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Nanomaterial Case Study: A Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles

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U.S. Environmental Protection Agency
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Key Terms

Upholstery textiles	Fabric or cloth material that is fixed to furniture (e.g., chairs), mattresses or transportation industry components (e.g., seating, roof linings)
Flame retardant	A chemical or other manufactured material that has the ability to inhibit the combustion process and increase the resistance of textile products to degradation associated with fire and flame.
DecaBDE	The only polybrominated diphenyl ether (PBDE) that is fully brominated (i.e., all available hydrogen atoms in the diphenyl rings have been substituted with bromine atoms) and therefore exists as a single isomer (see BDE-209); commercial formulations of decaBDE may contain trace amounts of lower brominated congeners (e.g., nona- or octaBDEs) as impurities
BDE-209	The single isomer of deca-substituted BDE (see decaBDE) named as the final of the 209 possible congeners of PBDE (many lower brominated PBDEs [e.g., heptaBDE] are composed of many different congeners based on the exact position of the bromine atoms in the chemical conformation)
Multiwalled carbon nanotube	Hollow nanoscale (i.e., with one or more dimensions in the range of approximately 1–100 nm) tubes composed of multiple concentrically nested graphene sheets

Abbreviations and Acronyms

A549	human lung epithelial cells
ACC	American Chemistry Council
ACGIH	American Conference of Government Industrial Hygienists
ADME	absorption, distribution, metabolism, and excretion
Ag	silver
Al	aluminum
APA	alkaline phosphatase (enzyme)
APPI	atmospheric pressure photoionization
ASTM	American Society for Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry
B6C3F$_1$	mouse strain
BAF(s)	bioaccumulation factor(s)
BAF/BCF(s)	bioaccumulation or bioconcentration factor(s)
BALB/c	mouse strain
BCF(s)	bioconcentration factor(s)
BDE	brominated diphenyl ether
BDE-209	single isomer of decaBDE (congener)
BDL	below detection limit
BfFV	Bundesministerium für Frauenangelegenheiten und Verbraucherschutz (Germany's Federal ministry for women's interests and consumer protection)
BFR(s)	brominated flame retardant(s)
BHI	brain heart infusion broth
BMF	biomagnification factor
Br	Bromine
BSA	bovine serum albumin
BSEF	Bromine Science and Environmental Forum
BSI	British Standards Institution
bw	body weight
C	Carbon
°C	degrees in Celsius
^{14}C	radiolabeled carbon
C57BL/6	mouse strain
CA TB	California (Bureau of Home Furnishings and Thermal Insulation) Technical Bulletin
Ca	Calcium
Cal/EPA	California EPA
CalRecyle	California Department of Resources Recycling and Recovery
Ce	Cesium
CEA	Comprehensive Environmental Assessment
CFR	Code of Federal Regulations
CINAHL	Cumulative Index to Nursing and Allied Health Literature
Cl	Chlorine
CLF	Conservation Law Foundation
cm^3	cubic centimeters
CNF(s)	carbon nanofiber(s)
CNQ	could not quantify
CNT(s)	carbon nanotube(s)
Co	Cobalt
CO_2	carbon dioxide
COOH-MWCNT	carboxylated MWCNT
CPC	condensation particle counters
CPTC	Consumer Product Testing Company
CVD	chemical vapor deposition
decaBDE	decabrominated diphenyl ether
DI	deionized (water)
diBDE	dibrominated diphenyl ether
DIN	Deutsches Institut fur Normung (Germany)
DLS	dynamic light scattering
DNA	deoxyribonucleic acid
DOD	U.S. Department of Defense
doi	digital object identifier
DOM	dissolved organic matter
DWCNT(s)	double-walled carbon nanotube(s)
E	Element in CEA Framework
EC_{50}	median effective concentration
ECB	European Chemicals Bureau
ECHA	European Chemicals Agency

ECNI	electron capture negative ionization
ECNI-MS	electron capture negative ionization-mass spectrometry
EEA	electron capture negative ionization
EEB	European Environmental Bureau
EEC	European Economic Community
EI99	Eco Indicator 1999 (method)
ENM(s)	engineered nanoscale material(s)
EPA	U.S. Environmental Protection Agency
EROD	ethoxyresorunfin-*O*-deethylase enzyme
E-RRF	Element / Risk-Relevance-Factor (Pair in CEA Framework)
EU	European Union
F344	rat strain
FBCVD	fluidized bed chemical vapor deposition
Fe	iron
FLE	forelimb emergence
FLM	fluorescence microscopy
FMVSS	Federal Motor Vehicle Safety Standards
FTIR	Fourier transform infrared spectroscopy
g, mg, µg, ng, pg; kg	gram, milligram, microgram, nanogram, picogram; kilogram
GC	gas chromatograph(y)
GC/HR TOF MS	gas chromatography/high resolution time-of-flight mass spectroscopy
GD	gestation day
GHG	green house gas(es)
GLP	Good Laboratory Practices
GLRI	Great Lakes Research Institute
GPIIb/IIIa	glycoprotein integrin receptor
gpt	guanine phosphoribosyl-transferase
GSI	gonadosomatic index
GSRI	Gulf South Research Institute
GWERD	Ground Water and Ecosystems Restoration Division of NRMRL
heptaBDE	heptabrominated diphenyl ether
hexaBDE	hexabrominated diphenyl ether
HHPC-6	Hand-held airborne particle counter
HiPCO®	a high pressure carbon monoxide synthesis process
HMVEC	human microvascular endothelial cells
hpf	hours post fertilization
HR	high resolution
HRMS	High resolution mass spectroscopy
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
ICF	ICF International, Inc. (formerly Inner City Fund; ICF-Kaiser; ICF Consulting)
ICL	Israel Chemical Ltd.
ICP-MS	inductively coupled plasma mass spectrometry
ICR	mouse strain
ID	inner diameter
IF	Influential Factor
INEL	indicative (human) no-effect level
IO	Immediate Office
IPCS	International Programme on Chemical Safety
IPEN	International POPs Elimination Network's Nanotechnology Working Group
IRDC	International Research and Development Corporation
IRIS	(U.S. EPA) Integrated Risk Information System
ISO	International Organization for Standardization
kg	kilogram
K_{oc}	Soil organic carbon/water partition coefficient
K_{ow}	octanol/water partition coefficient
L	length
L, mL	Liter, milliliter
LC	liquid chromatography
LC/MS-MS	liquid chromatography tandem-coupled mass spectroscopy
LC_{50}	median lethal concentration
LCA	Life-cycle Assessment
LD_{50}	median lethal dose
LDH	layered double hydroxide
LOAEL	lowest-observed-adverse-effect level
LOEC	lowest observed effect concentration
LOEL	lowest observed effect level
LOI	limiting oxygen index
LRT	long-range atmospheric transport
LSRI	Life Science Research Israel
µ	mu symbol, denoting 'micro' or 10^{-6}
M, mm, µm	meter, millimeter, micrometer

m^2	square meters
m^3	cubic meters
Mg	magnesium
MN	micronucleus
Mo	molybdenum
MRL	minimal risk level
mRNA	messenger RNA
MS	mass spectrometer
MWCNT(s)	multiwalled carbon nanotube(s)
MWCNT-OH	hydroxylated MWCNT
MWCNT-NH_2	amine-functionalized MWCNT
MWCNT-NH_3^+	ammonium-functionalized MWNT(s)
MWNT	multiwalled nanotube(s)
MWNT-COOH	carboxylated MWCNT
n	sample number
NA	not applicable
Na	sodium
NaCl	sodium chloride (salt)
Nanomaterials	nanoscale materials
nC_{60}	nanofullerene
NCC	nanocrystalline cellulose
NCCT	National Center for Computational Toxicology (U.S. EPA /ORD)
NCEA	National Center for Environmental Assessment (U.S. EPA /ORD)
NCSL (2011)	National Conference of State Legislators
ND	Not determined; No data identified
NERL	National Environmental Research Laboratory (U.S. EPA /ORD)
NF	not functionalized
NFPA	National Fire Protection Association
NH_2-MWCNT	amine-functionalized MWCNT
NH_3^+-MWCNT	ammonium-functionalized MWCNT
NHDF	normal human dermal fibroblast cells
Ni	nickel
NICNAS	(Australia) National Industrial Chemicals Notification and Assessment
NIEHS	National Institute of Environmental Science (NIH)
NIH	National Institute of Health
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine (NIH)
NMAM	NIOSH Manual of Analytical Methods
NMRI	mouse strain
NOAEL	no-observed-adverse-effect level
NOE	no observed effect
NOEC	no observed effect concentration
NOEL	no-observed-effect level
NOM	natural organic matter
nonaBDE	nonabrominated diphenyl ether
NR	not reported
NRC	National Research Council
NRMRL	National Risk Management Research Laboratory (U.S. EPA, ORD)
NRMRL/GWERD	Ground Water and Ecosystems Restoration Division of NRMRL
NSTC	National Science and Technology Council
NTP	National Toxicology Program (NIEHS/NIH)
O	oxygen
OAF	overall assessment factor
OCSPP	Office of Chemical Safety and Pollution Prevention (U.S. EPA)
octaBDE	octabrominated diphenyl ether
OD	outer diameter; optical density
OECD	Organisation for Economic Co-operation and Development
OEL(s)	occupational exposure limit(s)
OH-MWCNT	hydroxylated MWCNT
OPC	optical particle counters
OPP	Office of Pesticide Programs (U.S. EPA)
ORD	Office of Research and Development (U.S. EPA)
ORISE	Oak Ridge Institute for Science and Education
OSCP	Office of Science Coordination and Policy (in OCSPP; U.S. EPA)
OST	Office of Science and Technology (in Office of Water; U.S. EPA)
OW	Office of Water (U.S. EPA)
P	purity
p	p-value, estimated probability, level of statistical significance
$p53^{+/-}$	mouse strain with impaired gene stability
PAH(s)	polycyclic aromatic hydrocarbon(s)
PBDD	polybrominated dibenzo-p-dioxin

PBDE	polybrominated diphenyl ether
PBDF	polybrominated dibenzofuran
PBS	phosphate buffered saline (solution)
PBZ	personal breathing zone
PCB(s)	polychlorinated biphenyl(s)
PEC(s)	predicted environmental concentration(s)
PEI	polyethyleneimine
PEL	permissible exposure limit
pentaBDE	pentabrominated diphenyl ether
pH	scale of acidity and alkalinity
PINFA	Phosphorus, Inorganic and Nitrogen Flame Retardants Association
PMMA	polymethyl methacrylate
PMN	premanufacturing notice
PND	postnatal day
POPs	persistent organic compounds
ppb	parts per billion
ppm	parts per million
PPM	Physicochemical Properties Map
ppt	parts per trillion
R&D	Research and Development
RAW 264.7	murine macrophage cell line
REACH	Registration, Evaluation, Authorisation and Restrictions of Chemicals (EU)
REL	recommended exposure limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RRF	Risk Relevance Factor in CEA Framework
RTI	Research Triangle Institute
$	cost in U.S. dollars
S	sulfur
SA	surface area
SAFENANO	Europe's Center of Excellence on Nanotechnology Hazard and Risk, based at the Institute of Occupational Medicine
SD	rat strain; standard deviation
SEM	scanning electron microscopy; standard error of mean
Si	silicone
SiO2	silicone dioxoide
SNUR	(TSCA) Significant New Use Rule
SOC(s)	synthetic organic compound(s)
SWCNT(s)	single-walled carbon nanotube(s)
T_3	free tri-iodothyronine
T_4	free thyroxine
TB	technical bulletin
TB	total body
TEM	transmission electron microscopy
tetraBDE	tetrabrominated diphenyl ether
TfM	Transformation Map
TGA	thermogravimetric analysis
Ti	titanium
TiO_2	titanium dioxide
TLV(s)	threshold limit value(s)
TOC	total organic carbon
TOF	time of flight
TpM	Transport Map
triBDE	tribrominated diphenyl ether
TSCA	Toxic Substances Control Act
TWA	time weighted average
U.K.	United Kingdom
U.S EPA	U.S. Environmental Protection Agency
U.S.	United States of America
UV	ultraviolet
V	volume
V79 cells	lung fibroblast cell line from Chinese hamster lung tissue
w/w	weight-for-weight measurement
WHO	World Health Organization
wt	weight
XPS	x-ray photoelectron spectroscopy
Zn	zinc

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Preface

This document is part of continuing efforts by the U.S. Environmental Protection Agency (EPA) to understand the scientific issues and information gaps associated with nanotechnology, consistent with recommendations in the U.S. EPA *Nanotechnology White Paper* (2007) and U.S. EPA *Nanomaterial Research Strategy* (2009). Although no national or international consensus definition for nanomaterials exists, a current working definition is a material having at least one dimension on the order of 1 to 100 nm (NSTC, 2011).

Previous EPA documents similar to this one focused on nanoscale titanium dioxide used in drinking water treatment and in topical sunscreen (U.S. EPA, 2010d) and nanoscale silver used in disinfectant spray (U.S. EPA, 2010e). The nanomaterials considered in this document are multiwalled carbon nanotubes (MWCNTs), as incorporated into flame-retardant coatings for upholstery textiles. This document does not represent a risk assessment, nor is it intended to serve as a basis for near-term risk management decisions on possible uses of MWCNTs. Rather, it is a case study, the external review draft (U.S. EPA, 2012b) of which served as the starting point for identifying and prioritizing research gaps that, if pursued, could inform future assessments and subsequent risk management decisions for MWCNTs in this application. In revising the external review draft of the case study (U.S. EPA, 2012b) to create this peer review draft, EPA streamlined the document to clearly reflect the identified research priorities and input from public comments and expert stakeholders.

Like the previous case studies, this case study of MWCNTs is based on the comprehensive environmental assessment (CEA) approach, which consists of both a framework and a process. The organization of this document reflects the CEA framework, the principal elements of which are described in Chapter 1 of this document and largely represented in Chapter 2 through Chapter 5.

This document also contains information about a traditional (i.e., "non-nanoenabled") product, decabromodiphenyl ether flame-retardant upholstery coatings, against which the MWCNT flame-retardant upholstery coating (i.e., the "nanoenabled" product) is compared. The primary purpose of including a comparative element in the draft case study (U.S. EPA, 2012b) was to provide a more robust database as a foundation from which to identify data gaps related to the nanoenabled product. Because it has served its primary purpose, most of this comparative information has been moved to an appendix; how the information about the traditional product might inform research planning for MWCNTs is included in succinct textboxes in appropriate areas of the document.

Following a general introduction to the materials and selected application in this case study in Chapter 1; Chapter 2 highlights stages of the product life cycle for the nanoenabled product. Chapter 2 also identifies which stages in the product life cycle present opportunities for releases to the environment. Chapter 3 then provides information on the transport, transformation, and fate processes affecting the behavior of the nanomaterials, by-products, and transformation products in environmental compartments. Chapter 4 characterizes exposure, uptake, and dose for nanomaterials, by-products, and transformation products for different human populations and ecological receptors, after which Chapter 5 describes the human health, ecological, and other impacts related to those exposures.

Collectively, these chapters represent the assembly of information across the vertical spectrum of the CEA framework (Figure 1-1); as outlined in Chapter 1, however, this step is merely the first in the CEA process (Figure 1-2). Next, a group of expert stakeholders representing a variety of technical backgrounds and sectors used the draft case study document (U.S. EPA, 2012b) in a collective judgment process to rate areas of the CEA framework in terms of importance for future risk assessments of MWCNTs and their confidence in the data to support risk management decisions. Concurrently, the case study was posted for public comment. Traditionally, the Agency has responded to expert feedback and public comments by making in-text edits directly to case study documents as appropriate. In the current case study, EPA not only addressed feedback and comments through in-text edits, but also placed greater emphasis on highlighting the outcomes of the collective judgment step through incorporation on new elements and highlighting key sections of the case study; by doing so EPA hopes to facilitate research to support the compilation of new information in the CEA framework for future iterations of the approach. Chapter 2 through Chapter 5 now reflect the areas of the framework expert stakeholders judged essential for future risk assessment and management decisions. Areas identified as lower priorities are discussed in appendices of the document. In addition, new information identified through public or expert comments on the draft (U.S. EPA, 2012b) is highlighted throughout this document in text boxes.

As described in more detail in Chapter 6, the identification of priority areas by a diverse group of expert stakeholders is a key part of connecting research, risk assessment, and risk management for MWCNTs (areas that were not identified as priorities are discussed in Appendix G). The next critical step in this process is to engage the broader scientific community in implementing research in areas identified as important to consider in future risk assessments but which lack sufficient data to support risk management decisions for MWCNTs. Doing so will support the subsequent steps of the CEA process, which involve a continued, iterative communication flow across the continuum of research, risk assessment, and risk management.

Executive Summary

Chapter 1: Introduction to this Document

Background

As part of an ongoing effort to identify research needs and data gaps in assessing the broad environmental implications of nanomaterials, this case study focuses on a specific nanomaterial in a particular application: multiwalled carbon nanotubes (MWCNTs) in flame-retardant coatings applied to upholstery textiles. The selection of this specific nanomaterial and particular application was made with input from representatives across the U.S. Environmental Protection Agency (EPA) and was based in part on its relevance to EPA programmatic interests and the similarity in the potential for release and exposure over the product life cycle compared to conventional flame-retardant materials that are being phased out of use.

Like previous case studies of nanoscale titanium dioxide and nanoscale silver, this case study is built on the comprehensive environmental assessment (CEA) approach, which is both a framework and a process. The CEA framework (Figure 1-1) starts with the inception of a material and encompasses environmental fate, exposure-dose, and impacts associated with that material. The framework also considers differences in environmental media and the physical, chemical, biological, and social conditions in which the material occurs. Here, the framework is used to organize information about MWCNTs in the case study systematically. This information does not represent a completed or even preliminary risk assessment; rather, it is intended to inform research planning. The External Review Draft of the document provided a basis for identifying and prioritizing data gaps and research needs for MWCNTs and other nanomaterial assessments as part of the CEA process (Figure 1-2). Specifically, a group of expert stakeholders representing diverse technical (e.g., toxicology, ecology, material science) and sector (e.g., industry, academia, government) perspectives engaged in a structured, collective judgment workshop process such that each individual had equal input in identifying research priorities. To facilitate the identification of key research gaps related to assessing MWCNTs in this application, the External Review Draft case study provided a comparative perspective by also presenting information on a traditional flame retardant, decabromodiphenyl ether (decaBDE). The prioritized research gaps that emerged are intended to inform decision-makers in the EPA and the broader scientific community in developing research agendas that support future risk assessment and risk management goals for MWCNTs. These Priority Research Areas for MWCNTs are the primary focus of this revised document, with information on

decaBDE that supported identifying the priorities in the previous draft (U.S. EPA, 2012b), and are presented primarily in Appendix H. Background information on decaBDE, however, is provided in Chapter 1 to give the necessary context for reviewing the research priorities identified for MWCNTs. In addition, text boxes with the title "DecaBDE Can Inform MWCNT Assessment" are provided throughout the document to succinctly note how information on the conventional material might inform research planning for MWCNTs. Information on MWCNTs that pertains to areas that were not prioritized for research is now located in Appendix G. Input on the External Review Draft case study from public and expert stakeholders also is highlighted throughout the document and is recorded in Appendix I.

Given the purpose of the document, this case study does not purport to be a comprehensive literature review; rather, available sources were incorporated specifically to support prioritizing and subsequently planning research, as described above. As this case study involves an emerging technology, some information, particularly regarding background or general concepts, was occasionally obtained from non-peer-reviewed sources to supplement the published literature available. The most recent literature search for this case study was conducted on May 11, 2012, using specific criteria to search the PubMed database, Academic Search Complete, Environment Complete, and CINAHL (Cumulative Index to Nursing and Allied Health Literature) for records published since previous searches in November 2011 and January 2012. Search terms included carbon nanotube*, carbon nanofiber*, CNT*, CNF*, MWNT*, MWCNT*, and SWCNT*. Additional targeted literature searches were conducted on November 13, 2012, using search terms specific to topic areas identified in public and expert comments.

Introduction to decaBDE and MWCNT flame-retardant textiles

Production and importation of decaBDE are currently being phased out in the United States as a result of voluntary commitments within the industry and EPA actions in response to concerns regarding potential human health and ecological impacts. As a result, a range of alternative flame-retardant technologies, including nanotechnologies, is being evaluated as potential replacements for this extensively used material. This document presents information on a potential alternative flame-retardant technology, MWCNTs, in the context of the research priorities that could support future assessments of this product. The primary purpose of this document is to inform research planning efforts for MWCNTs across the scientific community. In doing so, the document supports a key objective of the CEA approach; to link research, risk assessment, and risk management efforts iteratively.

In developing research plans for MWCNTs, understanding the considerations involved in their potential use in flame-retardant textiles is informative. Many manufacturers incorporated flame-retardant materials into textiles to comply with state, federal, and industry fire-safety standards (i.e., certain flame test performance criteria that must be met). Once applied, flame retardants act to inhibit the combustion

process through a variety of physical or chemical means (e.g., producing inert gases that dilute the oxygen supply available to the flame, producing protective char barriers) (Section 1.2).

Both decaBDE and MWCNTs can be mixed with binding agents and applied as coatings to increase the flame resistance of upholstery textiles. In this application, the two materials are both referred to as barrier technologies because they exhibit similar mechanisms of flame-retardant action: decaBDE forms a protective char barrier and MWCNTs form a network floccules layer (i.e., network of loosely bound MWCNT bundles). The similarity in potential applications for decaBDE and MWCNTs was a primary reason for including the comparison of the two materials as flame-retardant coatings in upholstery textiles in the External Review Draft of the case study, as the comparison informed the identification of data gaps related to assessing possible risks and benefits associated with MWCNTs. Moreover, the comparison of these materials highlighted MWCNT- and nano-specific factors that might influence future research directions for nanomaterials and nanoenabled products. For example, unlike with decaBDE, the physicochemical properties of MWCNTs are often intentionally altered during synthesis; thus MWCNTs are not a single material with a defined set of characteristics, but rather a variety of materials—often present as mixtures—with vastly different physicochemical characteristics. Such variation in the physicochemical characteristics of MWCNTs presents challenges in describing the releases, behavior, and effects of exposure to MWCNTs as a class of materials (Section 1.3). Importantly, MWCNTs likely will be used in combination with other flame-retardant materials to provide sufficient efficacy for the standards noted above (Section 1.2). In addition to introducing greater variability in MWCNT behavior, exposure, and effects, the use of MWCNTs in combination with other materials raises important implications for the potential use of MWCNTs in this application (Additional Information Highlight Box 3).

Chapter 2: Product Life Cycle

Little information is available on the commercial production and use of MWCNT flame-retardant coatings, as few commercial-scale products currently exist. The manufacturing stages of MWCNT flame-retardant textile coatings (Section 2.2), along with the use (Section 2.4) and reuse/recycling/end-of life stages (Section 2.5), were identified as Priority Research Areas for upholstery textiles treated with MWCNT flame retardants.

Based on the available data, releases of MWCNTs to the environment are expected to occur throughout the life cycle of MWCNT flame-retardant upholstery textiles. The projected increase in MWCNT production likely will result in increased environmental releases of MWCNTs from flame-retardant textiles or other MWCNT products. Most MWCNTs released in the manufacturing stages are anticipated to be in the free or bundled form (Footnote 11 in Chapter 2 explains this terminology), while

most releases later in the life cycle are anticipated to be in the polymer or textile matrix-bound form. Upholstery textile products are expected to have a long lifespan and likely will be disposed of in municipal landfills or incineration facilities.

Air and water releases of MWCNTs during manufacturing are expected to occur based on the activities performed in manufacturing stages of the product life cycle. Although release is particularly likely during mixing, handling, and equipment cleaning, releases are expected to be fairly well controlled when proper ventilation and environmental controls are in place. Air releases of MWCNTs have been measured during material synthesis but no data are available regarding release to water during manufacturing. Additionally, MWCNTs typically require purification and functionalization, which also could result in releases due to chemical and physical processing methods (Section 2.2). Activities like textile and furniture processing might take place outside of closed systems and could result in environmental releases of MWCNTs. Abrasion, washing, unintended use, and accidental exposure to high heat or fire during the use stage could result in releases of MWCNTs (Sections 2.4 and 2.5).

No data are currently available on the volume or potential release of MWCNTs in the use stage of the flame-retardant upholstery textile product life cycle. Based on decaBDE data, however, the potential for release during this stage of the product life cycle could be relatively high. Similarly, no data currently exist on the volume or potential release of MWCNTs in upholstery textiles at end of life. Nevertheless, the physical and chemical processes (e.g., shredding, milling, chemical treatment) used to recycle textiles also could lead to releases of MWCNTs. Air releases from land-filling of MWCNT flame-retardant upholstery also could occur due to mixing and compacting. In addition, release in leachate from landfills is possible if the product or polymer matrix degrades. Although incineration at end of life presents the potential for airborne release of MWCNTs and by-products, preliminary experimental data suggest that MWCNTs will not be released to the environment when exposed to the sufficiently high temperatures of municipal incinerators (Sections 2.4 and 2.5). Incomplete incineration during other stages of the product life cycle, however, is one of the most likely airborne release scenarios for CNT textile coatings.

Chapter 3: Transport, Transformation, and Fate

Although MWCNTs are incorporated into polymer matrices after the flame-retardant production stage, little information exists that describes the environmental behavior of these polymer matrices. As a result, Chapter 3 focuses on the transport, transformation, and fate of MWCNTs and not the polymer matrices in which they are incorporated. Environmental transport, transformation, and fate of MWCNTs in air, wastewater, and sediment were identified as Research Priority Areas. The environmental behavior of MWCNTs is dictated by their physical and chemical properties—surface area, surface chemistry, morphology (shape), solubility, presence or absence of functionalization and surface coatings (e.g.,

engineered coatings or natural organic matter), and hydrophobicity. The nanostructured morphology, small size, and high surface area-to-volume ratio of MWCNTs can enhance chemical reactivity and propensity of MWCNTs to form bundles; single MWCNTs, as compared to bundles, will differ in their behavior in the environment (Section 3.1).

Recent literature regarding the behavior of airborne MWCNTs is extremely limited, and dominant fate, transport, and transformation processes for MWCNTs in indoor and outdoor air are unknown. In aqueous media, such as wastewater, the hydrophobicity and van der Waals interactions of pure MWCNTs suggest they will bundle together or sorb to particles and be removed during the sewage treatment process, or settle out into sediment in receiving water bodies. Physicochemical characteristics of the MWCNTs and environmental conditions, however, can alter this behavior. For example, the presence of dissolved organic matter has been shown to debundle MWCNTs causing to them to remain in solution. Similarly, surface coatings can affect the sorption behavior of MWCNTs in these systems and influence their mobility, dispersion, and bioavailability in environmental media (Sections 3.2, 3.3, and 3.4).

Scientists have demonstrated the use of simple, deterministic models and more complex probabilistic models to simulate movement of carbon nanotubes through, and predict environmental concentrations in, environmental compartments. Differences in modeling approaches, model scale, and model input data make comparisons across models for predicting environmental concentrations of CNTs difficult. Nevertheless, a recent life-cycle-based analysis predicted the impacts of CNT synthesis in aquatic systems by using output data from a single model of environmental concentrations. Nevertheless, output data from a single model predicting environmental concentrations were used in a recent life-cycle-based analysis to predict the impacts of CNT synthesis in aquatic systems (Section 3.5).

Chapter 4: Exposure-Dose

Several analytical challenges for nanomaterials combined with the lack of historical use of MWCNTs in consumer products have so far prevented MWCNTs from being detected in ambient media, which could inform decisions related to potential exposures in human and ecological populations (Section 4.1). Human exposures to MWCNTs released throughout the flame-retardant textile coating life cycle are expected to differ for workers, consumers, and the general public. Based on available information, occupational and consumer exposures were identified as Priority Research Areas in the CEA collective judgment workshop process for MWCNTs. Workers can be exposed to various forms of MWCNTs (e.g., adsorbed to dust, as part of the polymer or textile matrix) via inhalation and ingestion of, and dermal contact with, these substances during manufacturing, storage and distribution, and end-of-life activities. In the workplace, the inhalation route is expected to represent the greatest potential for exposures, and

MWCNTs are expected to be in the particulate phase when inhaled. Little is reported about consumer exposures to MWCNTs, especially those incorporated into flame-retardant textiles. Yet, based on activities expected to occur during use, repurposing, or reuse of upholstered products, consumers might be exposed to MWCNTs during each of these points in the product life cycle. The MWCNTs released from finished products also are expected to be in particulate form, generally adsorbed to dust or constituents of the polymer or textile matrix. The primary route of exposure (i.e., inhalation, ingestion, or dermal) for consumers is unknown.

Developing exposure standards, guidelines, or recommendations for MWCNTs is complicated by the heterogeneity in MWCNT configurations and challenges measuring MWCNTs in occupational or environmental settings. The National Institute for Occupational Safety and Health (NIOSH) established a recommended exposure limit for elemental carbon, and several other occupational exposure limits have been proposed by industry and international agencies (Section 4.2.5). In general, MWCNTs appear to be biopersistent and might remain in the lung for several months after inhalation. Limited studies show that, after oral exposure, most ingested MWCNTs are eliminated with no detectable metabolism or transport into the blood. Distribution to the liver, lungs, and spleen, however, has been reported following intravenous exposure (Section 4.2). Notably, the bioavailability, and thus dose, of MWCNTs likely will be based on whether they are bound in a textile matrix, bundled, or free (Footnote 11 in Chapter 2 explains this terminology).

No evidence is currently available to determine whether portions of the population might experience higher exposure levels to MWCNTs compared to the general population; however, the activity of children and workers might increase total exposure levels of MWCNTs relative to the general population (Section 4.2).

Exposure and dose in ecological populations were not deemed Priority Research Areas for MWCNTs in the CEA collective judgment workshop process, and thus information on these areas is now located in Appendix G and Appendix H for MWCNTs and decaBDE, respectively. The anticipated increase in MWCNT production (Section 2.2.2) along with increases in potential applications of the material could lead to an increase in the number and type of exposures experienced by workers, consumers, and ecological populations. These changes are expected to increase aggregate and cumulative exposures to different formulations of MWCNTs, transformation products, and by-products.

Chapter 5: Potential Human Health, Ecological, and Other Impacts

Expert stakeholders participating in the CEA collective judgment workshop process identified human health impacts as a Priority Research Area for MWCNTs. Toxicology studies conducted on animals are the only identified data on human health impacts of MWCNTs because no human data on

effects of MWCNT exposure exist. All routes of exposure were examined in this case study because each route (dermal, inhalation, and oral) offers potential for human exposures (Section 5.1). Toxicological effects from MWCNT exposure in animal models have been evaluated predominantly after dermal and inhalation exposures, rather than after oral exposure. Effects were generally localized and included irritation (skin and ocular), sensitization (respiratory), and inflammation (respiratory). In addition, MWCNTs altered immunological function after exposure via inhalation for 14 days or via a single intranasal injection. The carcinogenicity of MWCNTs following inhalation exposure has not been investigated; however, several studies using methods such as instillation indicate that some types of MWCNTs behave like asbestos, potentially inducing mesotheliomas, and might be more toxic than asbestos (Section 5.1).

Expert stakeholders identified impacts in aquatic, but not terrestrial, biota as a Priority Research Area. Considerations for the ecological impact of MWCNTs include the toxicity toward different species, types of effects, and potential for bioaccumulation and biomagnification. More than 20 studies have investigated the effects of MWCNTs on aquatic species or aquatic systems; those studies indicate low acute toxicity potential, with the effect level varying based on size and functionalization properties of the MWCNTs. Chronic studies show that MWCNTs can elicit immune responses and produce developmental impacts (Section 5.2).

Other impacts, including economic or societal effects and alterations in environmental resources, were identified as a Priority Research Area by expert stakeholders. No empirical data exist relating MWCNTs to other impacts, but the background literature on processes involved in manufacturing similar materials (e.g., carbon nanofibers, single-walled carbon nanotubes) provides some basis for concern regarding potential impacts of MWCNTs on energy demand, resource depletion, climate change, and economics. These related studies provide a plausible foundation for suggesting that MWCNT manufacturing can be an energy-intensive process potentially causing the depletion of nonrenewable natural resources like fossil fuels, and that the synthesis of MWCNTs can result in emissions of other compounds causing adverse environmental effects (e.g., volatile organic compounds; Section 5.3).

Chapter 6: Identifying and Prioritizing Research Needs to Support Risk Assessment and Risk Management

The External Review Draft of this document served as the foundation from which expert stakeholders participating in the CEA process could identify key data gaps and determine research priorities. The information presented in this revised document focuses on those priorities to inform ongoing research planning for nanotechnology in the general scientific community and at EPA. Results of these research efforts could subsequently support future assessments and risk management efforts for

MWCNTs or other nanomaterials. Future evaluations of nanoenabled products, such as MWCNT in flame-retardant textile coatings, could involve the consideration of risk-related trade-offs, for example, thyroid health effects versus pulmonary health effects and environmental justice considerations versus energy costs. This document therefore strives to inform research planning efforts that would support conducting risk assessments that can inform risk management decisions about such trade-offs.

The research priorities discussed in the case study were identified by a group of diverse expert stakeholders independently rating areas of the CEA framework based on two factors:

- Importance: how important an area is to consider in risk assessments of MWCNTs,
- Confidence: the availability and utility of current data to support risk management decisions for MWCNTs.

For those areas they identified as "Important" to consider in future risk assessments of MWCNTs, stakeholders were asked to rate the relative importance and confidence in data related to the relationship of the area with risk factors that might be considered in risk assessment or risk management efforts for the area. Areas that experts most commonly identified as being of high importance to risk assessment, and were not confident in the data to support risk management decisions, are considered high priorities for research. In contrast, areas rated as of high importance and for which experts had confidence in the data might be of interest to decision-makers for evaluating risk management options for MWCNTs.

Most of the prioritized CEA framework areas were considered research priorities, including release rates across the product life cycle; persistence and bioavailability in air, wastewater, or sediment, and inhalation exposure in workers and consumers. Other areas identified as high Research Priority Areas include absorption, metabolism, and excretion in humans, as well as impacts on human health, aquatic biota, and other considerations (i.e., economic, societal, environmental resources). For a subset of these areas, experts identified potential risk managment decisions in the context of an example risk scenario for that area and noted the type of assessment(s) that could inform those decisions. Specific research questions to support such assessments also were identified, along with estimates of the financial and time resources to carry out the research. Risk management decisions generally centered on choosing appropriate control technologies or personal protective equipment, modifications to MWCNTs (e.g., reducing residence time in air by increasing aggregation potential), or limits on production and use of the materials. Assessments to inform these and other types of risk management efforts included human health risk assessments, cost benefit analyses, and life cycle assessments. Research areas to support such assessments can be grouped into five general themes: (1) the influence of MWCNT characteristics on release from the product matrix; (2) the influence of MWCNT characteristics and the product matrix both on environmental transport and transformation, and on absorption across biological barriers (e.g., gastrointestinal tract); (3) development of analytical methods or tools to detect MWCNTs in complex

matrices and measure exposures; (4) human health impacts of MWCNTs and co-factors (e.g., solvents) after acute and chronic exposures; and (5) improving public engagement in and understanding of potential benefits and risks of nanotechnology.

The connection of specific questions within Priority Research Areas to the assessments and risk management decisions they would subsequently support demonstrates the focus within the CEA approach on linking communication across the continuum of research, risk assessment, and risk management. Moreover, the specific questions are intended to provide more concrete support for strategic research planning that informs future decision-making about MWCNTs.

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Chapter 1. Introduction to this Document

1.1. Background

Nanoscale materials (nanomaterials) have been described as having at least one dimension approximately 1–100 nm (NSTC, 2011). Although this definition is not universally accepted and continues to evolve, 100 nm is typically used as an upper bound, and this working definition is used as the size standard in this case study. Engineered nanomaterials are intentionally synthesized at the nanoscale, rather than being produced as incidental by-products of combustion or a natural process such as erosion, to exploit the unique or novel properties that can arise from their small size. Like all emerging technologies, engineered nanomaterials offer the potential for both benefits and risks, the assessments of which depend on the availability of relevant data and other information.

This document is part of an endeavor to identify what is known and, more importantly, what is not known that could be of value in assessing the broad environmental implications of nanomaterials. As a case study, this document presents information about a specific nanomaterial in a particular application. It does not represent completed or even preliminary assessments; rather, the External Review Draft provided a starting point in a process to identify and prioritize possible research directions to support future risk assessments of nanomaterials. The prioritized research gaps that emerged are the focus of this revised case study document. As with previous case studies, these research priorities are intended to inform decision-makers in the U.S. Environmental Protection Agency (EPA) as well as the broader scientific community in developing research agendas that support future risk assessment and risk management goals. Such information is expected to be considered in the context of the particular focus, budgetary constraints, ongoing research, and other considerations of any organization; however, as discussed below, by using a holistic framework paired with input from a diverse group of expert stakeholders, the priorities identified through the comprehensive environmental assessment (CEA) approach employed in this case study can provide a unique perspective on research directions to support future risk management goals.

The focus of this document is a specific application of a selected nanomaterial: the use of engineered multiwalled carbon nanotubes (MWCNTs) as an agent in flame-retardant coatings on

upholstery textiles.[1] As described in detail in Appendix A, several candidate carbon-based nanomaterials and applications were identified as options for this case study using a systematic approach, and professional judgment was then applied to narrow down the selection to a single nanomaterial and application. First, candidate carbon-based nanomaterials were identified through initial strategic literature and Internet searches, news reports, and basic literature search statistics (e.g., number of total hits, number of hits in scientific databases). This approach provided an initial indication of overall data availability and research interest within the nanotechnology and scientific communities for several different broad groups of carbon-based nanomaterials (e.g., carbon nanotubes, carbon nanofibers, nanocrystalline cellulose). This group was further narrowed using a more judgment-based approach to evaluating suitability, including consideration of the available data for multiple applications of each nanomaterial. Finally, five feasible candidates of unique nanomaterial and application pairs—carbon nanofibers in cement, MWCNTs in flame-retardant coatings, single-walled carbon nanotubes in textiles, nanocrystalline cellulose in biodegradable packaging, and MWCNTs in rubber tires—were selected based on additional professional judgment of suitability.

The process for selecting the material-application pair of MWCNT flame-retardant coatings for upholstery textiles as a CEA case study involved individuals representing EPA program offices, regional offices, and Office of Research and Development laboratories and centers. Individuals were appointed by their organization within EPA to be involved with development of nanomaterial case study documents. They were encouraged to share information on the five selected candidate carbon-based nanomaterials and applications with colleagues in their organization and to represent the views of their organization in voting for their preferences. The two candidates receiving the most votes were MWCNTs in flame-retardant coatings and composites and SWCNTs in textiles. Rationale for selecting MWCNTs and SWCNTs in each respective application included: relevance of both materials to Agency programs, similarity in potential release and exposure over the product life cycle of textiles compared to existing flame-retardant materials being phased out of use, greater availability of data compared to other candidate applications, and potential for market expansion of CNTs (see Appendix A). Based on input that MWCNTs were of greater interest (i.e., more widely produced than SWCNTs and might contain more contaminants) and that an application involving textiles would be preferable, a hybrid option was selected as the topic of this case study: MWCNTs in flame-retardant coatings applied to upholstery textiles. This selection does not imply that MWCNTs in flame-retardant coatings applied to textiles represents the

[1]Although flame retardants are commonly used in both upholstery textiles and furniture foam, this case study focuses only on information relevant to the use of flame retardants as coatings on upholstery textiles. The extent to which the information presented might be relevant to the use of flame retardants in furniture foam is not addressed.

carbon-based nanomaterial and application with the largest current market share (see Section 1.3.2), but rather was based on the selection factors noted above.

Using a similar selection process, EPA completed case studies of nanoscale titanium dioxide used for drinking water treatment and for topical sunscreen (U.S. EPA, 2010d) and nanoscale silver used as an agent in disinfectant spray products (U.S. EPA, 2010e). Unlike previous case studies, this case study incorporates information about a traditional (i.e., "non-nanoenabled") flame-retardant product, decabromodiphenyl ether (decaBDE), against which the MWCNT flame-retardant coating (i.e., the "nanoenabled" product) can be compared (see Section 1.1.4). As discussed in greater detail below (see Section 1.1.3), the primary purpose of including comparative information on decaBDE was accomplished with the External Review draft of this case study document (U.S. EPA, 2012b), and that information is now primarily contained within Appendix H.

Part of the rationale for compiling a series of nanomaterial case studies is that the properties associated with different nanomaterials are often complex and vary considerably within, between, or among specific types of nanomaterial groups, nanomaterials in general, and different applications of nanomaterials. As a result, applying generalities could result in overlooking key characteristics or information. Focusing on a single example of an application of MWCNTs is not intended to represent all ways in which this nanomaterial could be used or all issues that other applications might raise. By considering this single application of MWCNTs, however, research directions can be identified that would support future assessments of this material. Such information might be used more broadly as an analog for other applications of MWCNTs or types of nanomaterials. For instance, research investigating the influence of MWCNT surface treatment on potential release from flame-retardant textile coatings and subsequent behavior in environmental media can also inform efforts to understand the influence of surface treatment on the environmental behavior of MWCNTs in other applications.

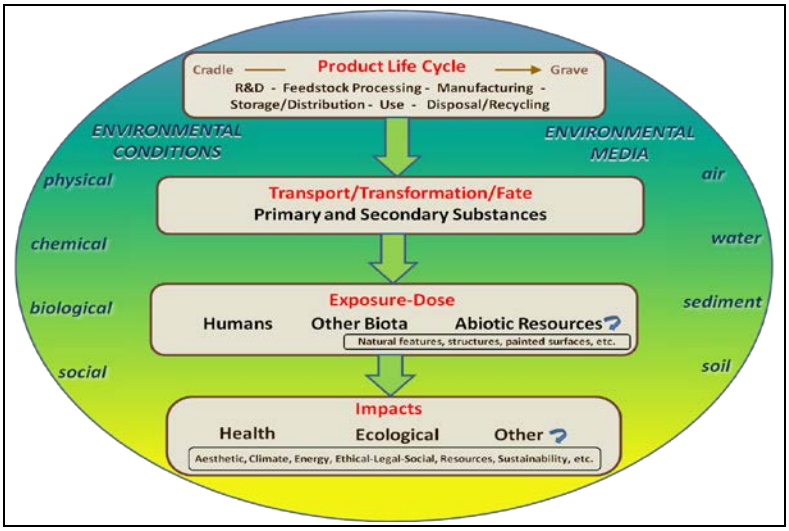
1.1.1. Introduction to Comprehensive Environmental Assessment

This case study of MWCNTs, like the previous case studies of nanoscale titanium dioxide (U.S. EPA, 2010d) and nanoscale silver (U.S. EPA, 2010e), is built on the CEA approach, which consists of both a framework and a process, the principal elements of which are illustrated in Figure 1-1 and Figure 1-2, respectively. The uppermost box of Figure 1-1 lists typical stages of a product life cycle: research and development (R&D), feedstock processing, manufacturing, storage and distribution, use, and disposal (which would include reuse or recycling, if applicable).

Although not considered a life-cycle stage in typical life cycle analyses, R&D is included in business models of product value chains. Because of the relatively large portion of resources and

information associated with this stage for emerging materials, such as nanomaterials, R&D is considered in the CEA framework. The actual volume of the material used in R&D is likely small but could represent a significant proportion of the total market, particularly during product development, given the limited number of full-scale commercial manufacturing efforts early in the life cycle for emerging materials. For these materials, processes in R&D lend insight to full-scale commercial processes and might constitute an important source of material release into the environment, as well as occupational exposures. Other CEA applications focusing on traditional or more mature materials or technologies might provide minimal or no information on the R&D portion of the product lifecycle, given that R&D would be less active.

Regardless of the material of focus, releases to the environment associated with any stage of the product life cycle lead to what is depicted in the second box in Figure 1-1, which refers to transport, transformation, and fate processes. These processes can result in the spatial distribution of both primary and secondary contaminants in the environment. The chains of events represented in the CEA framework occur within multiple environmental media (air, water, sediment, soil) and under various conditions (physical, chemical, biological, social). Also of note are the single arrows connecting one facet of the CEA framework to the next, which represent a variety of linkages, transfers, and feedback loops. For example, the transfer of material from one organism to another through the food chain would represent a bidirectional exchange between transport, transformation, and fate and exposure, uptake, and dose.



Source: (U.S. EPA, 2011a)

Figure 1-1. Comprehensive environmental assessment framework.

The CEA framework is used to systematically organize complex information in evaluations of the environmental implications of selected chemicals, products, or technologies (i.e., materials). The framework starts with the inception of a material and encompasses the environmental fate, exposure-dose, and impacts. Notably, the sequence of events is not always linear when, for example, transfers occur between media or via the food web. In addition, a variety of factors influence each event, including differences in environmental media and the physical, chemical, biological, and social conditions in which the material event occurs. Details on these influential factors are thus included throughout the framework when possible.

The third box in Figure 1-1, exposure-dose, goes beyond characterizing the occurrence of contaminants in the environment, as exposure refers to actual contact between a contaminant and a receptor, whether living or nonliving. Living

organisms include humans and other biota.[2] Examples of nonliving, or abiotic, receptors include features of the natural landscape, structures such as buildings and statues, and painted surfaces of vehicles and other objects. Exposure can involve aggregate exposure across routes (e.g., inhalation, ingestion, dermal), cumulative exposure to multiple contaminants (both primary and secondary), and various spatiotemporal dimensions (e.g., activity patterns, diurnal and seasonal changes). Dose is the amount of a substance that enters an organism by crossing a biological barrier or which deposits on an inanimate object.

As part of a chain of cause-effect events, dose links exposure with potential impacts of various types, as indicated in the last box of Figure 1-1. Human health effects might result when a certain delivered dose reaches a target cell or organ. In an ecological context, effects might occur when a stressor reaches a level sufficient to cause an adverse outcome in biotic or abiotic receptors. Impacts encompass both qualitative hazards and quantitative exposure-response relationships and can extend to aesthetic (e.g., alterations in visibility, taste, and odor), climate change, energy consumption, resource depletion, socioeconomic, and other effects. Such effects are considered in the CEA framework, but their ultimate inclusion would depend on whether the compiled information indicates that such effects could reasonably be expected to occur. As discussed below, the inclusion of such information in the CEA framework should influence the selection of the technical experts for the next step of the CEA process.

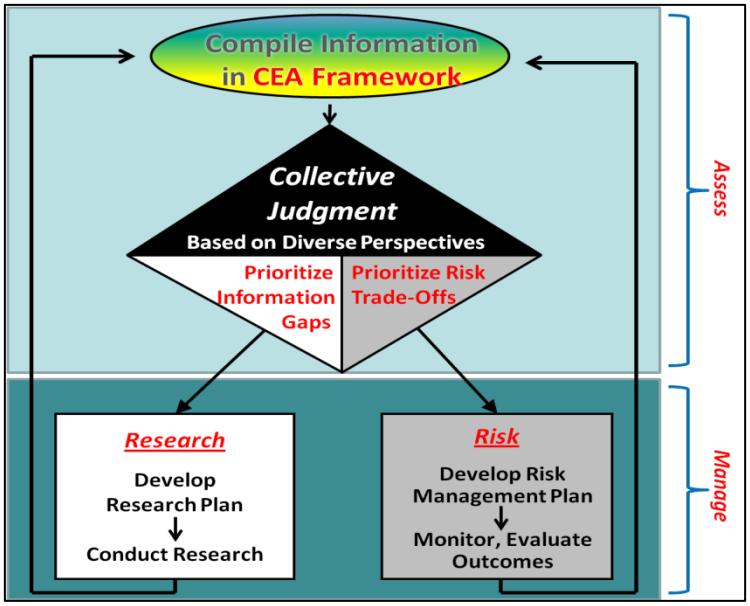
Not reflected in Figure 1-1 is the role of analytical methods that make detecting, measuring, and characterizing nanomaterials in the environment and in organisms possible. Characterizing a substance of interest (e.g., determining its chemical identity, reactivity, purity, and other properties) is fundamental to the assessment of any material. Thus, if adequate analytical techniques have not yet been developed or need refinement, methods development must be included in research efforts to inform future assessments. For simplicity, such information is not included in this high-level view of the CEA framework. For the purpose of this document, analytical methods for the materials in this case study are presented in detail in Appendix B.

As previously mentioned, the CEA approach consists of both a framework and a process. Compiling the information described above into the CEA framework is the first step of the CEA process (Figure 1-2). Starting with the holistic perspective of the CEA framework facilitates identifying information pertinent to consider for the material of focus, which in turn supports problem formulation and scoping for assessment purposes. Next, a collective judgment process is used to evaluate and prioritize this information. Collective judgment, as applied in the CEA process to date, refers to a formal, structured procedure enabling a range of participants to be heard individually and to be represented in a transparent record of the collectively reached outcomes. Collective judgment supports an essential feature

[2]The term biota is used throughout this document to refer to all living organisms other than humans.

of CEA: the inclusion of diverse technical and stakeholder perspectives to ensure that a holistic evaluation is achieved (U.S. EPA, 2010h).

Prioritization is a key objective in this holistic evaluation within the CEA process. Depending on one's objectives and the state of the science surrounding an issue, CEA can be used to prioritize (1) information gaps leading to development of a research plan that will support future assessment efforts and (2) risk trade-offs leading to development of an adaptive risk management plan. As depicted in Figure 1-2, these uses of CEA cross over from conducting assessments into management efforts after the initial identification and prioritization of information. Specifically, this transition encompasses the use of prioritized information by research planners and risk managers in their evaluations, which subsequently inform research and risk management decisions. In either instance, CEA is meant to be iterative; thus, the results of research, assessments that are carried out with new research results, and risk management efforts would be used to update the CEA framework after some period of time determined by those conducting the CEA process. At present, the CEA framework and process are being applied to help refine research planning for nanomaterials, with particular focus on a specific nanomaterial application. As the knowledge base grows for nanomaterials, the availability of more complete information will make the identification and prioritization of risk-risk and risk-benefit trade-offs feasible, and the path leading to risk management (as shown in Figure 1-2) will be pursued. Such prioritized risk-related trade-offs would be only one source of information that risk managers could consider when making judgments about risk management options in the context of relevant legal, political, and other considerations. Yet, the use of the holistic CEA framework together with diverse stakeholder input in the development of such priorities will make them a unique resource that



Source: (U.S. EPA, 2011a)

Figure 1-2. Comprehensive environmental assessment process.

The CEA process involves a series of steps that result in judgments about the implications of information contained in the CEA framework. Compiling information in the CEA framework is fundamental for a given material, but is only a first step in the CEA process. Next, the information in the framework is evaluated using a collective judgment technique (i.e., a structured process that allows the participants representing a variety of technical and stakeholder viewpoints to learn from one another, yet form their own independent judgments). The result of the collective judgment step is a prioritized list of risk trade-offs or information gaps that then can be used in planning research and developing adaptive risk management plans. The knowledge gained from these research and risk management activities feeds back in an iterative process of periodic CEA updates.

is responsive to current recommendations to further refine risk assessment and management approaches (see Chapter 6).

1.1.2. Purpose of this Document

This document has been revised from the External Review Draft that was used in the collective judgment step of the CEA process applied to MWCNTs (Figure 1-2). As a revised case study, it provides a basis for considering the outcomes of the collective judgment process to aid research planning that supports long-term assessment efforts; it does not, however, purport to present an exhaustive review of the literature. Furthermore, this case study is not an actual risk assessment and does not provide conclusions on potential ecological or human health impacts related to MWCNTs. As discussed further below, this document is focused on highlighting data gaps to inform risk assessment and risk management processes related to MWCNTs, and, as such, it does not discuss benefits. A variety of potential economic, social, and other benefits would likely need to be considered in future evaluations of risk-related trade-offs for nanomaterials such as MWCNTs [e.g., Wang and Shapira (2012), Bonner (2011)].

It must be emphasized that this case study has been developed without a specific regulatory or policy objective in mind. Within the United States, regulatory decisions for nanomaterials may be made by a number of federal agencies (e.g., EPA, Food and Drug Administration, Consumer Product Safety Commission, Occupational Safety and Health Administration) under a variety of legislative frameworks (e.g., Toxic Substances Control Act [TSCA], Federal Food Drug and Cosmetic Act). As discussed in Chapter 6, TSCA is one of the statutes under which EPA currently considers nanoscale substances. Considerations of nanoscale substances under TSCA begin with a determination of whether the substance is already included on the TSCA Chemical Substance Inventory based on whether the substance has the same molecular identity as a substance listed on the Inventory (U.S. EPA, 2008c). Determinations of whether nanoscale substances are new or existing substances are currently made on a case-by-case basis (U.S. EPA, 2008c).

A variety of efforts are underway to increase the scientific body of knowledge such that regulatory decisions through TSCA or other statutes could move beyond a case-by-case approach. These include several research frameworks applicable to, or exclusively for, nanomaterials and intended to support future assessments and subsequent risk management of these materials [e.g., (U.S. EPA, 2009), (NRC, 2012), and (OECD, 2012). These frameworks and the CEA approach share a number of common elements (e.g., focus on product life cycle, identifying environmental fate mechanisms and exposure sources, importance of stakeholder engagement), yet as described above, the CEA approach incorporates decision-support tools to engage stakeholders beyond that seen in other frameworks to date (Figure 1-2).

This document presents information in the CEA framework for MWCNTs, as potentially used in flame-retardant coatings applied to upholstery textiles, in the context of the outcomes that emerged from engaging expert stakeholders in the CEA process for this material. This case study begins with a general overview in Chapter 1 of textiles and flame-retardant systems and where MWCNTs fit into that context, as well as detailed introductory information on decaBDE in the context of textiles and flame-retardant systems. Throughout the main body of this document (Chapter 2 through Chapter 5), the focus is on highlighting what is known and not known related to each portion of the CEA framework identified as a research priority in the CEA collective judgment step for MWCNTs in flame-retardant coatings. As such, in these chapters readers are referred to Appendix H for the detailed information regarding decaBDE at each stage of the CEA framework; however, highlight-level information on decaBDE is presented in select tables, figures, and text boxes (see Section 1.1.4 and Appendix I) to provide a succinct comparison between MWCNTs and decaBDE in this particular application with the intention that such comparisons might inform MWCNT research planning.

1.1.3. How the CEA Framework and Process Were Applied

An important aspect of the CEA approach is the ability to examine the relative risks and benefits of, for example, different products or different formulation options, to aid in risk management decisions. The particular comparison to focus on in an application of CEA would be guided by risk management objectives. For example, MWCNT flame-retardant coatings applied to upholstery textiles might be compared to conventional flame-retardant products, a different nanoenabled flame-retardant formulation, a flame retardant not applied as a coating, or some other variable. Although several different options could be of interest to risk managers, considering every potential option in the present case study is not feasible. Therefore, this document focuses solely on a comparison of MWCNTs and a traditional flame retardant, decaBDE, as they might be used in flame-retardant coatings for upholstery textiles, including those used in homes and nonresidential areas such as public buildings and automobiles.

In the External Review Draft of this case study, the comparison between decaBDE and MWCNTs provided: (1) a more robust database (i.e., that of a traditional product that has been relatively well characterized) as a reference for identifying data gaps relating to a nanoenabled product; and (2) a context for identifying key factors and data gaps related to assessing the risk-risk and risk-benefit trade-offs between a nanoenabled product and a non-nanoenabled product. Although the specific characteristics, exposure patterns, and effects associated with the use of MWCNTs and decaBDE are expected to differ substantially, the data needed to inform risk assessment and risk management decision-making are comparable; thus, the comparative framework was used to help determine whether relevant information

(e.g., dominant exposure pathways, sensitive populations) is available and sufficient to inform future risk decision-making, and by extension, to identify key data gaps that could be pursued.

The External Review Draft of this document represented the "Compile Information in CEA Framework" step of the CEA process (Figure 1-2), and thus supported the next step of the process: evaluating the data in the framework using a collective judgment technique to identify and prioritize information gaps about MWCNTs. The collective judgment prioritization technique used for this case study was funded by EPA and conducted independently by an EPA contractor, RTI International. Details related to the collective judgment method and its outcomes are described in a separate report prepared by RTI International (RTI, 2012). A summary of that process is described here with the outcomes discussed in greater detail in Section 6.3.

In the collective judgment step of CEA applied to MWCNTs, selected experts representing diverse sector (e.g., industry, academia, government) and technical backgrounds (e.g., toxicology, ecology, material science) were first asked to read the External Review Draft of the case study. Next, they were asked to consider what elements of the CEA framework were most important to understanding, and therefore managing, the most significant risks associated with MWCNTs.

The experts identified important areas by independently rating areas of a more detailed view of the CEA framework (Figure 1-3). This detailed CEA framework illustrates discrete elements (blue boxes in top left of Figure 1-3), or discrete pathways within the broad levels of the CEA framework (e.g., Product Life Cycle, Exposure in Figure 1-1). Each element is associated with "risk relevance factors" (green boxes in top left of Figure 1-3), which might be considered in risk assessment or management efforts of a material, such as MWCNTs.

Experts were asked to rate the importance of each element of the detailed CEA framework as important, possibly important, or least important. If they rated the element important, they were then asked to rate (1) the importance of each element-risk relevance factor pair (E-RRF) using the same scale, and (2) their confidence in the availability and utility of current data for the E-RRF to support risk management decisions (as confident, somewhat confident, or not confident).

These ratings were collected in each of the three rounds of collective judgment prioritization used for this application of CEA:

Round 1: Thirty-one selected participants entered their individual opinions on the E-RRF pairs in a spreadsheet and submitted the spreadsheet to a secure online platform (website);

Round 2: Twenty-eight of the original 31 participants[3] viewed the compiled opinions of the wider group through a series of bar charts and tables available via the website and were given the opportunity to re-enter their opinions;

Round 3: A subset of participants (13) attended a structured workshop where they:

a. discussed their opinions in a structured collective judgment technique,

b. finalized research priorities through a third round of individually rating all E-RRFs and compiling these ratings,

c. developed detailed research questions for a subset of those priorities.

The finalized priority areas determined in Round 3, part b of the technique, hereafter referred to as "Priority Research Areas," are summarized in Figure 1-3 and discussed in greater detail in Section 6.3. As discussed below, these outcomes were used to focus the information in this case study document.

How the Case Study Was Streamlined to Emphasize Research Priorities

Compared to the External Review Draft (U.S. EPA, 2012b), this draft of the case study document has been streamlined to clearly reflect the outcomes of the collective judgment step of the CEA process. New text boxes have been embedded in the document immediately following section headings that correspond to elements of the detailed CEA framework (see Figure 1-3) to highlight the outcomes of the RTI workshop (RTI, 2012) related to the E-RRFs discussed in that section of the case study.

Boxes **outlined in red** with the title "Priority Research Area Highlight" (e.g., Section 2.2.2) indicate that the E-RRFs discussed in that section were deemed to be priorities for continuing research by participants in the RTI workshop, based on (1) high importance of that area to risk assessment and risk management, and (2) low confidence in the utility and availability of the data on the topic. Boxes **outlined in gray** with the title "Unprioritized Research Area Highlight" (e.g., Section 2.1) indicate that the E-RRFs discussed in that section were not identified by workshop participants as Research Priority Areas (i.e., the most commonly selected rating was "possibly important" or "least important" rather than "important"; therefore, the majority of participants did not rate the Importance and Confidence for those E-RRFs). For these sections, all text relevant to decaBDE and MWCNTs was moved to Appendix H and Appendix G, respectively, to focus the main body of the document on the priority research areas.

[3] Three participants from the first round of prioritization were unable to participate in the second round.

In each "Priority Research Area" and "Unprioritized Research Area" highlight box, a graphic appears that summarizes information on how the 13 workshop participants individually rated the Importance of each element; and, for the subset of participants who stated the element was of highest importance, their Importance and Confidence ratings for each E-RRF. The collective Importance and Confidence for each E-RRF is expressed using an Importance/Confidence Matrix image, where the three Importance categories are shown on the Y-axis and the three Confidence categories are shown on the X-axis, creating nine bins representing unique importance-confidence pairings (see lower left of Figure 1-3). E-RRFs were assigned to a particular bin of the Importance/Confidence Matrix based on which ratings were most commonly selected by expert stakeholders for Importance and for Confidence.[4,5] The prioritization of the framework areas (i.e., E-RRFs) is therefore based on the most frequently selected rating for each factor (Importance or Confidence), rather than on the most commonly selected combination of Importance and Confidence for each E-RRF. E-RRFs in Unprioritized Research Areas were not assigned to a particular bin since only a small subset of participants rated the Importance and Confidence of the E-RRF.

In most instances, the most commonly agreed-upon Importance and Confidence ratings align with the portion of the matrix with the largest number of stakeholders; however, in three instances, this is not the case. This lack of concordance reflects a difference in how individuals combined Importance/Confidence ratings compared to the overall rating combination of all stakeholders. In all cases, the most commonly selected rating for Importance and the most commonly selected rating for Confidence determines the placement of the E-RRF in the Importance/Confidence Matrix.

Finally, some case study sections present necessary supporting information for E-RRF pairs, but do not directly discuss a specific E-RRF pair. These sections have been identified as "Neutral Research Areas," and a small text box **outlined in black** with that title has been placed under the section heading. For these cases, the text that originally appeared in the section remains, as it supports understanding of other E-RRFs that are priorities for research.

[4]In instances of a tie (i.e., six out of 13, or 46% of stakeholders rated an E-RRF "Important" and the same number rated the E-RRF "Possibly Important") the more conservative rating was used as the most commonly selected rating (i.e., the E-RRF was rated as "Important"). The same rule applies for Confidence ratings.

[5]For example, if six out of 13 stakeholders rated an E-RRF "Important" and three out of 13 stakeholders rated the E-RRF "Possibly Important," the E-RRF was collectively rated "Important." Similarly, if four out of 13 stakeholders, 31%, rated their confidence in an E-RRF as Not Confident and three out of 13, 23% rated their confidence in the E-RRF as Somewhat Confident, the E-RRF would be rated as "Not Confident." Based on both ratings, the E-RRF would be placed in the "Important"/"Not Confident" bin of the matrix).

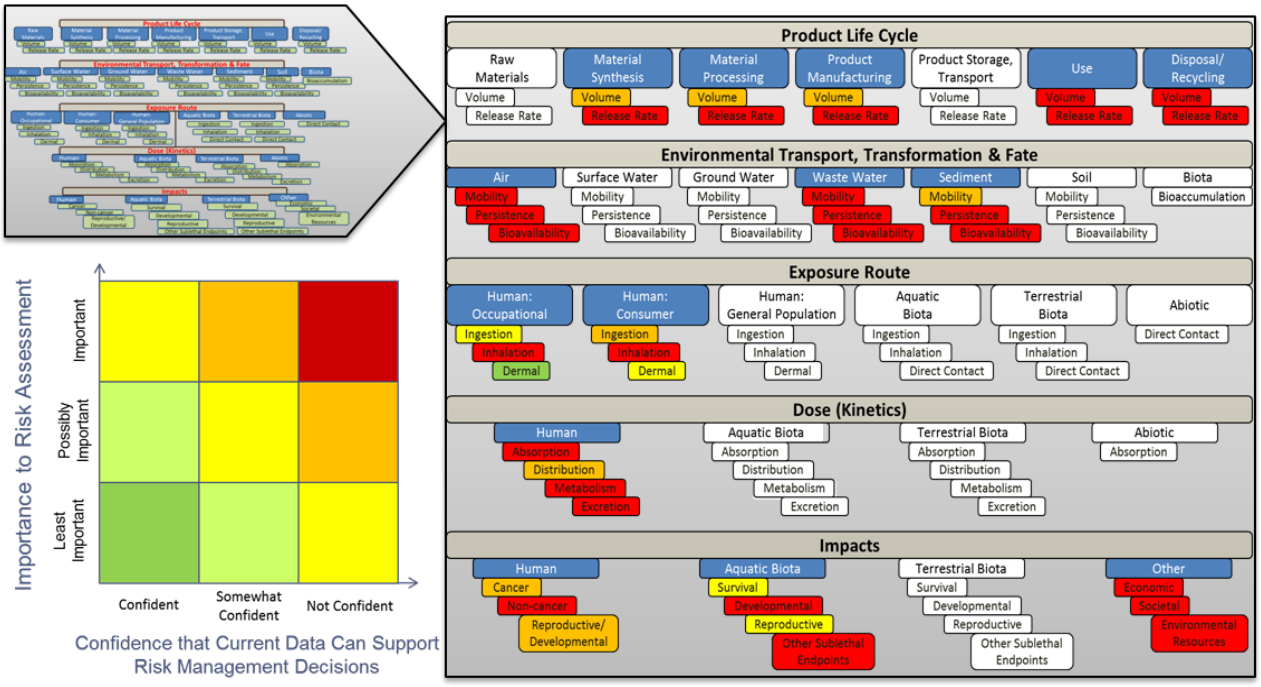


Figure 1-3. Detailed CEA framework used for the collective judgment prioritization process.

The detailed CEA framework contains "elements" at each CEA level (product life cycle; environmental transport, transformation, and fate; exposure route; dose (kinetics); and impacts). Each element is associated with several "risk relevance factors." In the original detailed CEA framework presented to participants in the collective judgment prioritization process, each element was represented by a blue bar and each risk relevance factor was represented by a green bar (shown in the upper left of this figure). During the prioritization process, participants assigned each element-risk relevance factor (E-RRF) pair a rating of "importance" and "confidence," placing each E-RRF into a bin of the Importance/Confidence Matrix (shown in the bottom left of this figure). Ratings among all participants were tallied to determine the collective assignment for each E-RRF, which is shown in the detailed CEA framework on the right side of this figure. Areas in white denote those deemed of lesser importance for future MWCNT risk assessments, while those colored in represent areas collectively identified as of high importance for future assessments. Areas in red are those of highest priority for research since participants most commonly rated the area as "Important" to MWCNT risk assessments and were "Not Confident" that data could currently support risk management decisions. More information on the collective judgment results for each E-RRF is presented in the "Priority Research Area Highlight" and "Unprioritized Research Area Highlight" boxes throughout the rest of this case study document.

How the Case Study Was Revised to Respond to Public and Peer Comments

Additional changes were made to the case study document, and new elements were added in response to written feedback from 23 experts involved in the prioritization process, and in response to comments from several members of the public (see Appendix I for more detail). Consistent with the discussion above, these changes were implemented to emphasize research priorities identified through the RTI workshop process, and to improve the scientific accuracy and rigor of the compiled information.

First, as mentioned in Section 1.1.3 and discussed above, detailed information on decaBDE was moved to Appendix H and replaced with text boxes that include highlights comparing information known about decaBDE to what is known about MWCNTs in Research Priority Areas. These highlights are meant to illustrate how understanding the data on decaBDE in flame-retardant upholstery textiles might help

guide research planning to elucidate potential risks of MWCNTs. These text boxes are consistently titled "DecaBDE Can Inform MWCNT Assessment" and are **outlined in green** (e.g., Section 2.2.2).

Second, a series of "Additional Information Highlight Text Boxes," new figures, and new tables were embedded in the case study to draw attention to scientific concepts related to the priority areas that commenters felt were under-represented in the External Review Draft of the case study. These elements were added to emphasize scientific topics that were included in the External Review Draft; but, were unclear or not clearly described, or to discuss a topic that was not included previously but is relevant to the topic and discussion. Additional Information Highlight Text Boxes, new tables, and new figures are **outlined in blue** (e.g., Table 2-2).

Finally, Chapter 6 was expanded to include a final section (Section 6.3) that discusses the priority research areas in more detail. Section 6.3 builds on the red outlined "Priority Area Highlight" text boxes described above, which are intended to briefly outline how participant ratings resulted in the area being collectively identified as a priority. Examples of the rationale for prioritizing these areas are presented in Section 6.3, along with factors that might be important to include in planning research for each area. In addition, for some priority areas, commenters, workshop participants and targeted literature searches identified relevant literature that had not been included in the External Review Draft of the case study. This literature is discussed in Section 6.3 in the context of how it might influence research planning for the area. Finally, specific research questions identified by expert participants (or based on the available literature) are listed for each priority area.

1.1.4. Selection of DecaBDE for Comparison

DecaBDE has been used widely in the textile industry to meet fire safety standards (see Section 1.2.1). Concern, however, is growing regarding the potential impacts of decaBDE on ecological and human health. For example, despite previous assumptions that decaBDE is relatively stable and inert in the environment, recent studies have suggested that it can debrominate, or break down into lower-weight congeners, which have been much more widely studied and are known to be highly toxic [(Environment Canada, 2010; U.S. EPA, 2010b; Siddiqi et al., 2003; Rahman et al., 2001); see Section 3.1 and Text Box H.3-1]. In response to these concerns regarding potential adverse impacts on human health and the environment (see Chapter 5), limitations or bans on the use of decaBDE have been imposed recently both in the United States and abroad. As summarized in Table 1-1, several states have begun to phase out or restrict the use of decaBDE.

In December 2009, the two largest U.S. producers and the largest U.S. importer of decaBDE announced voluntary commitments to phase out decaBDE in the United States by 2013 (U.S. EPA,

2010a). As summarized in the EPA PBDE Action Plan dated December 30, 2009, several reports provided evidence for the human and environmental effects of this compound. A finding of "suggestive evidence of carcinogenic potential" was reported in the 2008 *Toxicological Review of DecaBDE* (U.S. EPA, 2008b). Neurobehavioral effects also were identified in IRIS assessments for decaBDE and additional congeners (tetraBDE, pentaBDE, and hexaBDE). Environmental hazards associated with PBDEs include persistence, potential for biomagnification, and breakdown of some PBDEs to more toxic congeners to produce effects at environmentally relevant concentrations (based on reports from Environment Canada and studies from other authors). Furthermore, in 2012, EPA initiated proposed amendments to (1) the Toxic Substances Control Act (TSCA) § 5(a)(2), a Significant New Use Rule (SNUR), and (2) TSCA § 4, a Test Rule for decaBDE. The SNUR would require any entity planning to manufacture or import decaBDE or articles to which decaBDE has been added to notify EPA at least 90 days in advance, which would provide the Agency an opportunity to review and evaluate data related to the new use and to take action to limit or prohibit the new use if necessary. The Test Rule would require laboratory studies to determine the effects that decaBDE has on human health and the environment (U.S. EPA, 2012c).

Table 1-1. Existing state regulatory initiatives for decaBDE.

Regulatory Initiative	State
Implemented studies to assess environmental and human health impacts of decaBDE to inform regulatory action	Illinois, Minnesota, Rhode Island
Restricted the use or sale of products containing decaBDE	Oregon
Prohibited the manufacture, use, or sale of certain products containing decaBDE	Vermont, Maryland, Maine, New York

Source: National Conference of State Legislators (2011).

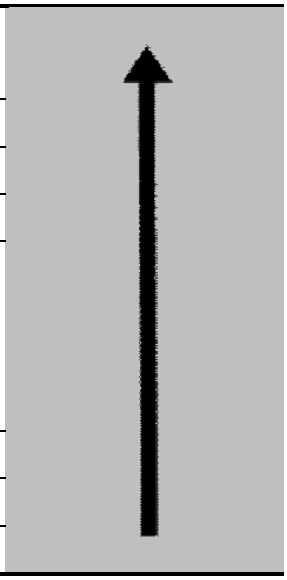
Although commercial MWCNT flame-retardant products are available, their presence is relatively new, and they are by no means abundant on the market. Given the projected decline in decaBDE use, as described above, investigating these nanoenabled products as a potential emerging alternative is relevant. The use of flame retardants in textiles is of interest to EPA and also aligns with the needs of other organizations (e.g., Consumer Product Safety Commission, National Institute of Standards and Technology). DecaBDE was chosen as the traditional flame-retardant product to compare to MWCNTs due to its extensive use since the 1970s and the robust scientific database available for it and for the brominated flame retardant (BFR) family in general.

The comparison of the larger body of information on decaBDE with the relatively small database for MWCNTs was intended to help pinpoint data gaps relating to this specific MWCNT product. For this reason, with the exception of Chapter 1, comparable information for decaBDE is included for each CEA framework area in Appendix H as a reference. Additionally, "Comparison Highlight Boxes" are included throughout the document to guide the reader to aspects of decaBDE that are particularly useful for drawing parallels to MWCNTs (see Appendix I). Because Chapter 1 is intended to provide relevant introductory information for both the traditional and nanoenabled product, it discusses relevant information on both MWCNTs and decaBDE while the rest of the document focuses solely on the "Priority Research Areas" relevant to MWCNTs.

1.2. Introduction to Flame Retardants in Textiles

Textiles and fabrics, which are networks of fibers composing flexible woven or nonwoven materials, are flammable to varying degrees due to their ignitability and their potential to propagate flame and produce burning droplets (PINFA, 2010). The behavior of various untreated textiles when exposed to flame depends on the chemical composition of the raw materials. Table 1-2 lists several common categories of textile fibers along with their flammability characteristics. The flammability of these fibers, when incorporated in different textile products, has led to the development of numerous fire safety standards (PINFA, 2010), as discussed in Section 1.2.1.

Table 1-2. Common textile fibers and degrees of flammability.

Fiber	Flammability Characteristics of Untreated Fibers	Increasing Fire Hazard
Cotton	Ignite easily, burn heavily; do not melt away from flame[1]	
Flax		
Viscose	Burns rapidly, similar to cotton	
Acetates	Burn heavily; can melt away from flame; form burning droplets[2]	
Acrylics	Burn rapidly; form burning droplets; produce dense black smoke	
Polyesters	Burn slowly and hot;[3] can melt away from flame; form burning droplets	
Polyolefins		
Polyamide		
Other synthetics		
Wool	Difficult to ignite; burns slowly; might self-extinguish	
Modified acrylics	Burn very slowly; tend to melt away from flame; might self-extinguish	
Aramide	Does not burn; strong char formation	

[1]Melting away from the flame refers to the burning characteristic where the fiber essentially melts more quickly than the flame can spread, thereby removing the amount of fiber that is available to the flame to continue burning.

[2]Burning droplets can form if the fiber melts slowly while in contact with the flame.

[3]Burning hot refers to a high peak heat release rate.

Source: PINFA (2010).

1.2.1. Standards for Textiles

Upholstery textiles, particularly those used outside of residential settings (e.g., in hospitals, airports, airplanes, penal institutions, public transportation, office buildings), are subject to various state, federal, and voluntary fire safety standards (see Table 1-3 for examples). Technical standards specify the types of products to which standards apply, methodologies for conducting specific tests, measured parameters of interest (e.g., time to ignition, heat release rate), and performance criteria for each test and product of interest (Illinois Environmental Protection Agency, 2007).

Table 1-3. U.S. and international fire regulations for upholstery textiles.[1]

Product Category	Standards	Description
Automotive vehicle (bus and car) passenger compartments; curtains or blinds used in automotive vehicles	FMVSS 302/DIN 75200/ISO 3795; DIN 50051	Specimen subjected to Bunsen burner flame for 15 seconds. The rate of flame spread should be <101.6 mm/min (for a 245-mm sample); requires test specimen to have a burning rate <100 mm/min (560-mm sample length) when subjected to a vertical flame test.
Federal flammability standard for mattresses and mattress pads	16 CFR 1632 (2000; updated 2007); 16 CFR 1633 (2006); CA TB 603 (2005); CA TB 129; CA TB 121	Cigarette test for ignition resistance sets requirements for testing of prototype designs of mattresses and mattress pads (based on CA TB 106). Open flame tests: the mattress set must not exceed a peak heat release of 200 kW at any time during a 30-minute test, and the total heat release for the first 10 minutes of the test must not exceed 15 megajoules (25 megajoules in California).
Filling materials used in upholstered furniture	CA TB 117	Furniture that meets the CA TB 117 standard is less likely to ignite rapidly, and if ignited, less likely to burn quickly or to sustain burning.
Passenger equipment in railroad trains	49 CFR Part 238 (2002); ISO 5658-2; ISO 9705	Safety and flammability standards for components of fixed items in passenger cars, seating upholstery, etc. Lateral flame spread test with heat radiator and ignition flame: specimen 800 mm by 155 mm is measured for critical heat flux at extinguishment; flame should not exceed 100 cm above the highest point of the seat surface.
Seating furniture for use in public occupancies	CA TB 133	Requires full-scale flame test[2] for furniture manufactured for use in public buildings in California. Many other states have adopted TB 133.
Cigarette testing of upholstered furniture fabric	Upholstered Furniture Action Council; CA TB 116; NFPA 701	Component standard. All upholstered furniture sold in California must pass this flame test; applies to buildings under NFPA 701 code.

[1]This list is not meant to be definitive or complete; some fire regulations are being re-evaluated and the contents of this table might not be current.

[2]Full-scale flame test refers to the use of a full piece of furniture or mockup (composite)

Note: FMVS = Federal Motor Vehicle Safety Standards and Regulations; DIN = Deutsches Institut fur Normung (Germany); ISO = International Organization for Standardization; CFR = Code of Federal Regulations; CA TB = California Technical Bulletin; NFPA = National Fire Protection Association

Sources: Lowell Center for Sustainable Production (2005); U.S. EPA (2012a); PINFA (2010).

1.2.2. Flame-Retardant Materials as Solutions to Flammability

The flammability of textiles and the standards described above have created a growing market demand for technologies to increase flame resistance and meet fire safety regulations (Alaee, 2003). One way to achieve this is through the use of flame-retardant materials, which are chemicals or other manufactured components that have the quality of resisting or inhibiting the spread of fire. Even where regulatory standards do not mandate flame resistance, market pressures and concerns about brand image often cause manufacturers to incorporate flame-retardant materials into their products (Illinois Environmental Protection Agency, 2007). In fact, the global market for flame-retardant materials is

expected to increase 4–5% by 2015 from the base market value of $3 billion in 2009 (Grzybowski, 2009; Sullivan, 2009).

The most commonly used flame-retardant materials are usually broadly categorized by chemical structure (e.g., halogenated, phosphorous-based, nitrogen-based, inorganic). Each broad class represents many possible flame-retardant compounds. Additionally, a variety of inert fillers (e.g., talc), manufactured components (e.g., glass fibers and microspheres), and more technologically advanced solutions (e.g., advances in polymer chemistry [see Section 1.2.2.2], nanotechnology) offer flame-retardant properties to increase the flame resistance of textiles (PINFA, 2010; U.S. EPA, 2005; Zhang and Horrocks, 2003).

The standards and regulations do not specify which flame-retardant materials, if any, must be used in textiles. Thus, various industry stakeholders must decide which flame-retardant materials to use based on several key criteria.

Additional Information Highlight Box 1:
Factors influencing flame retardant selection

Significant uncertainty surrounds which, if any, MWCNT flame-retardant applications are most likely to be developed for commercial use. The formulation of flame retardants is largely dictated by performance criteria, including flame test performance, efficiency, cost, and effect on textile characteristics (see Section 1.2.2.1). Although this case study discusses MWCNT flame-retardant coatings in textiles, alternative flame-retardant products might better meet these performance criteria than this selected application. Consequently, these alternative applications might be more prominent in the future than the application explored in this case study. Additional Information Highlight Box 3 details some of the challenges in developing MWCNT flame-retardant applications that meet fire safety standards and references some potential MWCNT flame-retardant applications.

1.2.2.1. Performance Criteria

Performance criteria help determine which flame-retardant materials are appropriate for which applications and provide a preliminary basis for stakeholders to compare these materials. Such comparisons are also useful in considering what materials are suitable alternatives to existing technologies. Some performance criteria proposed by EPA (U.S. EPA, 2005) include:

- **Flame test performance:** a measure of the efficacy of the flame-retardant material; different measures are included in specific regulatory standards;[6]
- **Efficiency:** the degree of flame-retardant action relative to the amount of material needed to obtain the result;
- **Cost:** expense associated with raw materials and downstream production;
- **Impacts on textile characteristics:** effect on features that can alter a product's desirability to consumers (e.g., enhanced strength, reduced aesthetic appeal).

[6]For example, the cigarette ignition test and vertical flame test measure aspects such as char length and afterglow of a sample. Flame test parameters and standards are specific to products and end uses [see (Exponent, 2010; ICL, 2010; Babrauskas and Krasny, 1985)].

Another important aspect of performance is durability. Durability is a measure of the ability of a flame-retardant material to maintain an acceptable level of flame-retardant behavior throughout the lifetime of the textile as it undergoes abrasion, laundering, weathering, or other expected processes (PINFA, 2010; NRC, 2000). The durability standard required depends on the intended use of a textile product. Durability classifications for flame-retardant finishes in textiles are presented in Table 1-4.[7] In some cases, an evaluation of durability is a component of the flame tests (e.g., both pre- and post-wash tests are required for some product uses).[8] Importantly, these criteria pertain only to the performance of a specific flame-retardant material in a specific application.

Table 1-4. Durability classifications of flame-retardant finishes.

Durability Classification	Example Flame-Retardant Materials	Example Application in Textiles
Nondurable – not resistant to washing	Boric acid, aluminum sulfate, ammonium salts, phosphates, some halogenated compounds	Mattresses, draperies, rarely washed textiles
Semidurable – resistant to limited number of washes	Cyanamide and phosphoric acid, phosphorylation of cellulosic fibers, some halogenated compounds	Tents, carpets, curtains (resistant for up to 50 washings)
Durable – resistant to many washes	Organic phosphorous compounds, some brominated compounds	Clothing, other frequently washed fabrics

Sources: BfFV (1998) and PINFA (2010).

1.2.2.2. Flame-Retardant Application Methods

Two principal processes are used for incorporating flame-retardant materials into the textile matrix: reactive and additive. Generally, flame retardants *incorporated into* the textile matrix using the reactive process produce durable finishes; flame retardants simply *added to* the textile matrix produce nondurable or semidurable finishes (U.S. EPA, 2005; Rahman et al., 2001).

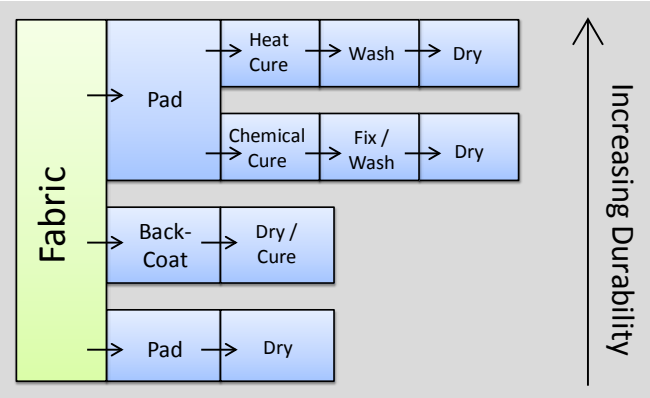
In the reactive process, flame-retardant materials are incorporated directly into polymeric materials during the manufacturing process such that they are chemically (i.e., covalently) bound to the raw materials of the final product (U.S. EPA, 2005; Rahman et al., 2001). Direct incorporation also can

[7]Durability should not be confused with leachability, which refers to the percent removal of a flame retardant from the textile matrix (NRC, 2000). Leachability is an important measure from a risk evaluation perspective while durability is more important from a product performance perspective.
[8]The *Federal Register* specifies which textile types and products require flame resistance for up to a specific number of washes.

be accomplished using a chemical reaction between two monomers to form a strong polymer chain or in a post-reaction process such as chemical grafting (functionalization) (PINFA, 2010; Laoutid et al., 2009). Flame-retardant materials produced by the reactive mechanism are often considered to be "inherently" flame resistant, as is the case with a variety of polyester blend fabrics.

In the additive mechanism, flame-retardant materials are applied to the fibers, the finished textile, or the finished product without the formation of chemical bonds and without a chemical reaction (Laoutid et al., 2009; U.S. EPA, 2005; Rahman et al., 2001). In some cases, binding agents, resins, or copolymers are used to increase the durability of the flame-retardant properties of the textile.

This case study focuses on the additive application of flame retardants to upholstery textiles. This method can be distinguished further as illustrated by the schematic in Figure 1-4, which shows the simple "pad/dry" technique and variations. In the pad/dry technique, the textile is immersed in a bath of flame-retardant solution and then squeezed through rollers at a specific pressure to remove excess solution. Back-coating describes several related application methods where a bonding resin containing the flame retardant is spread and smoothed across the reverse surface of a textile using a knife or blade (PINFA, 2010).



Source: Adapted from NRC (2000).

Figure 1-4. Durability of additive flame retardants.

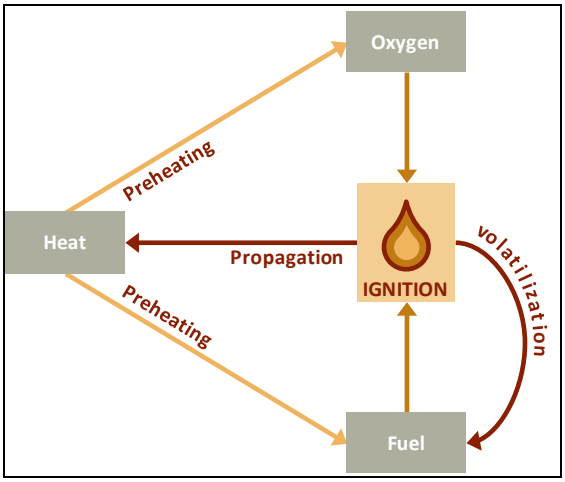
This general schematic of the "additive" application method of flame-retardant materials for textiles demonstrates the steps in the additive flame-retardant process that increase durability. The curing process can result in cross-linking, thermal fixation, or ionic linkage between the flame-retardant material and the fibers to increase durability.

Although additive flame retardants typically produce a nondurable finish (NRC, 2000), Figure 1-4 illustrates methods of addition that produce more durable finishes than the simpler pad/dry additive techniques. Thermal or chemical curing, for example, allows for interaction between the flame-retardant material and the fiber that results in a more durable finish than those produced using the simpler techniques (PINFA, 2010). Curing provides the opportunity for cross-linking (polymerization of the flame retardant onto the substrate), thermal fixation (deposition of the flame retardant within the fibers), or ionic linkage (negatively charged complexes bind to positively charged groups). These processes essentially "trap" the flame-retardant material within the polymer chains, producing a finish that is similar to those produced by the reactive method (PINFA, 2010; NRC, 2000). After curing, the textile is subjected to other processes (oxidation, neutralization, or washing) to remove by-products before the material is dried. Although a more durable finish can be obtained with heat curing or chemical curing,

leaching of flame-retardant material remains of greater concern for additive flame retardants than for reactive flame retardants (not shown in Figure 1-4) because the material is not covalently bound to the substrate (Rahman et al., 2001).

1.2.2.3. Mechanism of Flame-Retardant Action

Once incorporated into the textile, flame-retardant materials physically or chemically inhibit the combustion process. Combustion occurs through a series of chemical reactions including heating and ignition, volatilization, and decomposition, which are self-propagating in the presence of oxygen and a fuel source (U.S. EPA, 2005; Alaee, 2003) (see Figure 1-5).



Source: Adapted from Alaee et al. (2003) and Laoutid (2009).

Figure 1-5. The combustion process.

The combustion process consists of distinct but overlapping reactions between a fuel source and an oxidant in the presence of heat. Ignition and volatilization in the presence of oxygen produce additional heat, which propagates the cycle.

The mechanism of flame-retardant action can be categorized generally as follows, although many flame retardants actually inhibit the combustion process through a combination of these mechanisms (U.S. EPA, 2005; Alaee, 2003; Rahman et al., 2001):

- **Physical Dilution:** The flame-retardant material (1) reduces the fuel content available for combustion below the concentration needed to sustain flame propagation or (2) increases the heat capacity of the product, which increases the amount of heat required for product ignition.
- **Chemical Interaction/Gas-Phase Radical Quenching:** The flame-retardant material thermally degrades and releases chemical radicals that are highly reactive with oxygen, which reduces the amount of free oxygen available to supply the combustion process.
- **Inert Gas Dilution:** The flame-retardant material produces a large volume of noncombustible gases that dilute the oxygen supply available to propagate the flame.
- **Thermal Quenching:** The flame-retardant material endothermically degrades, which removes heat from the substrate and cools the material.
- **Protective Coatings:** The flame-retardant material forms a liquid or char coating that acts as an insulation barrier to prevent heat transfer from the flame to unaffected areas of the product.

These five processes act individually or in combination to increase the time to ignition, prevent spread of the flame, or decrease extinguishing time (Alaee, 2003). Table 1-5 provides examples of each major chemical class of flame retardant described in Section 1.2.2 along with a description of how the

flame retardants are added to textiles, and the general mechanism of flame-retardant action for each class of flame retardant.

Table 1-5. Flame retardants summarized by chemical class, method of application, and mechanism of flame-retardant action.

Chemical Class	Examples	Application Method	Flame-Retardant Mechanism
Halogenated	Chlorinated (polychlorinated biphenyls), Brominated (polybrominated diphenyl ethers)	Variations of padding and drying or back-coating	Gas-phase radical quenching/chemical reaction to slow the burning rate; also can form a solid protective layer
	Monomers and copolymers (vinyl bromide), Tetrabromobisphenol A	Combined with copolymeric modifications or grafted onto polymer chains for reactive application	Decreases thermal degradation; reduces extinguishing time
Phosphorous-based	Organophosphorous, Inorganic phosphates	Coatings; chemical bath	Protective coatings or layers; char formation
Nitrogen-based	Melamine, Melamine salts	Intumescent coatings; back-coatings; can be added to polymer melt	Inert gas dilution (inhibits formation of flammable gases); char formation
Inorganic	Metal hydroxides, Minerals	Fillers; back-coatings; can be added to polymer melt	Endothermic degradation/thermal quenching or inert gas dilution; forms protective layer; physical dilution; thermal shielding

Sources: U.S. EPA (2005); BfFV (1998); NRC (2000); Xusen (2010); PINFA (2010); and Laoutid (2009).

1.3. DecaBDE and MWCNTs in Flame-Retardant Textiles

As noted previously, the purpose of this case study is to present available information that supports research planning for conducting a comparative CEA in the future of a traditional flame retardant (e.g., decaBDE) and a nanoenabled flame-retardant technology using MWCNTs, specifically in upholstery textile coatings. The following sections provide a general overview of decaBDE and MWCNTs, their use in textiles, and a brief comparison of observed flame-retardant action and efficacies.

1.3.1. Introduction to DecaBDE

DecaBDE is part of a larger group of BFRs called polybrominated diphenyl ethers (PBDEs), a group of 209 structurally similar BFRs that differ in the number and location of bromine atoms

(Table 1-6) (Rahman et al., 2001; NRC, 2000). Although PBDEs are typically categorized into classes by number of bromine atoms (e.g., PBDE with two bromine atoms is a diBDE; ten bromine atoms is a decaBDE), a single class might contain several different PBDE congeners with the same number of bromine atoms in different locations (i.e., PBDE BFRs can have many isomers). As the only fully brominated PBDE, decaBDE is the exception, existing only as a single congener (BDE-209).

Table 1-6. Major PBDE congeners.

PBDE Class	Congeners
DiBDE	BDE-7, BDE-8, BDE-11, BDE-12, BDE-13, BDE-15
TriBDE	BDE-17, BDE-25, BDE-28, BDE-30, BDE-32, BDE-33, BDE-35, BDE-37
TetraBDE	BDE-47, BDE-49, BDE-66, BDE-71, BDE-75, BDE-77
PentaBDE	BDE-85, BDE-99, BDE-100, BDE-105, BDE-116, BDE-118, BDE-119, BDE-126, BDE-138, BDE-140
HexaBDE	BDE-153, BDE-154, BDE-155, BDE-166
HeptaBDE	BDE-181, BDE-183, BDE-190
OctaBDE	BDE-196, BDE-197, BDE-203
NonaBDE	BDE-206, BDE-207, BDE-208
DecaBDE	BDE-209

Source: U.S. EPA (2010b).

Commercial formulations of decaBDE (see Table 1-7) are generally 97–98% BDE-209 with less than 3% nonaBDE congeners present as impurities (Rahman et al., 2001; NRC, 2000) (see Appendix B, Table B-1 for analytical techniques used to distinguish PBDE congeners in samples). Although the terms decaBDE and BDE-209 often are used interchangeably, this case study primarily uses the term decaBDE to refer generally to the flame-retardant formulation and BDE-209 to refer to the specific decaBDE congener analyzed in scientific studies.

DecaBDE is the most widely used of the PBDEs and has been well studied. In 2001, decaBDE use accounted for 83% of total PBDE production worldwide (U.S. EPA, 2010b); an estimated 10–20% of decaBDE use is in the textile industry (Pure Strategies Inc., 2005). At the end of 2004, both octa- and pentaBDE were voluntarily withdrawn from the United States marketplace due to evidence of environmental persistence and toxicity, which left decaBDE as the sole PBDE available for use in commercial products in the United States (U.S. EPA, 2010b). As mentioned in Section 1.1.4, two U.S. producers made a commitment on December 17, 2009, to phase out decaBDE in the United States by 2013, due to similar concerns over environmental persistence and toxicity. Several standard

physicochemical properties are used to describe traditional chemicals: melting point, boiling point, molecular weight, and others. Such values are presented for decaBDE in Table 1-8.

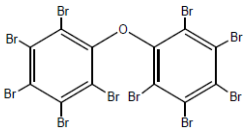
Table 1-7. Commercial formulations of PBDEs used as flame retardants.

Name	Congener Makeup and Percent Composition	
Penta formulation[1]	Penta	BDE-99 (35–50%), BDE-100 (6–10%)
	Tetra	BDE-47 (25–37%)
	Hexa	BDE-153 (5–10%), BDE-154 (1–5%)
Octa formulation	Hexa	BDE-153 (5–10%), BDE-154 (1–5%)
	Hepta	BDE-183 (40%)
	Octa	BDE-197 (21%), BDE-203 (5–35%), BDE-196 (8%)
	Nona	BDE-208 (10%), BDE-207 (7%)
Deca formulation[2]	Nona	BDE-206 (2.2%), BDE-207 (0.24%), BDE 208 (0.06%)
	Deca	BDE-209 (>97%)

[1]Trace amounts of additional congeners might be present in commercial formulations: <0.2% triBDE congeners.
[2]Trace amounts of additional congeners might be present in commercial formulations: <0.003% heptaBDE congeners; <0.001% hexaBDE congeners; <0.002% pentaBDE congeners; <0.00003% tetraBDE congeners; <0.00001% triBDE congeners.
Source: U.S. EPA (2010b).

DecaBDE can be applied to textiles by a variety of mechanisms, but this case study focuses on the application of decaBDE as a back-coating. This application method is used most frequently for decaBDE (Pure Strategies Inc., 2005; NRC, 2000) and is most similar to the application method expected for MWCNTs used in textiles (see Section 1.3.2). The back-coating process usually involves mixing decaBDE with a copolymer or resin binder (Pure Strategies Inc., 2005; NRC, 2000). DecaBDE combines the flame-retardant mechanism of most BFRs (i.e., releasing halogens during combustion to compete with the availability of oxygen for the flame) with formation of a protective char barrier (NRC, 2000) that interferes with the spread of the flame and helps the material to self-extinguish (Pure Strategies Inc., 2005).

Table 1-8. Physical properties and chemical identity of decaBDE.

	Physical property/chemical identity	Reference
CASRN	1163-19-5	NLM (2011)
Synonyms	2,2',3,3',4,4',5,5',6,6'-decaBDE; BDE-209; benzene, 1,1'-oxybis[2,3,4,5,6,-pentabromo]-; decabromodiphenyl oxide; decabromodiphenyl ether; decabromobiphenyl ether; ether, bis(pentabromophenyl)	NLM (2011); ATSDR (2004)
Physical state	Solid	Hardy (2002b)
Melting point,	300–310 °C	ECB (2003)
Boiling point	Decomposes at >320 °C	ECB (2003)
Vapor pressure	4.63×10^{-6} Pa at 21 °C	Hardy (2002b)
Henry's law constant	1.93×10^{-8} L atm/mol 0.04 Pa m3/mol at 25 °C	Hardy (2002b); Cetin and Odabasi (2005)
Density	3.0 grams/cm^3	NRC (2000)
Water solubility	<0.1 µg/L at 25 °C	Hardy (2002b); ECB (2003)
Log K_{ow}	6.3–12.6	Hardy (2002b)
Log K_{oc}	6.3	Hardy (2002b)
Molecular weight	959.17	NLM (2011); ECB (2003)
Chemical formula	$C_{12}Br_{10}O$	NLM (2011)
Chemical structure		

Note: K_{ow} = Octanol water partition coefficient, K_{oc} = Soil organic carbon-water partition coefficient.

1.3.2. Introduction to MWCNTs

MWCNTs are carbon nanostructures composed of multiple concentrically nested graphene sheets that look similar to nested rolls of chicken wire. Unlike many traditional chemicals, MWCNTs are not a homogeneous group of molecules; many of the characteristics of MWCNTs can be intentionally or unintentionally altered using different laboratory procedures, treatments, and synthesis methods (see Sections 2.2 through 2.2.3 and Appendix G, Sections G.2.1 through G.2.2.2). As described in Text Box 1-1, altering the physicochemical properties of MWCNTs can alter their behavior during all stages of the life cycle, in environmental compartments, and in humans and other biota. As a result, MWCNTs with different physicochemical properties might produce different impacts downstream, but which

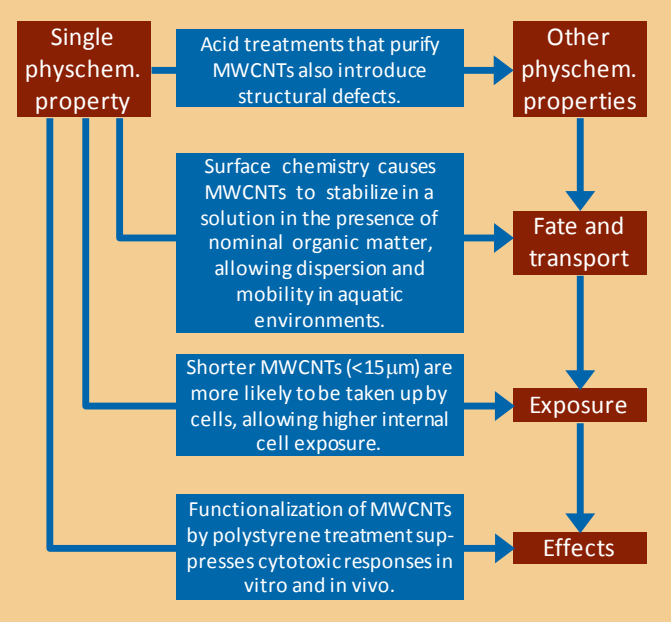
physicochemical properties might drive these differences and to what degree are not fully understood. MWCNTs are not a single homogeneous substance; ranges of values describing MWCNT physicochemical properties are provided in Table 1-9 to illustrate the array of characteristics recorded for MWCNTs in the literature (see Appendix B, Table B-2 for analytical techniques used to characterize MWCNTs).

Text Box 1-1. Physicochemical Properties of Multiwalled Carbon Nanotubes (MWCNTs) Affect Their Release, Behavior in the Environment, and Interaction with Biota

A substance's physicochemical characteristics largely determine the environmental fate and transport and potential for release, exposure, and impacts associated with that substance. Yet, the key characteristics that determine behavior differ between conventional materials and engineered nanomaterials. Driving characteristics for conventional materials include boiling point, melting point, and density. These are replaced at the nanoscale by size, surface area, surface chemistry, and morphology. Altering just one of these characteristics influences the behavior of nanomaterials. A single type of nanomaterial, such as MWCNTs, can be created with dozens of variations of these properties. MWCNTs are generally nested tube-like structures with a very high length-to-diameter ratio, but they can be engineered to have various lengths, surface coatings, and functionalizations.

Important Physicochemical Properties of Nanomaterials:

- Size, including agglomeration/aggregation tendencies
- Morphology, including shape and crystal structure
- Surface area
- Chemical composition
- Surface chemistry and reactivity
- Solubility and dispersion
- Conductive, magnetic, and optical properties



Demonstrating and quantifying relationships between individual characteristics and MWCNT behavior is complicated due to the difficulty in altering only one characteristic at a time. For example, oxidizing MWCNTs can shorten them and make them more straight (Johnston et al., 2010). Equally difficult is assigning mechanisms of toxicity to the observed effects. For instance, long, straight MWCNTs injected under the skin of rats can produce more inflammogenic effects than shorter bundles of MWCNTs administered in the same manner (Johnston et al., 2010), but whether the length of the materials, their tendency to bundle and how tightly, or all of these factors directly affect inflammation is unclear. The complex relationships among physicochemical properties, and between these properties and the life cycles of nanomaterials, have not been fully elucidated. The impacts of these properties on nanomaterial behavior also have not been analyzed adequately, particularly in terms of understanding the potential environmental and health effects of nanomaterials.

Table 1-9. Physical properties and chemical identity of MWCNTs.

Physical property/chemical identity[1,2]		Reference
Physical state	Solid	
Morphology	Concentric cylinders	Johnston et al. (2010)
Physical structure		Hirsch and Vostrowsky (2005)
Purity,[4] min. wt% C	Usually >90%; 7.5–40% reported for "multi-wall, powdered cylinder cores" and "multi-wall, as produced" by Sigma-Aldrich	See Appendix F study summaries; Sigma-Aldrich (2012)
Outer diameter	5–170 nm[3]	Aschberger et al. (2010); Li and Huang (2011); Desai et al. (2012); He et al. (2012); Dawson et al. (2011); Golovin et al. (2011); Lu et al. (2011b); Liu et al. (2011a); Ji et al. (2011); Sigma-Aldrich (2012)
Length	20 nm–200 µm	Aschberger et al. (2010); He et al. (2012); Aranberri et al. (2011); Golovin et al. (2011); Lu et al. (2011b); Liu et al. (2011a); Ji et al. (2011); Sigma-Aldrich (2012)
Aspect ratio	Up to 1,000	Cipiriano et al. (2007)
Chirality	Varies; chiral angles, described by vectors (n, m), produce different graphene sheet conformations (e.g., "zigzag" [m = 0], armchair [n = m]), and influence other properties (e.g., mechanical, optical, electrical)	Gustavsson et al. (2011)
Axial and radial strength	Axial: rigid; 10 times stronger than steel Radial: flexible; can be bent up to 90 degrees	Gustavsson et al. (2011)
Surface area	253–400 m^2/gram	Aschberger et al. (2010); Aranberri et al. (2011); Lu et al. (2011b);
Bundle size	0.9–100 µm	Li and Huang (2011); Baitinger et al. (2011);
Surface composition	Pristine or modified with various functional groups	Johnston et al. (2010)
Vapor pressure	No information available	
Melting point	3,652–3,697 °C	Sigma-Aldrich (2012)
Stability	Stable up to 600 °C (CNTs)	Nanoshel (2011)
Density	2.1 grams/mL at 25 °C	Sigma-Aldrich (2012)
Zeta potential, mV	−23–0	Li and Huang (2011)
Solubility in water	Insoluble; functionalization treatments result in different degrees of solubility	Lam et al. (2006); Johnston et al. (2010)

[1]Values reported represent total ranges reported in literature.
[2]Values are provided for MWCNTs where available, or values for single-walled CNTs or CNTs in general are provided, when not.
[3]Depending on the number of walls.
[4]Impurities include cobalt, iron, nickel, and molybdenum (commonly used as catalysts in production; see Sections 2.2 through 2.2.3, and Appendix G, Sections G.2.1 through G.2.2.2). Percent purity depends on purification methods (see Appendix C).

According to the scientific literature, MWCNTs can act as flame retardants in a variety of textiles, including plastics, polymers, assorted fabrics, and technical materials (Gonçalves et al., 2012; Alimohammadi et al., 2011; Binetruy and Boussu, 2010; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a). To date, at least one MWCNT flame-retardant textile coating is commercially available, but this application does not appear to be widespread (Nanocyl, 2009). Goncalves et al. (2012) describe the incorporation of MWCNTs into cotton or polyester using a process similar to industrial dyeing methods. In addition, a patent is currently on record for a method to incorporate MWCNTs into several different textile types (e.g., cotton, wool, silk, flax, nylon, polyester, acrylic) that includes documentation of flame-retardant properties compared to raw cotton (Alimohammadi et al., 2011). Both the work by Goncalves et al. (2012) and the recent patent indicate that more commercial applications of MWCNTs in textiles might be available in the near future. MWCNTs primarily inhibit flames in a manner similar to that of one of the mechanisms of decaBDE, that is, by forming a protective layer that seals against combustion. When formed by MWCNTs, this protective char-like layer often is referred to as a "network-structured layer" that can act as a thermal shield (Laoutid et al., 2009; Cipiriano et al., 2007; Kashiwagi et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004), reduce the peak heat release rate, and increase thermal conductivity (Laoutid et al., 2009; Cipiriano et al., 2007; Kashiwagi et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Beyer, 2004; Kashiwagi et al., 2004).

The flame-retardant behavior of MWCNTs depends on the formation of a highly uniform, network-structured layer of floccules, which are loosely bound MWCNT bundles, with no breaks or cracks. The formation of the floccule layer, and in turn the flame-retardant behavior, varies according to a variety of factors, including dispersion (which can be enhanced with surface treatments), size, shape,

Additional Information Highlight Box 2:
MWCNTs are not widely used in flame-retardant textiles

Use of MWCNTs in flame-retardant textiles is not currently a widespread application, nor is it anticipated to become one of the more widespread applications of MWCNTs in the near future. While global annual production capacity for MWCNTs has increased rapidly (Köhler et al., 2008) and is projected to reach 9,400 tons by 2015 (Innovative Research and Products Incorporated, 2011), most MWCNT production in the United States currently occurs in research labs or small-scale pilot manufacturing facilities (Schubauer-Berigan et al., 2011). Although one commercial MWCNT flame-retardant coating has been developed [(Luizi, 2009); Personal Communication: Nicolas Messin (Nanocyl). 3/2/2012],the proportion of total global MWCNT production used in textiles is anticipated to be very low (see Table 1-10 and Table 2-2). Future use of MWCNTs in flame-retardant textiles will be determined by their ability to pass specific flame retardant regulatory tests (see Additional Information Highlight Box 1, Additional Information Highlight Box 3, and Table 1-12), as well as the feasibility of large-scale production processes. Although researchers have already demonstrated the ability to incorporate MWCNTs into fabrics using a process that mirrors industrial dyeing methods (Gonçalves et al., 2012), other applications of MWCNTs (e.g., electrodes, electronic components, filters and membranes, sensors, cosmetics, molecular computing and data storage, fuel cells) currently occupy a larger percentage of the MWCNT market (Schnorr and Swager, 2011; Köhler et al., 2008). Although greater production volumes of other MWCNT applications was one consideration in developing this case study, other factors, such as exposure potential, also were important (see Section 1.1).

aspect ratio,[9] and loading concentration (Cipiriano et al., 2007; Kashiwagi et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004). Cipiriano et al. (2007) were able to produce a more uniform floccule layer at lower concentration loadings, resulting in enhanced flame-retardant properties, by using MWCNTs with a higher aspect ratio. In nanoclay, the incorporation of organomodified montmorillonite, but not sodium-layered montmorillonite, stimulated char formation in polymer matrices, indicating that surface functional groups can be instrumental in flame-retardant action (Laoutid et al., 2009).

1.3.3. MWCNTs as Alternative Flame-Retardant Materials in Upholstery Textiles

As the use of decaBDE begins to decline, cost-effective and feasible alternatives to replace this widely used flame retardant are being evaluated. MWCNTs are one of many possible alternatives to replace decaBDE. Given the current, albeit limited, availability of a MWCNT product for textile applications[10] and the projected decline in cost (Sullivan, 2009), the use of such nanoenabled products is likely to increase in the future as an emerging application. Table 1-10 provides a comparative summary of decaBDE and MWCNTs, which illustrates several similarities in application method, flame-retardant action, and relevant uses. Many parallels can also be drawn in the performance criteria (discussed in Section 1.2.2.1) as shown in Table 1-11.

A summary of information available from actual flame tests for decaBDE and MWCNTs is provided in Table 1-12. Note that information available for flame tests for both materials is not standardized. Some information is qualitative, while other data are quantitative. In both cases, only a few representative examples are described; in the absence of specific data on MWCNTs used in textiles relevant to this case study, available information has been provided on a similar MWCNT flame-retardant product used as a coating for a variety of materials. This product is used on foam and other structural materials, but might prove useful for comparison to the current application because it generally has been shown to increase flame resistance, increase the heat barrier and charring, and reduce the amount of smoke created. Furthermore, the manufacturer advertises that their MWCNT flame-retardant coating is appropriate for application to textiles (Mezzo, 2010). Table 1-13 describes properties of MWCNTs that impact performance as a flame retardant.

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[9]This dimension refers to the proportional relationship between the length and width of the nanotube; CNTs (carbon nanotubes) typically are characterized as having large aspect ratios (i.e., greater length than width).
[10]Personal Communication: Nicolas Messin (Nanocyl). 3/2/2012.

Table 1-10. Overview of decaBDE and MWCNTs for flame-retardant textile application.

	MWCNTs	DecaBDE
Method of incorporation into textile products	Integrated by "melt blending" with polymer (Cipiriano et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Zhang and Horrocks, 2003); dispersed in resin (e.g., silicon base) and applied as a coating (Nanocyl[1]) (Köhler et al., 2008); applied by "dyeing-like" method to fabrics (e.g., cotton) (Gonçalves et al., 2012); "layer-by-layer coating" (foam applications) (Uddin and Nyden, 2011a; Davis and Kim, 2010)	Applied as a back-coating to textiles (NRC, 2000), often with a binding agent such as latex (ECB, 2003), or a copolymer (NRC, 2000)
Mechanism of flame-retardant action	MWCNT network acts as a sealing or shielding agent (i.e., a barrier) (Berger, 2007; Cipiriano et al., 2007; Kashiwagi et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004)	Gas-phase radical quenching; creates a char barrier (NRC, 2000)
Approximate production volume/ capacity[2]	From 2005 to 2009, global annual production capacity increased from 294 tons (approximately 267 tonnes) to more than 1,500 tons (approximately 1,361 tonnes) (Köhler et al., 2008); projected to reach 9,400 tons (approximately 8,528 tonnes) by 2015 (Innovative Research and Products Incorporated, 2011); percent of MWCNTs produced for textile use expected to be very low	Worldwide demand in 2001 reported as 54,000–56,000 tonnes (Law et al., 2006; Pure Strategies Inc., 2005); >60,000 tonnes reported in 2007 (Illinois Environmental Protection Agency, 2007); 10–20% of decaBDE produced is used in textiles[3]
Relevant use in textile applications	Has been tested in "nanocomposites" with polyvinyl acetate, and ethylene vinyl acetate (Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004); marketed as coating on cables, metal, foam, and textiles (Nanocyl); marketed as "additives" for flame-retardant textiles or as industrial coatings for fabrics (Siegfried, 2007); tested in various textiles (e.g., cotton, wool, polyester, acrylic) with flame-retardant action reported (Gonçalves et al., 2012; Alimohammadi et al., 2011)	Used in mattresses, draperies, commercial upholstered furniture, and in transportation industry fabrics (Pure Strategies Inc., 2005)

[1]See (Nanocyl, 2009; Sullivan, 2009).

[2]Note: not all of the production capacity is relevant for flame retardants or for use in upholstered textiles.

[3]According to U.S. EPA (2010b), production volumes for PBDEs are not readily available. The most recent industry reporting year for market demand was 2001. At that time, 83% of all PBDE consumed worldwide was decaBDE.

Table 1-11. General qualitative comparisons of performance criteria for decaBDE and MWCNTs.

	MWCNTs	DecaBDE
Flame test performance	Reduces peak heat release rate; formation of network-structured protective layer; reduced rate of pyrolysis (Cipiriano et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004); increased limiting oxygen index (LOI)[1] (Alimohammadi et al., 2011)	Allows textiles to comply with fire safety standards in public places and public buildings. Also used to comply with more stringent fire safety requirements for home upholstered furniture in countries such as Ireland, the United Kingdom, and the United States (Pure Strategies Inc., 2005)
Efficiency	Effective at very low concentrations (0.5–4% by mass) (Grzybowski, 2009; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004); commercial formulations for textile use are reported to be effective at 100 μg thickness[2]	Very efficient, can be used at relatively low concentrations (Pure Strategies Inc., 2005; Rahman et al., 2001); maximum of approximately 20% w/w added as a back-coating (NRC, 2000);[3] applied 10–15% by weight to polymers in conjunction with resin binder (U.S. EPA, 2010b)
Cost	Relatively low cost of production ($100/kg) compared to other nanocarbon products, projected to decrease to $10–$20/kg (Sullivan, 2009); commercial prices vary with purity, size, and functionalization (e.g., $7,000/kg for functionalized, $2,000/kg for 95 wt% <8 nm; $700/kg for 95 wt% >50 nm) (Cheap Tubes Inc., 2009)	Described as "cost effective" (Pure Strategies Inc., 2005) and "relatively cheap" (Posner, 2004); decaBDE/antimony oxide mixture is roughly $3.09/kg when used for draperies (Pure Strategies Inc., 2005)
Impacts on textile characteristics	Can improve physical and mechanical properties (Siegfried, 2007; Hirsch and Vostrowsky, 2005; Kashiwagi et al., 2005b), as well as conductivity and optical properties4 (Siegfried, 2007); fatigue resistant; particle embedding can prevent cracks (Grzybowski, 2009)	Must be applied to reverse side of fabric because of negative effect on aesthetics.
Durability	Commercial product has not been tested for durability in laundering, but flame-retardant performance is resistant to other chemical treatments;[2] potential for nanotextiles to release individual nanoparticles or clusters of nanoparticles (Greßler et al., 2010)[5]	Semidurable (Rahman et al., 2001); resin applied with decaBDE bonds to the fiber to increase durability (Pure Strategies Inc., 2005)

[1]Limiting Oxygen Index (LOI) is a measure of the minimum percent concentration of oxygen that will support combustion.

[2]Personal Communication: Nicolas Messin, Global Sales and Marketing Manager for Thermosets (Nanocyl). 3/2/2012.

[3]Depends on the PBDE used (both decaBDE and hexaBDE referenced), the resin binder used, and the fabric to be treated.

[4]Optical properties of textiles include fluorescence or color-changing effects (theoretical; not necessarily relevant for MWCNTs in upholstery).

[5]Based on the fact that textiles are known to lose 5–20% of their weight during use (abrasion, mechanical influence, washing, etc.); authors note that textiles made from fibers with integrated nanoparticles are more likely to have longer lasting functionality compared to those with nanoparticle surface coating or impregnation.

Additional Information Highlight Box 3:

MWCNTs are likely used in combination with other chemicals in flame-retardant applications

Although MWCNT applications demonstrate the ability to confer flame-retardant properties to a wide range of polymers and textiles (Gonçalves et al., 2012; Grzybowski, 2009; Mahy, 2009; Howlett, 2008), the physical barrier properties (i.e., the ability of MWCNTs to produce a barrier to seal or shield materials from igniting) of MWCNTs alone are not sufficient to pass flammability tests for composites and polymeric materials (e.g., UL 94, Limiting Oxygen Index) (see Table 1-3 and Table 1-12 for example fire regulations and flame test performance, respectively) (Morgan, 2006; Bartholmai and Schartel, 2004). In many instances, however, nanomaterials can be combined with other flame retardants to decrease flammability synergistically (Morgan, 2006). For example, Beyer (2006) concluded that the addition of a microfiller (e.g., aluminum trihydrate) is essential to generate nanocomposites with flame-retardant properties sufficient for industry and government standards. Isitman and Kaynak (2010) observed similar synergies when carbon nanotubes were added to poly(methyl)methacrylate filled with an organophosphorus flame retardant that acts through intumescence. Therefore, MWCNTs likely would be used in combination with conventional fire retardants to pass flammability tests in most applications, including upholstery textiles (Morgan, 2006; Schartel et al., 2006; Bartholmai and Schartel, 2004). In support of this likelihood, additional examples of MWCNTs in combination with traditional flame retardants are available in the literature (Ma et al., 2011; Lu and Wilkie, 2010; Beyer, 2005).

Table 1-12. Flame test performance of decaBDE and MWCNTs.

	Sample	Without Treatment	With Treatment	Source
MWCNTs[1]	Polyurethane foam	Burns quickly, dense smoke forms, burning droplets fall	Spray coating forms "shell" to keep molten foam contained (no burning or flaming drops)	Mahy (2009); Howlett (2008)
	Polyvinyl chloride	Burns easily, melts, structure destroyed	Does not melt, structure is retained	Mahy (2009)
	Wires/Cables	Burns completely, releases dense smoke and burning droplets, copper core becomes exposed	No burning droplets; low smoke density; copper core protected; passes UL94,[2] IEC-332-3[3] tests	Mahy (2009)
	Polypropylene	Heat release rate = 2,800 kW/m^2	1–2% addition = heat release rate of 800 kW/m^2	Gryzybowski (2009)
	Cotton	Burned distance = 77 mm; burning time = 19 sec; burning rate = 243 mm/min	Burned distance = 80 mm; burning time = 21 sec; burning rate = 229 mm/min	Goncalves et al. (2012)
	Polyester	Burned distance = 66 mm; burning time = 26 sec; burning rate = 152 mm/min	Burned distance = 66 mm; burning time = 53 sec; burning rate = 75 mm/min	Goncalves et al. (2012)
DecaBDE	Sofa	Burns quickly (<5 minutes), temperature increases from 20 °C to 800 °C	Burns slowly, increases amount of time to escape by up to 15 times	BSEF (2012)
	50/50 polyester/ cotton twill	Sample burns completely	Char length reduced (<6.3 in.)	ICL Industrial Products (2010)

[1]Due to the limited availability of information relevant to upholstery textiles, data for flame-retardant coatings for foam, polyvinyl chloride, and other materials are included for additional context.

[2]Horizontal and vertical burning tests associated with American Society for Testing and Materials (ASTM) International standards.

[3]Large-scale flammability test for wire bundles under 20.5 kW flame.

Table 1-13. Physicochemical properties of MWCNTs related to flame-retardant performance.

Property	Influence on Flame-Retardant Performance
Dispersion	Dispersion, which is influenced by surface chemistry, functionalization, or use of surfactants, plays an important role in the flame-retardant properties of MWCNTs. For example, MWCNTs or SWCNTs that were "well dispersed" in a polymer resulted in significantly reduced heat release rate compared to "poorly dispersed" MWCNTs or SWCNTs (Kashiwagi et al., 2007; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004).
Size	Commercially available MWCNTs for flame resistance are approximately 1.5 µm in length [Nanocyl; (Howlett, 2008)]. Shorter MWCNTs (1–2 µm) are more flame-retardant than longer MWCNTs (0.5–40 µm) in polymer blends (Pack et al., 2009).
	MWCNTs that are "crushed" increase the time to ignition compared to uncrushed MWCNTs in polymer nanocomposites (Laoutid et al., 2009).
Functional Groups and Impurities	MWCNTs coated with high density polyethylene are better dispersed and result in more homogenous char formation compared to uncoated MWCNTs when producing nanocomposites within an ethylene-vinyl acetate copolymer (Laoutid et al., 2009).
	MWCNTs with triphenylphosphine functional groups have increased char production and flame resistance compared to purified MWCNTs in experimental tests where the MWCNTs were not incorporated into another material, such as polymer or foam (Muleja et al., 2012).
	Similar reduced heat release rates were reported for "crude" and "pure" MWCNTs in polymer matrices, indicating that Co, Fe, and alumina contaminants on the crude MWCNTs do not interfere with or enhance flame-retardant action (Beyer, 2004).
	MWCNTs with higher acidity (highest quantity of surface oxygen-containing groups like carboxylic acid, phenols, and carbonyls) have better flame performance than less acidic MWCNT treatments in cotton and polyester (Gonçalves et al., 2012).
	Chemical grafting of intumescent flame-retardant compounds onto the outer shell of MWCNTs improves dispersion in polymer matrix and improves flame retardancy at lower mass loadings relative to unmodified MWCNTs (Ma et al., 2011).
Aspect Ratio	Commercially available MWCNTs for flame resistance have an aspect ratio larger than 100 [Nanocyl; (Howlett, 2008)].
	CNTs significantly increase melt viscosity and reduce flammability of polymers due to high aspect ratio and formation of jammed network (floccules layer) (Song et al., 2012).
	Increased aspect ratio improves flame retardancy (reduced heat release rate as evidenced by increased storage modulus) at similar mass loadings (aspect ratio 49 versus 150) in polymer matrices (Cipiriano et al., 2007).

Table 1-13, cont.: Physicochemical properties of MWCNTs related to flame-retardant performance.

Property	Influence on Flame-Retardant Performance
Loading Concentration	Loading concentrations of 0.1–0.5% are positively correlated with reduced heat release rate, as long as the loading concentration does not cause the CNTs to be poorly dispersed (i.e., to agglomerate) in polymers (Kashiwagi et al., 2005b; Kashiwagi et al., 2005a).
	Loading concentrations of 0.5–4% MWCNT by mass show a shortened ignition delay time at 0.5%, followed by an increased ignition delay time with increase in concentration up to about 1% and an increase in peak heat release rate above 1% (loading; 2% and 4%). The ignition delay time and peak heat release rate observed at 1% loading is reported to be due to the balance between the effect of thermal conductivity and shielding performance of external radiant flux, although the authors do not discuss why higher loading mass resulted in poorer performance in polymer matrices (Kashiwagi et al., 2004).
	Mass loadings of 1–2% form solid protective layers with low mass loss rates; however, 4% loading of the same MWCNTs have a higher peak mass loss rate. The authors attribute this to increased thermal conductivity, which initially slows mass loss rate; but, once thermal energy accumulates in the polymer sample, the mass loss increases more quickly (Cipiriano et al., 2007).
	Increased loading (from 100 ppm to 1,500 ppm) increases the LOI from 17.6% (raw cotton) to a max of 23.8% (at 1,500 ppm), however concentrations of 250 ppm and above result in less dramatic increases in LOI compared to the first 100 ppm (with an LOI of 22.2%) (Alimohammadi et al., 2011).

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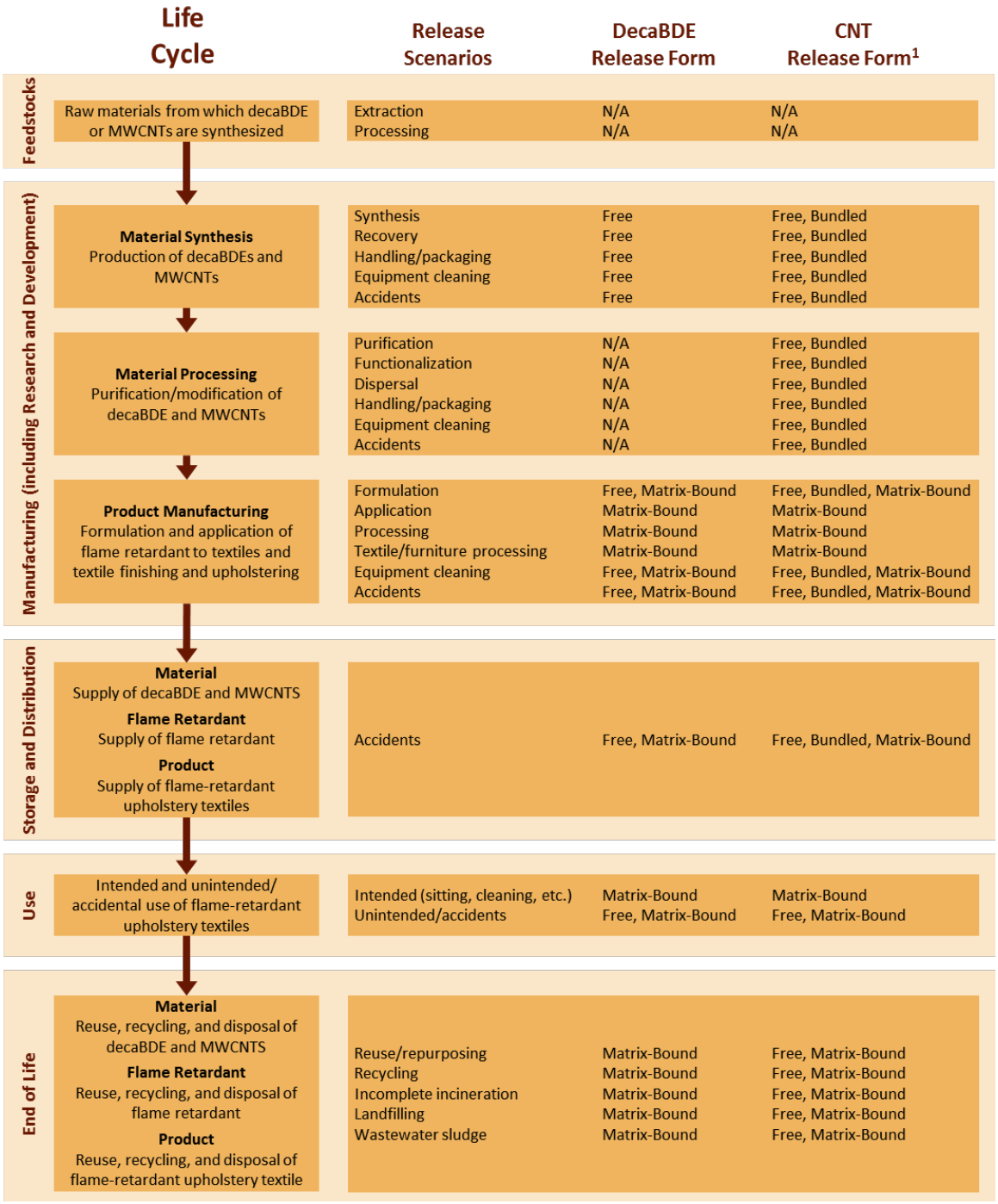
Chapter 2. Product Life Cycle

A product's life cycle encompasses all stages of its existence from "cradle to grave," starting with the extraction of raw materials from the earth for the manufacture of the product and continuing downstream until these materials are returned to the environment following disposal (U.S. EPA, 2006). The components of the life cycle determine the potential for releases and possible impacts on human health, ecological populations, and the environment (Som et al., 2011), which can be evaluated systematically within the framework of a comprehensive environmental assessment (CEA). Potential environmental impacts of a product throughout its life cycle can be estimated using a life-cycle assessment (LCA) approach, which involves four steps: goal definition and scope, inventory analysis, impact analysis, and interpretation (U.S. EPA, 2006). The CEA approach incorporates information from available LCAs in the "product life cycle" and "impacts" portions of the CEA framework to combine this knowledge with other analyses or qualitative indicators related to transport, transformation, and fate, exposure-dose, and additional impacts not considered in available LCAs. As discussed in Chapter 1, if a plausible reason exists to include an impact in the CEA framework, information (qualitative or quantitative) on that effect can be included from LCAs or other sources (if an LCA has not been completed) to evaluate that particular impact.

A generalized depiction of the life cycle for multiwalled carbon nanotube (MWCNT) coatings used to confer flame-retardant properties to upholstery textiles is presented along with comparable information for decabromodiphenyl ether (decaBDE) in Figure 2-1. This figure breaks down the life cycle of these materials into five main stages: (1) acquisition and processing of feedstocks, (2) manufacturing (including research and development (R&D) processes), (3) storage and distribution, (4) use, and (5) end-of-life processes (including disposal, reuse, and recycling). These stages correspond roughly to the four primary life-cycle stages outlined by the U.S. Environmental Protection Agency (U.S. EPA, 2006), including raw materials acquisition, manufacturing, use/reuse/maintenance (with storage and distribution discussed as a distinct stage in this case study), and recycle/waste management. As mentioned in Chapter 1, R&D is included in the product life-cycle portion of the CEA framework, given its importance regarding emerging materials such as MWCNTs. For such materials, R&D efforts can elucidate potential risks associated with commercial-scale manufacturing. In fact, because it often takes place when health and safety information is being developed for a material, R&D presents an ideal opportunity to gather data on a product's potential impacts and to make design adjustments if appropriate.



Sources: Chaudhry et al. (2009); Kohler et al. (2008); Johnson et al. (2010); Zhou and Gong (2008); Som et al. (2011); U.S. EPA (2005); Lassen et al. (1999); NRC (2000); Palm et al. (2002); Agrell et al. (2004); EU (EU, 2002).

Figure 2-1. Life-cycle stages, potential release scenarios, and forms of release for decaBDE and MWCNTs in flame-retardant coatings applied to upholstery textiles.

[1]No data available that specifically describe release form of MWCNTs, thus, release forms of CNTs in general, are discussed here.
N/A = not applicable; CNT = carbon nanotube

Similarly, as discussed below, differences between R&D activities and the commercial manufacturing process (e.g., use of protective equipment, volume of material produced) could be important considerations in mitigating potential risks to individuals involved in R&D versus commercial manufacturing.

To conduct a comparative CEA, relevant information on life-cycle inventories from existing LCAs would be incorporated into the product life cycle to characterize the inputs (e.g., raw materials, energy) and outputs (e.g., emissions to air and water, coproducts) associated with each material's manufacture. Impacts information from existing LCAs also would be considered (see Chapter 5). Other LCA aspects also might apply, including using an appropriate functional unit, which is a quantitative measure of a product's function or a process that facilitates comparison (U.S. EPA, 2006). In the current case study, a functional unit might correspond to the degree of flame retardancy conveyed by incorporation of a certain amount of MWCNTs. In general, for this case study, data that specify appropriate functional units were not identified; the reader might, however, consider how this aspect of existing or future LCAs could be incorporated into a future CEA when evaluating data gaps and needs. This chapter outlines important aspects of each of the five life-cycle stages outlined in Figure 2-1 for MWCNTs used in upholstery textiles. This chapter also includes descriptions of the important environmental release scenarios for MWCNTs across the product life-cycle stages based on current knowledge. A variety of release scenarios are possible throughout the life-cycle stages described in this chapter. Figure 2-1 also outlines potential release scenarios for MWCNT flame-retardant upholstery textile coatings throughout the life cycle along with potential forms of the released substances (i.e., free, bundled, or matrix bound). The term free MWCNTs refers to pure, unbound materials. The term MWCNT bundles refers to clusters of MWCNTs loosely or tightly bound together.[11,12]. The terms matrix-bound decaBDE and MWCNTs refer to these materials as a part of a polymer matrix (e.g., the flame-retardant formulation). Additionally, as illustrated in Figure 2-2, MWCNT formulations can be altered at multiple stages of the product life cycle, meaning the formulation of the MWCNT released at different stages of the product life-cycle can vary.

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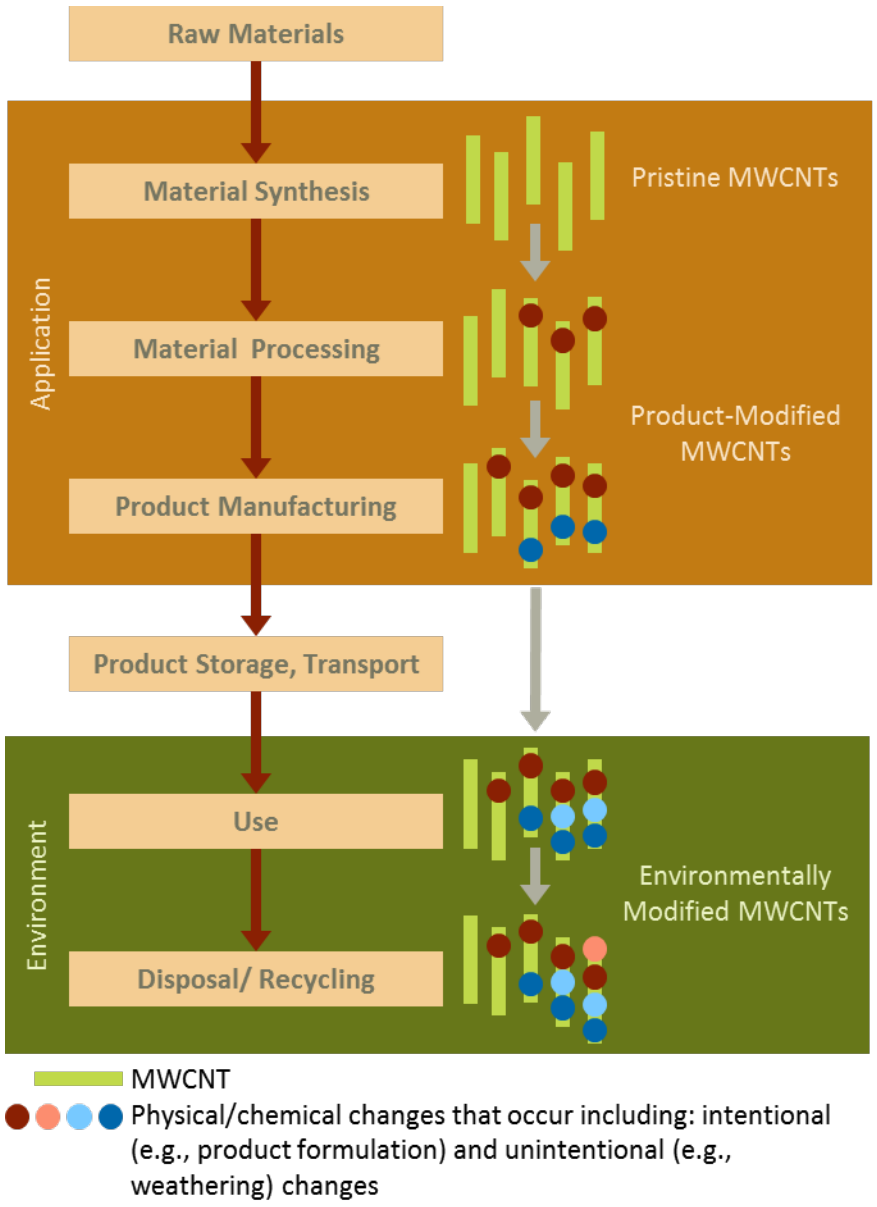
[11]The term "bundle" is used to subsume aggregates, agglomerates, and other clusters of MWCNTs reported in the supporting literature because of the inconsistency in usage and, more importantly, the frequent lack of adequate information to determine which specific term might be more appropriately applied to a particular dispersion state observed in a study or report. Where possible, this case study describes the relative characteristics of different dispersion states (e.g., more loosely or tightly bundled, ropier or more entangled) and quantifies the differences between these characteristics if this information is provided by the study authors.

[12]MWCNTs, could adsorb to dust particles (see Section 3.2). Although the ways that adsorption to dust could facilitate release (i.e., offer a transport vector) from a product matrix are discussed in this chapter, the dust-MWCNT complex is not considered a "release form" because dust was not included in the original product matrix.

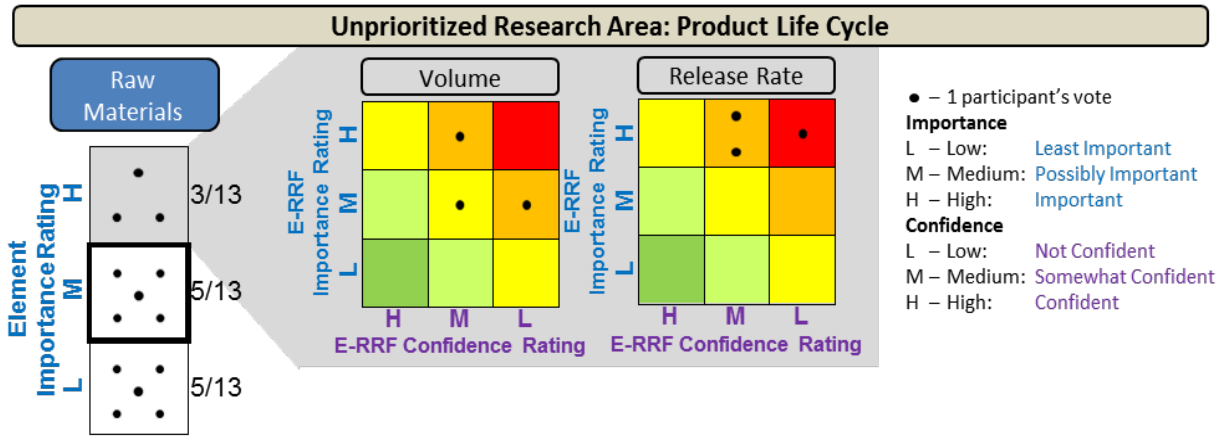


Adapted from: Nowack et al. (2012)

Figure 2-2. Variations in MWCNT formulations and functionalization along the product life-cycle.[1]

[1]This figure illustrates how MWCNT formulations can be altered at multiple stages of the product life cycle. Alterations can occur intentionally as part of product formulation, or unintentionally as the MWCNT moves through the environment. Alterations include both physical and chemical changes, for example, the addition or removal of functional groups, changes in surface charge reactivity, aggregation/agglomeration, physical shortening of tubes, or association with natural organic matter or contaminants. As a result of the multitude of changes that could occur as the MWCNT formulation moves through the product life cycle, risk assessors and risk managers must consider not only the hazards associated with the original material, but also the hazards associated with the various altered materials that could be traced back to the original material.

2.1. Feedstocks



Three out of 13 RTI workshop participants (23%) identified the raw materials stage of the product life cycle as important to risk assessment. Based on this information, this stage in the product life cycle was determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

2.2. Manufacturing

The manufacturing stage for MWCNT flame-retardant upholstery can be viewed as a sequential process involving synthesis, material processing (i.e., purification and modification), and product manufacture (i.e., formulation of the flame-retardant mixture, application of the flame-retardant mixture to textiles, and incorporation of the flame-retardant textile into consumer or commercial goods). R&D also is included in this section, given the similarities to key aspects of synthesis, processing, and manufacture.

2.2.1. Research and Development

Neutral Research Area: Product Life Cycle

The research and development stage of the product life cycle was not considered during the RTI collective judgment prioritization process. This section of text is included in the main document because it supports an understanding of the priority research areas of material synthesis and material processing (see Section 1.1.1 and Introduction to Chapter 2).

2.2.1.1. Life-Cycle Processes

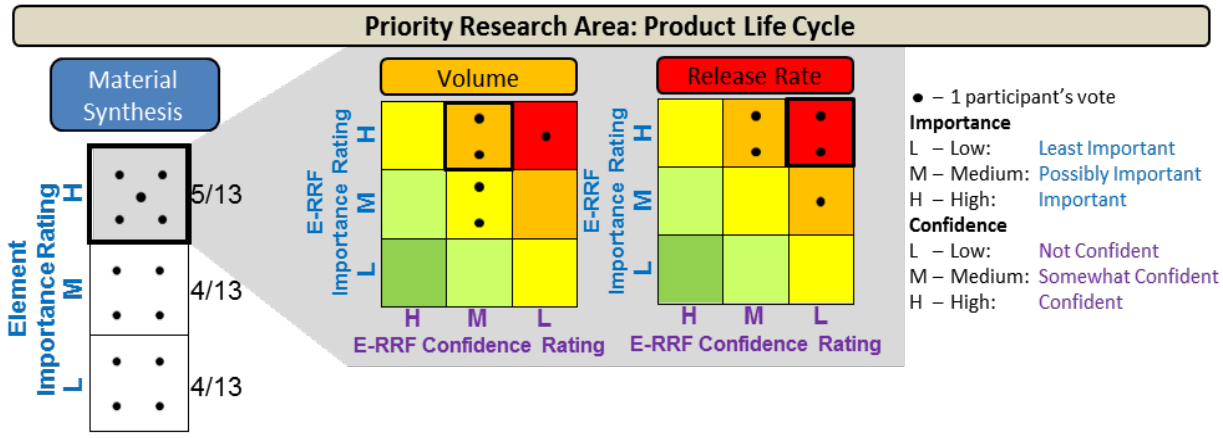
Research on MWCNTs and on flame-retardant coatings involving MWCNTs is principally conducted in specialized laboratory environments. Research and development (R&D) activities are expected to be carried out by individuals rather than automated mechanisms used in commercial-scale manufacture. The processes of interest to researchers are similar to those used in commercial-scale manufacture of these materials: synthesis, purification, modification, dispersion, incorporation into flame-retardant formulations, and application to textiles. Current research efforts focus on synthesis and purification methods to improve CNT quality and purity (Köhler et al., 2008). The following sections (material synthesis, material processing, and product manufacturing) provide detailed information on the processes of potential interest for R&D.

2.2.1.2. Potential Releases during the R&D Stage

Release scenarios during the R&D stage are expected to be similar to release scenarios from commercial synthesis described in the following sections, but the quantities released are anticipated to be much smaller in the R&D stage. The quantities of MWCNTs handled in research laboratories are much smaller than those handled in commercial-scale manufacturing facilities. Although R&D activities are typically carried out in laboratories with specialized pollution control systems in place, including fume hoods, ventilation systems, and environmental control systems, not all facilities have standardized engineering controls. For example, these practices might not be in place for small start-up operations. Given the experimental and somewhat unpredictable nature of R&D, releases from handling materials during synthesis, processing and purification, storage, and analysis are possible.

As discussed in more detail in Section 4.1.2.4, multiple studies have collected particles and fibers in workplace air to attempt to estimate MWCNT concentrations at the emission source, in area air, and in the personal breathing zone of workers in small laboratories or research and development facilities (Johnson et al., 2010; Lee et al., 2010; Methner et al., 2010; Bello et al., 2008; Han et al., 2008). One industry report measured airborne release of CNTs (0.25 μg/m^3) in the R&D facilities for a company that manufactures Thermocyl®, an MWCNT flame-retardant coating application (Luizi, 2009). No data were found that describe how releases in academic labs compare with releases in commercial R&D labs, though it is noted that estimates in Bello et al. (2008) were based on university laboratory settings.

2.2.2. Material Synthesis



Five out of 13 RTI workshop participants (38%) identified the material synthesis stage of the MWCNT-product life cycle as important to risk assessment. These five participants were asked to rate the importance of volume and release rate at this stage in the product life cycle as well as their confidence that the existing data on these subjects could support risk-management decisions. Based on this information, release rate was deemed the highest priority for research in this area, followed by volume. See Section 6.3.1.1 for more information on this priority area, and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

Releases of decaBDE and by-products or transformation products during material synthesis can be classified as incidental or accidental. Larger production volumes can result in larger incidental release volumes and a greater potential for accidental releases, and so the total production volume is important to consider.

Incidental releases—such as release of decaBDE into the air as vapor from the reactor vessels is released or into wastewater as equipment is cleaned—are minimal compared to the total volume of decaBDE produced, in part because large manufacturing facilities typically use control mechanisms that limit release volume. One study found, for example, that wastewater releases of decaBDE are unlikely to exceed 0.5 kg/ton if equipment is washed after every batch (EU, 2002). Fugitive releases of decaBDE vapor from a reactor vessel have been estimated as 1.1×10^{-5} mg/ton, and releases from the bagging of synthesized PBDEs have been estimated as <70 grams/ton PBDE produced [(EU, 2002); EEC (1993) as cited in EU (2002)].

Accidental releases, such as leaks arising from faulty equipment or malfunctioning ventilation systems, can result in larger environmental releases because control mechanisms like those for handling incidental releases are absent. Accidental releases also might contain transformation products (e.g., polybrominated dibenzofurans from high heat exposure to decaBDE) that typically would not be included in incidental releases. Accidental releases, however, occur less often than incidental releases.

Similar to decaBDE, MWCNT releases could be incidental or accidental. As shown in Table 2-3, decaBDE and MWCNTs can be released to air during synthesis and purification, recovery, handling/packaging, cleaning, and accidents, while release to water is generally limited to periods when equipment is being cleaned. Based on information for decaBDE, research planning to inform future MWCNT risk assessments might consider the differences between the potential for, and implications of, both incidental and accidental releases of MWCNTs during synthesis, including: Which is more frequent? Which would result in a greater volume of compound entering the environment? Are systems in place to limit the occurrence of both? See Appendix H for more information regarding release of decaBDE during material synthesis.

2.2.2.1. Life-Cycle Processes

In 2010, chemical vapor deposition (CVD) synthesis produced approximately 83% of the global supply of CNTs, followed by arc-discharge synthesis (12%) and laser-ablation synthesis (5%) (Patel, 2011) (see Table 1-10 for information on MWCNT global production capacity). What proportion of MWCNTs is synthesized using each method, however, is unclear. Table 2-1 summarizes some of the performance characteristics of these three synthesis methods. Table 2-2 summarizes the current scale and projected growth of the CNT manufacturing industry, with details on the percentage of companies using each synthesis methods.

Table 2-1. Summary of common CNT synthesis methods.[1]

Characteristic	CVD	Arc discharge	Laser ablation
Growth temperature	600–1,100 °C	2,500–3,000 °C	1,200 °C
Production	Continuous	Batch	Batch
Scalability	Scalable	Not currently scalable	Not currently scalable
Product quality	Many structural defects Long tubes Low crystallinity[2]	Few structural defects Short tubes Carbon-containing metal impurities	Few structural defects Diameter control
By-products	Over 45 side products, including polycyclic aromatic hydrocarbons and volatile organic compounds	Black carbon and airborne inorganic compounds	No Data

[1]No data available that specifically describe MWCNTs.
[2]Low degree of structural ordering.
CVD = Chemical vapor deposition
Sources: Li et al. (2010), Healy et al. (2008); Karthikeyan et al. (2009); Rafique and Iqbal (2011); Plata et al. (2009).

CVD synthesis takes place in two furnaces connected by a quartz tube (Healy et al., 2008). The catalyst mixture is heated before it is added to the furnace along with a carbon-containing gas (Karthikeyan et al., 2009; Healy et al., 2008). CNTs are recovered once the furnaces cool to room temperature (Karthikeyan et al., 2009). MWCNTs can be grown on a substrate (e.g., Si/SiO_2) or without a substrate (Tsai et al., 2009). CNTs produced using deposition substrates are recovered by automated or manual mechanical removal (Köhler et al., 2008); however, specific details regarding the method of recovery were not identified.

Table 2-2. Current scale and projected growth in the CNT industry.

Parameter		Manufacture Scale	Pilot/Developmental Scale	Combined Manufacture and Pilot/ Developmental Scale
Number of Employees per Company[1]		2–100	1–30	1–130
Quantity of CNT Produced per Year (kg/year)[1]		0.2–2,500	0.1–300	0.1–2,800
Projected Industry Growth	Employee Count Year 1[2]	172	20	192
	Employee Count Year 2 (% change from Year 1)[2]	196 (+14%)	43 (+115%)	239 (+24%)
	Employee Count Year 3 (% change from Year 2)[2]	214 (+9.2%)	62 (+44%)	276 (+15%)
	Total Percent Change from Year 1 to Year 3[2]	+24%	+210%	+44%
CNT Synthesis Method Used (% of companies using method)[3]	CVD	62%	NR	NA
	Arch Discharge	23%	NR	NA
	Flame Combustion	15%	NR	NA
	Laser Ablation	8%	NR	NA

[1]At the time of the survey (Oct 2008 to May 2009) there were 61companies manufacturing engineered carbonaceous nanomaterial (ECN) or applying ECN in other manufacturing processes in the United States at full, pilot, or research scale with plans to scale up within 5 years. Of these 61 companies, approximately 43 were CNT manufacturers. Approximately 59% of these 43 CNT companies (i.e., 25) were at "full manufacturing scale," 11% were pilot scale (i.e., 4), and 11% were research and development scale with plans to scale up (i.e., 4). The remaining ~ 18% (i.e., 10) did not participate so publicly available information regarding employee numbers was used but data regarding production quantity were not.

[2]Year 1 was 2004 for nonparticipating companies (n = 5) and 2006 for participating companies (n = 26), therefore Year 2 was 2005 and 2007 and Year 3 was 2006 and 2008 for nonparticipating and participating companies, respectively.

[3]33% (i.e., 14) of manufacturers reported as "primary," 42% (i.e., 18) reported as "secondary," and 26% (i.e., 11) reported as both primary and secondary manufacturers.

NA = not applicable; NR = not reported

Adapted from Schubauer-Berigan et al. (2011).

Synthesis by arc discharge involves passing an electric current between two graphite electrodes (Healy et al., 2008) in the presence of an inert gas. The anode contains a hole filled with carbon powder and a catalyst, and the electric current results in the vaporization of the graphite anode and subsequent condensation on the cathode and the walls of the reaction vessel (Baddour and Briens, 2005). CNTs deposits form as black powder in the reaction vessel (Healy et al., 2008). CNTs are generally recovered from a receptacle after arc-discharge synthesis (Köhler et al., 2008), but whether recovery is usually a manual or automated process is unclear.

Laser-ablation synthesis of MWCNTs involves vaporizing a metal-graphite composite block in the presence of an inert gas and a catalyst (Karthikeyan et al., 2009). The composite block is placed inside an oven, a laser is pointed at the block, and argon gas is pumped parallel to the laser beam. As the laser ablates the target at high temperatures, CNTs form and are carried by the gas flow onto a collector (Karthikeyan et al., 2009). See Sections 5.3.2 and 5.3.4 for information on the estimated energy requirements and costs of CNT synthesis.

2.2.2.2. Potential Releases during the Material Synthesis Stage

The potential release of MWCNTs during synthesis primarily depends on the synthesis and processing methods and the physical properties of the MWCNTs (e.g., size, bundling, density) (Köhler et al., 2008). Because few data were available that describe releases from commercial-scale manufacture of MWCNTs, this section also relies on CNT release data from R&D facilities. Although releases of MWCNTs could occur during the synthesis stage, evidence describing the likelihood and quantity of release is mixed. In general, MWCNTs grown on substrates are likely to produce fewer airborne releases than vapor-phase synthesis methods (Bello et al., 2009; Tsai et al., 2009). Mechanical removal (either automated or manual) of CNTs from the substrate, however, can cause airborne release of CNTs (Köhler et al., 2008). In one study, CVD synthesis, both with and without a substrate, resulted in a concentration at the source of synthesis of more than 2 to 3 × 10^6 particles/cm^3 that measured less than 560 nm in diameter (Tsai et al., 2009), but another study found no measurable airborne release of CNTs during substrate-bound CVD growth of CNTs (Bello et al., 2009). One study conducted in three commercial facilities and four research laboratories concluded that during synthesis, processing, and product manufacturing, nanoparticle releases occurred most frequently when opening the CVD vessel and when preparing the catalysts (Lee et al., 2010). No data were found on potential releases from laser-ablation synthesis of MWCNTs, but low levels of SWCNT clusters were released as aerosols during laser-ablation synthesis of SWCNTs in laboratory and field conditions (Maynard et al., 2004). This study intentionally agitated the SWCNTs, however, which would not be a normal component of the synthesis stage.

Synthesis of MWCNTs might release even greater quantities of CNTs, by-products, and feedstock materials than SWCNTs due to the larger quantities of precursor materials required for synthesis (Tsai et al., 2009). CNT powder generally comprises large bundles of CNTs and air release of these bundles is likely to occur during operations involving agitation (e.g., scraping, shaking) (Fleury et al., 2011), but local exhaust ventilation substantially reduces airborne releases to the environment (Lee et al., 2010; Han et al., 2008). Loose MWCNTs and the equipment used during synthesis are likely to be cleaned up with a vacuum, which appears to be effective in reducing the airborne concentration of nanoparticles (Lee et al., 2010). Vacuuming, rinsing, and changing dust filters and other cleaning and

maintenance activities also could result in subsequent release of MWCNTs to air or wastewater (Köhler et al., 2008).

MWCNTs released during synthesis can contain significant impurities (see Section 2.2.3.1). In addition, by-products from materials used in synthesis can be released at multiple points during the synthesis process (Plata et al., 2009). Some by-products, such as phenol, can be formed from general combustion processes used in CNT synthesis (Eckelman et al., 2012). Air release of synthesis by-products including polycyclic aromatic hydrocarbons and volatile organic compounds has been observed during CVD synthesis of CNTs in the absence of engineering controls (Plata et al., 2009); if employed, control technologies would be expected to limit these releases.

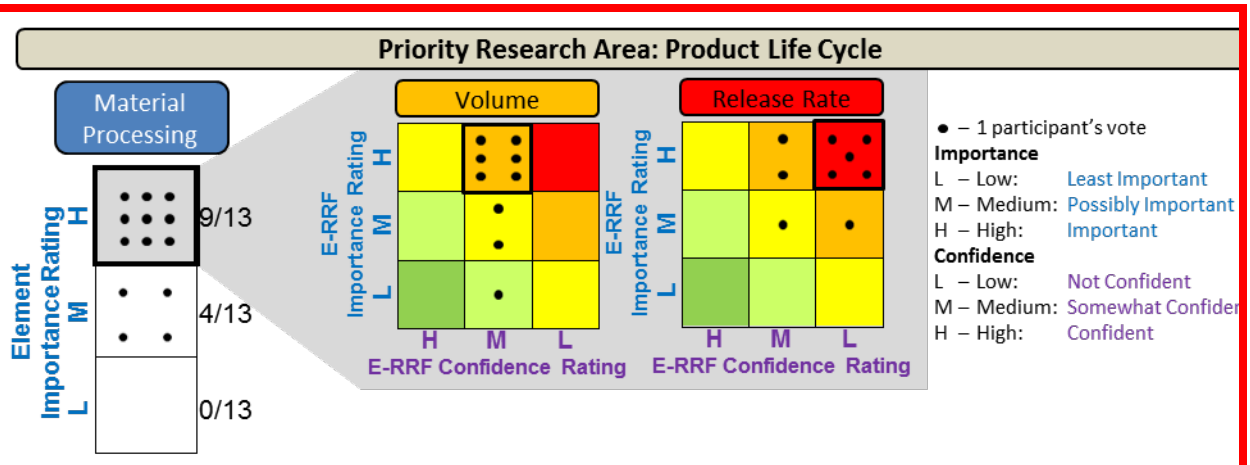
Accidental releases could also occur during MWCNT synthesis. These accidental scenarios include fugitive equipment leaks, malfunctioning ventilation systems, and exposure to fire and high heat. MWCNTs will not necessarily be destroyed at high temperatures (i.e., those possible in accidental fires) (Köhler et al., 2008), which could lead to airborne release or creation of ash containing elevated levels of MWCNTs (Chaudhry et al., 2009). Additionally, damaged filters that collect MWCNTs could result in airborne release during synthesis (Köhler et al., 2008). Such accidental events, while unlikely, could result in potentially large releases of MWCNTs to the environment.

Table 2-3 summarizes the anticipated potential release scenarios from the material synthesis stage of MWCNTs. Information for decaBDE is provided for comparison, with more detailed information on decaBDE available in Appendix H.

Table 2-3. Potential release scenarios during material synthesis.

Processes included in material synthesis life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Synthesis and purification	Occurs in closed vessel, but fugitive air emissions could occur; release depends on synthesis method	Occurs in closed vessel, but fugitive air emissions could occur
Recovery of synthesized substance	Air release could occur during removal from substrate and bagging	Air release could occur during bagging
Handling/packaging	Air release could occur	Air release could occur
Equipment cleaning	Air and water release could occur	Air and water release could occur
Accidental releases (equipment malfunction, etc.)	Air release could occur	Air release could occur

2.2.3. Material Processing



Nine out of 13 RTI workshop participants (69%) identified the material processing stage of the MWCNT-product life cycle as important to risk assessment. These nine participants were asked to rate the importance of volume and release rate at this stage in the product life cycle as well as their confidence that the existing data on these subjects could support risk-management decisions. Based on this information, release rate was deemed the highest priority for research in this area, followed by volume. See Section 6.3.1.2 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

Although post-synthesis processing is an important part of the life cycle for MWCNTs, it does not occur for decaBDE and so is not a consideration for assessment or risk management of decaBDE. Therefore, decaBDE does not provide useful information that could be applicable to research planning to support future assessments of MWCNTs during material processing.

2.2.3.1. Life-Cycle Processes

Material processing includes any modification of MWCNTs after synthesis and before incorporation into a flame-retardant formulation. These modifications can include purification, functionalization, and dispersal in solvents.

MWCNTs undergo physical and chemical processing before they are incorporated into flame-retardant applications. Commercial MWCNTs that have not been purified can contain large amounts of impurities, such as amorphous carbon, graphite, and encapsulated metallic particles (Hou et al., 2008). After synthesis, MWCNTs are typically purified using physical (e.g., flocculation, microfiltration, centrifugation) or chemical (e.g., acid treatment) techniques (Hou et al., 2008). Appendix C presents various CNT purification methods and their efficacies in removing various classes of impurities. By-products of purification techniques are expected to differ according to the technique used; one study

reported waste products of sodium hydroxide, ethanol, water, filtrate, and scrap membrane following general purification of SWCNTs (Healy et al., 2008).

One analysis found that samples of MWCNTs purified by the manufacturer contained metal impurities ranging from 0.44 to 1.75 (wt%) (Ge et al., 2011). After further purification with an acid treatment, significant quantities of catalyst residues (e.g., cobalt, chromium, iron, manganese, molybdenum, and nickel) remained (Ge et al., 2011). Additionally, trace noncatalyst impurities (mostly transition metals such as cerium, gadolinium, holmium, etc.) were also found in purified CNTs, which the authors theorize can form during production/post-purification processes or might be introduced as catalyst synergists to improve the quality of synthesized CNTs (Ge et al., 2011). Additionally, the purification process itself also can damage the CNTs by introducing structural defects (Gustavsson et al., 2011).

Before application, MWCNTs generally require surface functionalization (Saeed, 2010). Functionalization—the modification of materials by covalently or noncovalently attaching new molecular components—can alter the physicochemical properties of MWCNTs dramatically (Köhler et al., 2008; Ma et al., 2008; Hirsch and Vostrowsky, 2005). Often, the goal of functionalization of MWCNTs is to increase solubility, which facilities dispersion into solvents and polymers (Saeed, 2010). One example of functionalization consists of the covalent grafting of MWCNTs to traditional flame retardants (Ma et al., 2008). Table 2-4 presents examples of MWCNT functionalization. After functionalization, MWCNTs are often dispersed in water or organic solvents before they are incorporated into products (Saeed, 2010). Most dispersion methods use dry mixing or liquid-phase sonication (agitation of particles with ultrasound energy) to break up clumps and disperse MWCNTs in water or organic solvents.

2.2.3.2. Potential Releases from the Material Processing Stage

During the recovery, processing, handling, and packaging stages, CNTs are more likely to be released as bundles from bulk powder than as individual CNTs (Köhler et al., 2008) (see Table 2-3). In general, releases resulting from liquid-phase processing of CNTs will be lower relative to those resulting from dry handling, which can result in greater nanoparticle release (Köhler et al., 2008). What proportion of MWCNT processing occurs in the liquid versus the dry phase, however, is unclear. Handling of MWCNTs can cause airborne release of particles (Methner et al., 2010). Dispersal of MWCNTs in suspensions can reduce the likelihood of aerosolization (Johnson et al., 2010), but mixing and sonicating (common processes used to disperse MWCNTs in solution) might also result in airborne release of raw and functionalized MWCNTs (Johnson et al., 2010; Lee et al., 2010; Methner et al., 2010). Environmental control mechanisms likely would be in place to reduce environmental releases in facilities that process MWCNTs (Fleury et al., 2011; Methner et al., 2010). Cleaning of processing equipment and facilities can

lead to release of MWCNTs to air or wastewater (Fleury et al., 2011). MWCNTs released during this stage might still contain some of the impurities listed in Section 2.2.3.1 and Appendix C.

Table 2-4. Examples of functionalization of MWCNTs.

Functionalization technique	Goal of functionalization	Additional reagents	Reference
Amidation – Formation of carbon nanotube-acyl amides	Creation of anchor groups for further modification	thionyl chloride, dicyclohexylcarbodiimide	Hirsch and Vostrowsky (2005)
Fluorination	Solubility in polar solvents	elemental fluorine	Hirsch and Vostrowsky (2005)
Chlorination	Solubility in polar solvents	chlorine gas	Hirsch and Vostrowsky (2005)
Noncovalent exohedral functionalization	Solubility in polar solvents	streptavidin	Hirsch and Vostrowsky (2005)
Covalent grafting on intumescent flame retardant	Better dispersion in matrix; solubility and stability in polar solvents; enhanced network structure at very low nanotube loading	poly(diaminodiphenyl methane spirocyclic pentaerythritol bisphosphonate)	Ma et al. (2008)
Atom transfer radical polymerization	Creation of anchor groups for further modification	styrene and methyl methacrylate	Baskaran et al. (2004)
In situ surface reversible addition-fragmentation chain transfer polymerization	Solubility in polar solvents	styrene and *N*-isopropylacrylamide	Xu et al. (2007)
Electrografting	Solubility in polar solvents	polyacrylonitrile	Petrov et al. (2004)
Radiation polymerization	Solubility in polar solvents	ethanol, poly(acrylic acid), acrylic acid	Chen et al. (2006)
Liquid- and gas-phase oxidization with thermal treatment	Increased acidity or alkalinity; improved flame-retardant properties	nitric acid	Goncalves et al. (2012)

Release of by-products from CNT processing also might occur. One modeling study notes the potential for release of phenol from the production of nitric acid, a substance commonly used in CNT purification (Eckelman et al., 2012). The release of other substances used during purification is also possible.

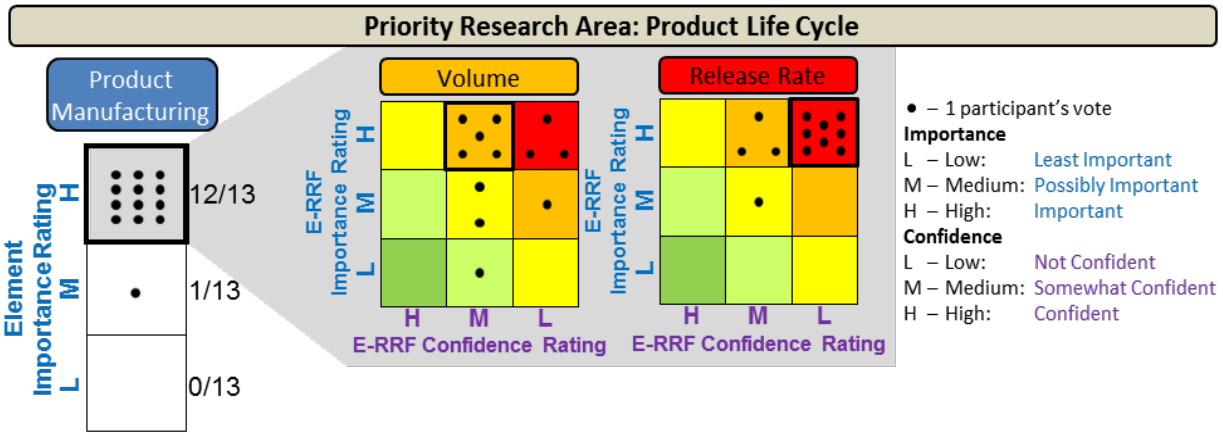
The accidental release scenarios for MWCNTs during processing are similar to those in the material synthesis stage (see Section 2.2.2.2). Additionally, spills of solutions containing dispersed

MWCNTs might occur during the processing stage, which could result in the release of MWCNTs to wastewater. Table 2-5 summarizes potential release scenarios from the material processing stage of MWCNTs.

Table 2-5. Potential release scenarios during material processing of MWCNTs.

Processes included in material processing life-cycle stage	Information on release
Purification	Air release possible due to physical purification methods such as flocculation, microfiltration, centrifugation, etc. (see Appendix C)
Functionalization	Air and water release possible during functionalization reactions; release depends on method of functionalization
Dispersion	Air release possible, especially during dry mixing
Handling/packaging	Air release possible during dry processes
Equipment cleaning	Air and water release possible
Accidental releases (spills, equipment malfunction, etc.)	Water release possible from spills in liquid-phase reactions and once MWCNTs are dispersed in solution; air release possible from fugitive emissions

2.2.4. Product Manufacturing



Twelve out of 13 RTI workshop participants (92%) identified the product manufacturing stage of the MWCNT-product life cycle as important to risk assessment. These 12 participants were asked to rate the importance of volume and release rate at this stage in the product life cycle as well as their confidence that the existing data on these subjects could support risk-management decisions. Based on this information, release rate was deemed the highest priority in this area, followed by volume. See Section 6.3.1.3 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

The volume of decaBDE used in textiles depends on the type of fabric used (e.g., 30–40 grams/m^3 in cotton to 70–80 grams/m^3 for velour fabrics) (EU, 2002), which also influences the volume of impurities and compounds used in conjunction with decaBDE (e.g., antimony trioxide).

The potential releases of decaBDE and other impurities during product manufacture are similar to those discussed in the material synthesis stage (see the DecaBDE Comparison Box on Material Synthesis in Section 2.2.2), but with some notable differences. First, any decaBDE released during product manufacture is likely to be matrix-bound. Second, the release rate of decaBDE during the product manufacturing stage is smaller than the release rate during material synthesis. Formulation of flame retardants generally occurs in closed systems with engineering controls that regulate temperature and pressure to minimize potential releases; however, processes that occur before or after the substance enters the closed system could result in environmental release. Indeed, one study found that environmental release was most likely to occur during the mixing of decaBDE powder and cleaning operations of the flame-retardant formulation stage (EU, 2002).

Similar to observations with decaBDE, MWCNTs likely would be released in matrix-bound form in smaller quantities during the product manufacturing stage compared to the material synthesis stage. As such, understanding the life cycle and releases of decaBDE flame-retardant coatings can aid efforts to characterize the life cycle and potential releases of MWCNT flame-retardant coatings more fully.

Considerations for MWCNT research planning to inform future risk assessments might include additional variables that are unique to MWCNTs based on post-synthesis processing (e.g., purification by-products, surface functionalization) (see Section 2.2.3.1 and the DecaBDE Comparison Box on Material Processing). For example: What is the relative production volume of MWCNT flame-retardant formulations with different physicochemical characteristics? Do different MWCNT chemistries, application methods to textiles, and textile characteristics increase or decrease the volume used in textiles, or the rate of release during product manufacturing? At what stages of product manufacturing are releases of free or matrix-bound MWCNTs most likely to occur? See Appendix H for more information regarding release of decaBDE during product manufacture.

In this section, product manufacturing for MWCNTs is described. This life-cycle stage is considered to include the manufacture of flame-retardant formulations, the manufacture of textiles containing MWCNT-based flame retardants, and the manufacture of end-use products containing flame-retardant materials, such as furniture.

2.2.4.1. Life-Cycle Processes

CNTs can be dispersed in polymers by in situ polymerization or by using a twin-screw extruder (a specialized machine using two screws to mix, compound, and react polymers) [Laxminarayana and Jalili (2005) as cited in Kohler et al. (2008)]. One study described the manufacture of a "high heat" acrylonitrile-butadiene-styrene polymer matrix filled with CNTs (Fleury et al., 2011). According to this study, master batch granules (1–4 mm long) consisting of thermoplastic resin and 15% CNTs by weight are mixed with the pure polymer matrix in injection molding and extrusion processes (where thermoplastics are fed into a heated vessel and forced into a mold cavity where they cool) (Fleury et al., 2011). Little information is available regarding the ingredients and characteristics of MWCNT flame-retardant formulations and possible by-products from their manufacture. Thermocyl®, an MWCNT flame

retardant, includes silicone resins containing MWCNTs (Luizi, 2009). In another formulation, MWCNTs have been used in place of ammonium polyphosphate, a traditional phosphorus-based flame retardant, as a filler with polymethyl methacrylate (PMMA) and polyamide-6 (Motzkus et al., 2012). General components of MWCNT flame-retardant formulations include epoxies, polyesters, and vinylesters (Alberding et al., 2011).

MWCNTs can be applied to textiles as a flame-retardant coating by (1) soaking the textile or (2) spray coating the surface of the textile (Luizi, 2009). The soaking application method for MWCNTs is similar to that used to apply decaBDE flame-retardant coatings (see Figure 1-4). In a recent study, researchers immersed cotton and polyester textiles in an MWCNT dispersion and maintained constant motion to embed functionalized MWCNTs in the textiles (Gonçalves et al., 2012). The authors reported acetic acid, sodium chloride, sodium carbonate, and sodium hydroxide as auxiliary reagents for this embedding process (Gonçalves et al., 2012). An alternative immersion method involves soaking a textile in a solution containing CNTs and then treating it with a crosslinking agent (similar to a binder), heating, rinsing, and drying the textile (with or without heat) (Alimohammadi et al., 2011). Uddin and Nyden (2011a) and Davis and Kim (2010) described a similar immersion method involving multiple treatments with polymeric solutions to create a coating consisting of layers of polyacrylic acid/MWCNT-polyethylenimine/ polyethylenimine. Flame retardant-treated materials also can be cured using UV radiation (Lu et al., 2011a). Lee et al. (2010) mentioned the spray application of CNTs in solution to thinly coat wafers, but they did not describe the process in detail. The few laboratory-scale studies investigating MWCNT flame retardants in textiles have reported MWCNT loadings ranging from 0.5 to 4% by mass (Grzybowski, 2009; Kashiwagi et al., 2005b; Kashiwagi et al., 2005a; Kashiwagi et al., 2004), which are about an order of magnitude lower than those for decaBDE. Thermocyl®, a commercial MWCNT flame retardant, has been incorporated into polyethylene at a loading of 1% (Luizi, 2009). After application, the MWCNT flame-retardant upholstery is cut, shaped, and glued or stapled to furniture.

2.2.4.2. Potential Releases during Product Manufacture

Environmental releases during the manufacture of MWCNT flame-retardant textiles can occur as a result of the following activities: mixing, handling/packaging, application of the flame retardant to textiles, textile processing/finishing, and accidents (Zhou and Gong, 2008). Few data are available that describe releases from commercial-scale manufacture of MWCNT flame-retardant textiles. Therefore, this section also relies on CNT release data from R&D facilities. Release of MWCNT bundles is possible when nanotubes are blended with polymers to formulate the flame retardant; however, releases are anticipated to be smaller for blending of master batches as opposed to blending of pure CNT powders (Fleury et al., 2011). The most critical phase for air and water releases during the formulation stage is the

discharging and the cleaning of the mixing chamber (Fleury et al., 2011). Release from the formulated flame retardant is expected to be minimal, but packaging of the formulated flame retardant could result in releases. Airborne releases of CNTs (1.45 μg CNT/m^3) were measured in a facility that packages Thermocyl®, an MWCNT flame-retardant coating (Luizi, 2009).

Application of MWCNT flame retardants to textiles also could lead to air or water releases. Currently, how a particular production method used to incorporate MWCNT flame retardant in the textile matrix might influence release potential and subsequent exposure potential is unknown. Any spray application could lead to the potential airborne releases of matrix-bound MWCNTs if the application does not occur in a closed environment. One study observed airborne release of both nanoparticles and fine particles when spraying an MWCNT solution onto wafers as a coating (Lee et al., 2010). The dominant particle size released during this study ranged from 50 to 110 nm and subsequent heating of the treated wafers also led to the release of particles smaller than 30 nm (Lee et al., 2010). Other data suggest that thermal processing (i.e., exposure to high temperatures and UV) might not lead to air release of MWCNTs from polymer matrices (Nguyen et al., 2011). In an analysis of an epoxy containing MWCNT, exposure to UV radiation and high temperatures (50 °C) degraded the polymer matrix, but the MWCNTs formed a dense network on the composite surface and no evidence of particle release was observed (Nguyen et al., 2011). If the MWCNT flame-retardant coating is applied by soaking the textile, water release of matrix-bound MWCNTs could occur when the textile is rinsed. Additional cutting, sewing, shaping, stapling, and other textile finishing processes could result in the airborne release of free or matrix-bound MWCNTs through abrasion (Köhler et al., 2008). One study found that grinding a nanocomposite containing CNTs created a substantial amount of airborne particles made up of polymer fragments containing CNTs (Fleury et al., 2011). How applicable release from grinding of plastic nanocomposites is to release from textile applications, however, is unclear. Airborne releases of CNTs (1 μg CNT/m^3) have been measured in a facility processing textiles treated with Thermocyl® (Luizi, 2009). Most manufacturing facilities, however, would be expected to have controls in place to prevent or minimize airborne releases to the environment. Equipment cleaning at any point in this life-cycle stage could lead to release of MWCNTs to wastewater. Not enough is known about the other components of MWCNT flame-retardant formulations to hypothesize about other substances that might be released as a part of the flame-retardant product matrix, but the use of different substances in MWCNT flame-retardant formulations might lead to different release characteristics.

The accidental release scenarios for MWCNTs during product manufacture are similar to those in the material synthesis stage (see Section 2.2.2.2). In the product manufacturing stage, spills of MWCNT flame-retardant formulation might also occur and could result in the release of MWCNTs to wastewater. Table 2-6 outlines potential release scenarios from the product manufacturing stage of MWCNT flame-retardant textiles along with decaBDE for comparison.

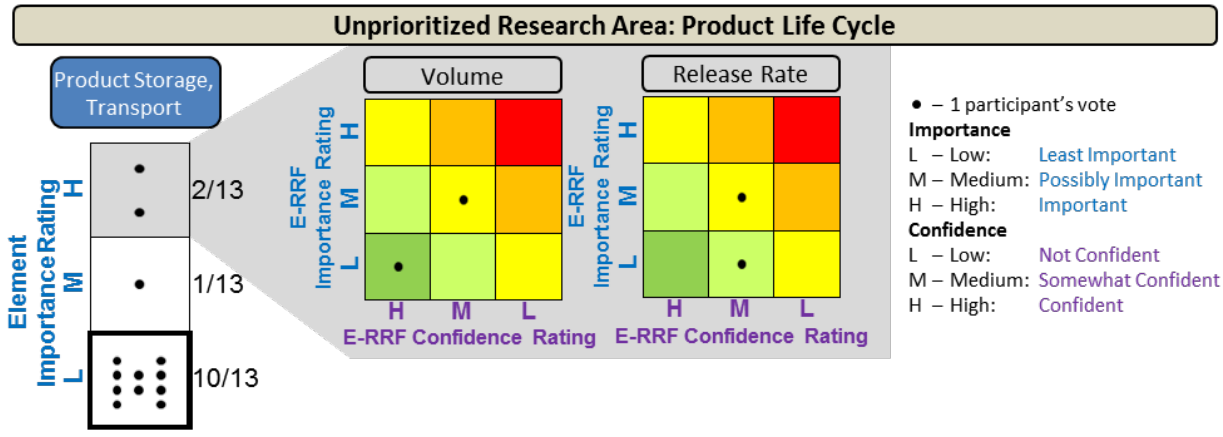
Additional Information Highlight Box 4:
MWCNT release from various product matrices informs predictions of release from textiles

Although little information describing release of MWCNTs from flame-retardant textile coating applications was found in the literature, information on similar applications might help inform future assessments of release potential during product manufacture. For example, Takaya et al. (2012) studied the likelihood of MWCNT release from MWCNT-coated yarn during the weaving process used to produce conductive fabric. The authors concluded that, although the likelihood of release of individual MWCNT fibers during the weaving process was low, micron-sized yarn particles containing MWCNT were released into the air around the weaving loom. The authors hypothesized that this release occurred as a result of the mechanical forces applied to the yarn during weaving. These findings suggest that the weaving processes used to produce textiles coated with MWCNT flame retardant might lead to similar releases of micron-sized textile particles containing MWCNTs. The potential for release of MWCNTs or matrix-bound MWCNTs from textiles during other stages of the product life cycle (see Figure 2-1) is similarly unknown.

Table 2-6. Potential release scenarios during product manufacturing.

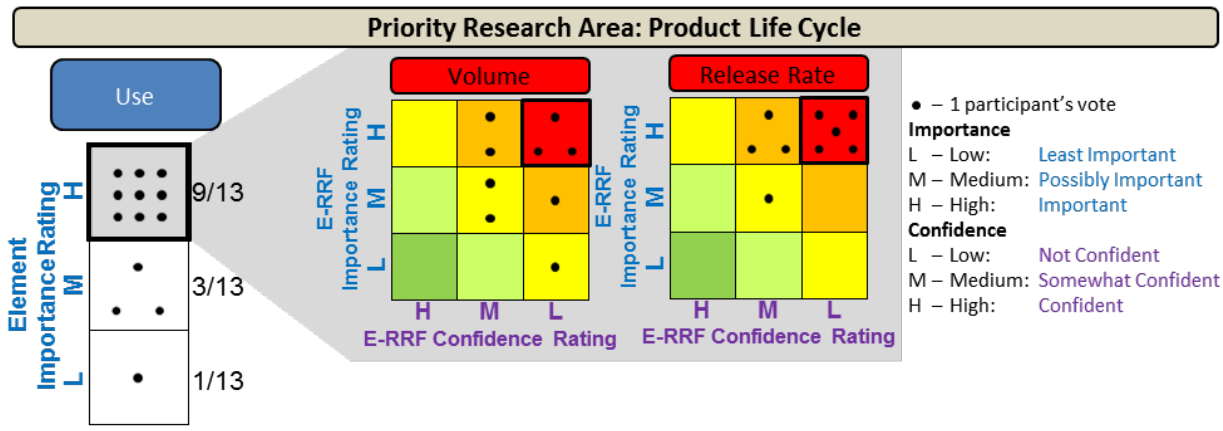
Processes included in product manufacturing life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Formulation of flame retardant	Air release possible when mixing dry MWCNTs into product formulation	Air release possible when mixing dry decaBDE into product formulation
Handling/packaging	Air release possible	Air release possible
Flame retardant application to textile	Air or water release possible depending on application method; for example, if substances are sprayed onto textiles, release to air can occur	Air or water release possible depending on application method
Thermal processing	Preliminary evidence on air release due to high heat is mixed	Air release possible
Rinsing/drying	Water release possible	Water release possible
Equipment cleaning	Air and water release possible	Air and water release possible
Textile processing	Air release possible due to cutting, sewing, shaping, and other finishing processes	Air release possible due to cutting, sewing, shaping, etc.
Furniture production	Air release possible due to cutting, stapling, and other finishing processes	Air release possible due to cutting, stapling, etc.
Accidental releases (e.g., spills, equipment malfunction)	Air and water release possible	Air and water release possible

2.3. Storage and Distribution



Two out of 13 RTI workshop participants (15%) identified the product storage and transport stage of the MWCNT product life cycle as important to risk assessment. Based on this information, storage and transport were determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

2.4. Use



Nine out of 13 RTI workshop participants (69%) identified the material processing stage of the MWCNT-product life cycle as important to risk assessment. These nine participants were asked to rate the importance of volume and release rate at this stage in the product life cycle as well as their confidence that the existing data on these subjects could support risk-management decisions. Based on this information, these areas were deemed a priority for research. See Section 6.3.1.4 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

2.4.1. Life-Cycle Processes

A wide variety of textiles contain flame-retardant coatings (see Section 1.2). Upholstery textiles are expected to be used in public places where people of all ages will sit, lie, or walk on them. Some unintended uses of upholstery textiles include outdoor use, repurposing for use in other products, burning as kindling, or mouthing by children. Repurposing for use in other products and burning as kindling are covered in Section 2.5 and Appendix H.2.5. In general, upholstery textiles are likely to have a lifespan of at least 10 years (EU, 2002).

DecaBDE Can Inform MWCNT Assessment

Information on volume during the product use phase for decaBDE must be inferred from production volumes reported by manufacturers; although production volumes are expected to decrease due to the withdrawal of decaBDE from the market (see Section 1.3.1), its volume during the product use phase likely greatly exceeds that of MWCNTs due to both higher historic production volumes (see Table 1-10) and larger volumes incorporated into textiles (see Table 1-11).

Studies measuring the concentration of BDE-209, the single isomer of decaBDE, in building dust and indoor/ambient air are presented in Appendix Sections H.4.1.2 and E.1. The studies show relatively high concentrations of decaBDE in dust of buildings and homes containing products treated with decaBDE. These concentrations are primarily attributed to the sorption of decaBDE to particles and dust in these settings (see the DecaBDE Comparison Box on Transport, Transformation, and Fate in Air in Section 3.2). DecaBDE-treated plastics are expected to have the greatest release potential during the use phase of the product life cycle (Lassen et al., 1999); in textiles, the frequently used decaBDE/antimony trioxide flame-retardant formulations result in improved durability (i.e., reduced likelihood of release) due to the copolymer resin that bonds to the textile fibers [(Pure Strategies Inc., 2005); see Appendix H.2.4.2]. Nevertheless, some estimates indicate that the principal source of decaBDE release in wastewater is due to textile washing during the product use phase (EU, 2002). Regular use of upholstered furniture is also expected to result in wear and tear or abrasion that could result in the release of small amounts of free or matrix-bound decaBDE.

In general, decaBDE release scenarios during the product use phase are similar to those anticipated for MWCNTs due to the similar application in question. For example, similar to decaBDE, MWCNTs are not expected to be released due to their stability and lack of degradation. As the product matrix degrades during normal use or is washed, however, MWCNTs could be released in either the free or matrix-bound form.

Based on information for decaBDE, research planning to inform future risk assessments of MWCNTs might consider: Whether the use of MWCNTs in combination with other chemicals or materials (similar to decaBDE/antimony trioxide example) results in increased or decreased rate of release from textiles. Will differences in physical-chemical properties and mechanism of flame-retardant action increase or decrease likelihood of release during exposure to high heat or fire? How does aging or weathering influence the potential release of MWCNTs from the textile matrix? What type of activities (e.g., washing) during the product use phase might result in the most frequent or greatest environmental releases? See Appendix H for more information regarding release of decaBDE during the use stage of the product life cycle.

2.4.2. Potential Releases during the Use Stage

Environmental releases are expected from upholstery textiles coated with flame retardants due to (1) the potential use scenarios for the upholstery textiles and (2) the physicochemical properties of MWCNTs. The anticipated long lifespan of upholstery textiles (>10 years) suggests that releases in this stage could occur over several years (EU, 2002). Although no concentration data resulting from consumer use are available for MWCNTs, the following characteristics of flame-retardant upholstery textiles are expected to reduce releases MWCNTs (EU, 2002):

- Flame-retardant coatings must meet durability requirements to comply with regulations (see Section 1.2.1);
- Flame retardant is often applied to the back of the fabric, minimizing wear and tear; and
- Upholstery textiles are unlikely to be washed frequently.

The integrity of the flame-retardant coating depends on the strength of the formulation that bonds it to the textile surface (Som et al., 2011; NRC, 2000). MWCNT flame-retardant textile coatings considered in this case study are additive, suggesting that release from upholstery textiles could occur during the use stage (see Section 1.2.2.2). While in general, CNTs are not likely to be released because they are very stable and do not readily degrade, they could be released if the polymer matrix degrades (Köhler et al., 2008), or they could be released as a component of the polymer matrix. Factors that could lead to MWCNT release from textiles include:

- Regular use of upholstered furniture (e.g., sitting, walking, lying) could abrade the textile surface and release small amounts of free or matrix-bound MWCNTs either into the air or onto the skin of users. However, early unpublished evidence presented at a public meeting indicates that very small amounts of MWCNTs could be released as aerosols after subjecting an MWCNT-polymer nanocomposite to simulated wear and tear tests (Uddin and Nyden, 2011b).
- Washing of textiles also could lead to water release of matrix-bound MWCNTs.
- Even though CNTs might be embedded in a matrix, depending on the production method, a portion of a tube or a group of tubes could be left partially exposed in the final product.

Importantly, although most releases initially will be to the indoor environment, they could spread outdoors through environmental transport mechanisms (see Chapter 3). In contrast, factors that suggest minimal MWCNT release from textiles include:

- Most flame-retardant upholstery textiles will be used indoors, minimizing exposure to UV light and weathering.
- Upholstery textiles that are back-coated (a common application method) with MWCNT flame retardant likely will not be subject to significant abrasion, washing, or UV light.

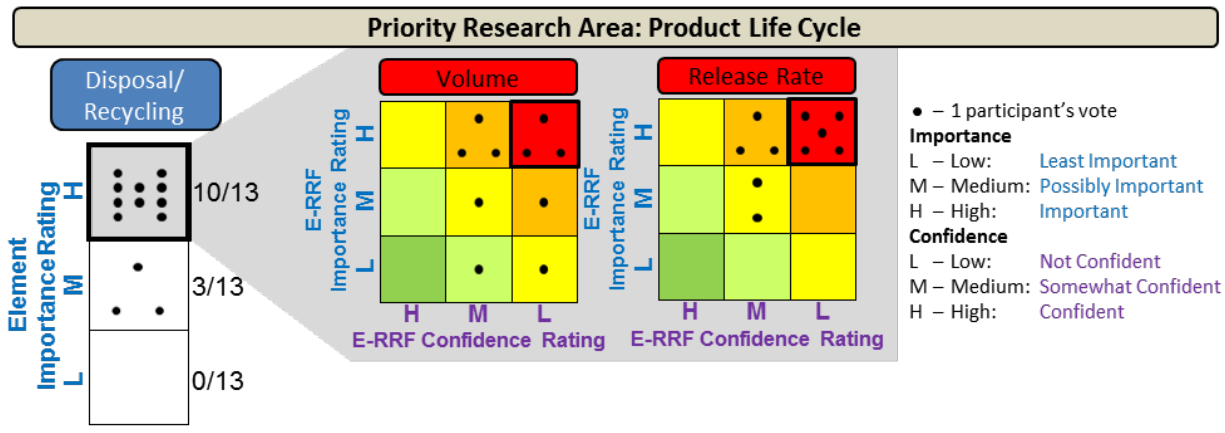
Although these processes also could result in release of MWCNTs to the air or to wastewater, less degradation of upholstery textiles is expected for MWCNT-treated composites than for traditional materials (see Section 1.3.3). As mentioned in Section 2.2.4.2, Nguyen et al. (2011) found that exposure of an epoxy containing MWCNTS to conditions of high heat and UV radiation can cause MWCNTs to form a dense network on the surface of composites, which might minimize environmental release. The authors also found that the epoxy containing MWCNTs degraded more slowly than unfilled epoxy or an epoxy containing another nanoscale material (Nguyen et al., 2011). A similar study found that when PMMA is filled with silane-coated MWCNTs the amount of submicrometric airborne particles emitted decreased when the polymer is exposed to fire compared to pristine PMMA (Motzkus et al., 2012). The authors noted that the release of airborne particles depends on a variety of factors, including the type of polymer matrix, the combustion process, and the type of surface treatment (Motzkus et al., 2012). A lack of data precludes a determination of whether similar MWCNT releases could be expected to occur in textiles that contain them.

Unintended uses also could lead to the release of MWCNTs from flame-retardant textiles. Use of flame-retardant upholstery textiles outdoors could lead to weathering, which could degrade the polymer matrix resulting in a release. Mouthing by small children, pets, or rodents on flame-retardant textiles could lead to release directly into the mouths of children, pets, or rodents if the back-coating is exposed and the integrity of the fabric is compromised. Preliminary unpublished evidence presented at a public meeting, however, suggests that few MWCNTs are released from a flame-retardant nanocomposite when subjected to simulated chewing tests (Uddin and Nyden, 2011b). Accidental contact of flame-retardant textiles with fire and high heat also could occur and would lead to possible airborne releases (see Section 2.2.2.2 for more details). No data were found, however, that describe the likelihood of this release from this application. Table 2-7 outlines potential release scenarios from the use stage of MWCNT flame-retardant textiles. Similar data on decaBDE are provided in the table for comparison; more detailed information on decaBDE can be found in Appendix H.

Table 2-7. Potential release scenarios during product use.

Processes included in use life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Intended use (e.g., sitting, standing)	Release possible due to abrasion or other physical/mechanical activities, resulting in direct release to individual in contact with the textile or to air as particle-bound substance (e.g., due to abrasion, release to dust)	Release possible due to abrasion or other physical/mechanical activities, resulting in direct release to individual in contact with the textile or to air as particle-bound substance (e.g., due to abrasion, release to dust)
Cleaning	Water release possible, but infrequent	Water release possible, but infrequent
Unintended use (outdoor use)	Air release possible due to weathering/degradation of the polymer; outdoor use could result in release to water or soil	Air release possible due to weathering/degradation of the polymer; outdoor use could result in release to water or soil
Unintended use (mouthing)	Direct release to mouth likely if polymer matrix surface is accessible and degraded	Direct release to mouth likely if polymer matrix surface is accessible and degraded
Accidental releases	Preliminary evidence suggests that air release due to high heat is unlikely	Air release possible due to exposure to high heat or fire

2.5. Reuse, Recycling, and End of Life



Ten out of 13 RTI workshop participants (77%) identified the disposal/recycling stage of the MWCNT-product life cycle as important to risk assessment. These 10 participants were asked to rate the importance of volume and release rate at this stage in the product life cycle, as well as their confidence that the existing data on these subjects could support risk-management decisions. Based on this information, these areas were deemed a priority for research. See Section 6.3.1.5 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

No information specific to the volume of decaBDE, decaBDE flame-retardant formulations, or decaBDE-treated upholstery textiles that are disposed of or recycled was identified. Nevertheless, volumes of decaBDE and decaBDE flame-retardant formulations are expected to decrease as the product is phased out of use. Disposal, recycling, and reuse of decaBDE treated textiles might continue for some time, however, given that upholstery textiles have a lifespan of at least 10 years (EU, 2002). The disposal, recycling, and reuse volumes of MWCNTs, MWCNT flame-retardant formulations, and MWCNT flame-retardant upholstery textiles are likely to be much smaller than for decaBDE (see Table 1-10 and Table 1-11), but the potential for release of MWCNTs generally is expected to be similar to that of decaBDE during such disposal, recycling, reuse, and repurposing of flame-retardant textiles.

Recycling

Although disposal or recycling of decaBDE and decaBDE flame-retardant formulations is expected to be minimal and only occur when manufacturing facilities are cleaned, research from a plastic recycling plant suggests that some release of decaBDE in the product matrix can occur during the recycling and disposal of plastics (Sjödin et al., 2001). Although releases from recycling of upholstery textiles containing decaBDE flame retardant might be similar to those of plastics, the processing of plastics differs from that of textiles.

Landfilling

Although no information quantifying the release of decaBDE from the landfilling of flame-retardant textiles was identified, release to air, soil, or water is possible (Rahman et al., 2001; Lassen et al., 1999). Such releases are expected to be small, however, based on key physicochemical properties, including low volatility and low leaching potential [Kim et al. (2006) as cited in Wright et al. (2008) and Palm et al. (2002); see Table 2-10 and Table H-4].

Wastewater Treatment

The removal efficiency of decaBDE in wastewater treatment plants is not well characterized. DecaBDE, however, likely sorbs onto particles during wastewater treatment that are then removed in sludge (Som et al., 2011; Lassen et al., 1999). Depositing sludge in landfills or spreading it on agricultural soil is one of the most significant potential releases of decaBDE to soils (Ciparis and Hale, 2005; EU, 2002; Lassen et al., 1999).

Incineration

Based on available data, release of decaBDE from municipal incinerators is expected to be limited due to the use of high temperatures and other pollution control technologies (Köhler et al., 2008; Palm et al., 2002; Lassen et al., 1999). Incomplete incineration outside of municipal incineration facilities, however, could result in airborne release of decaBDE and the formation of PBDFs, PBDDs, polychlorinated dibenzo-p-dioxins, and nonhalogenated substances such as polycyclic aromatic compounds (see Appendix H).

Based on decaBDE information, research planning to support future risk assessments of MWCNTs might consider: What volume of MWCNTs, MWCNT flame-retardant formulations, and MWCNT-treated upholstery textiles is likely to be disposed of, recycled, or reused? Under what incineration conditions could release occur? Could specific conditions be modified (e.g., incineration temperature) to increase or decrease the release of MWCNTs to air? Are MWCNTs likely to partition in sewage sludge? See Appendix H for more information regarding the potential release of decaBDE during disposal or recycling.

The reuse, recycling, and end-of-life stage encompasses a variety of different transformation and disposal processes for (1) MWCNTs, (2) MWCNT flame-retardant formulations, and (3) MWCNT flame-retardant upholstery textiles. What the primary reuse, recycling, and end-of-life treatments are for MWCNTs and MWCNT flame-retardant formulations are unclear. The reuse, recycling, and end-of-life treatments for flame-retardant upholstery textiles containing MWCNTs, however, are expected to be similar to those of traditional flame-retardant upholstery textiles (see Appendix H.2.5).

2.5.1. Reuse and Recycling

2.5.1.1. Life-Cycle Processes

Reuse or recycling of MWCNTs or MWCNT flame-retardant formulations is unlikely. On the other hand, textile waste often is recovered and reused or recycled (Köhler et al., 2008); upholstered furniture is sometimes reused, but is rarely recycled (CalRecycle, 2002). Upholstery could be donated to charitable organizations and resold for residential use. Additionally, upholstery textiles could be informally repurposed into clothing, blankets, and other textile products. Due to the difficulty of recycling furniture and flame-retardant materials, flame-retardant furniture is typically land-filled (CalRecycle, 2002; Lassen et al., 1999). Of the small portion of upholstered furniture that is recycled, about 60% of the material is recycled and 25–30% is composted (CalRecycle, 2002). No data were found that describe the proportion of other upholstery textiles (e.g., mattress ticking or curtains) that are typically recycled.

The main types of textile recycling processes are fiber-to-fiber recycling and polymer reduction recycling. During the fiber-to-fiber process, textiles are shredded and blended with other fibers to create a new mixture ready for spinning (Köhler et al., 2008). During the polymer reduction process, textiles are cut and granulated to form pellets that are processed to break down the polymer to the molecular level to be reused as raw material (Köhler et al., 2008). No data were found that described the prevalence of each recycling process.

2.5.1.2. Potential Releases during the Reuse/Recycling Stage

Release of MWCNTs beyond releases described in the use stage is unlikely to occur during reuse of flame-retardant upholstery textiles. Older textiles could release greater levels of MWCNTs, however, due to increased degradation of the material. Informal repurposing of flame-retardant textiles likely would require cutting and shredding, resulting in possible air release of MWCNTs. Airborne releases of MWCNTs could occur during recycling of flame-retardant textiles. Recycling subjects textiles to a variety of mechanical, thermal, and chemical treatments that could result in the airborne releases of additive flame retardants from fibers (Köhler et al., 2008). Recycling processes, such as shredding, milling, and thermal processing, could lead to the airborne release of CNTs from upholstery textiles if carried out in uncontrolled environments (Chaudhry et al., 2009). Airborne releases during recycling of textiles likely would be in the form of CNTs in a polymer matrix (Chaudhry et al., 2009). Downcycling, the conversion of waste materials into new materials of lesser quality and reduced functionality, could lead to cross-contamination of other materials with CNTs, for example, if MWCNT-treated textiles were shredded and mixed with other textiles for use as insulation (Chaudhry et al., 2009). Release of MWCNTs to water also

could occur during chemical treatment and processing. Although release of MWCNTs is possible during recycling of flame-retardant textiles, no data were found that indicate the likelihood of release from recycling processes.

Table 2-8 outlines potential release scenarios from the reuse/recycling stage of MWCNT flame-retardant textiles along with decaBDE for comparison.

Table 2-8. Potential release scenarios during reuse and recycling.

Processes included in reuse/recycling life-cycle stage	Information on release	
	MWCNTs	DecaBDE
General reuse (product kept intact)	Air release possible if textile degrades	Air release possible if textile degrades
Repurposing (product manipulated)	Air release possible due to cutting, shredding, and other abrasive processes	Air release possible due to cutting, shredding, and other abrasive processes
Recycling (product broken down)	Air and water release possible due to mechanical, thermal, and chemical treatment	Air and water release possible due to mechanical, thermal, and chemical treatment

2.5.2. Incineration

2.5.2.1. Life-Cycle Processes

The incineration of MWCNTs or MWCNT flame-retardant formulations is unlikely, but any incineration likely would occur in a hazardous waste incinerator. Upholstery textiles treated with MWCNT flame-retardant coatings might be sent to municipal incinerators for processing. Municipal incinerators generally provide a well-controlled environment with pollution control mechanisms and sufficiently high temperatures (850 °C) to destroy most materials (Köhler et al., 2008). Processing in municipal facilities is likely to result in complete incineration of the upholstery textiles. Alternatively, upholstery textiles also might be incinerated in less well-controlled facilities or burned in open fires as a rudimentary form of waste management or as kindling. These incineration methods are likely to result in incomplete incineration of the upholstery textiles. No data were found that describe the prevalence of incineration as a form of disposal for upholstery textiles or what proportion of incinerated textiles is processed at well-controlled incineration facilities.

2.5.2.2. Potential Releases during the Incineration Stage

Airborne releases of MWCNTs from well-controlled incineration are expected to be negligible, but incomplete incineration (e.g., open fires) could lead to some airborne release. MWCNTs are likely to be destroyed at the high temperatures used by municipal waste incinerators (Chaudhry et al., 2009; Sobek and Bucheli, 2009). Any CNTs remaining following municipal incineration could be expected to bind to other particles and be removed by the incinerator's filter (Köhler et al., 2008); however, incinerator removal efficiency for CNTs has not been studied (Som et al., 2011). Alternatively, incomplete incineration of products containing CNTs could result in the airborne release of CNTs in a polymer matrix (Chaudhry et al., 2009). Nguyen et al. (2011) found that exposure to moderately high temperature (50 °C) and UV radiation, however, caused MWCNTs to form a dense barrier on the surface of the polymer that prevented the release of MWCNTs to the environment. No data were found that describe potential by-products of incinerating upholstery textiles coated with MWCNT flame retardant in either municipal incinerators or in incomplete incineration scenarios.

In sum, due to the high temperatures and pollution control mechanisms at municipal incinerators, MWCNTs in flame-retardant textiles are expected to be destroyed during well-controlled incineration. Preliminary evidence suggests that MWCNTs might not be released to the environment during incomplete incineration. Table 2-9 outlines potential release scenarios from the incineration stage of MWCNT flame-retardant textiles along with decaBDE for comparison.

Table 2-9. Potential release scenarios during incineration.

Processes included in incineration life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Complete incineration, controlled	Release unlikely	Release unlikely
Incomplete incineration, uncontrolled	Preliminary evidence suggests that air release is unlikely	Air release of decaBDE and harmful by-products likely, likely will reach environment

2.5.3. Land-Filling

2.5.3.1. General Processes

Land-filling of MWCNTs or MWCNT flame-retardant formulations is unlikely, except in the case of floor sweepings from manufacturing facilities. Upholstered furniture and textiles generally are

disposed of in municipal landfills (Köhler et al., 2008). Remaining parts from recycled furniture, such as cover cloth materials, also are sent to the landfill (CalRecycle, 2002). Additionally, some textiles might be disposed of in uncontrolled landfills or open dumping sites that have no pollution control mechanisms in place. No data were found that describe the proportion of upholstery textiles disposed of in landfills or any further processing that might occur at the landfill.

2.5.3.2. Potential Releases during the Land-filling Stage

Land-filling of MWCNT flame-retardant textiles could lead to water and air releases. Mechanical land-filling processes (e.g., mixing and compacting) could lead to the airborne release of CNTs in a polymer matrix (Chaudhry et al., 2009). Airborne release of CNTs after land-filling is complete, however, is not likely (Chaudhry et al., 2009). Degradation of the polymer matrix material in textiles could lead to release of CNTs into leachate/soil because CNTs are very stable and do not readily degrade (Köhler et al., 2008). No data were found, however, that identify MWCNTs in land-fill leachate. Few data were identified that measure releases of MWCNTs from land-filling flame-retardant textiles, but the physicochemical characteristics of these materials suggest that such releases likely would be small. Table 2-10 outlines potential release scenarios from the land-filling stage of MWCNT flame-retardant textiles along with decaBDE for comparison.

Table 2-10. Potential release scenarios during land-filling.

Processes included in land-filling life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Disposal	Air release possible due to mixing and compacting	Air release possible due to mixing and compacting
Degradation	No data exist; air and water release possible but unlikely	Air and water release unlikely

2.5.4. Wastewater Treatment Plants

2.5.4.1. Life-Cycle Processes

The wastewater treatment process consists of filtering and treating wastewater to remove solids and contaminants. Large facilities that manufacture MWCNTs and MWCNT flame retardants might

divert their wastewater to an on-site wastewater treatment plant. Alternatively, some wastewater from these facilities might be directly processed by municipal wastewater treatment plants. Water releases of MWCNTs that occur during the storage and distribution, use, and reuse/recycling/end-of-life stages also would be treated in municipal wastewater treatment plants.

2.5.4.2. Potential Releases during the Wastewater Treatment Stage

Release of MWCNTs or MWCNT flame-retardant formulations into wastewater could occur throughout the life cycle. Primary releases to wastewater during manufacturing stages are due to equipment cleaning, formulation and application of the flame retardant, and accidental spills. Washing processes (which can involve abrasion, detergents, and water), particularly in the product manufacturing stages, are likely to result in the release of additive flame retardants from textiles to wastewater (Som et al., 2011). Due to the physicochemical characteristics of MWCNT flame retardants (see Table 1-8 and Table 1-9 in Section 1.3), MWCNTs are likely to sorb to particles during water treatment and be removed in sludge (Som et al., 2011). The potential nonetheless exists for releases from filter backwash and other wastewater treatment plant equipment (EU, 2002). Additionally, some of this removed sludge is deposited in landfills or spread on agricultural soil (EU, 2002; Lassen et al., 1999). However, the potential release of MWCNTs due to the spread of sludge on agricultural soil is unknown. The releases of MWCNTs from wastewater treatment facilities are expected to be small, but release potential greatly depends on surface chemistry.

The removal efficiency of wastewater treatment plants is not well characterized MWCNTs and the spread of sewage sludge onto agricultural soil could represent a significant source of MWCNTs to soil. In addition, negative impacts on WWTP functionality due to MWCNT contamination and subsequent antimicrobial activity are possible (see Appendix G.5.1.1.1 and Table F-18). See Section 3.3.3 for information regarding MWCNT removal efficiency of these wastewater treatment plants.

Additional Information Highlight Box 5:
Impact of MWCNT release into wastewater treatment plants

Petersen et al. (2011b) noted that most of the CNTs that are released into wastewater come from the tailoring, finishing, use, and degradation of textiles containing CNTs, or from research and development facilities. Because some evidence suggests that MWCNTs impact microorganisms (for example, see Appendix G.5.1.1 and Appendix F for data on impacts to soil microbes), important considerations for wastewater treatment facilities include: How will CNTs be removed from the aqueous phase, and what is the removal rate? How will MWCNTs impact diverse bacterial communities in wastewater, which are responsible for pollutant and contaminant removal in these systems? In a review of the available literature, Petersen et al. (2011b) found that the chemistry of CNTs is modified in activated sludge, microbial communities were often negatively impacted by the addition of CNTs, and that certain environmental conditions (e.g., extracellular polymeric substances) could lessen the negative impacts.

Table 2-11 outlines potential release scenarios from the wastewater treatment stage of MWCNT flame-retardant textiles along with decaBDE for comparison.

Table 2-11. Potential release scenarios during wastewater treatment.

Processes included in wastewater treatment life-cycle stage	Information on release	
	MWCNTs	DecaBDE
Release of effluent	Release unlikely due to sorption behavior, but filter backwash could lead to release	Release unlikely due to sorption behavior, but filter backwash could lead to release
Removal of sludge	No data exist, but release to soil possible if sludge spread on agricultural fields	Release to soil likely if sludge spread on agricultural fields

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Chapter 3. Transport, Transformation, and Fate

Releases throughout the product life cycles of upholstery textile coatings containing multiwalled carbon nanotube (MWCNT) flame retardant will, to some extent, lead to occurrence of primary and secondary contaminants in air, soil, and aquatic media. Chapter 3 examines what might happen to these substances after their release to the environment, including transport or transformation through chemical, physical, and biological processes. Studies investigating the transport, transformation, and fate of MWCNTs in the environment are summarized in Appendix D. In general, information on environmental concentrations of MWCNTs was not found.

MWCNTs can be released into the environment during the manufacturing, storage, distribution, use, disposal, reuse, and recycling of upholstery textiles treated with flame retardants (see Chapter 2). MWCNT flame-retardant formulations are used primarily as additives that are mixed with, not chemically bound to, polymers in textile products (see Section 1.3). Because they are not chemically bound, these substances can escape from the material and become a source of contamination to surrounding environmental media (Moniruzzaman and Winey, 2006). Although some, if not most, releases after the production stage are likely to be in the matrix-bound form, little information exists that describes the environmental behavior of MWCNT-polymer complexes. As a result, this chapter focuses on the transport, transformation, and fate of MWCNTs not embedded in a polymer matrix.

Section 3.1 provides a brief discussion of the chemical and physical characteristics and the processes that influence behavior (e.g., mobility, persistence, and bioavailability) of MWCNTs in environmental media. The sections that follow summarize the available information regarding their behavior in indoor and outdoor air (Section 3.2), aquatic systems (Section 3.3), and terrestrial systems (Section 3.4). A brief discussion of models that might be used for evaluating their fate and transport in environmental media is provided in Section 3.5.

Additional Information Highlight Box 6:
Transformation throughout the product life cycle

Engineered nanomaterials such as MWCNTs are unlikely to occur in the environment in their as-manufactured form (see Figure 2-2). The intended use and the disposal of consumer products that contain MWCNTs, such as upholstery textiles, often expose the product to a wide variety of environmental conditions that can alter the composite material and the behavior of MWCNTs after release (Nowack et al., 2012). Nowack et al. (2012) discuss the various processes that can alter or transform (e.g., photochemical transformation, oxidation, reduction, adsorption/desorption, combustion, abrasion) nanomaterials directly or nanomaterials in products. These processes can change how MWCNTs aggregate, disperse, and interact with biota (Nowack et al., 2012). Greater understanding of how these processes influence MWCNT flame-retardant coatings in upholstery textiles could support future assessments of the material.

3.1. Physicochemical Factors Influencing Transport, Transformation, and Fate

The environmental fate of MWCNTs will be dictated by their physical and chemical properties (see Text Box 1-1 and Figure 3-1). These properties influence behavior, including mobility, persistence, bioavailability, and likelihood for transformation in environmental media. A summary of key physicochemical factors that might affect partitioning of MWCNTs and their fate in the environment is provided in Table 3-1. Values for or descriptions of key physicochemical properties of MWCNTs (e.g., surface area, morphology, solubility) are provided in Table 1-9.

Table 3-1. Summary of physicochemical properties that affect partitioning and fate of nanomaterials such as multiwalled carbon nanotubes (MWCNTs).

Physicochemical property	How does this property affect chemical partitioning and fate?
Small size; single particle versus cluster	• Single particles versus bundles or clusters will differ in their mobility (and ultimate fate) in environmental media; generally, nanoparticle clusters are less mobile in the environment than individual nanoparticles Sources: Ma-Hock et al. (2007)
High surface area-to-volume ratio	• Large surface area enhances chemical reactivity and clustering • Might cause other molecules to adhere and be transported with MWCNTs Source: Kohler et al. (2008); O'Driscoll et al. (2010)
Distinct morphology	• Concentrically nested multiple graphene sheets, which frequently exhibit "disturbed wall texture" and irregular shape, increases chemical reactivity. • Differences in morphology based on variations in synthesis • Shape can affect the kinetics of deposition and transport in the environment; depending on surface structure and shape, MWCNTs might exhibit different reactivity Sources: Kohler et al. (2008); Oberdorster et al. (2005)

Table 3-1, cont.: Summary of physicochemical properties that affect partitioning and fate of nanomaterials such as multiwalled carbon nanotubes (MWCNTs).

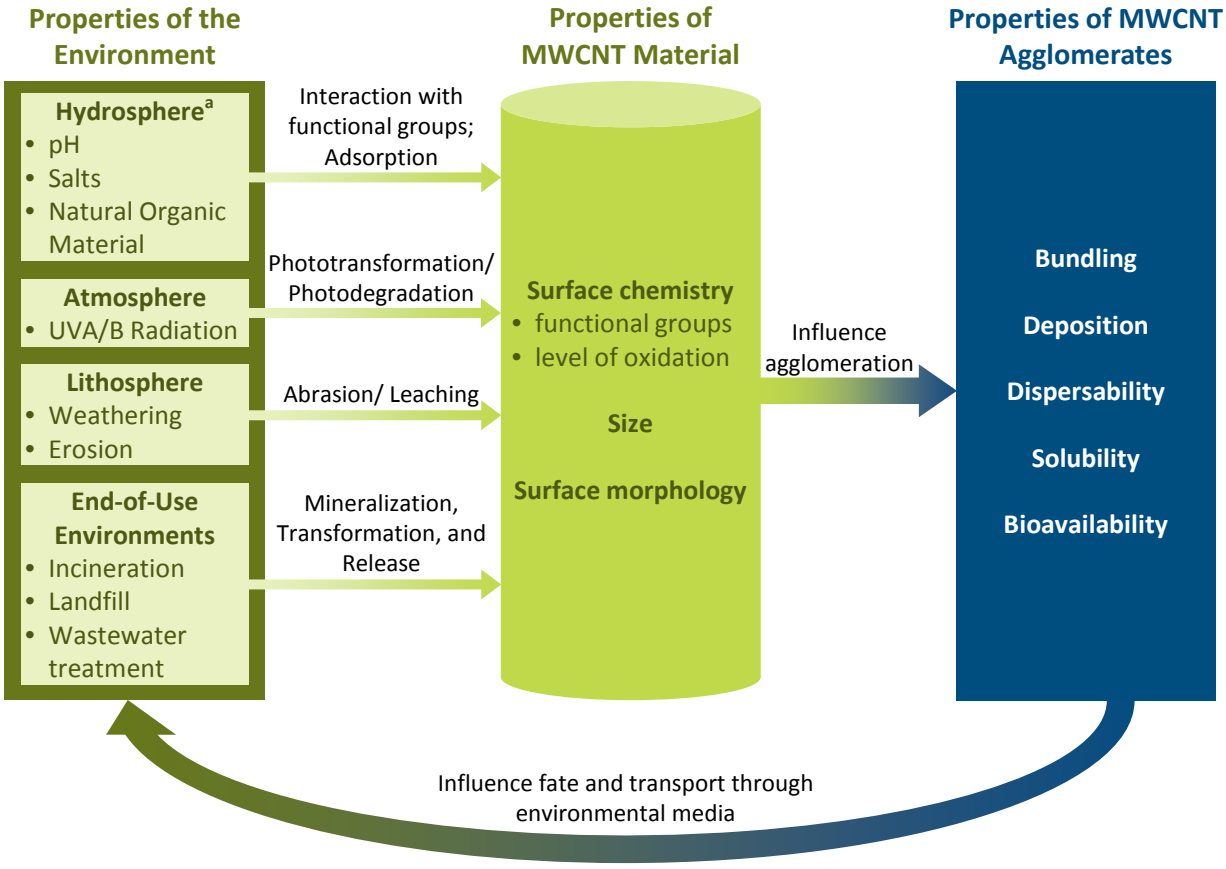
Physicochemical property	How does this property affect chemical partitioning and fate?
Low water solubility; hydrophobic (potentially lipophilic)	• Will result in poor dispersion • Prone to bundling in the water column and settling to sediments; though functionalization and surface chemistry can alter partition coefficients and rates • Hydrophobic interactions play major role in adsorption of organic contaminants • Functionalization and presence of surface-active agents (surfactants, dissolved organic matter) can improve their dispersion/increase solubility in aqueous media • Might interact with lipids in abiotic and biotic media; might be taken up by microbial communities and plant roots Sources: Helland et al. (2007); Christian et al. (2008); Klaper et al. (2010); Saeed (2010); Kohler et al. (2008); Luoma (2008); Li et al. (2011); Oberdorster et al. (2006); Wu et al. (2006); Kennedy et al. (2008)

Carbon nanotubes (CNTs) are not dispersed by simple mixing because they tend to form bundles through a van der Waals attraction among tubes. As shown in Table 2-4, MWCNTs, including those in commercial products such as textiles, can be engineered to include charged functional groups to improve their dispersion or to increase their solubility in aqueous media; the treated nanoscale materials (nanomaterials) that remain dispersed tend to exhibit greater persistence in the environment (Klaper et al., 2010; Saeed, 2010; Köhler et al., 2008; Luoma, 2008). CNTs in textiles might also be coated with a surface coating, such as a polymer (Köhler et al., 2008). These surface coatings could be degraded by chemical or biological reactions, affecting persistence of the MWCNTs over time in ways that depend on both the presence of a coating and the type of coating used.

Additional Information Highlight Box 7:
Properties of the MWCNT formulation impact environmental release and transformation

MWCNT physicochemical properties can vary substantially as a result of MWCNT purification (see Section 2.2.3.1 and Appendix C), functionalization (see Section 2.2.3.1 and Table 2-4), and formulation of MWCNT flame-retardant products (see Section 2.2.4.1). Because many MWCNT applications, including flame-retardant coatings in upholstery textiles, are still in research and development phases, however, it is unclear what type of modifications during production will dominate in the market.

The types of modification during production can alter product chemistry and thus influence MWCNT release (see Figure 2-2); transformation, transport, and fate; exposure; and human health and environmental impacts (see Text Boxes Text Box 1-1 and Text Box 5-1, Table 3-1, and Figure 3-1). For example, Nguyen et al. (2011) observed that exposure of an epoxy containing MWCNTs to high heat and UV radiation can cause MWCNTs to form a dense network on the composite surface, which might minimize environmental release (see Section 2.2.4.2). Although Nguyen et al. (2011) simply describe the MWCNTs used in their study as "commercially available," understanding which modifications of MWCNTs likely dominate a particular application market, and how such modifications can influence potential environmental releases throughout the product life cycle could inform future assessment and risk management efforts.



Adapted from: Misra et al. (2012)

Figure 3-1. Variability in MWCNT chemistry and implications in terms of life cycle, exposure, and risk.[b]

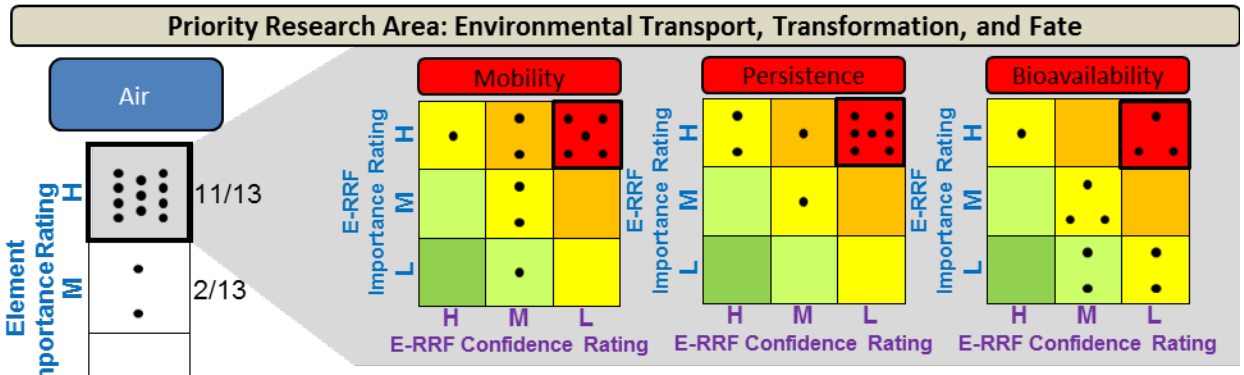
[a]Hydrosphere describes environmental media characterized by water (i.e., groundwater, surface water). Lithosphere describes media characterized by rock composition (i.e., soil, sediment).

[b]Environmental transport and fate – and therefore exposure, impacts, and risk – are intimately tied to the interactions between MWCNT formulation and environmental media conditions. As illustrated here, environmental conditions can result in transformation of the MWCNTs, for example, exposure to UV radiation can result in phototransformation, which alters the surface chemistry of the MWCNTs (Misra et al., 2012). In turn, the properties of the MWCNTs dictate how the compound moves through the environment and partitions across various environmental media. The result is a cycle of interactions between environmental conditions and MWCNT properties that influence movement and bioavailability of MWCNTs in the environment.

Environmental conditions (e.g., redox potential, pH, temperature, UV light, ionic strength, and characteristics of other contaminants present) are also likely to affect the behavior and environmental fate (e.g., mobility, persistence, bioavailability) of MWCNTs (Tóth et al., 2011; Zhang et al., 2011; Helland et al., 2007) (see Text Box 1-1 and Figure 3-1). The same is true for environmental processes such as interactions with natural organic matter (NOM), which will alter the surface chemistry of the MWCNTs (Petersen et al., 2011a). Metals, such as lead, cadmium, and copper; hydrophobic organic chemicals and other toxic organics (e.g., polycyclic aromatic hydrocarbons); and other pollutants (e.g., phenol,

dopamine) can sorb strongly to CNTs (Li et al., 2011; Tóth et al., 2011; Cho et al., 2008; Petersen et al., 2008; Chen et al., 2007; Helland et al., 2007). These associations might dictate CNT mobility and bioavailability. Factors that have been shown to influence adsorption of organic contaminants to MWCNTs include surface oxidation (adsorption capacity decreases with increasing oxygen content) and pH (effects differ based on the contaminant) (Li et al., 2011; Tóth et al., 2011; Cho et al., 2008).

3.2. Transport, Transformation, and Fate in Air



Eleven out of 13 RTI workshop participants (85%) identified environmental transport, transformation, and fate in air as important to risk assessment. These 11 participants were asked to rate the importance of MWCNT mobility, persistence, and bioavailability to environmental fate in air, as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based on this information, these areas were deemed a priority for research. In the event of a tie (e.g., confidence ratings for MWCNT mobility and bioavailability in air), the most conservative rating (i.e., higher importance, lower confidence) was chosen. See Section 6.3.2.1 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

In air, 99% of BDE-209, the single isomer of decaBDE, exists in the particulate phase, making its fate in air dependent on the characteristics of the particles to which it adsorbs. In indoor air, the tendency to sorb to particles likely would lead to higher concentrations of BDE-209 in house dust than in vapor in the air and to extended persistence (Kemmlein et al., 2003). In outdoor air, evidence suggests long-range atmospheric transport of PBDEs to remote ecosystems, including the Arctic (de Wit et al., 2010; Su et al., 2009; Agrell et al., 2004). This atmospheric deposition of BDE-209 is thought to be a main source of the background contaminants in waters and soils (Vonderheide et al., 2008). Notably, temperature changes and UV exposure influence BDE-209 concentrations; UV exposure results in lower brominated compounds in the environment due to photolysis of BDE-209 (Shih and Wang, 2009).

Based on decaBDE information, the following questions might be considered in planning research to inform future MWCNT risk assessments: Will differences in MWCNT physicochemical properties result in critical differences in mobility, persistence, and bioavailability in air? Could specific surface modifications be made to MWCNTs in flame-retardant applications that might increase or decrease the mobility, persistence, and bioavailability of MWCNTS in air? How do environmental conditions (e.g., temperature, UV) influence mobility, persistence, and bioavailability of MWCNTs in air? See Appendix H for more information about BDE-209 fate, transport, and transformation in air.

MWCNTs released from flame-retardant upholstery textile coatings could reach indoor and outdoor air in several ways. For example:

- They can be released directly into ambient air during all stages of the product life cycle, as previously described in Chapter 2 and can disperse through air away from the source of release.
- They can become suspended in the surrounding indoor or outdoor air during multiple stages of the product life cycle.
- They might remain suspended and be transported through the atmosphere or be deposited onto surfaces. Particles that have been deposited on surfaces could become resuspended in the air and redeposited elsewhere.

MWCNTs might distribute to indoor air and dust, and these sources could be a major contributor to outdoor air concentrations. Several processes and factors could influence the behavior (e.g., mobility, persistence, bioavailability) and ultimately the fate of airborne MWCNTs in indoor and outdoor environments, including: (1) size—whether they are traveling as individual particles of varying sizes or as larger bundles, (2) surface chemistry, (3) interactions with other airborne particles and chemical compounds, (4) residence time in the air, and (5) distance traveled prior to deposition (Köhler et al., 2008; U.S. EPA, 2007). The fate of airborne nanomaterials outdoors could be influenced by meteorological factors, including wind, temperature, and precipitation (Navarro et al., 2008).

Information in the recent literature regarding the behavior of airborne MWCNTs is limited. No studies have examined transport mechanisms for MWCNTs in air. Yang et al. (2009) examined the atmospheric aging of CNTs under normal ambient conditions (20 ± 0.5°C, relative humidity = 50 ± 1%) and found that CNT surface area and pore volume (volume of space [holes] per gram nanotube; provided in cm^3/gram) decreased over time (up to 7–15 months) and coincided with decreases in surface oxygen of the CNT as it aged. For MWCNTs, these conditions stabilized within 15–18 months. The total structural-defect concentration also appeared to be lowered as the CNTs aged. The authors theorized that during CNT aging under ambient conditions, oxygen leaves the surface of the CNTs. The structure then repairs itself and becomes more thermodynamically stable with fixed values of surface area, pore volume, and structural defects. Based on these results, the authors stated that CNT "physicochemical properties can be characterized with reliability only after samples have sufficiently aged" (Yang et al., 2009).

In the laboratory, Zhu et al. (2011) observed that MWCNTs exposed to air under ambient temperature were slowly oxidized and shortened. The degree of oxidation increased over time, and MWCNTs were almost totally transformed into amorphous carbon after 15 days.

Complete transformation of pure, airborne CNTs to carbon dioxide could occur during incineration at temperatures greater than 850°C and oxygen levels exceeding 21%. Under oxidative

conditions, MWCNTs have been shown to burn off completely at 740°C (Som et al., 2011; Köhler et al., 2008).

Section 4.1.2.4 describes MWCNT air concentration data collected in occupational settings. No data were found on residential or consumer exposures to MWCNTs in air. Literature containing concentrations of MWCNTs in outdoor air also was not found.

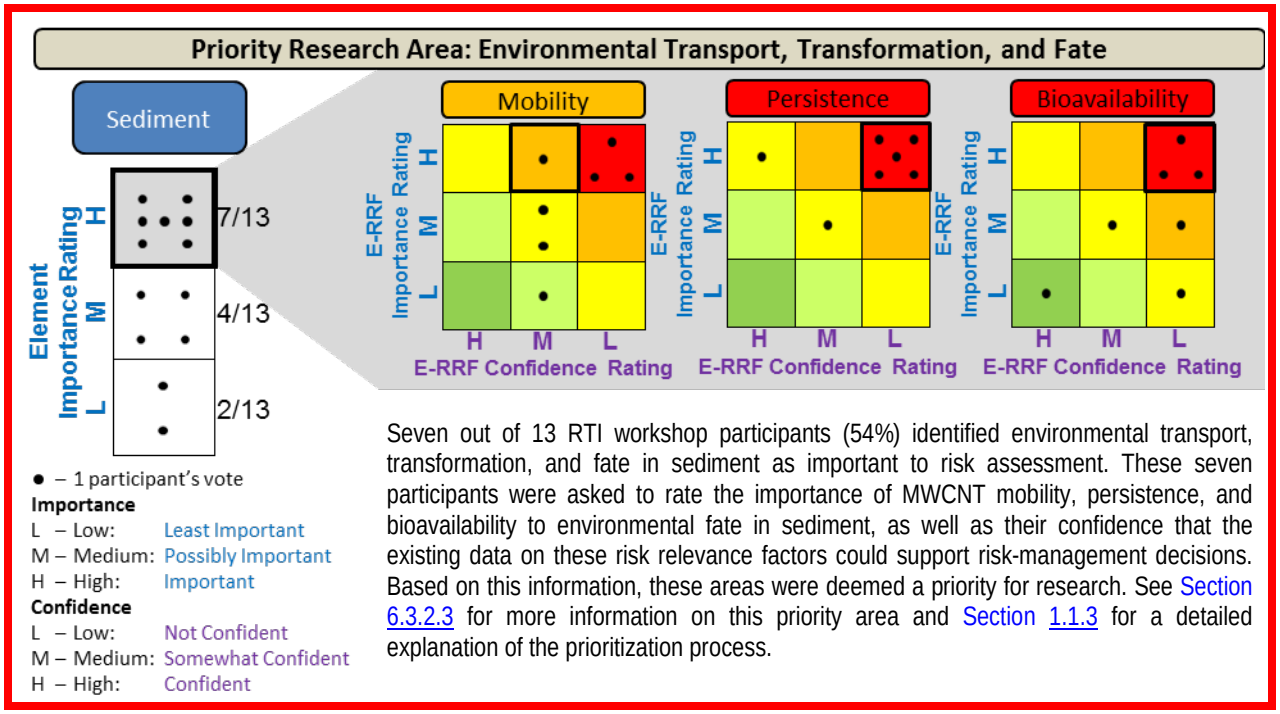
3.3. Transport, Transformation, and Fate in Water and Sediment

MWCNTs released from the flame-retardant upholstery textile coating life cycle could enter aquatic systems in several ways. For example:

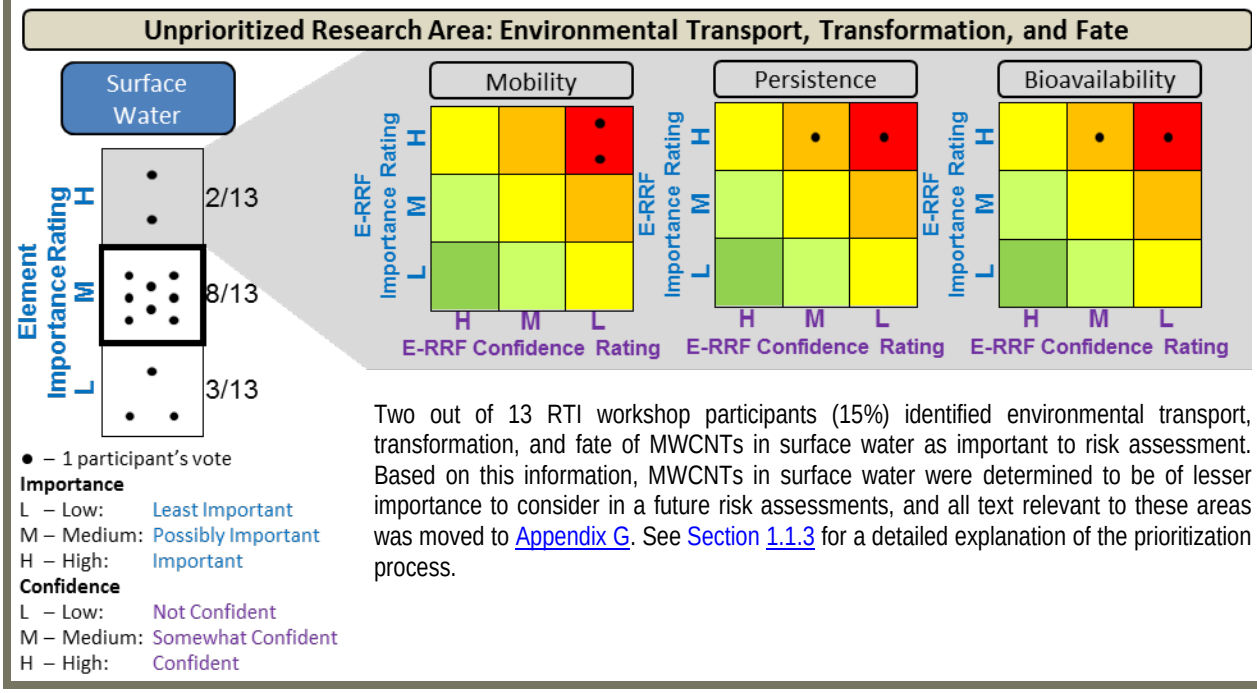
- MWCNTs in ambient air subsequently could be deposited or washed out to aquatic systems.
- Erosion of contaminated soil could release MWCNTs to surface waters.
- Runoff flowing along the ground surface could transfer MWCNTs in contaminated soil to nearby waterways.
- Wastewater effluents containing MWCNTs could be a source of contamination to receiving water bodies near the discharge location.
- MWCNTs could leach from land-filled sewage sludge into subsoil and ground water and migrate to surface water or sediment.

3.3.1. Surface Water and Sediment (Inland and Coastal)

The transport, transformation, and fate of MWCNTs in surface water (specifically, mobility, persistence, and bioavailability) was not identified as a priority area by workshop participants during the collective judgment step of the CEA process. However, mobility, persistence, and bioavailability in sediment was determined to be a priority area. Due to the limited available data, which overlaps between surface water and sediment, these topics are discussed together.



Seven out of 13 RTI workshop participants (54%) identified environmental transport, transformation, and fate in sediment as important to risk assessment. These seven participants were asked to rate the importance of MWCNT mobility, persistence, and bioavailability to environmental fate in sediment, as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based on this information, these areas were deemed a priority for research. See Section 6.3.2.3 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.



Two out of 13 RTI workshop participants (15%) identified environmental transport, transformation, and fate of MWCNTs in surface water as important to risk assessment. Based on this information, MWCNTs in surface water were determined to be of lesser importance to consider in a future risk assessments, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

The hydrophobicity and van der Waals interactions of MWCNTs imply they will partition to the particulate phase when introduced to aquatic systems (Kennedy et al., 2008). Pure MWCNTs are insoluble in water and are prone to bundling in the surface water column and settling to sediments—making benthic organisms potential vectors for the transport of MWCNTs through the food web (Christian et al., 2008) (see Section 4.3). MWCNTs suspended in NOM solutions have greater potential for dispersion in natural waters (ODriscoll et al., 2010). Results of the O'Driscoll et al. (2010) study suggested that smaller diameter MWCNTs stay suspended in NOM solutions much longer than larger diameter MWCNTs. Dissolved organic matter has been shown to debundle MWCNTs and induce conformational and electrostatic stabilization of carbon-based nanomaterials under environmentally relevant conditions (Hyung and Kim, 2008; Wang et al., 2008; Hyung et al., 2007).

DecaBDE Can Inform MWCNT Assessment

Water solubility and K_{ow} of BDE-209 indicate that it will partition to the particulate phase in water or bind strongly to sediments, making sediment a sink for PBDEs. BDE-209 is the dominant PBDE congener in sediment samples, although whether this is due to greater use of BDE-209 or its resistance to environmental degradation is unclear. Despite relatively high concentrations in sediment, the bioavailability of BDE-209 in sediment is expected to be limited due to its strong hydrophobicity and large molecular size (Liu et al., 2011b). Further, environmental transformations (e.g., debromination, See Appendix H, Text Box H.3-1) of BDE-209 likely influence its concentration in sediment because lower brominated congeners are more water soluble than higher brominated congeners, and are therefore more mobile in the water column (Söderström et al., 2004; Watanabe and Sakai, 2003). Environmental conditions such as the amount of organic matter and microbial or photolytic degradation processes also influence levels of PBDEs, such as BDE-209, in sediment or surface waters.

As with decaBDE, physicochemical properties and environmental conditions could be important to consider in planning research that informs future risk assessments of MWCNTs. For example, will environmental processes act on MWCNTs in a way that makes them more or less likely to partition to sediments? Will MWCNTs that have been functionalized to increase dispersibility in aqueous media be likely to sorb to particles in the environment? Can specific physicochemical formulations of MWCNTs make them more or less likely to partition to sediments even under environmental conditions? What environmental conditions (e.g., organic matter content, microbial community composition) influence mobility, persistence and bioavailability of MWCNTs in sediments? See Appendix H for more information about BDE-209 fate, transport, and transformation in surface water and sediment.

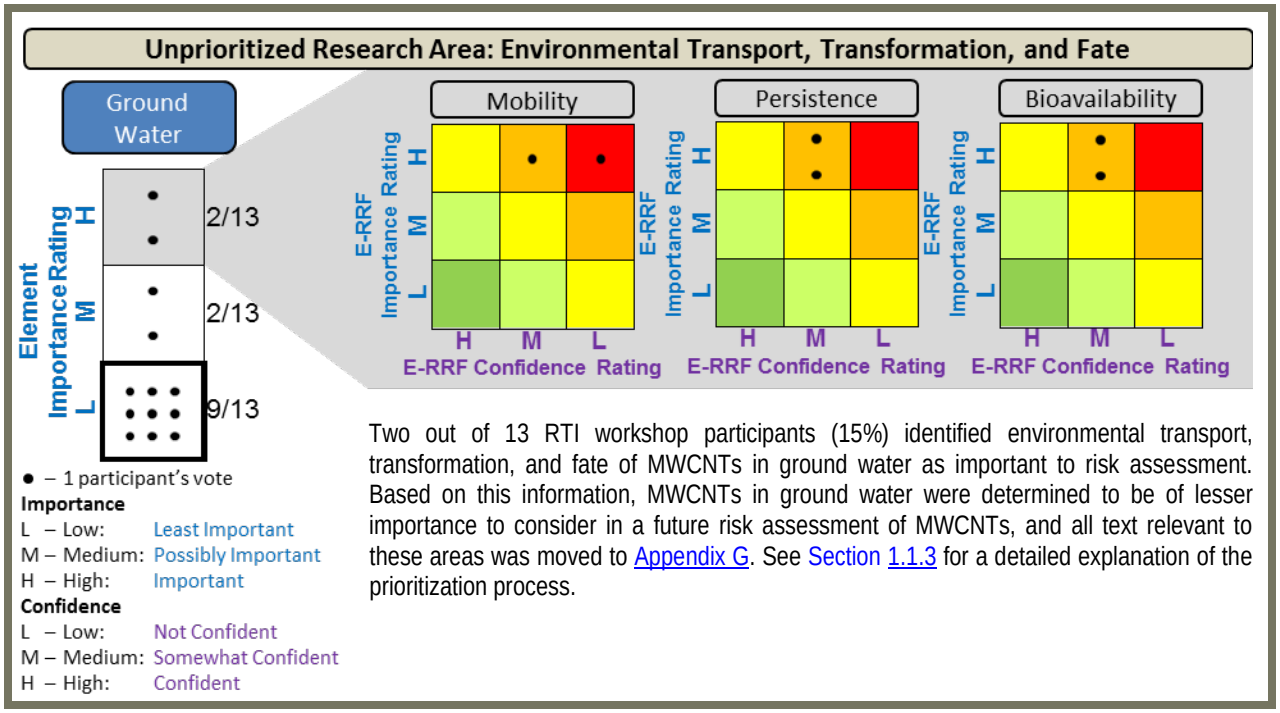
Changing conditions such as ionic strength and pH of an aqueous solution can influence sorption behaviors of CNTs and subsequently the mobility, persistence, and bioavailability of these compounds in water. Zhang et al. (2011) suggested that the overall effect of increasing ionic strength is that more MWCNTs transfer from the aqueous phase and sorption increases. The authors also indicated that, in general, decreasing the pH of aqueous solutions enhances MWCNT bundling. The presence of dissolved organic matter, however, contributes to stabilization of MWCNTs in solution and suspended MWCNTs become less sensitive to changes in ionic strength or solution pH (Zhang et al., 2011). Similarly, Hyung and Kim (2008) determined that adsorption capacity is directly proportional to the aromatic carbon content of the organic matter and the ionic strength of the solution and indirectly proportional to pH. Adsorption strength is indirectly proportional to ionic strength and is not significantly changed by pH.

Functionalization of MWCNTs can improve their dispersion or increase their solubility in aqueous media, thereby increasing their mobility. As mentioned previously, engineered surface modifications (e.g., functional groups and coatings) are used to improve CNT dispersion in aqueous suspension. Column stability and settling experiments have shown pure MWCNTs settle and sink to sediment as described previously. The presence of functional groups slows this settling, especially in combination with NOM (Kennedy et al., 2008; Hyung et al., 2007).

As discussed in Section 3.1, MWCNTs can act as environmental adsorbates of metals, hydrophobic organic compounds, and other toxic organics (Li et al., 2011; Cho et al., 2008; Petersen et al., 2008; Chen et al., 2007; Helland et al., 2007), and the properties of the adsorbants might dictate MWCNT mobility and dispersion in surface water.

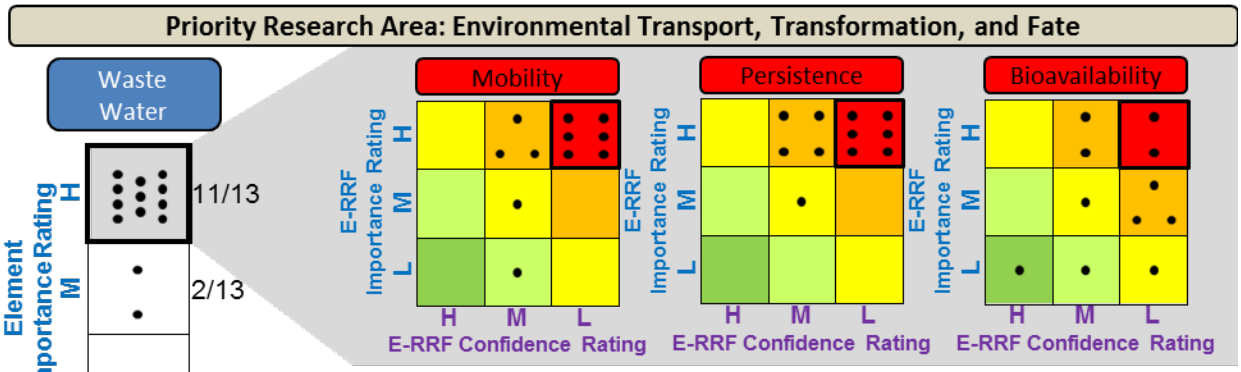
Studies relevant to MWCNT fate and transport in aqueous media are summarized in Appendix D, Table D-2. No data were found on concentrations of MWCNTs in surface water and sediment.

3.3.2. Ground Water



Two out of 13 RTI workshop participants (15%) identified environmental transport, transformation, and fate of MWCNTs in ground water as important to risk assessment. Based on this information, MWCNTs in ground water were determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

3.3.3. Wastewater



● – 1 participant's vote

Importance
L – Low: Least Important
M – Medium: Possibly Important
H – High: Important

Confidence
L – Low: Not Confident
M – Medium: Somewhat Confident
H – High: Confident

Eleven out of 13 RTI workshop participants (85%) identified environmental transport, transformation, and fate in wastewater as important to risk assessment. These 11 participants were asked to rate the importance of mobility, persistence, and bioavailability to MWCNT environmental fate in wastewater, as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based on this information, these areas were deemed a priority for research. See Section 6.3.2.2 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

Information in the recent literature regarding the behavior of MWCNTs in wastewater is limited. Because of their hydrophobicity and tendency to form bundles, however, pure MWCNTs likely would be removed from the effluent by settling during the sewage treatment process. Functionalized MWCNTs could have improved dispersion and increased solubility in wastewater, thereby increasing their mobility and persistence in wastewater effluents.

As discussed in Section 3.1, MWCNTs can act as environmental adsorbates of metals, hydrophobic organic compounds, and other toxic organics (Li et al., 2011; Cho et al., 2008; Petersen et al., 2008; Chen et al., 2007; Helland et al., 2007), and these adsorbants might dictate

DecaBDE Can Inform MWCNT Assessment

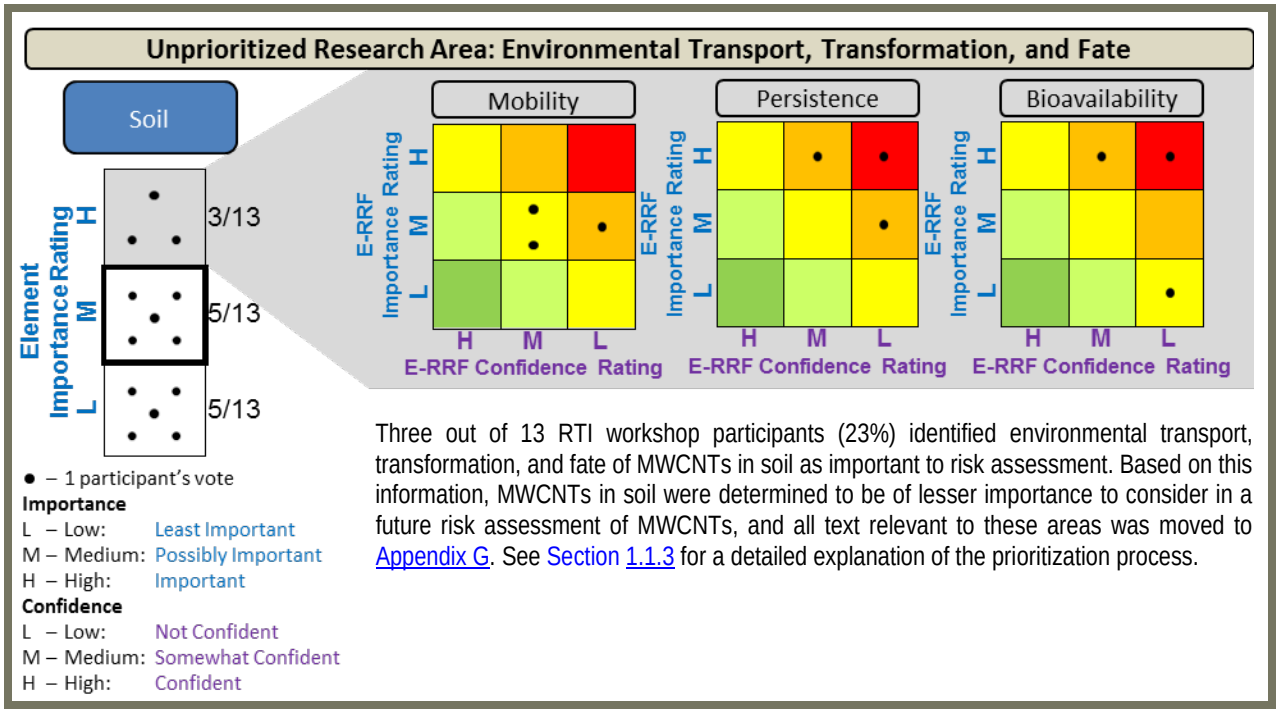
Because of its hydrophobicity, most (>99%) BDE-209 present in wastewater sorbs to sediments, making sewage sludge a major sink for this material (Ricklund et al., 2009; North, 2004). As mentioned in Section 2.5, the application of sewage sludge to agricultural fields is one of the most significant potential releases of decaBDE to soils (Ciparis and Hale, 2005; Lassen et al., 1999). Wastewater effluents, in contrast, could contain lower brominated transformation products of BDE-209 and thereby contaminate receiving water bodies or local aquatic ecosystems near the discharge location (Peng et al., 2009; Song et al., 2006).

Based on decaBDE information, considerations to include in planning MWCNT research to support future assessments are: Will MWCNT functionalization to increase dispersibility cause them to remain dispersed in wastewater? What concentrations of MWCNTs might end up in sludge applied to agricultural soils? What is the bioavailability of MWCNTs in sewage sludge and how does functionalization influence bioavailability? What types of transformation products might partition in wastewater sludge or effluents? See Appendix H for more information on fate, transport, and transformation of BDE-209 in wastewater.

CNT mobility and dispersion in wastewater. He et al. (2012) studied the behavior of MWCNTs stabilized by humic acid during the coagulation-flocculation-sedimentation process of drinking water treatment and found that humic acid-stabilized MWCNTs were effectively sequestered by this process.

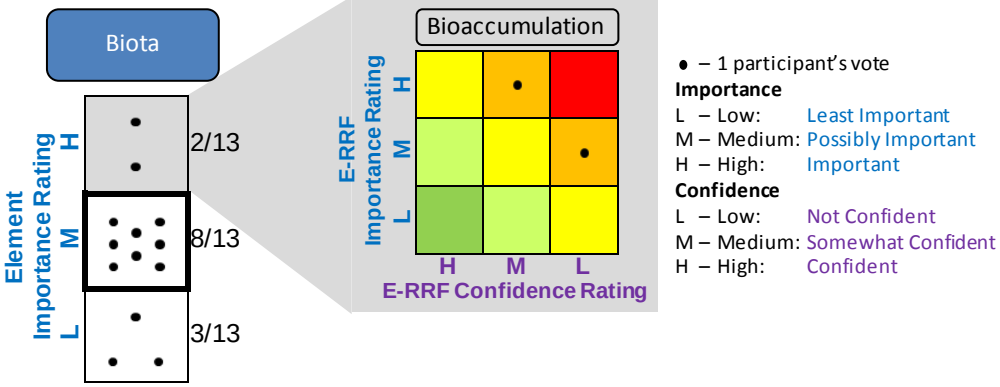
Literature containing concentrations of MWCNTs in wastewater effluent or sludge was not found.

3.4. Transport, Transformation, and Fate in Soil



Three out of 13 RTI workshop participants (23%) identified environmental transport, transformation, and fate of MWCNTs in soil as important to risk assessment. Based on this information, MWCNTs in soil were determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

Unprioritized Research Area: Environmental Transport, Transformation, and Fate



Two out of 13 RTI workshop participants (15%) identified environmental transport, transformation, and fate of MWCNTs in biota as important to risk assessment. Based on this information, MWCNTs in biota were determined to be of lesser importance to consider in a future risk assessment of MWCNTs. In the draft document (U.S. EPA, 2012b) reviewed by RTI workshop participants information pertinent to this area was primarily identified for plants in soil; since transport, transformation, and fate in both biota and soil were not identified as priorities all relevant text was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

3.5. Multimedia Models to Predict Environmental Fate and Transport

Neutral Research Area: Environmental Transport, Transformation, and Fate

Multimedia models predicting environmental fate and transport of MWCNTs were not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports an understanding of the priority research areas presented in this chapter.

Although empirical data on MWCNT concentrations in the environment are lacking, some researchers have used modeling to simulate movement of CNTs through environmental compartments and to derive predicted environmental concentrations (PECs). Mueller and Nowack (2008) used substance flow analysis to model CNTs in air, soil, and water (not sediment) in Switzerland based on simplifying assumptions. PECs were calculated for "realistic" and "high exposure" scenarios and are provided in Table 3-2.

Gottschalk et al. (2009) described a probabilistic material flow analysis framework to derive probability distributions of PECs for engineered CNTs in soil, sludge-treated soil, air, surface water,

sediment, and sewage treatment plant effluent and sludge for the United States, Europe, and Switzerland (see Table 3-2). As noted in Gottschalk et al. (2010), although both studies were designed to estimate PECs in environmental media, the two study designs were quite different and the methodologies used varied considerably, making a direct comparison of PECs difficult. The differences included the model type (deterministic versus probabilistic); model scale [Gottschalk et al. (2009) considered additional environmental compartments (sediment and ground water), more flows associated with these additional compartments, as well as production, manufacturing, and recycling processes]; model input data [newly available model input data were used in Gottschalk et al. (2009)]; and amended categorization of the products and allocation of the CNT mass to the product categories.

Another study employed the USEtox model to carry out a life cycle-based analysis of the aquatic toxicity impacts associated with CNT synthesis (Eckelman et al., 2012). This study used information on the physicochemical properties of CNTs to model fate and transport of CNTs in freshwater systems under "realistic" and "worst-case" or "conservative" scenarios, as described by the authors. Based on information from Gottschalk et al. (2009), the realistic scenario assumed the fraction of CNTs removed from the water column due to clustering and settling to be 90%. For the 10% remaining in the water column, this scenario assumed a CNT exposure factor (defined by USEtox as the dissolved fraction of CNTs in the water column) of 98%, with most of the remaining 2% partitioning to suspended solids. This realistic scenario, which utilized Monte Carlo analysis, calculated a mean residence time in fresh water to be on the order of days. The conservative scenario assumed an exposure factor in the water column of 100% and estimated the freshwater residence time for CNTs as 143 days. This study did not distinguish between single-walled and multiwalled CNTs.

Table 3-2. Predicted environmental concentrations of CNTs using fate and transport modeling.

Medium	Mueller and Nowack (2008)	Gottschalk et al. (2009)[1]
Air (μg/m^3)	1.5×10^{-3} (realistic); 2.3×10^{-3} (high exposure)	1×10^{-6} (United States) 3×10^{-6} (Europe) 8×10^{-6} (Switzerland)
Soil (μg/kg or Δμg/kg-year)	1×10^{-2} (realistic); 2×10^{-2} (high exposure)	5.6×10^{-4} (United States) 1.5×10^{-3} (Europe) 1.9×10^{-3} (Switzerland)
Sludge-treated soil (Δμg/kg-year)	ND	3.1×10^{-2} (United States) 7.4×10^{-2} (Europe) ND (Switzerland)[2]
Surface water (μg/L)	5×10^{-4} (realistic); 8×10^{-4} (high exposure)	1×10^{-6} (United States) 4×10^{-6} (Europe) 3×10^{-6} (Switzerland)
Sediment (Δμg/kg-year)	ND	4.6×10^{-2} (United States) 2.4×10^{-1} (Europe) 2.3×10^{-1} (Switzerland)
Sewage treatment plant (STP) effluent (μg/L)	ND	8.6×10^{-3} (United States) 1.5×10^{-2} (Europe) 1.2×10^{-2} (Switzerland)
STP sludge (mg/kg)	ND	6.8×10^{-2} (United States) 6.2×10^{-2} (Europe) 6.9×10^{-2} (Switzerland)

[1]For Gottschalk et al. (2009), air, surface water, STP effluent, and STP sludge concentrations are modes (most frequent values) from 2008. For soil, sludge-treated soil, and sediment, values are modes that represent annual increases in concentrations (Δμg/kg-year).
[2]In Switzerland, sewage sludge is not applied to soil.
ND = no data

Cullen et al. (2010) simulated subsurface mobility of MWCNTs compared with nanofullerenes (nC_{60}) under a range of hydrologic and geological conditions (homogeneous and heterogeneous) using a two-dimensional finite element model. In general, nanoparticles in systems with the same average hydraulic properties were predicted to be less mobile if the systems were heterogeneous as opposed to homogeneous. For the conditions evaluated, MWCNTs were predicted to be much more mobile compared with nC_{60} because of two factors—nanoparticle shape and size. The smaller, spherical nC_{60} were more efficiently collected on soil surfaces compared with the larger, cylindrical MWCNTs.

Additional Information Highlight Box 8:
Multimedia modeling of MWCNT environmental transport

Multimedia modeling is challenged not only by a lack of empirical data on environmental concentrations of MWCNTs, but also by a lack of knowledge regarding the predominant MWCNT fate and transport mechanisms in specific media and how MWCNT physicochemical properties might impact these processes. For example, although classical filtration theory can model particle transport in soil, additional mechanisms (e.g., deposition, straining) might play an important role in removal of non-spherical, high-aspect colloidal particles, such as CNTs, from suspensions (Mattison et al., 2011). Classical filtration theory, therefore, might not be applicable to CNTs due to the large aspect ratio and unique surface properties of these chemicals. Mattison et al. (2011) tested the suitability of several parameters for describing MWCNT transport in subsurface environments, including porous subsurface media. They concluded that a dual deposition model coupled with site blocking better described MWCNT transport than traditional colloid filtration theory. In developing the dual deposition model, Mattison et al. (2011) used column experiments in the lab and observed that initial mobility in the first pulse of MWCNTs (acid modified with an diameter of 36 ± 11 nm, length of 540 ± 340 nm, and low level of metal impurities) that they evaluated was slower than a conservative tracer (NaBr), although mobility increased relatively rapidly after initial breakthrough. During the second pulse, MWCNT effluent in the sand-packed column reached a near-maximum concentration at the same time as the conservative tracer, and then gradually rose to a maximum value more slowly than the tracer. Smaller grain size of sand or silt (e.g., 50-µm versus 80-µm grains) resulted in slower mobility of MWCNTs through media, while pore-water velocity and ionic strength had fairly limited influence on MWCNT mobility (Mattison et al., 2011). Notably, normalized effluent concentrations of MWCNTs were greater than 60% of the influent concentration. These results (Mattison et al., 2011) differ from results with humic acid-stabilized MWCNTs, which moved more quickly through media than the conservative tracer [(Wang et al., 2008) as cited in Mattison et al. (2011)]. Several recent laboratory studies have shown that humic acids (representing natural organic matter) in peat soil bind to MWCNTs (Tian et al., 2012; Wang et al., 2011), which alters the surface functionalization and electronegative charge and increases sorption of heavy metal ions (Tian et al., 2012). These alterations of surface functionalization could alter transport of MWCNTs through soil. For example, Wang et al. (2008) observed that humic acid-coated CNTs are highly mobile in porous media. Results from these studies suggest that, although empirical data on MWCNT fate and transport outside of the laboratory are lacking, modeling efforts can identify environmental factors such as grain size and media composition that can alter the environmental behavior and physicochemical properties of MWCNTs, which could affect their exposure and toxicity potential for human and ecological receptors.

Chapter 4. Exposure-Dose

Releases of multiwalled carbon nanotubes (MWCNTs) to the indoor and outdoor environments can occur at multiple stages of the product life cycle for flame-retardant upholstery textile coating (Chapter 2). Subsequent transport, transformation, and fate processes dictate how MWCNTs distribute through various environmental media once released (Chapter 3). Exposure describes the pathways through which contact occurs between contaminants in the environment and living organisms and abiotic receptors. Toxicokinetics (i.e., absorption, distribution, metabolism, excretion [ADME]) describes the processes that relate exposure (or dosage) to the internal dose, which refers to the quantity of a chemical or material that is taken up and absorbed by living organisms (U.S. EPA, 2010c).[13]

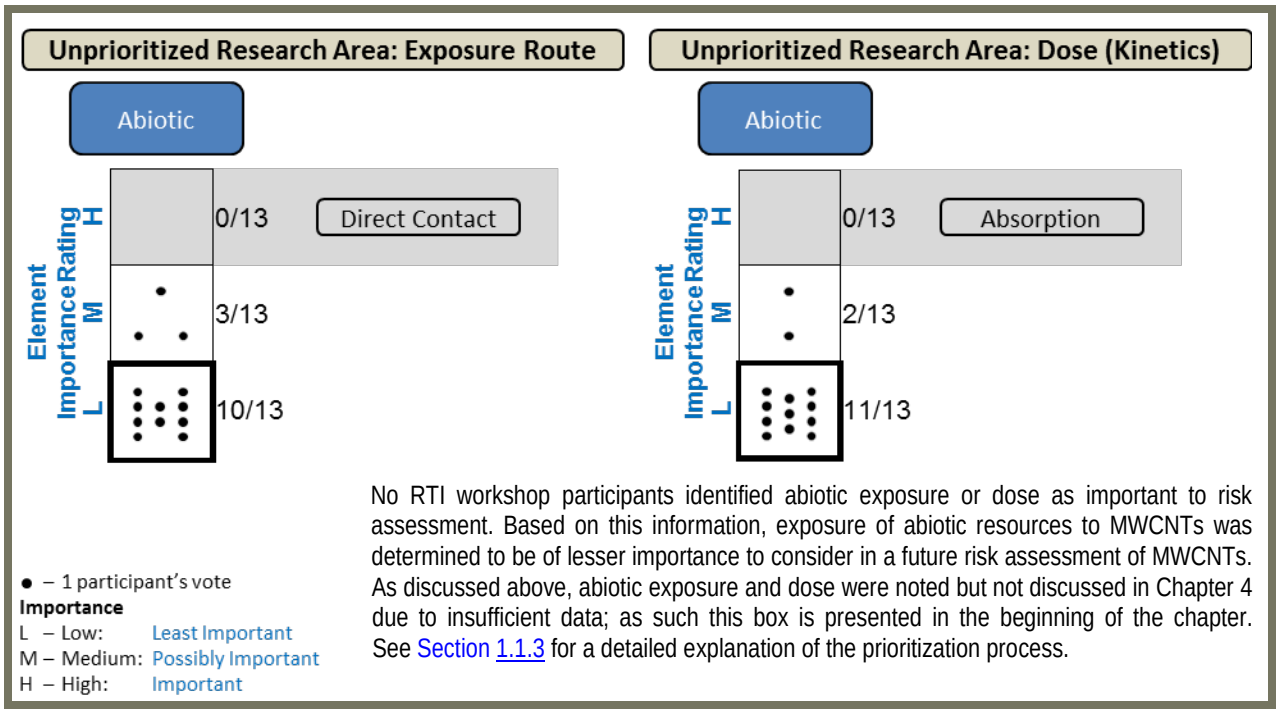
Section 4.1 introduces analytical techniques for identifying, characterizing, and measuring MWCNTs in various matrices. The various metrics recommended for characterizing exposure and dose of MWCNTs are also discussed, and available concentration data in various indoor and outdoor media are presented. In the absence of data quantifying MWCNT exposures at the point of contact, measured concentrations of MWCNTs in surrounding media can be used to estimate exposures using a scenario evaluation approach. Section 4.2.1, Appendix G.4.1, and G.4.2 expand on the release scenarios presented in Chapter 2 to discuss the potential human and ecological exposure pathways that link those releases to receptors. No data were identified regarding relevant exposure pathways leading to impacts on abiotic resources (e.g., the manmade environment); as a result, this comprehensive environmental assessment case study does not include a discussion of exposure scenarios that would influence abiotic receptors. Although broad potential impacts on society and the global environment are discussed in Section 5.3, exposure is either not considered germane to the discussion of the impact (such as for economic impacts of manufacturing MWCNTs) or the exposure characteristics related to the impact are already included in

[13]The term "dose" is described generally by the U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) as "[t]he amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism." Several specific forms of dose are also described by IRIS, but the definitions of these terms are not used consistently across the risk assessment community. The following definitions of specific forms of dose are provided by IRIS: "The POTENTIAL DOSE is the amount ingested, inhaled, or applied to the skin. The APPLIED DOSE is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The ABSORBED DOSE is the amount crossing a specific absorption barrier (e.g. The exchange boundaries of the skin, lung, and digestive tract) through uptake processes. INTERNAL DOSE is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by any particular organ or cell is termed the DELIVERED or BIOLOGICALLY EFFECTIVE DOSE for that organ or cell."

the general discussion that follows (such as for higher potential exposure levels in certain populations related to socioeconomic impacts).

The scenarios described in Sections 4.2.1 and Appendix G.4 describe the conditions under which exposures might occur; this information can be used in combination with measured or modeled concentrations in environmental media from Section 4.1 and exposure factors to estimate exposures. Kinetic information then can be used to determine or estimate the internal dose that results from external exposures. When available, point-of-contact measurements, administered dosages, tissue or body burdens, scenario-specific exposure guidelines and recommendations are provided, and the toxicokinetics of MWCNTs are described in Section 4.2.2 and Appendix G.4.2. Studies describing toxicokinetics of carbon nanotubes (CNTs) in mammals are summarized in Appendix F. Finally, Section 4.4 discusses aggregate exposures to MWCNTs from multiple sources and Section 4.5 discusses cumulative exposures to multiple related stressors.

As described in Section 2.2.4, MWCNTs likely would be incorporated into a polymer or other type of matrix in the flame-retardant formulation applied to upholstery textiles, and both the free and matrix-bound forms might be released during the product life cycle. Very little data relevant to MWCNT exposures, however, have been generated for the matrix-bound form of MWCNTs. This lack of data necessitates a reliance on the existing data for free MWCNTs in the discussion throughout this chapter. The extent to which exposure characteristics and dose implications differ between the free and matrix-bound form of MWCNTs, however, is unknown at this time.



4.1. Detection, Measurement, and Characterization

Neutral Research Area: Environmental Transport, Transformation, and Fate

Detection, measurement, and characterization of MWCNTs—including dose and exposure metrics and concentrations in environmental media (outdoor air, aquatic and terrestrial ecosystems) and indoor environments (occupational, residential, and nonresidential settings)—were not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports understanding of occupational exposure pathway scenarios (see Section 4.2.1) and consumer exposure pathway scenarios (see Section 4.2.2), which were deemed priority research areas.

Exposure scenario evaluation requires information on measured, modeled, or reasonably estimated concentrations of a stressor in exposure media. As introduced in Chapter 1, MWCNTs represent a group of compounds, encompassing substances that span a range of physicochemical characteristics and properties. As a result, developing reliable analytical techniques for detecting, measuring, and characterizing the full range and makeup of MWCNTs in environmental media can present challenges. Text Box 4-1 provides a brief discussion of a few common analytical techniques and the general challenges associated with them. Appendix B summarizes common analytical techniques and presents the strengths and limitations of each technique.

Configurations of MWCNTs vary depending on the type of material or substrate used in their manufacture (see Section 2.2). Text Box 4-2 provides examples of the specific physicochemical properties of MWCNTs that influence exposure, uptake, and dose. Single analytical techniques used alone are generally not sufficient for characterizing all of the properties of MWCNTs that can influence exposure; to characterize the presence and form of MWCNTs in media adequately, multiple analytical methods must be used in tandem (see Text Box 4-1 and Appendix B).

Text Box 4-1. Detecting, Measuring, and Characterizing MWCNTs

Because multiwalled carbon nanotubes (MWCNTs) tend to clump, multiple, orthogonal techniques are recommended to characterize MWCNTs adequately in exposure media (Petersen and Henry, 2012). Analytical techniques for detecting, measuring, and characterizing MWCNTs are summarized in Appendix B. Several detection and quantification techniques are available for MWCNTs in aqueous media, but fewer are available for evaluating MWCNTs in other media. Due to the challenges associated with detecting, measuring, and characterizing very small concentrations of highly reactive and polydispersed particles, successful protocols for extracting MWCNTs from relevant matrices or media (e.g., textiles, polymers, body fluids) could differ from those used to extract traditional compounds for exposure studies based on preliminary, unpublished evidence presented at a public meeting (Uddin and Nyden, 2011a; Uddin and Nyden, 2011b). Additionally, many detection methods rely on knowledge of properties of the material as produced, which can change dramatically during subsequent stages of the product life cycle. Currently, the main application for detection methods is to verify concentrations of as-manufactured MWCNTs during laboratory-based experiments.

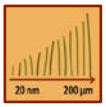
Radioactive labeling is a precise quantification method that works in any medium, but CNTs must be radioactively labeled prior to dispersal in environmental media for this method to work. In aqueous suspensions, the most straightforward method for quantification is gravimetric assessments of suspended materials. The nominal concentration at the start of the study must be known, however, because deviation from that nominal value is what is measured.

The potential for human exposure from upholstery textiles coated with flame retardants is currently difficult to assess because data are not yet available on production of MWCNTs for flame-retardant upholstery textiles (see Section 2.2.4). Furthermore, very little information is available on whether or how MWCNTs might migrate out of a product matrix; or on what methods could be used to quantify exposure concentrations of matrix-bound MWCNTs and partially exposed MWCNTs (i.e., ends of MWCNTs "sticking out" from the matrix). Understanding the behavior of the material requires comparing potentially similar applications. For example, machining of CNT composites and the resultant exposure could be compared to migration of MWCNTs out of textiles and the resultant exposure. The reason for this is that machining of CNT composites could generate particles or fibers similar to those generated from the wear and breakdown of MWCNT textiles, so these studies are useful from an exposure assessment perspective. Estimating exposures during other product life-cycle stages also might be possible by evaluating similar applications or alterations of materials containing MWCNTs. Such assumptions, however, could yield conclusions that are very different from the actual behavior and exposure potential of the MWCNTs in flame-retardant upholstery textile applications.

Text Box 4-2. Specific Physicochemical Properties of MWCNTs Shown to Influence Exposure, Kinetics, and Dose

As introduced in Text Box 1-1, the physicochemical characteristics of multiwalled carbon nanotubes (MWCNTs) can be altered (both intentionally and unintentionally) by using different methods, materials, and processing techniques under different ambient conditions, and these characteristics can change further over the course of the life cycle. Several studies have explored how changes in individual MWCNT characteristics can affect exposure, kinetics, and dose. The following physicochemical characteristics have been identified as contributing to changes in the behavior of CNTs in vitro and in vivo [as summarized by Johnston et al. (2010)]. Because most studies have focused on the inhalation and dermal routes of exposure, data are extremely limited for the oral route.

Dispersion State. Individual CNTs often form larger bundles that range from tightly aggregated (i.e., thick and ropy) to loosely agglomerated (i.e., tangled, like steel wool). Following inhalation, long, well-dispersed CNTs are more likely to deposit deeper in the respiratory tract, where they might be taken up by cells via phagocytosis (i.e., engulfed by the cell membrane). Well-dispersed CNTs are more likely to translocate to other sites following deposition in the lung, leading to a shift in CNT presence from the active airways to the interstitium and alveolar walls, and ultimately to the circulatory system. Up to a certain size limit, bundles of CNTs tend to be more biopersistent in the lung than well-dispersed CNTs, remaining in the conducting airways or entering macrophages at the point of contact. Studies of skin cells (keratinocytes) have also demonstrated that dermal uptake of free MWCNTs can depend largely on the dispersion state of the MWCNTs, with limited uptake in the absence of large bundles.



Morphology. Short (usually defined as <15 µm) CNTs are more readily taken up into cells, but they are also more readily cleared (for example, via macrophages following inhalation). Longer CNTs, on the other hand, are more persistent at the deposition site and might get "stuck" in the cell membrane, resulting in "frustrated" phagocytosis or endocytosis. The length of CNTs might be more important than functionalization, as neutral and positively or negatively charged CNTs are consistently internalized when CNT length remains <2 µm. CNTs engineered with rounded or open ends will also exhibit different uptake mechanisms into cells. CNTs with rounded tips enter cells at a perpendicular angle, whereas CNTs with open ends enter cells parallel to the cell surface (Shi et al., 2011). The ratio of MWCNT length to diameter (i.e., aspect ratio), which can be a relevant exposure metric for fibers like asbestos, can also help predict the deposition sites of CNTs in the respiratory tract, the internalization success of CNTs into cells, the speed at which uptake will occur, and the potential for subsequent translocation. CNTs with higher aspect ratios, for example, are more likely to deposit deeper in the lung, undergo frustrated internalization, take longer to achieve the ideal entry angle into cells, and are more likely to translocate to pleura than CNTs with lower aspect ratios.

Surface Functionalization. CNTs often are treated or complexed with surfactants or other compounds designed to functionalize them for a specific purpose (e.g., remain dispersed in water, interact with specific proteins). Some surface functionalizations can also influence biopersistence of CNTs; for example, some CNTs functionalized to be water soluble will be eliminated rapidly from the body, and CNTs functionalized to interact with specific proteins might be more readily taken up by cells, including macrophages, which contribute to CNT clearance.

Contaminants. Several contaminants can be introduced during the manufacture of CNTs, including metals like iron and nickel and various forms of carbon. Such impurities can "hitch a ride" with the CNTs to a biological surface or interior of a cell, and contaminants that are not trapped within the central cavity of the CNT could be bioavailable. Although purification processes often are used (with mixed success) to remove metal contaminants, these processes tend to alter other characteristics of the CNTs, including length and morphology, which makes isolating the effect of metal adsorbates on receptors difficult.

4.1.1. Dose and Exposure Metrics

Dosages of free MWCNTs usually are expressed or quantified by mass concentration or by particle/fiber count of individual MWCNTs or MWCNT bundles in a particular quantity of a medium over an established period of time (Aschberger et al., 2010; Pauluhn, 2010a). Because exposures to MWCNTs might involve only a small amount of mass but a large number of particles/fibers, the appropriateness of traditional mass-based exposure and dose metrics for estimating and measuring toxicologically relevant doses of engineered nanoscale materials (nanomaterials) is under debate (Aschberger et al., 2011).

Use of time-adjusted, mass-based metrics historically has been the accepted paradigm for quantifying exposure and dose for most chemical substances. For example, mass concentration has been used for more than 50 years as the metric for characterizing aerosol exposures. Recent research has challenged the ability of mass concentration to capture appropriate nanomaterial dose-response relationships, however, by illustrating that airborne nanoscale particles—including both engineered nanomaterials and nanoscale particulate matter—can be more toxic than larger airborne particles of the same composition on a mass-for-mass basis (Maynard and Aitken, 2007). Despite acknowledgment in the scientific community that mass-based dose metrics might not be appropriate for nanomaterials, an alternative unifying metric for characterizing dose has not yet been established, and no single metric appears to be suitable for all nanomaterials or exposure situations (Pauluhn, 2010b; Maynard and Aitken, 2007).

Additional Information Highlight Box 9:
Challenges related to MWCNT toxicokinetics

Although dosages of MWCNTs are often quantified using the standard toxicological practice of mass concentration measurements, this metric might not be appropriate for nanomaterials such as MWCNT (Holgate, 2010). Many nanoscale particles or fibers have greater toxicity on a mass-for-mass basis than larger particles (Maynard and Aitken, 2007). Similarly, free MWCNTs could be more toxic than bundled MWCNTs due to greater surface area-to-volume ratios and kinetic differences that influence distribution of free versus bundled MWCNTs (Johnston et al., 2010; Pauluhn, 2010a). The dose metric (e.g., mass, fiber number, surface area) is particularly important for inhalation exposures. Specifically, free MWCNTs (or those in smaller bundles) are in the respirable range and therefore can interact with biological receptors, with the potential to evoke toxic effects; however, nonrespirable particles (of greater mass) will likely not interact with receptors, and thus will not have the same toxic potential. In addition, larger or bundled particles might be targeted more effectively by macrophages as a part of the immune response (Johnston et al., 2010; Kim et al., 2010). Research supports this relationship: Increasing the mass of bundled MWCNTs causes the bundles to grow larger instead of creating more bundles (Tan and Fugetsu, 2007).

In addition to affecting the dose-response relationship, MWCNT bundling makes it difficult to measure MWCNTs in exposure media (to determine administered dose) and in tissues (to determine absorbed dose and dose uptake) (Chen et al., 2011; Ponti et al., 2010; Monteiro-Riviere and Inman, 2006). Currently available analytical techniques do not provide sufficiently accurate results, so using multiple techniques to characterize MWCNTs is recommended (see Text Box 4-1).

Some research in animal models has shown that toxic effects of some MWCNTs do follow a more traditional dose-related curve based on the administered mass concentration of MWCNTs [for example, Ma-Hock (2009), as described in Section 5.1.3, and Asharani et al. (2008), as described in Section 5.2.1.2], indicating that mass can be considered an appropriate dose metric for some MWCNTs under certain exposure conditions. To what degree variations in other MWCNT characteristics (e.g., length, width, bundling state) influence the appropriate application of mass-based metrics for MWCNTs is not well understood. CNTs might induce toxic effects beyond those expected based on mass concentration, however, which has been demonstrated in comparative tests of nanoparticulate carbon and quartz, commonly used indicator compounds (Donaldson et al., 2006).

Alternative characteristics that have been considered as potentially relevant dose metrics for some nanomaterials include particle size, surface area, surface chemistry, particle count per particle size, and particle charge (Aschberger et al., 2011; Maynard and Aitken, 2007). Although surface area has been shown to be a better dose metric than mass in several rodent studies (Aschberger et al., 2011; Sager and Castranova, 2009; Tran et al., 2000; Oberdorster, 1996), surface area has not been routinely measured or recorded when examining occupational exposures (Aschberger et al., 2011). Calculating surface area after study completion is complicated by the differences in measurement techniques, the dynamic behavior of MWCNTs (i.e., propensity to form bundles), and lack of thorough reporting.

Because the physical form of MWCNTs resembles fibers, other characteristics such as length, diameter, aspect ratio, bundling state, and fiber count have been considered as characteristics potentially relevant to quantifying potential exposures and doses of CNTs. Using fiber count as a dose metric can be challenging, however, because MWCNT fibers generally are not uniform in size, and different sizes might elicit different effects (see Text Box 5-1). The diameters of MWCNTs in general can range from 10 to 200 nm (Hou et al., 2008), and the lengths can vary widely, often by tens of microns (Donaldson et al., 2006).

Bundling also can be a relevant characteristic for considering dose-response relationships. Researchers have noted that MWCNTs tend to form bundles, which then can combine into small "clumps," some of which are nonrespirable (Pauluhn, 2010a). For inhalation exposures, these larger clumps are therefore less toxic than free MWCNTs and MWCNT bundles in the respirable range, despite the larger mass concentration. Characterization of inhalation exposure and subsequent dose based on bundle size or aerodynamic diameter could therefore be more appropriate than characterization based on mass or particle count. Bundling of CNTs also could result in a toxic impact that is not observed with the same mass of dispersed CNTs. For example, bundled CNTs could trigger an immune-system foreign-body response because larger structures are potentially better recognized by macrophages (Johnston et al., 2010) (see Text Box 5-1). In vitro plant assays have shown that clustered MWCNTs fail to disperse

throughout the culture, limiting exposure to a few cells (Tan and Fugetsu, 2007). Increasing the mass of clustered MWCNTs did not increase dispersion, rather this caused the clusters to grow larger and precipitate out of solution but did not cause a higher percentage of plant cells to be affected [Tan and Fugetsu (2007), described further in Appendix G.5.1.1.2].

Aspect ratio, which refers to the ratio of a compound's length to diameter, has been shown by some to be an important characteristic for driving exposure and dose of CNTs (Kim et al., 2011; Poland et al., 2008). The fiber-like structure of CNTs can be considered similar to asbestos, causing many researchers to predict that the toxicity of CNTs will be driven by differences in aspect ratio, with CNTs having higher aspect ratios more frequently depositing deeper in the lungs and translocating to the pleura, where mesothelioma, other cancers, and fibrosis (all effects of asbestos exposures) can occur (Kim et al., 2011) (see Additional Information Highlight Box 13). The utility of morphological parameters like length, width, and aspect ratio for dose quantification is limited, however, by inconsistencies in the literature regarding what constitutes "long" versus "short" or "high aspect ratio" versus "low aspect ratio." These distinctions are usually relative, based on the materials compared in an individual study; specific incremental changes in length, width, or aspect ratio have not yet been correlated to quantitative changes in dose.

Since no single dose metric has been identified to date as capable of accurately predicting the toxicity of MWCNTs, consideration of multiple characteristics together therefore has been proposed as a potential alternative. For example, aspect ratio and bundling state might need to be considered together. Long, thin CNTs (i.e., those with higher aspect ratios) can penetrate deeply into airways, while bundled CNTs are more likely to deposit in the upper airway. Particles in the upper airway can be removed though mucociliary processes, whereas deposits in deeper regions are more likely to persist or translocate from the lung to other tissues where they might shift the location of toxic effects (Johnston et al., 2010).

Measuring potential exposures outside of well-controlled experimental settings—for example, in occupational settings—introduces a different set of challenges that can only be addressed currently by using multiple instruments and analytical techniques. As described in Text Box 4-1 and Appendix B; however, many of the techniques needed for detection, measurement, and characterization of MWCNTs are limited by inadequate levels of detection or restrictive measurement ranges for morphological parameters. For example, a common method for counting fibers in workplace air, the National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods (NMAM) 7400 (NIOSH, 1994), does not detect fibers or bundles with diameters less than 0.25 μm and does not differentiate between MWCNTs and other fibers (Gustavsson et al., 2011). Another method that can be used to estimate MWCNT mass concentrations in workplace air is NMAM 5040 [highlighted in NIOSH (2010)],

but this method measures elemental carbon as a proxy for MWCNTs and does not automatically account for background contributions of other forms of particulate carbon (Birch, 2003).

The metrics primarily used to determine potential exposure levels of MWCNTs in occupational air are total particle count by size fraction, total dust or particle mass, respirable[14] dust or particle mass, inhalable[15] dust or particle mass, total elemental carbon mass, and total or respirable fiber count (Gustavsson et al., 2011). The instruments required to capture these measurements include a suite of real-time, direct monitoring particle samplers and particle counters and a variety of area and personal air filters. The particles and fibers collected by these samplers and filters, however, are not limited to MWCNTs; instead, all particles or fibers within a certain size range are collected and counted, which might lead to overestimation of exposure concentrations. This lack of specificity introduces a degree of uncertainty that can be reduced only with adequate characterization of the samples collected on the filters (Gustavsson et al., 2011). In general, characterization involves a form of electron microscopy to verify morphological features and energy-dispersive spectroscopy to verify the chemical identity of the samples. In summary, most estimates of workplace exposure are derived by relating real-time data on particle or fiber counts with filter samples analyzed to determine particle or fiber mass, particle or fiber morphology, and chemical composition; all analytical techniques involved in this multistep estimation of exposure concentrations have analytical limitations that produce estimates with varying amounts of uncertainty (Dahm et al., 2011a).

4.1.2. Concentrations in Environmental Media and Indoor Environments

As described in the previous section, exposures can be estimated by combining knowledge of concentrations in exposure media with assumptions about contact of humans, biota, or abiotic surfaces with those media. The following sections describe the information available on concentrations of MWCNTs and related substances in environmental media (i.e., air, water, soil).

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[14]The respirable particulate fraction is generally defined as the "fraction of inhaled airborne particles that can penetrate beyond the terminal bronchioles into the gas-exchange region of the lungs" (WHO, 1999). The National Institute for Occupational Safety and Health considers particles with aerodynamic diameters >10 μm to be larger than respirable (Bartley and Feldman, 1998).

[15]The inhalable particulate fraction is generally defined as the "fraction of a dust cloud that can be breathed into the nose or mouth" (WHO, 1999), which could include both particles with sizes within the respirable range and particles that are larger than respirable.

Additional Information Highlight Box 10:
Weaknesses of current analytical techniques

Although analytical techniques for identifying, quantifying, and characterizing MWCNTs are available, they often cannot accurately characterize MWCNTs in complex environmental matrices for several reasons. First, traditional analytical techniques were not developed for application to engineered nanomaterials (such as MWCNTs) at the low concentrations likely to be found in environmental matrices (Petersen et al., 2011b). Second, the chemical transformations that MWCNTs undergo during environmental transport might impede detection by standard analytical methods (von der Kammer et al., 2012). Third, due to the colloidal associations of many engineered nanomaterials (including MWCNTs) in the environment, their physicochemical properties depend on the environment in which they are found (von der Kammer et al., 2012). Finally, the processes involved in isolating, observing, and quantifying engineered nanomaterials could alter the physicochemical properties of the analyte of interest and introduce artifacts (von der Kammer et al., 2012). Appendix B describes some of the specific disadvantages of several analytical techniques for identifying, quantifying, and characterizing MWCNTs in different environmental matrices. Some additional analytical techniques used to detect CNTs (including both single-walled and multiwalled) include: near infrared fluorescence spectroscopy in aquatic systems (Schierz et al., 2012; Rocha et al., 2011); thermogravimetry in complex mixtures such as soot, coastal sediment, and biological macromolecules (Plata et al., 2012b); programmed thermal analysis in surface water, tap water, wastewater, sediments, and various biological matrices (Doudrick et al., 2012); combined programmed thermal analysis/Raman spectroscopy and thermal optical transmittance/reflectance in urban air (Doudrick et al., 2012); and microwave irradiation in agricultural samples (Irin et al., 2012). Although some new analytical techniques are producing promising results, better methods are needed to extract, clean up, separate, and store MWCNTs to improve efficiency, sensitivity, and specificity (von der Kammer et al., 2012). Further, the limited number of studies that use the same analytical technique(s) impedes comparison of results between studies (Petersen et al., 2011b), in a way similar to differences between studies of toxicity outcomes with different types of MWCNTs.

4.1.2.1. Outdoor Air

A recent review of toxicity and exposure to CNTs indicates that ambient exposure to CNTs is possible, but very little outdoor environmental sampling data are available (Aschberger et al., 2010). Dahm et al. (2011a) measured background elemental carbon (inhalable fraction) outside CNT primary and secondary manufacturing facilities. Concentrations ranged from not detected (limit of detection 0.2 to 0.5 µg elemental carbon/filter) to 0.76 $\mu g/m^3$ at MWCNT manufacturing facilities. This information is of limited utility, however, because elemental carbon particles can be produced by many sources, and no electron microscopic analysis was conducted to determine if the particles collected included CNTs.

Researchers have found MWCNTs in methane or propane flames from kitchen stoves, and automotive exhaust is thought to be a source of MWCNTs (Lagally et al., 2012; Aschberger et al., 2010). CNTs were found in the lung tissues of World Trade Center patients following the collapse of the buildings on September 11, 2001, which indicates that dust or smoke in urban environments can contain CNTs (Aschberger et al., 2010).

As summarized in Table 3-2, two life cycle-based models estimated flow of CNTs and other nanomaterials from the products containing them to environmental compartments (Gottschalk et al., 2009; Mueller and Nowack, 2008). The predicted environmental concentrations (PECs) of CNTs in the air were estimated by Mueller and Nowack (2008) as 1.5×10^{-3} and 2.3×10^{-3} $\mu g/m^3$ for the realistic exposure and

high exposure scenarios, respectively; concentrations in airborne dust were not examined. Gottschalk et al. (2009) estimated a mode PEC of 1×10^{-6} µg/m^3 CNTs in U.S. air for 2008. Differences between the models and the resulting estimates are discussed in Section 3.5.

4.1.2.2. Aquatic Systems – Sediment and Surface Water

No data were found on environmental concentrations of MWCNTs in aquatic environments, but as summarized in Table 3-2, two substance flow analyses have estimated PECs of CNTs in surface water (Gottschalk et al., 2009; Mueller and Nowack, 2008). Mueller and Nowack (2008) estimated surface water CNT PECs of 5×10^{-4} and 8×10^{-4} µg/L for the realistic and high exposure scenarios, respectively. Gottschalk et al. (2009) estimated not only a mode PEC of 1×10^{-6} µg/L for CNTs in surface water, but also an annual increase of 4.6×10^{-2} µg/kg-year to U.S. sediment.

4.1.2.3. Terrestrial Systems – Soil

No data were found on environmental concentrations of MWCNTs in surface soil samples, but as summarized in Table 3-2, two substance flow analyses have estimated PECs of CNTs in soil (Gottschalk et al., 2009; Mueller and Nowack, 2008). Mueller and Nowack (2008) estimated soil CNT PECs of 1×10^{-2} and 2×10^{-2} µg/kg for the realistic and high exposure scenarios, respectively. Gottschalk et al. (2009) estimated an annual increase of 5.6×10^{-4} µg/kg-year to U.S. soil.

4.1.2.4. Occupational Settings – Air

No studies were found that measured MWCNT concentrations in air in facilities where textiles containing MWCNTs are manufactured. Multiple studies have collected particles and fibers in workplace air to attempt to estimate MWCNT concentrations at the emission source, in area air, and in the personal breathing zone of workers in small laboratories or research and development facilities (Johnson et al., 2010; Lee et al., 2010; Methner et al., 2010; Bello et al., 2008; Han et al., 2008), as well as in larger pilot plants and manufacturing and handling facilities (Dahm et al., 2011a; Lee et al., 2010; Takaya et al., 2010). Some of these studies are discussed below, and Appendix E, Table E-6 presents additional information on particle, fiber, and MWCNT concentrations for the studies that reported quantitative concentration values associated with MWCNTs.

Concentrations in MWCNT Research Laboratories

Han et al. (2008) measured concentrations of total particles in the area air and personal breathing zones of workers in an MWCNT research facility. Two particle sizers were used to count particles with

sizes ranging from 14 to 630 nm and 0.5 to 20 μm, respectively, and a portable aethalometer measured the mass of carbon black in the total particulate matter in the air. All fibers with aspect ratios greater than 3:1 were collected on filters and analyzed using electron microscopy, and MWCNTs were distinguished from asbestos fibers using energy-dispersive spectroscopy. During the blending process, which creates a uniform size-distributed CNT powder, particulate matter concentrations in the air near the open blender ranged from 434.5 $\mu g/m^3$ without exposure controls to no detection (limit of detection not reported) with exposure controls. The maximum MWCNT number concentration ranged between 172.9 (area air sample) and 193.6 (personal air sample) fibers per cm^3 air during blending without exposure controls, and between 0.018 (personal air sample) and 0.05 (area air sample) fiber per cm^3 air during blending with exposure controls. During weighing and spraying, particulate matter concentrations ranged from 36.6 (area air sample) to 193.0 (personal air sample) $\mu g/m^3$ without exposure controls and from below the level of detection (area air sample; limit of detection not reported) to 30.9 $\mu g/m^3$ (personal air sample) with exposure controls. The maximum MWCNT number concentrations during weighing and spraying were below detection (limit of detection not reported) in the absence of controls, and up to 1.997 fibers per cm^3 air after controls (Han et al., 2008). The reason for the increase in MWCNTs following implementation of exposure controls (in this case, the control was "a simple fan") was not discussed. The maximum MWCNT length observed was 1.5 μm, which is smaller than the World Health Organization's minimum length of 5 μm for classification as a fiber (Aschberger et al., 2010).

Using a suite of real-time particle sizers, particle counters, and filters with electron microscopy and energy-dispersive spectroscopy analyses, Methner et al. (2010) measured and characterized particulate matter in carbon-based nanomaterial research and development facilities. The highest particle number concentration for particles ranging in size from 10 to 1,000 nm was measured when engineering controls were turned off during the opening of an MWCNT growth chamber of a pulsed laser deposition reactor. The maximum particle number concentration was 42,400 particles per cm^3 in the absence of engineering controls, but when the same activity was performed in a sealed system with vacuum exhaust, the particle number was reduced to 300 particles per cm^3 (Methner et al., 2010).

Johnson et al. (2010) used real-time particle sizers to count total particles per liter air for six size cuts (300, 500, 1,000, 3,000, 5,000, and 10,000 nm) and per cubic centimeter air for the cumulative 10- to 1,000-nm size fraction of particles released to the air in a laboratory while two tasks were being performed with raw and functionalized MWCNTs. The first task involved weighing MWCNTs and transferring them to a beaker of stirring water, and the second task involved sonicating a previously mixed solution containing reconstituted water and 100 mg/L MWCNTs with 100 mg/L natural organic matter. Filter samples also were collected at the emission source (i.e., as close as possible to the instruments used for each task) and in area air, and samples were analyzed using electron microscopy and

energy-dispersive spectroscopy. In general, particle number concentrations in the air were inversely proportional to particle size, with either zero or very few particles detected for the 5,000- and 10,000-nm size cuts for both types of MWCNTs used in both tasks. The maximum background-adjusted particle number concentrations for the raw MWCNTs occurred within the 300-nm size fraction; these concentrations were 123,403 particles/L air (above the upper limit of quantification) during weighing and transferring and 42,796 particles/L air during sonication (Johnson et al., 2010). The particle number concentrations measured for the functionalized MWCNTs (MWCNT-OH) exhibited different trends from those for the raw MWCNTs. First, no additional 300-nm particles were detected above the background level during weighing and transferring. Second, particle counts were higher during sonication of functionalized MWCNTs than during weighing and transferring, which is opposite of the trend observed for the raw MWCNTs. Whereas the maximum background-adjusted particle number concentration was 3,065 particles/L air (500-nm size fraction) during weighing and transferring, the maximum concentration was 144,623 particles/L air (above the limit of quantification; 300-nm size fraction) during sonication of functionalized MWCNTs. The particle number concentrations measured for the cumulative 1- to 1,000-nm size range were 1,576 and 2,776 particle/cm^3 air for the raw MWCNTs and 676 and 726 particles/cm^3 for the functionalized MWCNTs during weighing/transferring and sonicating, respectively. Johnson et al. (2010) proposed that the cumulative measurements do not follow the same trends as the size cut measurements because of the inclusion of particles smaller than 300-nm in the cumulative particle counter.

Bello et al. (2008) used a real-time particle sizer and a particle counter to count total particles with sizes ranging from 5.6 to 560 nm and 10 to 1,000 nm, respectively in the area air of a university research laboratory. Personal air samples also were collected on filters and analyzed using scanning electron microscopy and energy-dispersive spectroscopy. Bello et al. (2008) found that removal of MWCNTs from the reactor furnace and detachment of MWCNTs from the nanotube growth substrate during chemical vapor deposition (CVD) did not increase total airborne particle concentrations compared to background. Additionally, no MWCNTs were observed in the personal air sample of a furnace operator (Bello et al., 2008).

In a later study, Bello et al. (2009) measured particulate matter, respirable particulate matter, and respirable fibers in a laboratory during dry and wet machining of composite materials with and without CNTs. Particle sizers were used to detect and count all particles with sizes ranging from 5 nm to 20 μm, and particles and fibers in the respirable range were collected on filters near the source (i.e., 10 cm from the machined composite) and in the breathing zone of the operator; filter samples were analyzed using electron microscopy. Although the dry-cutting process did result in statistically significant increases in airborne particles and fibers, no statistically significant differences were noted in the particle number,

particle sizes, or total dust generated by dry cutting the composites with and without CNTs. Furthermore, analyses of filter samples revealed no single or bundled CNTs in the particles and fibers collected, and no CNTs were observed "sticking out" of the CNT composites (Bello et al., 2009).

Concentrations in MWCNT Manufacturing and Packing Facilities

Dahm et al. (2011a) used a series of filters to measure the inhalable size fractions of elemental carbon and determine CNT and carbon nanofiber "structure" counts (defined as "single CNTs to large agglomerates" viewed using electron microscopy) in the area air and personal breathing zones of six pilot-scale CNT or carbon nanofiber primary and secondary manufacturing facilities. Sampling was conducted while workers performed various tasks, including harvesting, sonicating, weighing, extruding, manually transferring, and mixing MWCNTs; spray coating a product with an MWCNT solution; milling MWCNT composites; and collecting and disposing of waste from MWCNT work areas. The elemental carbon concentrations in the personal breathing zone samples generally were higher than the area air samples. Inhalable elemental carbon concentrations in personal breathing zones ranged from 1.13 $\mu g/m^3$ (sonicating, sieving, and spray coating) to 2.74 $\mu g/m^3$ (harvesting) at the primary MWCNT manufacturing facilities and from 0.8 $\mu g/m^3$ (office work outside lab space) to 7.86 $\mu g/m^3$ (extrusion, weighing, and batch mixing) at the secondary MWCNT manufacturing facilities. The CNT structure counts in the personal breathing zones ranged from 0.010 structure/cm^3 (sonicating, sieving, and spray coating) to 0.399 structure/cm^3 (harvesting) at the primary facilities, and from none observed (weighing, sonicating, milling) to 0.242 structure/cm^3 (extrusion, weighing, and batch mixing) at the primary and secondary MWCNT manufacturing facilities (Dahm et al., 2011a).

Inhalable elemental carbon concentrations in area air samples from Dahm et al. (2011a) ranged from not detected (sonicating, sieving, and spray coating; limits of detection ranged from 0.2 to 0.5 µg elemental carbon/filter) to 4.62 $\mu g/m^3$ (harvesting) and from not detected (weighing, sonicating, milling, and mixing) to 1.01 $\mu g/m^3$ (extrusion, weighing, and batch mixing) at the primary and secondary MWCNT manufacturing facilities, respectively. The CNT structure counts ranged from none observed (production and harvesting) to 0.134 structure/cm^3 (harvesting at a different facility) and from none observed (weighing, milling) to 0.008 structure/cm^3 (extrusion, weighing, and batch mixing) in the area air samples at the primary and secondary MWCNT manufacturing facilities, respectively (Dahm et al., 2011a).

Lee et al. (2010) collected filter samples to measure respirable dust concentrations in the area air and personal breathing zones of workers at three MWCNT manufacturing facilities and four research and development laboratories throughout a normal workday. Fibers with aspect ratios greater than 3:1 were collected on the filters and analyzed using electron microscopy, and MWCNTs were chemically identified

using energy-dispersive spectroscopy. A suite of particle sizers, differential mobility analyzers, and particle counters also was used to count particles with sizes ranging from 14 to 500 nm, and a dust monitor was used to capture number concentrations of particle ranges from 0.25 to 32 μm in diameter. A portable aethalometer measured the mass of carbon black in the total particulate matter in the air. Lee et al. (2010) generally found that the highest increases in particle number concentrations compared to background were observed following the opening of the chemical vapor disposition (CVD) chamber after MWCNT synthesis. Increases in carbon black concentrations at this time were minimal, however, suggesting that most of the particles released were more likely to be metal catalysts than MWCNTs. Furthermore, the authors reported only one measurement of a detectable amount of MWCNTs on one filter from a single facility (0.00312 tube/cm^3); the study authors could not determine whether the lack of MWCNT detection reflected a lack of MWCNTs in workplace air or flaws in the sampling process or analytical methods.

Total dust and respirable dust concentrations were measured in a study of two MWCNT packing facilities, one of which was manually operated and the other automated [(Takaya et al., 2010) English translation available only for abstract]. Total dust concentrations in the area air, of both MWCNT packing facilities, were approximately 240 μg/m^3. Both total and respirable dust concentrations, however, were substantially higher in the manual packing facility (total: 2,390 μg/m^3; respirable: 390 μg/m^3) than in the automated packing facility (total: 290 μg/m^3; respirable: 80 μg/m^3).

4.1.2.5. Residential Settings – Air and Dust

No data were found on concentrations of MWCNTs in household air or dust.

4.1.2.6. Nonresidential Settings – Air and Dust

No data were found on concentrations of MWCNTs in nonresidential air or dust.

4.1.2.7. Transportation, Including Automobiles and Airplanes— Air and Dust

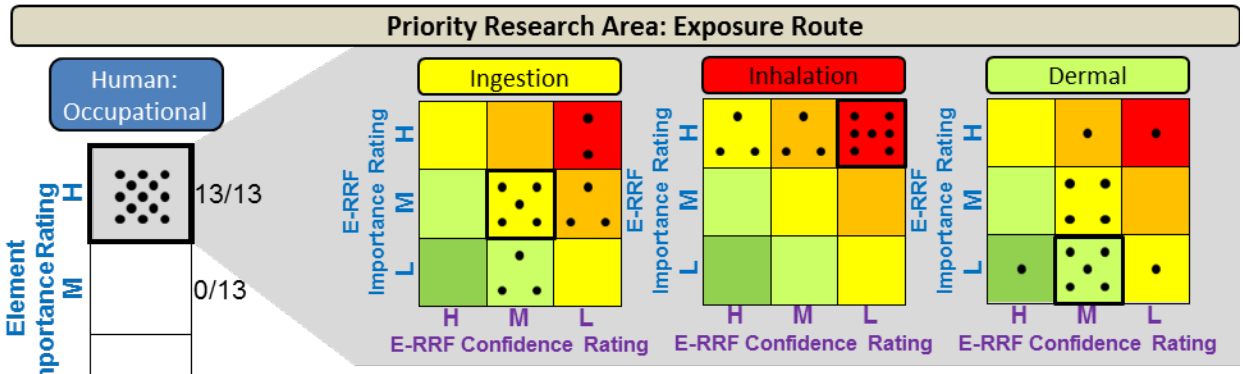
No data were found on concentrations of MWCNTs in air or dust in vehicles or aircraft.

4.2. Human Exposure and Kinetics Leading to Dose

Limited data were found that measured or quantified human exposure to MWCNTs. Data on concentrations of MWCNTs measured in media such as air, soil, or dust in various settings (described in Section 4.1.2), however, can be used in conjunction with activity pattern and other exposure factor data [such as those described in *The Exposure Factors Handbook* (U.S. EPA, 2011b)] to inform estimates of potential exposure through the various exposure pathways and scenario characteristics described in this section.

The types of human exposure scenarios described here can be divided into four broad groups: occupational, consumer, general public, and highly exposed populations. For the purposes of this case study, occupational exposures include occupational exposures during synthesis, processing, or handling of MWCNTs; manufacturing of flame retardants, application of the flame retardants to textiles, or textile finishing and upholstering; storage of the MWCNTs, flame-retardant formulations, treated textiles, or upholstered products; disposal of MWCNTs, flame-retardant formulations, treated textiles, or upholstered products; and repurposing or recycling of treated upholstery textiles and end-user products (e.g., furniture). Consumer exposure scenarios include the intended or unavoidable use of treated upholstery textiles in residential and nonresidential spaces, including on household or institutional/office furniture, in vehicles, and in aircraft; unintended uses of treated upholstery textiles or end-use products such as reuse or repurposing of furniture for something other than its original intended use; or recycling of upholstery textiles for new uses. General public exposure includes primary exposure to members of the community near manufacturing, disposal, or recycling facilities and secondary exposure to the general public through environmental routes such as air, soil, or water. Highly exposed populations refers to exposure scenarios that are expected to occur via similar pathways as outlined for consumers and the general public, but where exposure levels are expected to be higher due to key differences in population characteristics such as those described in *The Child-Specific Exposure Factors Handbook* (U.S. EPA, 2008a).

4.2.1. Occupational Exposure Pathway Scenarios



● – 1 participant's vote

Importance

L – Low: Least Important
M – Medium: Possibly Important
H – High: Important

Confidence

L – Low: Not Confident
M – Medium: Somewhat Confident
H – High: Confident

All 13 RTI workshop participants identified human occupational exposure as important to risk assessment. The 13 participants were asked to rate the importance of ingestion, inhalation, and dermal occupational exposures, as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based on this information, the inhalation exposure route was deemed the highest priority for research in this area, followed by ingestion and dermal exposures. See Section 6.3.3.1 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

The exposure routes through which workers might be exposed to decaBDE (i.e., inhalation, oral, and dermal) are similar across the material synthesis, product manufacturing, storage, and disposal stages of the product life cycle. Certain exposure routes, however, are more likely for occupations that are specific to certain life-cycle stages (e.g., working in material synthesis facilities compared to working in recycling facilities). Industrial hygiene and personal protective equipment can reduce exposure to decaBDE, although workers involved with some life cycle stages might be less likely to take these precautions. No data are available, however, on the relative or estimated amounts of exposure at each life-cycle stage.

- *Inhalation* exposure to decaBDE, by-products, or dust containing the material suspended in air could occur during the stages of material synthesis (e.g., handling decaBDE powders), product manufacturing (e.g., abrading treated textiles during tailoring), storage (e.g., volatilized components of coating, dust), and disposal/reuse/recycling (e.g., abrading or destroying textiles) (EU, 2002).
- *Oral* exposures could occur secondarily from inhaling decaBDE and then subsequently ingesting it or by ingesting decaBDE that deposits from the air onto the skin, food, or food-contact surfaces during all life cycle stages. Dust levels are expected to be higher in textile storage facilities, which could result in increased transport of decaBDE adsorbed to dust and therefore increased potential for exposure during this stage.
- *Dermal* exposures could occur from decaBDE present in dust that deposits on skin or skin-contact surfaces at all life cycle stages. During product manufacturing, the liquid flame-retardant coating could be spilled directly on skin; while during disposal stages, physical contact with decaBDE flame-retardant coating on upholstery textiles also is possible.

Occupational exposures to decaBDE are generally expected to be similar to MWCNT exposure throughout the product life cycle, given the similarity in application (see the DecaBDE Comparison Boxes in Section 2.4 and Section 2.5). Analysis of decaBDE data thus helps identify important research questions that could inform future risk assessments of MWCNTs. For example: Which stages of the MWCNT life cycle present the greatest occupational hazard to those working with MWCNTs and MWCNT products? Is occupational risk of exposure greater by a particular route for each life-cycle stage? Are MWCNTs expected to volatize in air or absorb to dust and deposit on surfaces in manufacturing or disposal facilities? Does modifying physicochemical characteristics of MWCNTs (e.g., aspect ratio, surface functionalization) influence the dominant occupational exposure routes? See Appendix H for more information on occupational exposure to decaBDE.

Limited data were found to determine the extent of occupational exposures to MWCNTs during the material synthesis, processing, and handling phases or to the flame-retardant product during formulation, application, storage, and disposal phases. See Section 4.1.2.4 for MWCNT concentrations measured in occupational settings, which could be applied with the exposure pathways and scenario characteristics described below to estimate potential exposures through scenario evaluation.

Additional Information Highlight Box 11:
MWCNT dermal absorption

Although several studies highlight the potential for dermal exposure to MWCNTs throughout the life cycle of MWCNT flame-retardant coatings in upholstery textiles (Uddin and Nyden, 2011b; Aschberger et al., 2010; Johnson et al., 2010; Lam et al., 2006; Maynard et al., 2004), dermal penetration by MWCNTs has rarely been observed. Numerous studies on applications of other engineered nanomaterials, such as sunscreen formulations containing nano-TiO_2, have shown that although dermal exposure might occur, dermal penetration is unlikely. With few exceptions (Sadrieh et al., 2008; Kertész et al., 2005; Menzel et al., 2004), most dermal penetration studies have found clear evidence that nano-TiO_2 in sunscreen formulations do not penetrate beyond the stratum corneum or hair follicles, and it does not penetrate into living cells of healthy skin (Kiss et al., 2008; Mavon et al., 2007; Pinheiro et al., 2007; Gamer et al., 2006; Lademann et al., 1999; Dussert and Gooris, 1997). In their summary of evidence regarding the interaction of various nanoparticles with skin, Elder et al. (2009) concluded that dermal absorption of nanoparticles does not appear to occur readily but can take place under certain conditions, especially when skin is damaged. Although the behavior of nano-TiO_2 and other nanoparticles cannot be extrapolated to MWCNTs, these findings demonstrate that dermal exposure to engineered nanomaterials, even when the intended use is dermal application (e.g., sunscreen), does not necessarily lead to dermal penetration. Data are lacking, however, on the extent to which modifications to MWCNTs that occur during production (see Additional Information Highlight Box 7) or transformation during subsequent stages of the product life cycle (see Additional Information Highlight Box 6) influence dermal absorption.

4.2.1.1. Synthesis, Processing, and Handling

As discussed in Section 2.2.2, synthesis of MWCNTs is achieved by one of three processes: CVD, arc discharge, and laser ablation. Although many facilities use engineering controls (e.g., fume hoods, closed production systems, high-efficiency particulate air-filtered vacuums) and require workers to wear personal protective equipment (e.g., gloves, respirators, paper face masks, safety glasses, lab coats, Tyvek clean suits) to minimize exposure to MWCNTs (Dahm et al., 2011a), not all facilities comply with the *General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories*, which outlines the recommendations by NIOSH (2012). Many facilities do not employ the same level of protective measures, and in many cases, the filtration technologies and personal protective equipment are not appropriate for or sufficiently protective against exposures to nanomaterials (Dahm et al., 2011a). Therefore, exposure during handling and other operations might still occur, for example, when a reaction chamber is opened to recover MWCNTs; while extracting, weighing, or manually transporting materials; or during maintenance and cleaning of equipment (Dahm et al., 2011a; Fleury et al., 2011; Aschberger et al., 2010). Workers performing each operation are expected to be exposed to peak concentrations of MWCNTs for only a short time while carrying out MWCNT handling tasks, but multiple production cycles might occur within a day, resulting in several opportunities for short-duration, acute exposures

throughout the workday (Dahm et al., 2011a; Lee et al., 2010). Most occupational exposure studies to date have examined these short-duration, task-specific exposures instead of full-shift exposures, and task-specific exposures have been evaluated only for a limited set of handling operations (see Section 4.1.2.4). In general, MWCNTs observed in air and settled on surfaces in occupational environments during synthesis, processing, and handling are in bundled form, but exposure to single MWCNTs is possible (NIOSH, 2010). The pathways through which workers might be exposed to MWCNTs and MWCNT bundles during synthesis, processing, and handling scenarios are described below:

- **Inhalation.** Handling dry powder might be the activity most likely to lead to inhalation exposures during production. Dahm et al. (2011a) and Johnson et al. (2010) observed that workers handling dry powder often turned off vents, hoods, fans and other engineering controls to avoid disturbing and dispersing MWCNTs. Handling processes such as weighing, blending, transfer to containers, or maintenance also could result in inhalation exposure (Dahm et al., 2011a; Fleury et al., 2011; Aschberger et al., 2010).
- **Oral.** Secondary oral exposures might occur if inhaled MWCNTs or MWCNTs that deposit on the skin, food, or food-contact surfaces are subsequently ingested.
- **Dermal.** Particles generated during manufacturing and processing of CNTs can settle on the skin of workers if proper personal protective equipment is not worn (Lam et al., 2006). A study evaluating occupational exposure to CNTs during synthesis, processing, and handling estimated (using adsorbed metals as proxy) that, on average, 0.2 to 6 mg of single-walled CNTs are deposited on the gloves covering each hand of workers during routine operations. Although the cotton gloves worn by workers could have adsorbed more CNTs than bare skin or latex, the study illustrates that dermal exposure to CNTs could occur in laboratory settings (Maynard et al., 2004).

4.2.1.2. Formulation of Flame Retardant, Application to Textiles, Upholstering

No data were found on occupational exposures to MWCNTs during formulation of the flame retardant, application of the flame retardant to textiles, or textile finishing and upholstering. Furthermore, information on the processes for preparing MWCNT flame retardants and for applying them to textiles are lacking. To confer the desired flame-retardant properties of MWCNTs to the textile product, however, MWCNTs must be well dispersed in a polymer medium. To promote dispersion, MWCNTs are sometimes ground or pulverized, which could lead to the release of single MWCNTs or bundles. MWCNTs also might be mixed or sonicated, which could generate airborne water droplets, or mists, containing nanomaterials that then can be inhaled or deposited on surfaces (Fleury et al., 2011; Aschberger et al., 2010; Johnson et al., 2010).

As described in Section 2.2.4.1, one industry representative reported that textiles can be immersed or spray coated with MWCNT flame retardants. The immersion method could result in worker exposures, and exposures are expected to be highest during equipment handling and cleaning. Should

MWCNT flame retardants be sprayed onto textiles, however, MWCNTs in the wet polymer matrix might be released as mists, which can occur even with nonvolatile liquids (U.S. EPA, 2005).

Exposures to MWCNTs also might occur when the treated upholstery textile is machined, drilled (Aschberger et al., 2010), or otherwise abraded during the textile finishing or upholstering processes. Wet machining and dry machining of advanced nanomaterial composite systems were evaluated for generation of respirable CNTs. Wet-cutting methods were not found to produce exposures significantly different from background, while dry-cutting methods created statistically significant quantities of nanoscale and fine particles and fibers composed of the composite material (i.e., no single or bundled CNTs were observed in the samples) (Bello et al., 2009).

Equipment cleaning can be a key contributor to work exposure during product manufacture, application, and upholstering. One study identified equipment cleaning as one of the most important occupational exposure scenarios because it often requires workers to be in direct contact with molten polymers and residues containing CNTs (Fleury et al., 2011).

The pathways through which workers might be exposed to single MWCNTs or MWCNT bundles during general formulation of the flame retardant, application of the flame retardant to the textile, and textile finishing and upholstering scenarios are expected to be comparable to those described in Section 4.2.1.1 on exposures during synthesis, processing, and handling. Additional considerations pertaining to exposures to MWCNTs in combination with polymer ingredients, textile fibers or scraps, or other product constituents during these scenarios are described below:

- **Inhalation.** Spray coating textiles with MWCNT flame retardants could result in inhalation exposures to mists containing MWCNTs embedded in a liquid polymer mixture. Dry-cutting MWCNT-treated textiles during tailoring and upholstering could lead to inhalation of fine and ultrafine particles comprising MWCNT-polymer composites and textile dusts.
- **Oral.** Secondary oral exposures might occur if inhaled MWCNTs in mists and particulate form or the MWCNT mists or particles that deposit on the skin, food, or food-contact surfaces are subsequently ingested
- **Dermal.** MWCNTs in mists and particulate form generated during product manufacturing can land on the skin of workers if proper personal protective equipment is not worn (Aschberger et al., 2010; Johnson et al., 2010; Lam et al., 2006). The liquid flame-retardant coating also can be spilled directly onto the skin.

4.2.1.3. Storage of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products

As described in Appendix G.2.2, MWCNTs and the flame-retardant formulations to which they are added are expected to be stored in sealed receptacles that would limit potential for worker exposures

to these materials during storage. Defective packaging and accidental spills or releases, however, could lead to rare exposures during storage operations.

Although no information was identified regarding procedures for storing treated upholstery textiles, these products are likely packaged to protect them from exposure to elements like water and light that could damage their aesthetics. Such packaging also is expected to limit exposures of workers to the flame-retardant coatings. Once the textiles have been applied as upholstery to end-use products, these products also are expected to be enclosed in protective packaging. Some surfaces of bulkier products (e.g., furniture), however, might remain uncovered, which could lead to worker exposures during storage operations, or exposures might occur during application and removal of packaging materials to and from the product. Dust also can accumulate in storage facilities that frequently store textiles and textile products, and MWCNTs that escape from the product matrix could sorb to dust particles. Ventilation technologies and other contamination-prevention strategies like those used by manufacturing facilities are not expected to be in place in storage facilities. Dust that has settled on surfaces in storage facilities can be disturbed by worker operations, resuspended, and transported to other locations.

Although MWCNTs are not expected to be highly volatile, off-gassing of more volatile components of the treated textiles might occur during storage of treated textiles or upholstered products. Furthermore, due to the additive nature of MWCNT flame retardants, covalent bonding between the flame retardant and the textile does not occur, suggesting that flame-retardant coatings that are loosely attached to the textile surface might slough off during storage or handling. Because MWCNT flame retardants are generally added to the back of the textile, however, the likelihood of this detachment seems low.

No data were found on occupational exposures to MWCNTs during storage throughout the product life cycle of flame-retardant upholstery textile coating. The pathways through which workers might be exposed to MWCNTs alone or MWCNTs in combination with polymer ingredients, textile fibers or scraps, dusts, or other product constituents during storage of MWCNTs and MWCNT flame-retardant formulations are expected to be comparable to those described in Sections 4.2.1.1 and 4.2.1.2 (exposures during synthesis, processing, and handling and during formulation of the flame retardant, application to textiles, and upholstering). The pathways through which workers might be exposed to MWCNT bundles or MWCNTs adsorbed to dust during storage of treated textiles and upholstered products are expected to be inhalation, oral, and dermal. Workers could inhale volatile components of the flame-retardant coating or MWCNTs adsorbed to dust in storage facilities, particularly facilities that are not well ventilated. Higher levels of dust in textile storage facilities could lead to increased transport of MWCNTs adsorbed to dust. This could result in oral exposures to MWCNTs in dust transported to break rooms, homes (via clothes), and other locations where MWCNTs adsorbed to dust can be unintentionally ingested while eating or due to hand-to-mouth activity. Additionally, MWCNTs adsorbed to dust could be

resuspended by worker activities and deposit on the skin of workers if proper personal protective equipment is not worn.

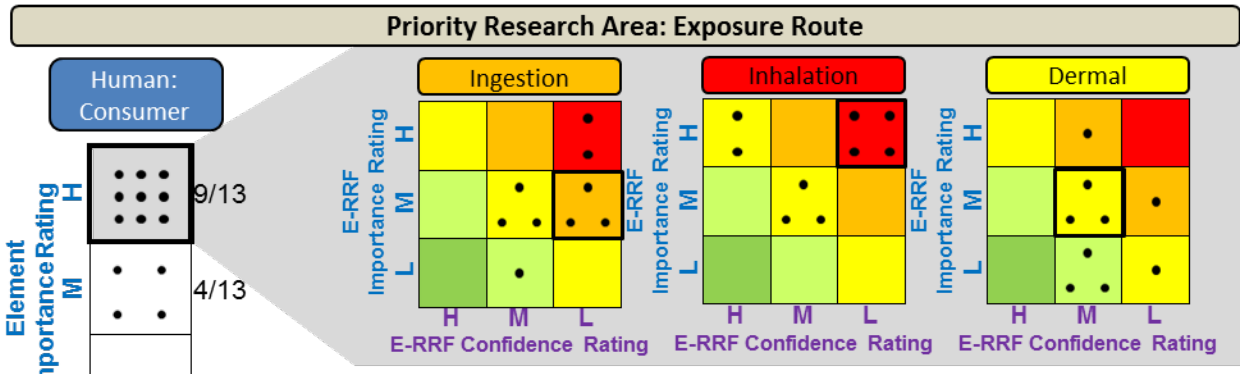
4.2.1.4. Disposal and Recycling of MWCNTs, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products

As described in Section 2.5, large-scale disposal, recycling, and reuse of MWCNTs and the flame-retardant formulations to which they are added are unlikely, but containers used to store these products might enter the waste stream, and workers at disposal and recycling facilities could be exposed to product residues remaining in these containers.

Disposal and recycling of treated textiles and upholstered products, however, is prevalent. Mixing and compacting of waste for land-filling; cleaning, shredding, blending, melting, and spinning scrap textiles for recycling; and incomplete incineration of treated upholstery textiles all could result in exposure of workers to MWCNTs (Chaudhry et al., 2009), primarily in combination with other product constituents and dusts.

No data were found on occupational exposures to MWCNTs during disposal and recycling throughout the product life cycle of flame-retardant upholstery textile coating. The pathways through which workers might be exposed to MWCNTs during general disposal and recycling of MWCNTs and flame-retardant formulations are expected to be comparable to those described in Section 4.2.1.1 (exposures during synthesis, processing, and handling); worker exposure pathways for MWCNTs in combination with polymer ingredients, textile fibers or scraps, or other product constituents during disposal and recycling of treated textiles and upholstered products are expected to be similar to those described in Section 4.2.1.2 (exposures during formulation of the flame retardant, application to textiles, and upholstering) and Section 4.2.1.3 (exposure during storage and distribution) for these products.

4.2.2. Consumer Exposure Pathway Scenarios



● – 1 participant's vote

Importance

L – Low: Least Important
M – Medium: Possibly Important
H – High: Important

Confidence

L – Low: Not Confident
M – Medium: Somewhat Confident
H – High: Confident

Nine out of 13 RTI workshop participants (69%) identified exposure to consumers as important to risk assessment. These nine participants were asked to rate the importance of ingestion, inhalation, and dermal occupational exposures as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based this information, the inhalation route was the highest priority within this area, while ingestion and dermal exposures were lower priorities. In the event of a tie (e.g., importance ratings for dermal exposure routes), the most conservative rating was chosen. See Section 6.3.3.2 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

As with occupational exposures (see the DecaBDE Comparison Box in Section 4.2.1), studies of decaBDE provide insight into possible routes of consumer exposure pathways to MWCNT flame-retardant coatings. During intended use, decaBDE present in upholstered products in residential, commercial, and public settings can be disturbed and released as dust. Research attributes most PBDE intake in toddlers, children, teenagers, and adults to household dust from combined oral and dermal exposure (Johnson-Restrepo and Kannan, 2009). Unintended uses (e.g., repurposing of treated upholstery textiles for clothing) or accidental releases (e.g., mouthing of textiles by children or animals, fire, or high heat) are also possible consumer exposure scenarios; however, no information was identified that directly addresses these potential exposures to decaBDE.

The extent of consumer exposure to decaBDE during intended or unintended use varies based on: differences in living space size and time spent indoors or in rooms where exposure to decaBDE is more likely (Allen et al., 2008b), the presence of new furniture (Rose et al., 2010), and the matrix or textile to which the flame-retardant chemical is applied. Similarly, weathering processes (e.g., UV exposure, abrasion) differ across settings relevant to consumers, such as indoor/outdoor use in homes and in airplanes or cars, and thus influence exposure differences between each type of setting. In planning research to inform future MWCNT risk assessments, considerations might include: Do consumer exposure pathways differ between intended and unintended consumer use? Are nonresidential settings (e.g., aircraft and automobiles) likely to contribute to consumer exposures? Are the MWCNT textile matrices or surface treatments likely to lead to MWCNT in suspended particles during intended use? What unintended uses of MWCNT flame-retardant products might pose a risk to consumers? See Appendix H for more information on human consumer exposure routes for decaBDE.

No studies were found that evaluated the potential for consumer exposure to MWCNTs from any consumer product. As a result, probable consumer exposure pathways and scenario characteristics for exposure to free MWCNTs, bundled MWCNTs, and MWCNTs in combination with the polymer matrix, textile fibers or scraps, or other product constituents cannot be differentiated at this time. As discussed in Chapter 2, different MWCNT flame-retardant production processes are expected to result in differences in release rates and release forms, which in turn will affect the magnitude of exposure during consumer use and the form of the material to which consumers are exposed (Motzkus et al., 2012). Based on the physicochemical properties of MWCNTs, the assumption that MWCNTs and associated substances released from consumer products will be present in the particulate phase is reasonable.

Additional Information Highlight Box 12:
Predicted dominant exposure routes for MWCNTs

Differences in production practices used to incorporate MWCNTs into fire retardants likely will result in different exposure scenarios for consumers, by influencing the magnitude and form of the material to which consumers are exposed (Motzkus et al., 2012) (see Section 1.2.2.2 and Additional Information Highlight Box 7). Based on the physicochemical properties of MWCNTs, MWCNTs and associated substances likely would be released from upholstery textiles in the particulate phase, in a manner similar to BDE-209 (Nowack et al., 2012) (see Section 3.1 and Appendix H.3.1). Yet, the primary exposure pathway(s) for consumers will vary depending on the types of upholstered products into which the MWCNTs are incorporated. No studies were found in the literature that evaluated the potential for human exposure to free or matrix-bound MWCNTs from any consumer product; however, because releases of MWCNTs in the particulate phase are expected to be similar to BDE-209 releases, inferences can be drawn from PBDE data to provide indications of primary exposure pathways for upholstery textiles in different scenarios (see the DecaBDE Comparison Box above, [in this Section 4.2.2]). Based on information from decaBDE and MWCNTs, predominant routes of exposure in consumer populations are likely to be oral and dermal in residential and nonresidential spaces and in transportation vehicles (e.g., automobiles and aircraft). During unintended uses, inhalation and dermal exposures are the likely primary exposure routes, with secondary oral exposure as the secondary exposure route. See Section 4.2.2 for more information on each consumer exposure scenario for MWCNTs in flame-retardant coatings applied to upholstery textiles.

4.2.2.1. Intended Use – Upholstered Products in Residential Spaces

Although flame-retardant upholstery textiles typically are used in nonresidential settings (see Section 4.2.2.2), some residential upholstered products, particularly mattresses, are known to contain flame retardants, and other upholstered furniture products, like couches, sometimes might be treated with flame retardants (Rose et al., 2010). As introduced in Section 2.4, upholstered products are expected to be used for many years, and contact with the textile might be frequent and prolonged, which could introduce substantial wear and tear to the textile product. In addition, upholstery in residential spaces might frequently be exposed to cleaning products, sweat, food, and other substances that could affect the properties of the textile and the flame-retardant coating.

The pathways through which consumers might be exposed in residential settings to MWCNTs during general consumer use scenarios for end products upholstered with MWCNT flame-retardant coatings are described below:

- **Inhalation.** Chronic inhalation of MWCNTs in combination with other product constituents and dust could occur following release from upholstered products over time (due to wear and tear from anticipated use, aging of materials, abrasion, UV light, water, cleaning chemicals, among other factors; see Section 2.4.2). MWCNTs could settle onto surfaces, where they might be disturbed and re-entrained, after which they could be inhaled by residents. Whether inhalation is a primary route of consumer exposure for MWCNTs, particularly when embedded in a polymer matrix, is unknown.
- **Oral.** MWCNTs in combination with other product constituents and dust could be ingested after settling on food and food-contact surfaces or following hand-to-mouth activity. Whether ingestion is a primary route of consumer exposure for MWCNTs, particularly when embedded in a polymer matrix, is unknown. Preliminary, unpublished studies presented at a public meeting indicate, however, that MWCNTs could be released from flame-retardant barrier fabrics and polyurethane foams in very small amounts during normal wear and tear (Uddin and Nyden, 2011b); these MWCNTs could settle onto food, food-contact surfaces, or other surfaces where children could be exposed via hand-to-mouth activity during use.
- **Dermal.** Dermal exposure to MWCNTs in combination with other product constituents and dust might occur while touching the textile surface (particularly if the portion of the textile that has been treated with the flame-retardant coating is exposed) or touching surfaces upon which particles have settled. Whether dermal uptake is a primary route of consumer exposure for MWCNTs, particularly when embedded in a polymer matrix, is unknown. Preliminary, unpublished studies indicate, however, that MWCNTs could be released from flame-retardant barrier fabrics and polyurethane foams in very small amounts during normal wear and tear; these MWCNTs could contact skin directly during use (Uddin and Nyden, 2011b).

4.2.2.2. Intended Use – Upholstered Products in Nonresidential Spaces

Due to regulations requiring that upholstery textiles used in nonresidential settings pass flame-retardancy tests (see Table 1-3), many upholstery textiles in public, commercial, and institutional settings are treated with flame retardants. The characteristics of the different settings in which these products are used can vary considerably. For example, flame-retardant upholstery textiles might be used in seating for airports and other transportation hubs and in waiting rooms, office buildings, penal institutions, and other nonresidential spaces that can range from very small to very large and where consumers might spend varying amounts of time. Some scenarios for nonresidential exposures are not likely to differ from those expected from residential exposures, but a few key differences do exist. For example:

- Exposures to flame-retardant upholstery coatings in public spaces might be unavoidable. Although consumers have some control over which products they bring into their home, consumers have no control over the products they encounter in public spaces.

- Some nonresidential exposures might occur over long periods of time and for extended intervals (e.g., sitting in the same office chair every day over the course of several work years), while some might occur infrequently and for short periods of time (e.g., sitting in seating at the airport waiting for a flight).
- Products in public spaces might experience higher activity levels, more frequent cleaning, and less care to the textile surface, all of which could damage or weaken the textile matrix and influence releases and exposures.

With the exception of these potential differences in exposure settings and activity patterns, the pathways and scenarios through which consumers might be exposed in nonresidential settings to MWCNTs during general consumer use scenarios for end products upholstered with MWCNT flame-retardant coatings are not expected to differ from those described previously in Section 4.2.2.1 on exposures from intended use of upholstered products in residential spaces.

4.2.2.3. Intended Use – Aircraft and Automobile Upholstery

Flame-retardant upholstery can be used for seating, draperies, carpets, and other textiles in passenger cars and public and private transportation.

The pathways through which consumers might be exposed in vehicles (including airplanes) to MWCNTs during general consumer use scenarios for end products upholstered with MWCNT flame-retardant coatings are described below:

- **Inhalation.** Inhalation of MWCNTs adsorbed to dust from worn or abraded automobile upholstery is expected to occur. The recirculation of air in aircraft cabins also might affect exposure to MWCNTs, if filters do not adequately remove these particles.
- **Oral.** Secondary oral exposures might occur if inhaled MWCNTs or MWCNTs that deposit on the skin are subsequently ingested.
- **Dermal.** Dermal exposures to MWCNTs are expected to occur, particularly when skin touches the treated part of the textile directly. Dermal exposure also can occur when particles in the air settle on the skin. Different exposure characteristics or scenarios (e.g., children sitting in safety seats) might influence whether dermal exposure occurs, or influence the extent to which exposure occurs through this pathway.

4.2.2.4. Unintended Use, Repurposing, or Reuse of Treated Textiles and Upholstered Products

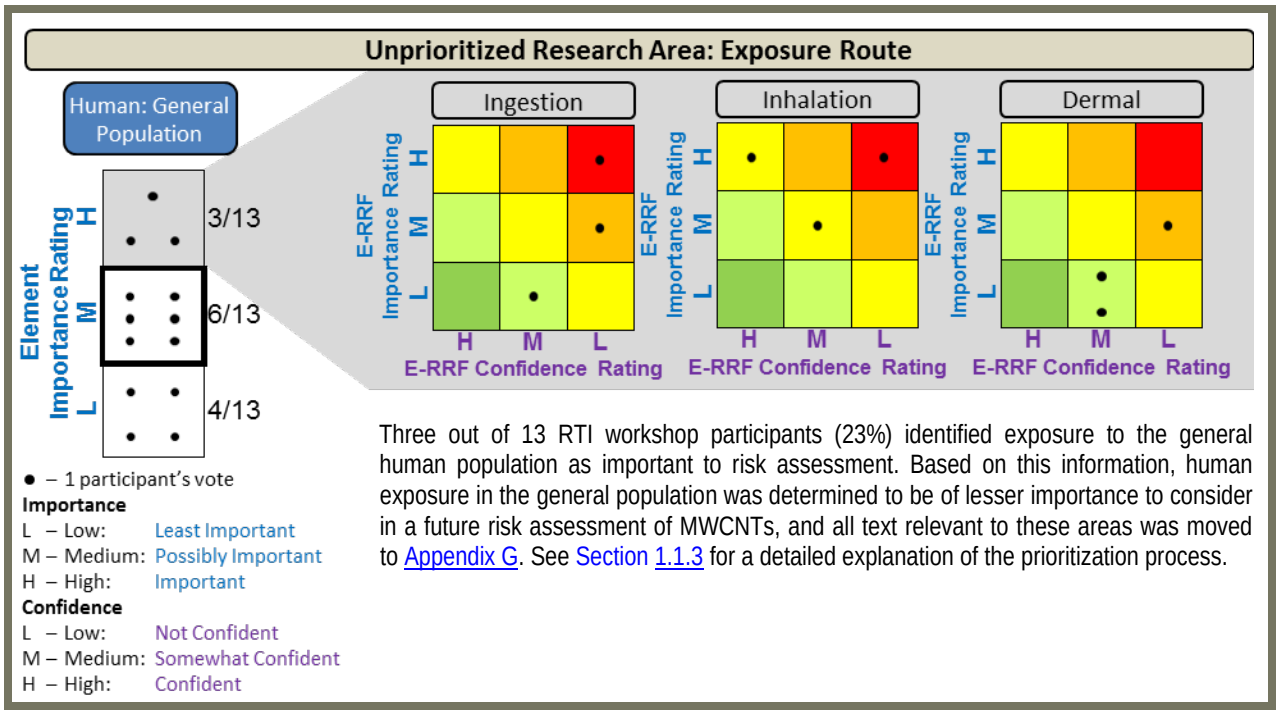
As introduced in Section 2.4, unintended uses of upholstery textiles treated with MWCNT flame-retardant coatings could include repurposing of treated upholstery textiles for clothing, building insulation, other in-home or outdoor furnishings, bedding, or other purposes. The repurposing stages could introduce occupational exposures similar to those discussed in Section 4.2.1.2 (exposures during formulation of the flame retardant, application to textiles, and upholstering) and Section 4.2.1.3 (exposure during storage and distribution), as products that are treated with flame-retardant coatings are broken down and reprocessed into new products.

Although no information was identified that directly addresses potential consumer exposures following unintended use or reuse of flame-retardant upholstery textiles, exposure pathways and scenarios from other life-cycle stages are relevant here. Most reuse scenarios might differ little from those for anticipated consumer uses, but a few key differences might occur, particularly when products are repurposed for new uses or used in unintended ways. For example:

- Similar processes to those involved with product manufacture (e.g., cutting, sewing) and storage of textiles also might be employed for repurposing treated textiles. In this scenario, however, these processes are not expected to occur in an occupational setting, but in the home or another private space, where no personal protective equipment is worn and limited control technologies are used. These processes, as employed for repurposing textiles, however, are not expected to occur as commonly or at the same scale as in a manufacturing facility.
- Older, more degraded textiles with weakened matrices might be handled directly and subjected to abrasion, thereby releasing the product constituents in the vicinity of the consumer conducting the repurposing.
- Although dermal contact with products used for their intended purpose (e.g., furniture seating) might be limited by a clothing barrier between the consumer and the treated textile, should flame-retardant upholstery textiles be repurposed into clothing, direct dermal contact might occur repeatedly over long periods of time.

With the exception of these potential differences in exposure characteristics, the pathways and scenarios through which consumers might be exposed to MWCNTs during repurposing, reuse, or unintended use of treated textiles and upholstered products are not expected to differ from exposure pathways associated with the cutting, tailoring other abrasive processes involved with product manufacturing (Section 4.2.1.2); storage of textile products (Section 4.2.1.3); and consumer use in residential and nonresidential spaces (Sections 4.2.2.1 and 4.2.2.2).

4.2.3. General Public Exposure Pathway Scenarios through Environmental Media



4.2.4. Highly Exposed Populations

Neutral Research Area: Exposure Route

Populations with high exposure to MWCNTs were not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports understanding of occupational exposure pathway scenarios (see Section 4.2.1) and consumer exposure pathway scenarios (see Section 4.2.2), which were deemed priority research areas.

Occupation could increase exposure to MWCNT relative to the general population. In occupational settings, the primary exposure pathway for MWCNTs is likely to be inhalation. Consumer exposure pathways might be similar to those identified for decaBDE, namely ingestion of household dust, but MWCNTs are less likely to be released from the polymer matrix (see Section 2.4.2; see Appendix H for detailed information regarding decaBDE). Given the lack of data on consumer exposure to MWCNTs, whether the primary route of exposure for highly exposed populations would be different from that of decaBDE is difficult to determine. Dust levels in the home can vary by socioeconomic status or the type and condition of housing (see Section 5.3.1). In turn, disproportionate levels of exposure can occur in specific populations, including low-income and low-educational-attainment populations. Additionally, for

pollutants for which inhalation exposure due to proximity to primary pollution sources is of concern, socioeconomic status has been associated with increased exposures, which also might be true for MWCNTs. Race and ethnicity do not present specific physiological conditions to increase susceptibility to exposure, but demographic factors such as socioeconomic and educational status might cause some populations to experience disproportionate exposures. The possibility of increased exposure to MWCNTs due to characteristics associated with low socioeconomic status has not yet been explored in the literature.

In general, children are more susceptible to increased inhalation exposures because of increased ventilation rates per unit of body weight and increased oral exposures due to hand-to-mouth and chewing (e.g., mouthing furniture or fabric) behaviors. The relevance of the inhalation and oral pathways for MWCNT consumer exposures, however, is unknown. In addition, lack of data on whether MWCNTs, if released from flame-retardant textiles, would partition to dust precludes a determination of whether children might experience elevated oral exposures to MWCNTs similar to those observed for decaBDE.

4.2.5. Exposure Reference Values and Recommendations

Neutral Research Area: Exposure Route

Exposure reference values for MWCNTs and recommendations from agencies or organizations were not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports an understanding of occupational exposure pathway scenarios (see Section 4.2.1) and consumer exposure pathway scenarios (see Section 4.2.2), which were deemed priority research areas.

A variety of exposure standards, guidelines, or recommendations are developed by different organizations with purview over specific portions of the population or situations during which exposure might occur (e.g., occupational exposures, general population drinking water exposures). Available information on these types of values for MWCNTs is presented below. Section 5.1.1 discusses how some of these values inform quantitative toxicity assessments.

MWCNTs can have features of both nanoparticles and fibers, and regulations exist to control particles and fibers in the workplace. MWCNTs can appear as clumps or ropes, which can be counted as single fibers if they fit the definition of a fiber. If the rope is not within the World Health Organization's definition of a fiber (greater than 5 μm in length, with an aspect ratio greater than 3:1), however, it would not be counted as a fiber under the current measurement system. Some MWCNTs could therefore be missed using current fiber classification methods (Donaldson et al., 2006).

Recently, NIOSH conducted a risk analysis for CNTs to establish a guideline exposure level for occupational workers (NIOSH, 2010). They estimated a working lifetime inhalation exposure of 0.2–2 $\mu g/m^3$ (8-hour time-weighted average) associated with a 10% excess risk of early-stage adverse

lung effects (95% lower confidence limit estimates) based on two subchronic animal inhalation studies (Pauluhn, 2010b; Ma-Hock et al., 2009) (see Section 5.1 for human health effects). The NIOSH-recommended exposure limit is 7 μg/m^3 for elemental carbon (see Table 4-1) as an 8-hour time-weighted average respirable mass airborne concentration (NIOSH, 2010). NIOSH also recommends that workplace airborne exposure to CNTs be measured by NIOSH NMAM 5040, which has an upper limit of quantitation of 7 μg/m^3 (NIOSH, 2010). Specifically, the animal-data-based risk estimates indicate that workers could have >10% excess risk of developing early-stage pulmonary fibrosis if exposed over a full working lifetime at the upper limit of quantitation for NIOSH NMAM 5040 (NIOSH, 2010). Other recommended occupational exposure limits (OELs) and general human health exposure limits for inhalation of MWCNTs and related materials are shown in Table 4-1.

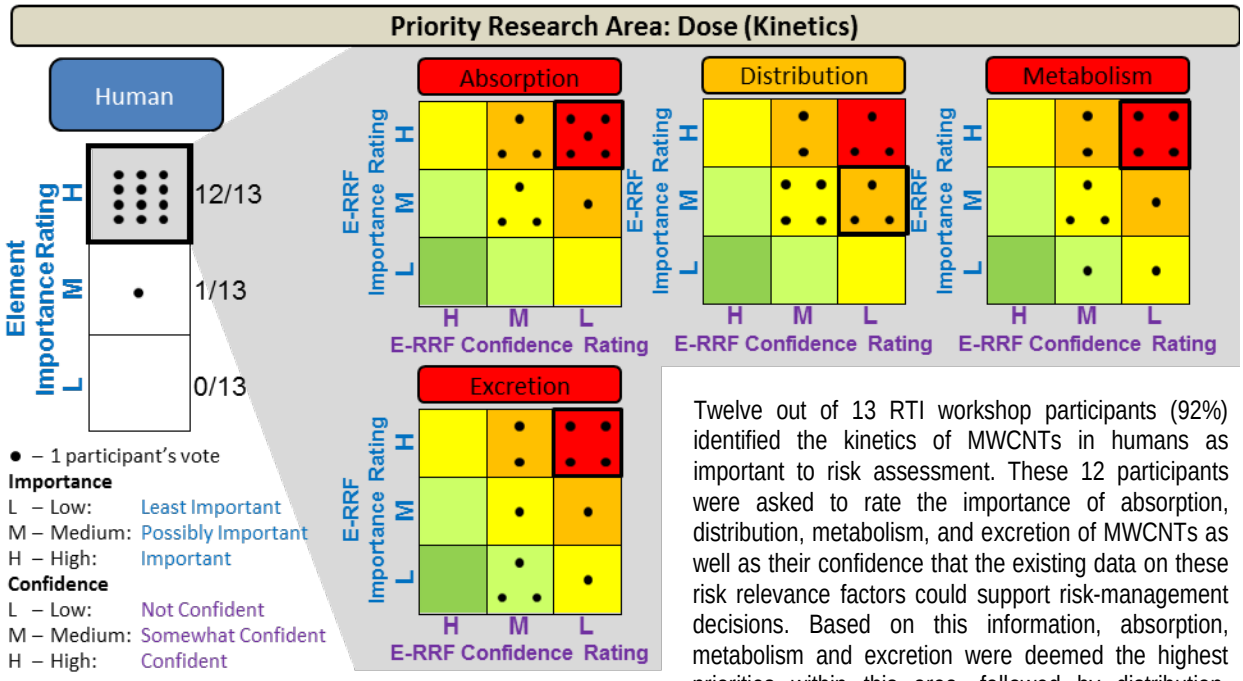
As discussed by Schulte et al. (2010), deriving OELs for MWCNTs and other nanomaterials is complicated by the challenges associated with measuring workplace exposures (see Text Box 4-1), coupled with the variation in configurations of physicochemical properties that can influence exposure and toxicity (see Text Box 4-2). The heterogeneity in MWCNT configurations could necessitate developing OELs specific to individual formulations of MWCNTs (Schulte et al., 2010). Alternatively, OELs could be developed for groups of nanomaterials based on composition or toxic mechanism, although such classifications could exclude physicochemical characteristics that influence biological activity (Schulte et al., 2010).

Table 4-1. Established inhalation reference values and recommendations applicable to MWCNTs.

OEL		Value	Reference
The Occupational Safety & Health Administration – permissible exposure limit (PEL) for respirable fraction of synthetic graphite		5,000 μg/m^3	Lam et al. (2006)
A review of CNT toxicity – human inhalation no-effect levels for workers derived from acute and subchronic inhalation studies with MWCNTs	$INEL_{acute}$	150 μg/m^3	Aschberger et al. (2010)
	$INEL_{chronic}$	1 μg/m^3 and 2 μg/m^3	
Bayer Pharmaceuticals – estimated OEL for TWA (6 hours/day, 5 days/week, 13 weeks) exposure to Baytubes® based on a no-observed adverse-effect level of 0.1 mg/m^3 divided by an inter-species dose-time adjustment factor of 2		50 μg/m^3	Pauluhn et al. (2010a)
NIOSH – recommended exposure limit for elemental carbon as an 8-hour TWA respirable mass airborne concentration		7 μg/m^3	NIOSH (2010)
Nanocyl – estimated OEL for an 8-hour TWA exposure to MWCNTs based on applying an overall assessment factor of 40 to the lowest-observed-adverse-effect level of 0.1 mg/m^3 in Ma-Hock et al. (2009)		2.5 μg/m^3	Nanocyl (2009)
Japanese New Energy and Industrial Technology Development Organization – Interim OEL for MWCNTs based on unpublished data by unpublished study		3.0 μg/kg-day	Kobayashi et al. (unpublished) as cited in NIOSH (2010)
British Standards Institute – benchmark exposure limit based on one-tenth of the Institute's asbestos exposure limit		0.1 fiber/cm^3 air	BSI (2007) as cited in NIOSH (2010)

TWA = time-weighted average

4.2.6. Toxicokinetics, Dose, and Body Burden



Twelve out of 13 RTI workshop participants (92%) identified the kinetics of MWCNTs in humans as important to risk assessment. These 12 participants were asked to rate the importance of absorption, distribution, metabolism, and excretion of MWCNTs as well as their confidence that the existing data on these risk relevance factors could support risk-management decisions. Based on this information, absorption, metabolism and excretion were deemed the highest priorities within this area, followed by distribution. See Section 6.3.3.3 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

The toxicokinetics of MWCNTs is neither well understood (see Sections 4.2.6.1 and 4.2.6.2, and Additional Information Highlight Box 14), nor expected to be similar to that of decaBDE, but the toxicokinetic questions that have been asked about BDE-209 can help inform research planning for MWCNTs. When planning research to inform future risk assessments of MWCNTs, investigators might consider the differences between acute and chronic studies or species, as well as other findings with decaBDE, for instance: How are MWCNTs absorbed, distributed, metabolized, and excreted across various exposure routes and durations? Does the type of solvent or dispersant used influence toxicokinetics of MWCNTs? Do these processes differ across species? Is bioaccumulation over an extended period of time possible? Do MWCNTs distribute to fetuses or neonates following in utero or early life exposures? See Appendix H for more information regarding the toxicokinetic behavior of decaBDE and BDE-209.

Toxicokinetics can be used to relate exposure and contact, such as those described in the scenarios above, with uptake and dose. Specifically, toxicokinetics describes how a material is absorbed, distributed, metabolized, and excreted in an organism. An understanding of the relationship between each of these concepts, which are often referred to as ADME, leads to an understanding of the concentration, or dose, of material that can reach—and potentially accumulate in—different tissues of the body.

4.2.6.1. Absorption, Distribution, Metabolism, Excretion

This section contains information regarding the toxicokinetic behavior of MWCNTs when administered to mammals. Information regarding birds and fish is not presented in this section because, when extrapolating toxicokinetic data to humans, studies conducted with rodents (rat or mouse) or nonrodent mammals (dog or monkey) are generally used. Additionally, the toxicokinetic behavior in response to MWCNTs might differ among birds, fish, and mammals. See Section 4.3 and Appendix G.4.2 for toxicokinetic information relevant to ecological exposures. Studies examining the toxicokinetics of MWCNTs in mammals are summarized in Appendix F.

As discussed in Section 4.2.2, humans might be exposed to free MWCNTs, bundled MWCNTs, and MWCNTs in combination with a polymer matrix, textile fibers or scraps, or other product constituents. The bioavailability (and therefore dose) of MWCNTs is expected to differ for MWCNTs in different forms or bundling states (see Text Box 4-2). In general, CNTs, including MWCNTs, appear to be biopersistent. After intratracheal administration, MWCNTs have been observed to deposit and persist within the lung for up to several months (Elgrabli et al., 2008b; Deng et al., 2007). Macrophage-mediated clearance of MWCNTs after exposure via inhalation (Elgrabli et al., 2008a) and translocation of some types of CNTs into the pleura and subpleura (Porter et al., 2010; Ryman-Rasmussen et al., 2009a) have been demonstrated. After oral exposure, most MWCNTs (administered at 10 µg/mouse by gavage) were evident within the feces and also remained within the stomach and small and large intestines, with no detectable transport into the blood or obvious metabolism through 28 days (Deng et al., 2007). Because only one study was identified that evaluated distribution after oral exposure, whether distribution is possible to other organs in the body following inhalation, dermal, and oral exposures to MWCNTs is not well understood.

Distribution of CNTs to various organs has been reported following intravenous exposure (Deng et al., 2007; Cherukuri et al., 2006), with predominant localization within the liver, lungs, and spleen. This pathway, however, is not likely relevant for the exposures of concern in this evaluation (i.e., MWCNTs used in flame-retardant coatings on upholstery textiles are unlikely to be intravenously applied).

4.2.6.2. Internal Dose and Body Burden

Based on toxicokinetic studies with rats, inhaled MWCNTs can remain in the lung following exposure for an extended period, up to six months (Aschberger et al., 2010). These studies reported qualitative data, however, and no studies were found that reported levels of MWCNTs in the lung. One study did report MWCNTs in the subpleura of mice following a single inhalation exposure to 30 mg/m^3;

no MWCNTs were detected in the subpleura following instillations of a lower concentration (1 mg/m^3) (Ryman-Rasmussen et al., 2009a). Another study reported MWCNTs with known length just under 4 μm in the pleura of mice following a single aspiration of 10–80 μg (Porter et al., 2010). This finding is notable because the pathogenic mechanism of asbestos fibers in the mesothelioma disease process occurs in the pleural cavity (Aschberger et al., 2010).

No detectable amounts of MWCNTs were observed in the blood following oral exposure in mice, but the MWCNTs did remain in the stomach and small and large intestines (Deng et al., 2007); the observed MWCNTs remained unchanged (Aschberger et al., 2010). As discussed in Section 4.2.6.1, MWCNTs were distributed to multiple organs following intravenous injection (Deng et al., 2007; Cherukuri et al., 2006), but this exposure pathway is unlikely to be relevant for this case study.

4.3. Ecological Exposure and Kinetics Leading to Dose

4.3.1. Factors Impacting Ecological Exposure

Neutral Research Area: Exposure Route

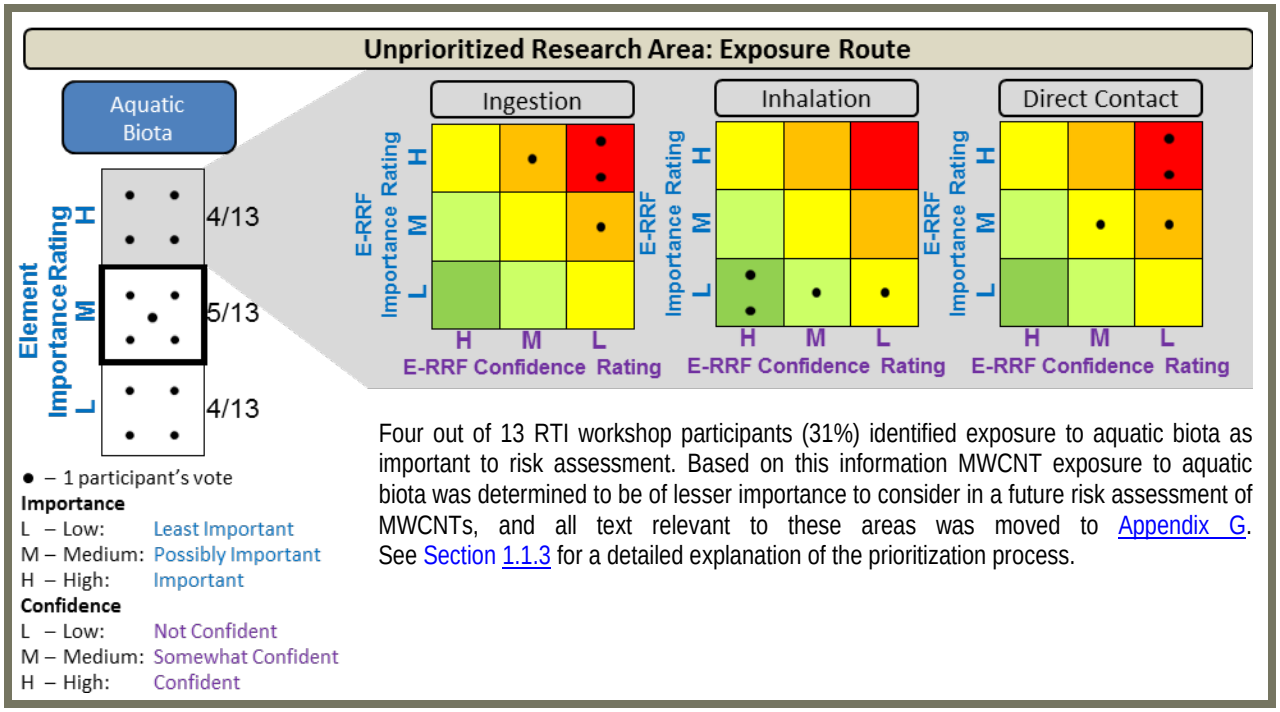
Factors impacting ecological exposure (e.g., properties of the environmental media and physiological and behavioral characteristics of aquatic and terrestrial organisms) were not considered during the RTI collective judgment prioritization process. Since this section of text supports understanding the unprioritized areas of exposure in aquatic and terrestrial biota, this text is now included in Appendix G.4.2.1. See Appendix H.4.3.1 for a similar discussion relevant to decaBDE.

4.3.2. Absorption, Distribution, Metabolism and Excretion in Ecological Receptors

Neutral Research Area: Dose (Kinetics)

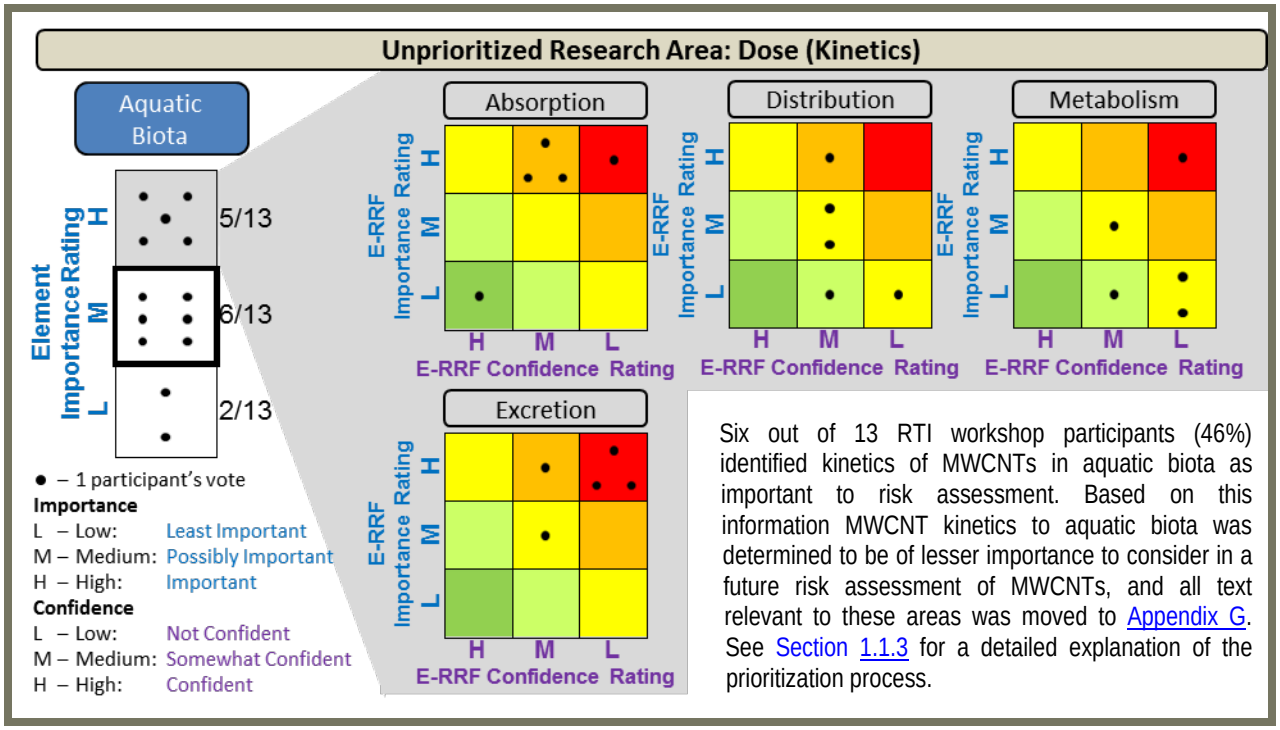
General factors influencing absorption, distribution, metabolism and excretion (ADME) processes in aquatic and terrestrial biota were not considered during the RTI collective judgment prioritization process. Because this section of text supports understanding the unprioritized areas of dose (kinetics) in aquatic and terrestrial biota, this text is now included in Appendix G.4.2.2. See Appendix H.4.3.2 for a similar discussion relevant to decaBDE.

4.3.3. Exposure Pathways in Aquatic Systems



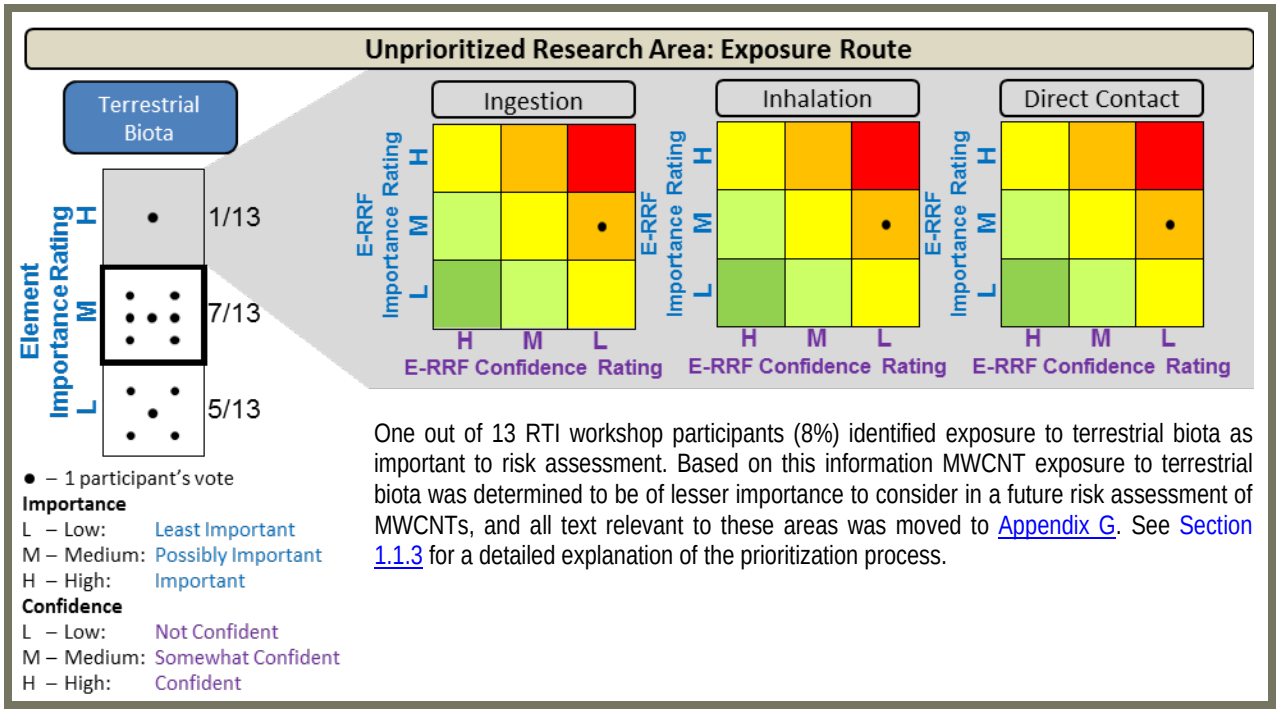
Four out of 13 RTI workshop participants (31%) identified exposure to aquatic biota as important to risk assessment. Based on this information MWCNT exposure to aquatic biota was determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

Toxicokinetics and Body Burden in Aquatic Systems



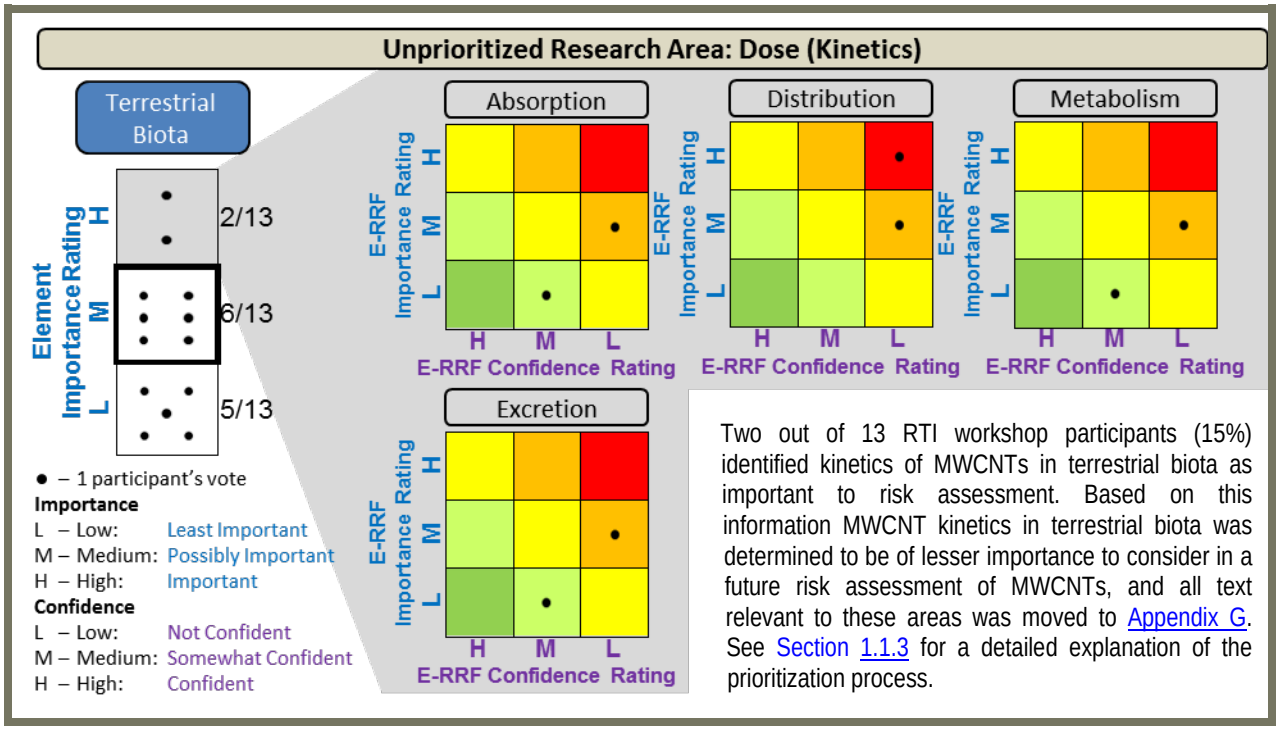
Six out of 13 RTI workshop participants (46%) identified kinetics of MWCNTs in aquatic biota as important to risk assessment. Based on this information MWCNT kinetics to aquatic biota was determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

4.3.4. Exposure Pathways in Terrestrial Systems



One out of 13 RTI workshop participants (8%) identified exposure to terrestrial biota as important to risk assessment. Based on this information MWCNT exposure to terrestrial biota was determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

Toxicokinetics and Body Burden in Terrestrial Systems



Two out of 13 RTI workshop participants (15%) identified kinetics of MWCNTs in terrestrial biota as important to risk assessment. Based on this information MWCNT kinetics in terrestrial biota was determined to be of lesser importance to consider in a future risk assessment of MWCNTs, and all text relevant to these areas was moved to Appendix G. See Section 1.1.3 for a detailed explanation of the prioritization process.

4.4. Aggregate Exposures

Neutral Research Area: Exposure Route

Aggregate exposure to MWCNTs across multiple exposure routes was not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports an understanding of occupational exposure pathway scenarios (see Section 4.2.1) and consumer exposure pathway scenarios (see Section 4.2.2), which were deemed priority research areas.

Assessing aggregate exposures involves characterizing exposures to a single chemical across multiple exposure routes. Due to the range of applications for which MWCNTs can be used, release from multiple products and subsequent exposure via multiple routes is anticipated.

As described in Text Box 4-2, the properties of MWCNTs are easily altered through manipulation of material characteristics such as size, bundling affinity, and surface treatments, and the degree to which these specific changes affect the overall exposure profile is unclear. Moreover, the composition of MWCNT formulations can vary with differences in synthesis techniques and remaining impurities from manufacturing stock. If small changes in MWCNT characteristics result in measurable changes in the nature and extent of exposure, each MWCNT formulation might be considered a unique substance; therefore, MWCNTs produced by different manufacturers using different techniques might introduce discrete sets of aggregate exposures. No consensus has been reached on which physicochemical characteristics drive changes in exposure potential or what magnitude of change to any specific characteristic or property is necessary to elicit a measurable change in exposure.

In addition to different material designs, MWCNTs can be used in a wide range of possible applications, including in coatings, electronics, adhesives, polymer composites, thermoplastics, and others. MWCNT applications can then be used in textiles, aerospace, construction, sporting goods, medical applications, and many other types of products (Aschberger et al., 2010). Thus, the potential for exposure to MWCNTs exists where humans interact with any of these products as producers or consumers or when CNTs are released to environmental media.

Exposure to MWCNTs is likely to occur through inhalation of MWCNT bundles and MWCNTs sorbed to dust produced during the manufacture and processing of MWCNTs and composites containing MWCNTs. A secondary pathway is through dermal exposure, which could occur in occupational settings from dust settling on work surfaces. For consumers, exposure could occur from the abrasion or wear of products containing MWCNTs. The general public could be exposed to MWCNTs via drinking water, contact with contaminated soil, ingestion and inhalation of household dust, dermal contact with surfaces upon which MWCNTs and dust have settled, and other pathways as a result of their release from product matrices. MWCNT releases from composite materials, such as those used in sporting goods, plastics,

touchscreens, and batteries are expected to be minimal, if not negligible, during consumer use because MWCNTs used for these products are bound in relatively strong matrices. End-of-life product dismantling, land-filling, and incineration, however, might offer greater potential for release of constituent materials to environmental compartments because many of the processes involved in end-of-life practices are intended to break down the strong matrices in which the MWCNTs are embedded (Aschberger et al., 2010). What the implications of these releases will be on exposures and impacts to human health, ecological receptors, and other receptors is not yet known.

The anticipated market trend for production of MWCNTs is strong growth in the near future, especially as production costs drop and a wider variety of applications is discovered (Lam et al., 2006). Strong market growth and diverse applications could lead to a greater diversity and number of exposure scenarios, thus increasing the aggregate exposure potential for MWCNTs.

4.5. Cumulative Exposures

Neutral Research Area: Exposure Route

Cumulative exposure to MWCNTs and substances produced or released as a result of the MWCNT product life-cycle across multiple exposure routes was not considered during the RTI collective judgment prioritization process. This section of text, however, is included in the main document because it supports understanding of occupational exposure pathway scenarios (see Section 4.2.1) and consumer exposure pathway scenarios (see Section 4.2.2), which were deemed priority research areas.

As stated in *The Exposure Factors Handbook* (U.S. EPA, 2011b), "Cumulative exposure is defined as the exposure to multiple agents or stressors via multiple routes." For the purpose of this case study, the "multiple agents or stressors" considered to contribute to cumulative exposure include those substances that are produced or released as a result of the product life cycle of MWCNT flame-retardant upholstery textile coatings, facilitate uptake of MWCNTs into humans and biota, are taken up as a result of MWCNT exposures, or induce effects in humans or biota through a comparable or synergistic mode of action. As mentioned in Section 4.4, different characteristics of different MWCNT formulations could result in the necessity to consider different formulations as unique stressors, in which case each formulation might represent a contribution to cumulative exposures.

Depending on which feedstocks are used in the manufacturing process, by-products might differ; therefore, coexposures to MWCNTs and other compounds might differ. Although the generation of impurities is likely during the manufacturing process, MWCNTs are typically purified after synthesis with varying degrees of success (see Appendix C). As described in Section 2.2.2.2, Plata et al. (2009) observed production of 45 side-products of CVD synthesis of MWCNTs, including polycyclic aromatic

hydrocarbons, methane, and volatile organic carbons. Single-walled carbon nanotube production can result in by-products of sodium hydroxide, ethanol, water, filtrate, and scrap membrane (Healy et al., 2008), but whether these by-products also will be generated by MWCNT synthesis is unclear.

Functionalization, which involves covalent attachment of submolecular components to the MWCNTs, is required before MWCNTs can be dispersed into polymers or organic solvents. Functionalization can involve several different reagents, depending on the process used, as listed in Table 2-3. Any of the MWCNT-containing textiles could include small amounts of the reagents. No data were found, however, on the by-products or impurities in textiles treated with MWCNT flame-retardant coatings.

CNTs released to the environment might bind or sequester pollutants in a form that is not bioavailable, thus reducing the impact of other toxic substances. For example, when MWCNTs are added to sewage sludge, seed germination and root growth increased, which could be because the MWCNTs bound pollutants (e.g., heavy metals, organic compounds) present in the sludge (Oleszczuk et al., 2011). On the other hand, MWCNTs might facilitate transport of these pollutants through environmental compartments, across biological boundaries, and into cells, where they could react with cell machinery (Johnston et al., 2010).

Increasing production and market growth for products containing CNTs likely will lead to increasing levels of CNTs, by-products, and related compounds in the environment, as well as an increase in exposures. Due to the heterogeneous nature of MWCNTs, the various manufacturing processes used, exposure to a wide variety of CNTs and by-products from many different sources is possible. In addition, the environmental persistence of CNTs could lead to long-term exposures or consecutive exposures in multiple receptors.

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Chapter 5. Potential Human Health, Ecological, and Other Impacts

The final step of compiling information into the comprehensive environmental assessment (CEA) framework is to link the information described in the previous chapters on the product life cycle; transport, transformation, and fate; and exposure-dose with potential impacts to receptors. The CEA framework includes information relevant to impacts on human health and ecological receptors, similar to what might be investigated in traditional risk assessment processes, as well as other plausible impacts that might be considered in life-cycle-focused assessments (e.g., socioeconomics, climate change, resource depletion).

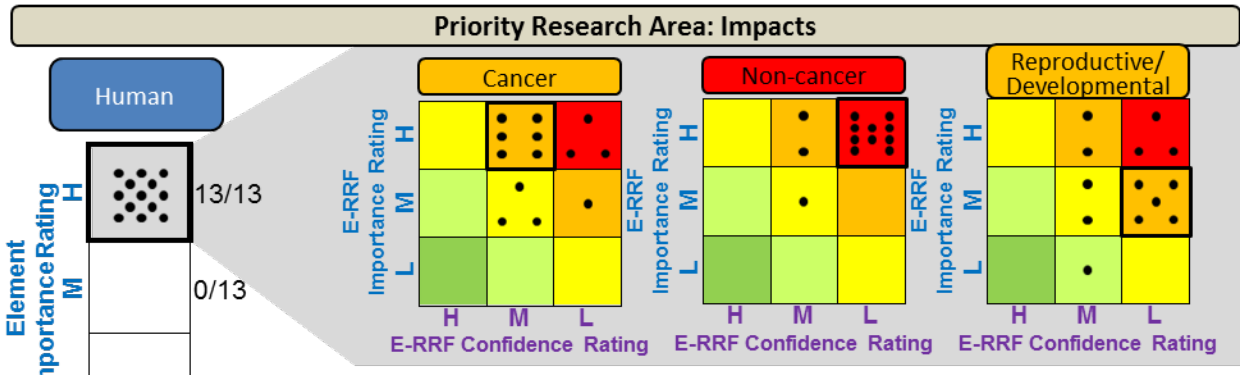
Section 5.1 discusses potential impacts of exposure to multiwalled carbon nanotubes (MWCNTs) and related contaminants on human health. This section relies heavily on evidence from experimental studies with laboratory animals, the results of which could be extrapolated to humans using methods established for quantitative toxicity assessment. As discussed in Chapter 4, humans could be exposed to MWCNTs from flame-retardant upholstery textiles through a variety of pathways, with the contaminants reaching receptors through dermal deposition, oral ingestion, or inhalation. This section discusses potential health impacts observed in studies with laboratory animals exposed to MWCNTs by these exposure routes; data are grouped to illustrate the types of impacts (e.g., pulmonary toxicity, skin irritation, reproductive effects) and sub-grouped by exposure routes for each impact.

Section 5.2 discusses the potential impacts of environmental media contaminated with MWCNTs on ecological health, which encompasses impacts at the organism, population, and ecosystem levels. This section is approached from an ecosystem perspective (aquatic vs. terrestrial), and data on groups of organisms within those ecosystems are summarized. The focus of the discussion of impacts on ecological health is on identifying and comparing data on exposure levels that might cause significant mortality, delayed growth or development, reproductive defects, or other impacts that could alter community structure and potentially cause ecosystem collapse.

Finally, Section 5.3 discusses other plausible impacts resulting from the product life cycles of MWCNTs in flame-retardant upholstery textiles. The section includes a consideration of the energy input requirements for synthesis of the MWCNTs, the economic impacts related to the cost of material production, and the potential for disproportionate impacts on populations with lower socioeconomic status.

As noted throughout this document, MWCNTs are not a single material, but rather a mixture of materials with different physicochemical properties. For the purpose of this case study, however, MWCNTs are generally regarded as a single class of materials. Text Box 5-1 provides introductory-level detail on how changes in physicochemical properties might influence toxicity. Throughout this chapter, where physicochemical properties can be related to effects on particular outcomes (e.g., fiber length on inhalation endpoints), these properties are described and their potential influences on effects are discussed. Additionally, Appendix F presents detailed toxicokinetic and toxicological study summaries in which the MWCNT characteristics and components of test designs that influence toxicological outcomes are provided.

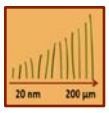
5.1. Human Health Effects



All 13 RTI workshop participants identified human impacts of MWCNT exposure as important to risk assessment. The 13 participants were asked to rate the importance of cancer, non-cancer, and reproductive and developmental effects as well as their confidence that the existing data on these subjects could support risk management decisions. Based on this information, non-cancer effects were deemed the highest priority for research in this area, followed by cancer, then reproductive and developmental effects. See Section 6.3.4 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

Text Box 5-1. Specific Physicochemical Properties of Multiwalled Carbon Nanotubes Shown to Influence Toxicity

As introduced in Text Box 1-1, the physicochemical properties and behavior of multiwalled carbon nanotubes (MWCNTs) vary. Many physicochemical characteristics of MWCNTs are interrelated, making it difficult to isolate a single characteristic and determine how it influences toxicity. For example, ground MWCNTs, which have undergone a grinding process, have been observed to induce more inflammation than their unground counterparts, but it is unclear whether this response results from reduced fiber length or reduced bundling, which is itself related to a change in surface properties introduced by the grinding process (Muller et al., 2005). In addition, dispersion state (and the characteristics that influence it, such as morphology and functionalization) appears to be a driving factor behind granuloma formation. Specifically, more highly bundled CNTs induce large intraluminal granulomas localized in the bronchi, while ground (and more dispersed) CNTs induce granulomas in the interstitial tissue of the alveolar spaces and interstitium. Nevertheless, general assumptions about CNT toxicity are rarely made without also presenting several exceptions. The following physicochemical characteristics contribute to changes in the toxicity of CNTs in vitro and in vivo [as summarized by Johnston et al. (2010)].



Morphology. Aspects of morphology, such as the diameter, length, and bundled state of CNTs might influence toxicity. Following peritoneal injection, long, relatively straight CNTs induce asbestos-like effects (i.e., mesotheliomas), whereas bundles of shorter CNTs do not. Longer MWCNTs also have been associated with a greater inflammatory response than shorter MWCNTs following dermal exposure. Cells might attempt to take up CNTs that are too long and straight to be fully engulfed, which results in high reactive oxygen species and pro-inflammatory cytokine release due to frustrated phagocytosis. In contrast, shorter bundled CNTs that are more easily engulfed by cells produce little inflammatory response. Most toxicological studies use shorter CNTs (typically only a few microns in length), and many studies do not characterize the length of the CNTs used due to the tendency of CNTs to bundle. Thus, the role of CNT length in toxicity is not well understood. Diameter might also play a role in toxicity; studies have shown that thin MWCNTs (diameters of 50 nm or less) are less toxic than thick MWCNTs (diameters of 70 nm or more) (Fenoglio et al., 2012; Nagai et al., 2011). According to Kim et al. (2011), although aspect ratio (the ratio of the CNT diameter and length) did not impact the direct genotoxicity of MWCNTs, it might impact other aspects of toxicity (e.g., oxidative stressor inflammation) that could indirectly induce genotoxicity. Similarly, others have suggested that aspect ratio plays a large role in toxicity (e.g., structural similarities with asbestos fibers) (Stella, 2011; Johnston et al., 2010; Pacurari et al., 2010; Saeed, 2010).

Surface Functionalization. Alterations of surface chemistry can both enhance and reduce toxicity. Some surface modifications, such as nitrogen-doping, result in less toxicity than pure CNTs because the modification makes the CNTs more biocompatible. Other surface modifications, such as oxidation, result in greater toxicity than pristine CNTs presumably because the modification promotes better dispersion of the CNTs and greater interaction with cells. Some surface modifications can result in altered CNT shape or form. For example, prolonged oxidation treatment results in shorter and straighter CNTs with different surface chemistry compared to nontreated CNTs. In a study by Jain et al. (2011), MWCNT toxicity depended on functionalization density; a higher density of surface carboxyl groups resulted in lower toxicity to male Swiss mice over a 4-week period.

Contaminants. Higher levels of metal impurities in CNTs are associated with an increase in toxicity. For example, cobalt and nickel catalysts that remain in trace concentrations after CNT purification are likely responsible for delayed hatching observed in zebrafish exposed as embryos to CNTs. Other potential contaminants remaining after the manufacturing process include iron, amorphous carbon, hydrocarbons, and endotoxins, all of which can induce unique toxic impacts. Although unpurified CNTs generally induce higher levels of toxicity (e.g., higher levels of cytotoxicity, morphological changes in cells, release of pro-inflammatory cytokines, glutathione depletion), many purification processes result in structural changes to the CNTs, making the attribution of increases in toxicity to contaminant content alone difficult. As such, excluding certain unavoidable contaminants that are integral to an MWCNT's life cycle from consideration in toxicity studies might not be appropriate, even though many existing studies use pristine materials (Johnston et al., 2010).

Wall Number. Several studies have illustrated that single-walled CNTs (SWCNTs) are potentially more toxic than MWCNTs (Inoue et al., 2008; Tian et al., 2006; Jia et al., 2005; Radomski et al., 2005; Warheit et al., 2004); however, other physicochemical properties likely varied between the SWCNTs and MWCNTs used in these studies, making conclusions on the impact of number of walls difficult to decipher (Johnston et al., 2010).

This section discusses the potential human health effects resulting from exposures to MWCNTs. As noted in Chapter 4, exposure to this material from aggregate sources is likely; no studies were found that investigated impacts to human health that could be attributed specifically to exposure to MWCNTs released during the life cycles of MWCNT flame-retardant upholstery textile coatings. Primary literature on MWCNTs was identified for most endpoints discussed in the following sections. When primary literature was not identified on MWCNTs, literature on single-walled carbon nanotubes (SWCNTs) was considered.

Toxicology studies conducted on animals provide much of the information discussed in this chapter because data from studies on humans are unavailable. Effects observed in animal studies are typically extrapolated to humans when conducting quantitative toxicity assessments (e.g., when calculating a reference dose [RfD] or reference concentration [RfC]; see Section 4.2.5). Potential health effects associated with all routes of exposure (dermal, inhalation, and oral) are presented in this section because each is plausible for humans (see Chapter 4 for additional exposure scenario information). Table 5-1 provides an overview of the findings for human health effects of decaBDE and MWCNTs and is followed by a detailed discussion of the available data for MWCNTs. Detailed discussion of the data for decaBDE can be found in Appendix H.

Table 5-1. Summary of effects observed after dermal, oral, and inhalation exposure to decaBDE and MWCNTs.

Route of exposure	Observed effect	MWCNTs			DecaBDE		
		Yes	No	No data	Yes	No	No data
Dermal							
Local effects	Skin irritation	X (weak[1])				X	
	Skin sensitization		X			X	
	Ocular irritation	X (weak[2])				X	
Other effects	Acute toxicity			X		X	
	Subchronic toxicity			X			X
	Chronic toxicity			X			X
Inhalation							
Local effects	Inflammation	X[3]					X
	Respiratory sensitization	X[3]					X
Other effects	Acute toxicity			X		X	
	Subchronic toxicity		X				X
	Chronic toxicity			X			X
	Immunotoxicity	X[4]					X

Table 5-1, cont.: Summary of effects observed after dermal, oral, and inhalation exposure to decaBDE and MWCNTs.

Route of exposure	Observed effect	MWCNTs			DecaBDE		
		Yes	No	No data	Yes	No	No data
Oral							
Effects	Acute toxicity			X		X	
	Subchronic toxicity			X	X[5]		
	Chronic toxicity			X	X[5]		
	Reproductive/developmental			X (weak)[7]	X[6]		

[1]Exposure resulted in a primary irritation index (PII) of 0.6 (calculated by mean dermal response score at 24 hours + mean dermal response score at 48 hours + mean dermal response score at 72 hours divided by 3; a PII score greater than 5 is considered positive) when animals were exposed to 1% Nikkiso-MWCNTs in an OECD 406-compliant study (Ema et al., 2011).

[2]Conjunctival redness and blood vessel hyperemia at 1 hour, but not at 24 hours (Ema et al., 2011).

[3]Inflammation was found in three OECD-compliant studies (Pauluhn, 2010b; Ellinger-Ziegelbauer and Pauluhn, 2009; Ma-Hock et al., 2009); respiratory sensitization was found in Park et al. (2009).

[4]Immunosuppressive results were found in Mitchell et al. (2009; 2007), and Nygaard et al. (2009).

[5]Effects included changes to thyroid and liver observed in subchronic and chronic oral studies (NTP, 1986; Norris et al., 1975; Norris et al., 1973);

[6]Effects reported in response to neonatal exposure include changes in sperm parameters (Tseng et al., 2006) and changes in locomotor activity or altered expression of proteins in the central nervous system (Johansson et al., 2008; Viberg et al., 2008; Viberg et al., 2007; Viberg et al., 2003).

[7]Effects reported to prenatal exposure (via intraperitoneal injection) included external and skeletal malformations (Fujitani et al., 2012); an oral study did not report any developmental effects (Lim et al., 2011b).

Most toxicological studies for MWCNTs exposed animals by the dermal or inhalation route (see Section 4.2.2 and Additional Information Highlight Box 12 for discussion of why dermal and inhalation might be primary exposure pathways for MWCNTs in occupational settings); effects are predominantly localized and include irritation (both skin and ocular), sensitization (respiratory), and inflammation (respiratory). When determining the toxicity of MWCNTs for humans, the following factors should be considered:

- Numerous in vitro and in vivo studies have shown that carbon nanotubes (CNTs) (both SWCNTs and MWCNTs) might induce prominent pulmonary inflammation (Pauluhn, 2010b; Ellinger-Ziegelbauer and Pauluhn, 2009; Ma-Hock et al., 2009) (see Section 5.1.3).
- At least some CNTs were found to contain a large proportion of metal catalyst (iron and nickel), which contributes significantly to oxidative stress, as indicated by the formation of free radicals and accumulation of peroxidative products, depletion of total antioxidant reserve, and a loss of cell viability (Shvedova et al., 2003). Transition metals such as iron can be important in the toxicity of a variety of pathogenic dusts because of their ability to cause oxidative stress (Pulskamp et al., 2007; Ghio et al., 1999; Donaldson et al., 1996; Kennedy et al., 1989).

Although no subchronic inhalation studies were identified for systemic toxicity (i.e., toxic effects resulting from absorption and distribution of a toxicant at a site distant from its entry point) (see Section 5.1.2.2), acute inhalation exposure to MWCNTs altered immunological function (Mitchell et al., 2009; Mitchell et al., 2007) (see Section 5.1.8). The carcinogenicity of MWCNTs following inhalation exposure has not been investigated. However, several studies using methods such as instillation and intraperitoneal injection (Sakamoto et al., 2009; Poland et al., 2008; Takagi et al., 2008) have demonstrated that certain forms of MWCNTs could behave in a manner similar to asbestos and induce mesotheliomas. Therefore, inhalation of certain forms of MWCNTs could be of human health concern.

Additional Information Highlight Box 13:
MWCNT fibers resemble asbestos fibers

Similarities between the shapes of MWCNTs and asbestos fibers have raised concern regarding potential health impacts related to inhalation of MWCNTs (Murphy et al., 2011). Asbestos inhalation can cause mesothelioma, which is directly linked to the aspect ratio (length/diameter) of the fiber (Donaldson et al., 2010). Asbestos fibers in the parietal pleura portion of the lung cause inflammation and fibrosis that are believed to lead to mesothelioma (Schinwald et al., 2012) (Donaldson et al., 2010). Some early-stage effects critical for the development of mesothelioma (e.g., inflammation and early fibrosis) have been demonstrated in studies using MWCNTs (Murphy et al., 2012; Murphy et al., 2011). Nevertheless, pre-existing inflammation might be needed for the generation of fibrosis (Ryman-Rasmussen et al., 2009b). Although the lung often can clear foreign fibers, the aspect ratio of some fibers (including some MWCNTs) might limit the effectiveness of biological clearance mechanisms (Donaldson et al., 2010). Importantly, a study by Murphy et al. (2011) investigated clearance of CNTs of varying lengths and demonstrated a deficit in clearance ability within the parietal pleura. The results of mode-of-action investigations for MWCNTs provide qualitative data to better determine the appropriateness of the comparison to asbestos; however no quantitative data were identified.

5.1.1. Quantitative Toxicity Assessment

Neutral Research Area: Impacts

Quantitative toxicity assessment and determination of health reference values were not considered during the RTI collective judgment prioritization process. This section of text is included in the main document because it supports the connection between specific research questions related to human health impacts (a priority research area) and subsequent human health risk assessments. To develop human health risk assessments, data would be needed to support reference value derivation, examples of which are described below.

In a quantitative toxicity assessment, appropriate toxicity information is collected and evaluated. These data are used to derive reference values, such as an RfD for oral exposure or RfC for inhalation exposure. Similar to an RfD (as defined in Section 4.2.5), an RfC is an estimate of a continuous inhalation exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. Both values, an RfC and an RfD, are derived from a benchmark dose lower confidence limit, no-observed-adverse-effect level (NOAEL), a lowest-observed-adverse-effect level (LOAEL), or another suitable point of departure, with uncertainty/variability factors applied to reflect limitations of the data used. Other types of reference values also can be derived for use with other exposure durations (e.g., acute or subchronic), more specific populations (e.g., healthy workers), or specific exposure contexts (e.g., emergency response or occupational exposure; see Section 4.2.5).

EPA has not evaluated MWCNTs to derive an RfD or an RfC. The only health effect based reference value for MWCNTs derived by a government agency is the draft recommended exposure limit (REL) proposed by the National Institute for Occupational Safety and Health (NIOSH) for CNTs (NIOSH, 2010) as discussed in Section 4.2.5. Acute and subchronic human no-effect levels for inhalation exposures to the general public also have been proposed in the open literature; derivation of these values is briefly discussed in the sections that follow.

5.1.1.1. Health Reference Values

To date, EPA has not evaluated MWCNTs to establish an RfD or RfC. As discussed in Section 4.2.5, NIOSH (2010) conducted a risk analysis for CNTs and established a draft REL of 7 $\mu g/m^3$ (the high estimate of the limit of quantification for NIOSH Method 5040) for carbon. The REL is based on a working lifetime inhalation exposure of 0.2–2 $\mu g/m^3$ (8-hour time-weighted average) associated with a 10% excess risk of early-stage adverse lung effects (95% lower confidence limit estimates) and was derived using two subchronic (90-day) animal inhalation studies (Pauluhn, 2010b; Ma-Hock et al., 2009).

Although not derived by a government agency, a subchronic human occupational no-effect level for MWCNT exposure to the general public of 0.25 μg/m^3 has been estimated by Aschberger et al. (2010) based on a LOAEL (Ma-Hock et al., 2009) and a NOAEL (Pauluhn, 2010b) of 1.0 μg/ m^3 from the same subchronic studies NIOSH (2010) used in their derivation of an REL. Aschberger et al. (2010) also calculated a human no-effect level for acute exposure to MWCNTs of 150 μg/m^3 from a LOAEL of 11 mg/m^3 based on the absence of inflammatory effects in a rat study (Ellinger-Ziegelbauer and Pauluhn, 2009). Although both values were calculated based on guidance provided by Registration, Evaluation, Authorisation and Restrictions of Chemicals (REACH) for chemical safety assessment (ECHA, 2008), the relatively limited and often conflicting database of currently available toxicological values for MWCNTs suggests that these values are preliminary estimates associated with a high degree of uncertainty.

The two subchronic animal inhalation studies (Pauluhn, 2010b; Ma-Hock et al., 2009) used to derive the draft NIOSH (2010) REL and the subchronic human no-effect level proposed by Aschberger et al. (2010) are described in detail in Section 5.1.3.

5.1.2. Systemic Toxicity

DecaBDE Can Inform MWCNT Assessment

For all routes of exposure, decaBDE exhibits low acute toxicity. Subchronic occupational exposure to decaBDE in humans, however, has led to evidence of toxicity. In addition, evidence suggests hepatic and thyroid effects in rats after subchronic oral exposure. Further, chronic exposure in test animals resulted in multiple non-cancer thyroid and hepatic effects. Yet, regardless of exposure duration, minimal pulmonary effects and no ocular or dermal irritation were observed in exposed test animals. Research planning to inform future risk assessments of MWCNTs might consider how impacts or effects might vary across multiple exposure routes and durations of exposure. See Appendix H for more detailed information on the non-cancer effects of decaBDE.

5.1.2.1. Acute

No data were identified on the acute systemic toxicity of MWCNTs following inhalation exposure (see Section 5.1.8 for Immune System Effects). Acute inhalation studies identified for MWCNTs, including key studies, are presented in Appendix F.1.2.

Limited data were identified on the acute toxicity of MWCNTs following oral or dermal exposure (see Section 5.1.5 for discussion of skin irritation). Based on the OECD TC 423, MWCNTs tested by Pauluhn (2010b) were not acutely toxic (oral LD_{50} > 5,000 mg/kg body weight). An acute dermal exposure study was not identified for MWCNTs. One acute oral toxicity study on SWCNTs was identified in which single doses of 1,000 mg/kg body weight of three different types of SWCNTs

(raw: 1 nm × 1–2 μm, 25% Fe; purified: 1 nm × 1–2 μm, <4% Fe; ultrashort: 1 nm × 20–80 nm, <1.5% Fe) were administered to mice (Kolosnjaj-Tabi et al., 2010). No signs of toxicity (e.g., reduced survival, delayed growth, behavioral abnormalities, clinical chemistry changes) were observed for any type of SWCNT.

One acute intraperitoneal toxicity study was identified for MWCNTs. Mice injected with 0.25, 0.5, or 0.75 mg/kg-day of purified, carboxylated MWCNTs for 5 days experienced decreased body weight gain, and increased markers of oxidative stress and hepatotoxicity (increased reactive oxygen species in liver, enhanced activity of liver enzymes such as serum aminotransferases and alkaline phosphatases) (Patlolla et al., 2011) (see Table F-8 in Appendix F).

5.1.2.2. Subchronic

No data were identified on the subchronic systemic toxicity of MWCNTs following exposure by any route. See Section 5.1.3 for discussion of pulmonary effects and Section 5.1.8 for discussion of immune system effects following subchronic exposure.

5.1.2.3. Chronic

No data were identified on the chronic systemic toxicity of MWCNTs following exposure by any route.

5.1.3. Pulmonary Toxicity

Material characteristics and study details associated with the acute and subchronic inhalation studies identified for MWCNTs are presented in Appendix F.1.2, Table F-6. No chronic inhalation studies were identified for MWCNTs. Toxicological responses generally have been consistent across studies administering MWCNTs into the lungs (by intratracheal instillation, aspiration, or inhalation), with exposed animals exhibiting pulmonary inflammation and fibrosis. Results reported for animals exposed to MWCNTs via intratracheal instillation (Park et al., 2009; Muller et al., 2008a; Muller et al., 2008b; Muller et al., 2005), however, generally resulted in more severe effects than those observed for inhalation (Pauluhn, 2010b; Ellinger-Ziegelbauer and Pauluhn, 2009; Li et al., 2009; Li et al., 2007; Mitchell et al., 2007).

Additional Information Highlight Box 14:
Applying traditional in vivo inhalation study design models to MWCNTs

Available evidence suggests that MWCNT inhalation exposure might occur and cause subsequent human health effects (e.g., fibrosis, inflammation) (see Sections 4.2.1, 4.2.2 and 5.1.3); however, the lack of chronic data, choice of exposure route, and differences in study design could impede the use of existing data in future risk assessments and the subsequent risk management of potential MWCNT human health effects (see Section 5.1).

Traditional particle exposure studies might not be relevant to human exposures because of known species differences and exposure methods that have been shown to alter health effects (Nikula et al., 2001; Osier and Oberdorster, 1997; Paxton, 1995). Several studies have attempted to improve on approaches to allow for better translation to human health effects by evaluating variables in experimental design that influence toxicity outcomes and by developing alternative methods to test MWCNT toxicity. For example, Wako et al. (2010) demonstrated in a rat intratracheal instillation model that the methods used to prepare the MWCNT suspensions necessary for intratracheal instillation can alter cellular responses in the lung and suggested a primary method for similar, future MWCNT studies. Other suggested improvements to MWCNT toxicity testing design have included alternative exposure methods in laboratory animals (as described above), cellular exposure models, and specific methods for MWCNT sample preparation (Geys et al., 2007) (Liu et al., 2012; Coccini et al., 2010; Alfaro-Moreno et al., 2008; Osier and Oberdorster, 1997). For example, optimization of an in vitro cell culture model of respiratory epithelium has improved the growth of a tight cell monolayer that could be used as a respiratory translocation model for nanomaterials (Geys et al., 2007). Coccini et al. (2010) tested the effect of varying degrees of functionalization on the MWCNTs, which were observed to alter the water solubility, dispersibility, and agglomeration, within two-cell culture models of cytotoxicity.

Pulmonary inflammation was observed in one acute (Ellinger-Ziegelbauer and Pauluhn, 2009) and two subchronic (Pauluhn, 2010b; Ma-Hock et al., 2009) Organisation for Economic Co-operation and Development (OECD)-compliant animal inhalation studies, with granulomas observed in both subchronic studies. In the study conducted by Ma-Hock et al. (2009), an exposure-related increase in the incidence of granulomatous inflammation in the lung and lung-associated lymph nodes was observed in exposed rats (head-nose exposure). At the mid and high exposures (0.5 and 2.5 mg/m^3, respectively), increased lung weights, pronounced multifocal granulomatous inflammation, diffuse histiocytic and neutrophilic inflammation, and intra-alveolar lipoproteinosis were observed in lung and lung-associated lymph nodes. Similar effects were observed in a study by Pauluhn (2010b), in which Wistar rats were exposed (nose only) to MWCNTs (0.1, 0.4, 1.5, 6 mg/m^3); inflammatory changes in the distal nasal cavities were observed at all but the lowest concentration. Additionally, exposure-related lesions of the upper respiratory tract (e.g., goblet cell hyperplasia or metaplasia, eosinophilic globules, and focal turbinate remodeling) and lower respiratory tract (e.g., inflammatory changes in the bronchioloalveolar region and increased interstitial collagen staining) were observed at higher concentrations. According to a study conducted by Kim et al. (2012), pulmonary DNA damage is initiated after only a few days of exposure; a significant increase in DNA damage was measured by Comet assay in lung cells from rats immediately following 5 days of exposure (6 hours per day) to 0.94 mg/m^3 MWCNTs. DNA damage remained detectable one month after the last exposure.

5.1.4. Eye Irritation

All in vivo eye irritation studies considered are presented in Appendix F.1.2 (Table F-4). In a key ocular irritation study conducted with rabbits, one of two types of MWCNTs administered via instillation to the conjunctival sac resulted in conjunctival redness and blood vessel hyperemia at 1 hour, but not at 24 hours (Ema et al., 2011). Differences in purity, diameter, and surface area (see Appendix F, Table F-4) between the two types of MWCNTs tested could explain why effects were observed with only one of the two types.

5.1.5. Skin Irritation

Material characteristics and study details associated with the in vivo dermal studies considered for MWCNTs are presented in Appendix F.1.2.

Based on the information available, even the most irritating of several MWCNTs tested appears to be only a very weak skin irritant when tested on healthy, intact skin (Ema et al., 2011; Kishore et al., 2009). The available studies were performed in accordance with accepted standard practices for conventional skin irritation tests, which use healthy, intact skin exposed for 4 hours under semioccluded conditions. No data were identified for dermabraded or damaged skin.

5.1.6. Reproductive Effects

DecaBDE Can Inform MWCNT Assessment

Most studies report that decaBDE does not induce reproductive or developmental effects when administered at high levels during gestation or adulthood. Some research does show reproductive and neurodevelopmental effects, however, when neonates are dosed directly. The data on decaBDE raise important questions that should also be considered for research planning to inform future MWCNT risk assessment, for example: Do reproductive and developmental effects of MWCNTs differ when administered during different developmental periods? See Appendix H for more details regarding the reproductive and developmental effects of decaBDE.

No in vivo reproductive studies using highly relevant exposure routes were initially identified for MWCNTs. See Section 6.3.4.2 for information on two studies (Lim et al., 2011a; Lim et al., 2011b; Bai et al., 2010) that were identified after the collective judgment prioritization process.

5.1.7. Developmental Effects

One developmental study was identified in which MWCNTs were administered via gavage to pregnant Sprague-Dawley rat dams at doses of 0, 40, 200, and 1,000 mg/kg-day on gestation days (GD) GD6–GD19; dams were sacrificed on GD20 (Lim et al., 2011b). Minimal maternal toxicity was observed at 1,000 mg/kg-day; a dose-dependent decrease in thymus weight was observed, but no effects were observed on maternal body weight, food consumption, and oxidant-antioxidant balance in the liver. No differences in gestation index, fetal death, fetal and placental weights, or sex ratio were observed as a result of MWCNT exposure. Therefore, the embryo-fetal NOAEL was 1,000 mg/kg-day.

When MWCNTs were administered via intraperitoneal or intratracheal injection to pregnant ICR mice in a single dose of 0, 2, 3, 4, or 5 mg/kg on GD9, teratogenic effects were observed (Fujitani et al., 2012). Fetal examinations performed on GD18 showed external and skeletal malformations such as short or absent tails, cleft palate, limb reduction deformities, fused ribs and vertebral bodies, and hypo/hyperphalangia (see Table F-8 in Appendix F).

5.1.8. Immune System Effects

Inhalation studies examining the immune system after exposure to MWCNTs are summarized in Appendix F.1.2. In one notable study, systemic immunosuppression (characterized by T-cell dependent antibody response to sheep erythrocytes and T-cell proliferative ability in presence of mitogen), was observed in mice exposed to 0.3, 1, or 5 mg/m^3 MWCNTs via inhalation for 14 days, however no significant lung inflammation or lung tissue damage was observed (Mitchell et al., 2007).[16] The immunosuppressive mechanism could involve a signal originating in the lungs that activates cyclooxygenase enzymes in the spleen (Mitchell et al., 2009). In addition, an acute inflammatory response was observed in female BALB/cAnCrl mice following administration of MWCNTs via single intranasal injection at 200 or 400 µg/mouse (Nygaard et al., 2009).

MWCNTs have been identified as respiratory sensitizers in several studies. Park et al. (2009) observed a potential allergic response in mice following intratracheal instillation of 50 mg/kg MWCNTs. The authors noted that the significantly increased immunoglobulin E concentrations coupled with pro-

[16]This study was questioned after publication primarily because an image in the study indicated that nanofibers, not nanotubes, were used. According to Lison and Muller (2008), although Mitchell et al. (2007) might be correct in their assertion that the results of these early installation experiments show immune effects in the lungs, these studies are "probably of little relevance to assess the hazard of MWCNT because they could not be reproduced upon inhalation exposure." They maintain that conclusions about immunological effects cannot be reached by Mitchell et al. (2007).

inflammatory responses likely resulted from B-cell activation by IL-10. Similarly, Inoue et al. (2009) demonstrated a potential allergic response in mice following six weekly intratracheal instillations of 50 μg MWCNTs. These authors reported a significant increase in the number of total immune cells (including macrophages, neutrophils, eosinophils, and lymphocytes) in the bronchiolar lavage fluid, concurrent with infiltration of eosinophils, neutrophils, and mononuclear cells in the lung. They also noted a significant induction of goblet cell hyperplasia in the bronchial epithelial tissue, indicating that MWCNTs exacerbate metaplasia in the presence or absence of other allergens. Of note, the Organisation for Economic Co-operation and Development currently has no guidelines for standardized respiratory sensitization studies, and the studies identified above used intratracheal instillation, not inhalation, as the route of exposure.

One study that used inhalation as the route of exposure was identified. Ryman-Rasmussen et al. (2009b) exposed mice with allergic asthma to 100 mg/m^3 MWCNT aerosol for 6 hours (approximately 10 mg/kg MWCNT total) and found that airway fibrosis occurred differentially in ovalbumin-sensitized mice versus nonsensitized mice. The authors concluded that airway fibrosis occurs as a result of MWCNT inhalation with preexisting inflammation, suggesting that individuals with preexisting allergic inflammation are susceptible.

Immune effects from oral exposure to MWCNTs have been suggested by one study. As described in Section 5.1.7, Lim (2011b) observed a decrease in thymus weight in rat dams following administration of MWCNTs at the highest dose tested (1,000 mg/kg-day).

5.1.9. In Vitro Data

In vitro data can be used to make judgments on the toxic potential of stressors, but the relevance of in vitro data to predicting toxicological responses of “real-world” exposures is not always clear.

Multiple in vitro studies were identified for MWCNTs; a few were selected for discussion here and inclusion in Table F-9 in Appendix F to highlight the major themes and important concepts covered in the literature.

One in vitro study was identified on ocular effects of MWCNTs. The study produced negative results (i.e., no irritation was observed) when two sizes of MWCNTs were evaluated using hen's egg test chorioallantoic membrane with white leghorn chicken eggs (Kishore et al., 2009).

Negative results also were observed in an in vitro dermal irritation study by Kishore et al. (2009), in which two sizes of MWCNTs were evaluated using the three-dimensional human epidermis model with human skin cells. The relevance of dermal in vitro studies to occupational, consumer, and general public exposures, however, depends on the ability of CNTs to penetrate the stratum corneum barrier in vivo, which is unknown at this time (Monteiro-Riviere and Inman, 2006).

Radomski et al. (2005) investigated effects of MWCNTs on platelet aggregation and found that MWCNTs could promote platelet aggregation. One possible mechanism for thrombus development following MWCNT exposure observed by the study authors was a change in the abundance of GPIIb/IIIa (glycoprotein integrin receptor), which triggers platelet adhesion. This study is an example of in vitro data that could potentially identify data gaps in in vivo data.

Other in vitro studies have found that MWCNTs induce proinflammatory effects, generate reactive oxygen species and oxidative stress, inhibit phagocytosis, and induce apoptosis, as reported in a review article (Donaldson et al., 2006). Similarly, in human T cells, MWCNTs were found to decrease cell viability and increase apoptosis in a dose- and time-dependent manner at concentrations between 40

Additional Information Highlight Box 15:
Developing NexGen-style models for MWCNT toxicity testing

The toxicokinetics and potential toxicity of MWCNTs are influenced by an array of factors aside from chemical composition, including particle agglomeration, fiber length, and functionalization (Coccini et al., 2010; Liu et al., 2010; Wako et al., 2010). Given the many ways that these factors can be combined to generate different types of MWCNTs, in vitro methods might prove invaluable to quickly evaluate the potential for these factors to influence MWCNT toxicity and to support future MWCNT assessment efforts.

For example, Gasser et al. (2012) used an in vitro cellular model to show that the ability of MWCNTs to cause oxidative stress, cytokine/chemokine release, and apoptosis was more related to pre-coating of the MWCNTs with pulmonary surfactants than to functionalization of the MWCNTs. Thus, understanding surfactant coating properties might be an important factor for assessing MWCNT toxicity. Similarly, Liu et al. (2012) recently used in vitro models to evaluate length-dependent cytotoxicity of MWCNTs in immune and epithelial cancer cell lines.

Application of an integrated testing strategy has been suggested for nanomaterials as it provides a framework for prioritization, screening, and targeted testing, using multiple approaches and existing data to address the health effect concerns regarding exposure to nanoparticles (U.S. EPA, 2009). A number of different mechanism-based high-throughput in vitro methods can be used predictively as screening tools and then validated using a limited amount of in vivo studies (Nel et al., In Press). These types of approaches for characterizing effects of MWCNTs must be carefully developed and interpreted, as there is uncertainty involved in extrapolating in vitro results to in vivo effects.

and 400 μg/mL (Bottini et al., 2006). The study authors noted that the level of toxicity was significantly greater for oxidized MWCNTs compared to their pristine counterparts (Bottini et al., 2006).

5.1.10. Genotoxicity/Mutagenicity

Standard and modified in vitro genotoxicity tests have been conducted to investigate the genotoxic potential of CNTs. However, their genotoxic potential is uncertain at this time, as available tests have shown contradictory results, which might be due to differences in composition and physicochemical characteristics of the CNTs (see Table F-9 in Appendix F).

MWCNTs were not found to be mutagenic when evaluated with the Ames test[17] using *Salmonella typhimurium* with and without metabolic activation (Di Sotto et al., 2009; Wirnitzer et al., 2009). However, bacterial mutagenicity-based assays might not be suitable for detecting genotoxicity induced by nanoscale materials because prokaryotes cannot perform endocytosis, and the nanoscale materials might not be able to diffuse across the bacterial cell wall. This lack of uptake could lead to false-negative results (Singh et al., 2009). Purified MWCNTs also did not show genotoxic activity in several other assays at different dose levels and in different test systems, including micronucleus and sister-chromatid exchange assays of human lymphocyte cells (Szendi and Varga, 2008) and a chromosome aberration assay of Chinese hamster lung cells (Asakura et al., 2010). The MWCNTs used in these tests were predominantly high purity and contained minimal metal impurities such as metal catalysts, which are included in the commercial MWCNT preparation as a result of the synthesis process. Such impurities could influence the genotoxic potential of MWCNTs.

Other micronucleus assays have reported significant MWCNT-induced increases in micronuclei of rat lung epithelial cells, Chinese hamster lung cells, and human lung carcinoma A549 cells (Asakura et al., 2010; Muller et al., 2008a; Kato et al., In Press). MWCNTs also have acted as clastogenic and aneugenic agents simultaneously in human blood cells (Cveticanin et al., 2010). Using the murine macrophage cell line RAW 264.7, Migliore et al. (2010) observed a significantly increased MWCNT dose-related percentage of DNA in comet tails in a Comet assay and a significant cytotoxic effect in a Trypan blue assay. Cavallo et al. (2012) also reported a MWCNT concentration-dependent, statistically significant induction of direct DNA damage in human lung epithelial A549 cells evidenced by percentage of DNA in comet tails in a Comet assay that corresponded with reduced cell viability; however, the authors noted that oxidative DNA damage was not statistically significant. Patlolla et al. (2010b; 2010a)

[17]The Ames test is a bacterial reverse mutation assay, designed to determine mutagenicity of the test compound.

observed a statistically significant, dose-dependent increase in the percentage of DNA in comet tails in a Comet assay in normal human dermal fibroblast cells.

5.1.11. Carcinogenicity

Carcinogenicity studies considered for MWCNTs are presented in Table F-11 of Appendix F. Currently, the carcinogenic potential of MWCNTs is unknown. No studies have investigated carcinogenicity of MWCNTs following oral or inhalation exposures; several studies indicate, however, that certain forms of MWCNTs behave in a manner similar to asbestos, inducing mesotheliomas when administered using methods such as injection (e.g., intrascrotal, intraperitoneal) (Sakamoto et al., 2009; Poland et al., 2008; Takagi et al., 2008). Therefore, the lung could be another target of MWCNT carcinogenicity.

DecaBDE Can Inform MWCNT Assessment

Research indicates that decaBDE does not induce genotoxicity. DecaBDE does appear, however, to target the liver and thyroid in studies of carcinogenicity (see Appendix H). Similar to many chemicals though, important differences have been observed between species, gender, and target organs. Based on observations with decaBDE, research planning to inform future assessments of MWCNT carcinogenicity might consider: Does exposure to MWCNTs induce genotoxicity? Is evidence of MWCNT carcinogenicity reproducible in multiple species, genders, and sites? See Appendix H for more information about the carcinogenic impacts of decaBDE on humans, including details on the NTP study (1986).

However, Muller et al. (2009) found that a single 20-mg injection of MWCNTs did not produce mesotheliomas in male Wistar rats observed for 24 months postexposure. Similarly, Varga and Szendi (2010) found that peritoneal injection of 10 mg MWCNTs did not result in development of mesotheliomas in F-344 rats examined at 12 months postexposure, but did result in a granulomatous reaction. Intratracheal instillation studies are useful for evaluating respiratory toxicity for particles, such as MWCNTs, because they produce results that are qualitatively similar to those from inhalation studies for endpoints such as pulmonary inflammation and fibrosis; however, such studies also have limitations because treatment with bundled particles can produce artifactual granulomatous lesions (Muller et al., 2005). One possible reason for the mesotheliomas observed in some studies is that MWCNTs are more cohesive than asbestos; consequently, MWCNTs bundle easily into granules after instillation or injection into animals (Schulte et al., 2010; Sakamoto et al., 2009; Takagi et al., 2008). Currently, the mechanism by which MWCNTs reach and persist in the pleura, including retention time and the importance of factors such as fiber length or bundle size, is not understood well enough to determine whether inhalation of MWCNTs could result in mesothelioma.

The carcinogenic potential of MWCNTs also might be influenced by the presence of metal contaminants (e.g., iron or nickel). These contaminants could play a role in carcinogenicity by accelerating the generation of reactive oxygen species (Johnston et al., 2010).

Additional Information Highlight Box 16:
Mechanisms of toxicity for cancer and non-cancer impacts of MWCNTs

MWCNTs have been reported to cause pathogenic or carcinogenic effects in several standard toxicity studies, which indicates that human health impacts might occur as a result of MWCNT exposures (Delorme et al., 2012; Murphy et al., 2011; Donaldson et al., 2010; Ryman-Rasmussen et al., 2009b). To date, data indicate that pathogenic or carcinogenic effects could arise from several mechanisms, including increased cellular permeability through reactive oxygen species production and effects on the actin filament system, as observed in a human microvascular endothelial cells (Pacurari et al., 2012). Muller et al. (2008) investigated the genotoxic potential of MWCNT using both an in vivo and in vitro rat model and showed that MWCNT exposure led to the formation of micronuclei resulting from chromosomal alterations in the lung epithelia.

As described in Additional Information Highlight Box 13, several studies have shown the potential for MWCNTs to act like asbestos, causing thoracic inflammation, early fibrosis (Murphy et al., 2012; Murphy et al., 2011), and fibrosis (Ryman-Rasmussen et al., 2009b). Additionally, MWCNTs have been shown to penetrate into the alveolar region of the lung (Delorme et al., 2012) and to cause inflammation due to accumulation of alveolar macrophages (Schinwald et al.). These biological events have been shown to lead to mesothelioma (Donaldson et al., 2010); however, the current science on MWCNTs is not yet sufficient to determine if these mechanisms are responsible for the observed effects. Continuing to build a greater understanding of the mechanisms of toxicity leading to potential health impacts is important for future MWCNT risk assessment efforts.

5.1.12. Susceptible Populations

Sacks et al. (2011) defined susceptibility as "individual- and population-level characteristics that increase the risk of health effects in a population, including, but not limited to, genetic background, birth outcomes (e.g., low birth weight, birth defects), race, sex, life stage, lifestyle (e.g., smoking status, nutrition), preexisting disease, socioeconomic status (e.g., educational attainment, reduced access to health care), and characteristics that may modify exposure … (e.g., time spent outdoors)." In this section, populations susceptible to MWCNT impacts based on characteristics such as age, genetic background, and disease are considered. Characteristics that could modify exposure and increase susceptibility are discussed in Section 4.2.4; for a discussion on impacts related to socioeconomic status, see Section 5.3.

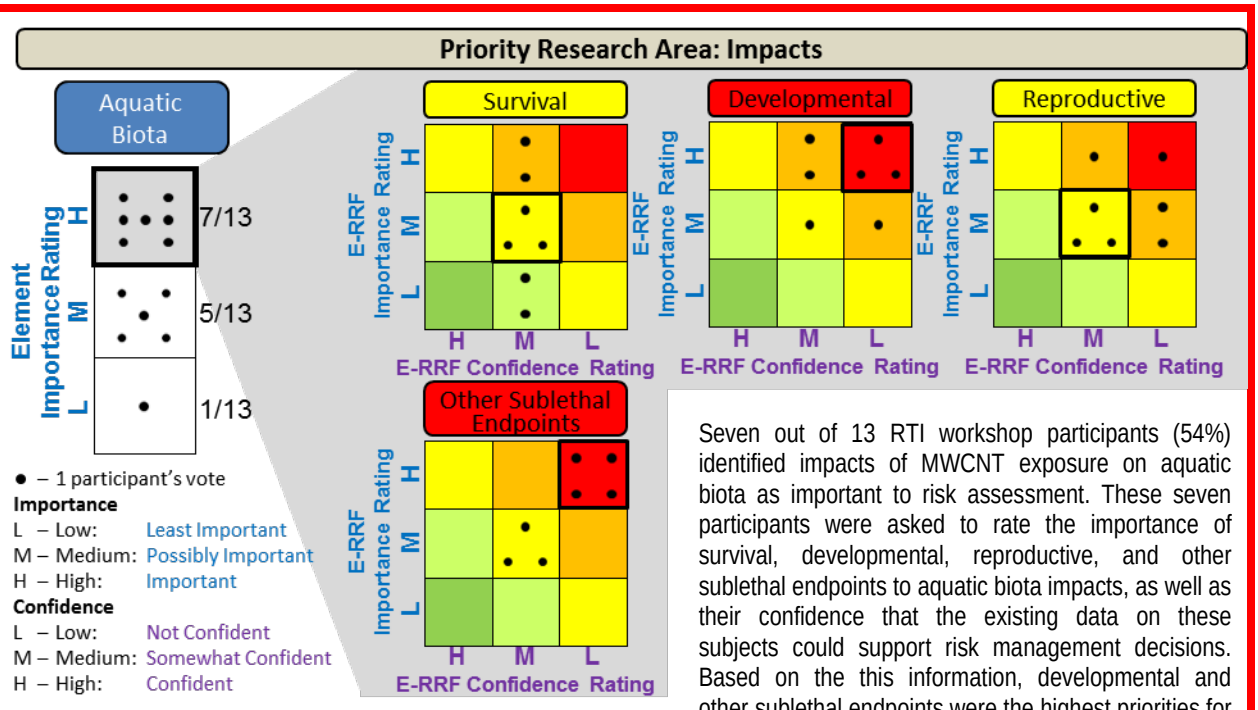
No information was identified regarding MWCNTs and susceptible populations. Because MWCNTs appear to induce inflammatory and fibrotic effects (see Sections 5.1.3 and 5.1.8), however, individuals with existing pulmonary disease and children with higher respiration rates could be susceptible populations.

5.2. Ecological Effects

This section presents a summary of data on the potential ecological impacts of environmental contamination with MWCNTs. Specific information from the studies reviewed for this case study can be found in Appendix F.2. Considerations for ecological impact include the absolute and relative toxicity of

MWCNTs and other factors such as bioaccumulation and biomagnification potential (see Appendix G.4.2). For aquatic ecosystems, little information was identified for MWCNTs; conversely, much information was identified on the potential effects of MWCNTs in terrestrial ecosystems. The terrestrial ecosystem studies focus on agriculturally relevant plants and soil microbes. In both aquatic and terrestrial ecosystems, studies are predominantly laboratory-based experiments on single species. Therefore, limited research on the broad ecological impact of MWCNT exposure is available, which might be the result of limited data on its presence in the environment. As mentioned in Appendix G.4.2, ecological receptors can be exposed to MWCNTs attached to textile fibers, embedded in polymers, or sorbed to other particles, all of which are more likely to occur in the environment than exposure to the pristine compound. Studies examining exposure to larger textile scraps, polymer particles, and other heterogeneous compounds containing MWCNTs, however, are lacking. The results of laboratory studies using pristine compounds must therefore be considered, recognizing that results might not translate directly into real-world exposure scenarios.

5.2.1. Aquatic Receptors



Seven out of 13 RTI workshop participants (54%) identified impacts of MWCNT exposure on aquatic biota as important to risk assessment. These seven participants were asked to rate the importance of survival, developmental, reproductive, and other sublethal endpoints to aquatic biota impacts, as well as their confidence that the existing data on these subjects could support risk management decisions. Based on the this information, developmental and other sublethal endpoints were the highest priorities for research in this area, followed by survival and reproductive effects. See Section 6.3.4.3 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

DecaBDE Can Inform MWCNT Assessment

Bioaccumulation and bioavailability of PBDEs in sediment and in the water column influence PBDE toxicity to marine and freshwater invertebrates and algae. Deca-, octa-, and pentaBDE are not acutely toxic to fish up to the limits of water solubility, but sublethal doses to decaBDE produced some endocrine effects in aquatic species. Histopathological alterations in thyroid gland shapes and decreases in thyroid hormone expression in tail tissue during metamorphosis were observed in African clawed frog tadpoles exposed to decaBDE, and these sublethal effects can influence tadpole growth and development (Qin et al., 2010). Decreased thyroid hormone expression also was observed in Chinese rare minnow and lake trout after exposure to decaBDE via water and diet, respectively (Tomy et al., 2004; Li et al., In Press). The relevance of studies exposing fish to decaBDE is complicated because decaBDE in the environment is often transformed into other congeners via biotic debromination. The impact of debromination on PBDE bioaccumulation, bioavailability, and effects in aquatic biota can be compared to the impacts of functionalization, surface treatment, and aggregation of MWCNTs. Research planning to inform future risk assessment of MWCNTs could consider: What is the impact of transformation, partitioning, and formation of mixtures when considering toxicity data? See Appendix H for more details regarding the effects of decaBDE on aquatic biota.

Limited information was identified on the toxicity of MWCNTs to algae and aquatic plants (see Section 5.2.1.1). Only a few studies have investigated toxicity of MWCNTs to aquatic invertebrates and aquatic vertebrates (see Sections 5.2.1.1 and 5.2.1.2). Although these studies provide information for acute effects, they vary with regard to endpoints, doses, functionalization, and other material characteristics (see Text Box 5-1). Little information was identified regarding toxicity to benthic invertebrates (see Additional Information Highlight Box 17), and most MWCNTs released to the aquatic environment are expected to accumulate in the benthic environment (see Sections 3.1 and 3.3). A limited amount of information was identified on ecosystem effects due to chronic MWCNT exposure.

As discussed in Sections 3.1 and 3.3, MWCNTs have low water solubility and are expected to partition to sediment where they might be available primarily to benthic organisms. Physicochemical properties of MWCNTs suggest potential for bioaccumulation in aquatic systems (Helland et al., 2007), but no studies were identified on this topic. The potential impact of bioaccumulation of MWCNTs in aquatic systems is therefore uncertain.

5.2.1.1. Algae, Aquatic Plants, and Aquatic Invertebrates

Table 5-2 provides a comparison of key reference values identified for the effects of decaBDE and MWCNTs on algae, aquatic plants, and aquatic invertebrates. More detailed information on decaBDE is available in Appendix H. Table F-12, Table F-14, and Table F-15 in Appendix F summarize details of the MWCNT studies identified and reviewed for this section.

Table 5-2. Effects of decaBDE and MWCNTs on aquatic receptors: Algae, plants, and invertebrates.

Organism	MWCNTs			DecaBDE		
	Effect	Effect level	Citation	Effect	Effect level[1]	Citation
Sediment oligochaetes	ND			Acute NOEC	>5,000 mg/kg	Hardy (2002a)
				28-day NOEC	>3,841 mg/kg	ACC (2001a, b)[2]
Algae	Growth inhibition LOEC	1 mg/L	Wei et al. (2010)	Growth inhibition, 96-hr EC_{50}	>1 mg/L	Hardy (2002a)
Zebra mussels	ND			DNA damage	0.1 to 10 µg/L	Riva et al. (2007)
Macrophytes	Positive effects on recolonization and community structure after 3 months of exposure in sediment		Velzeboer et al. (2011)	ND		
Sediment/ Benthic organisms	*Leptocheirus plumulosus:* LC_{50}	68 grams/kg	Kennedy et al. (2008)	ND		
	Hyalella azteca: LC_{50}	>264 grams/kg	Kennedy et al. (2008)			

Table 5-2, cont.: Effects of decaBDE and MWCNTs on aquatic receptors: Algae, plants, and invertebrates.

Organism	MWCNTs			DecaBDE		
	Effect	Effect level	Citation	Effect	Effect level[1]	Citation
Water fleas	*Ceriodaphnia dubia:* acute LC_{50}	2–100 mg/L	Li and Huang (2011)	*Daphnia magna:* 21-day LOEC (growth)	BDE-209: ND; pentaBDE: 9.8 µg/L	Wildlife International report submitted to Chemical Manufacturers Association (Drottar and Krueger, 1998)[2]
	C. dubia: Subchronic growth inhibition EC_{50}	50.9 mg/L	Kennedy et al. (2008)	21-day EC_{50} (survival, reproduction)	BDE-209: ND; pentaBDE: 14 µg/L	Wildlife International report submitted to Chemical Manufacturers Association (Drottar and Krueger, 1998)[2]
	3-generation reproduction EC_{50}	4–17 mg/L	Li and Huang (2011)			
	C.dubia: LC_{75}	26 mg/L (un-derivatized MWCNTs)	Kennedy et al. (2009)			

[1]Concentration in media (water [units: µg/L or mg /L] or sediment [units: mg/kg]).

[2]As cited in Environment Canada (2006).

ND = No data identified, NOEC = No-observed-effect concentration, EC_{50} = Median effective concentration

Additional Information Highlight Box 17:
Toxicity to benthic invertebrates

The complexity of ecological systems combined with the wide variety of MWCNT chemistries can make determining how parameters of the material (e.g., surface charge, aspect ratio) and the environment (e.g., pH, UV light) influence toxicity in aquatic receptors difficult. For example, Mwangi et al. (2012) recently conducted 14-day toxicity tests in several benthic species, including an amphipod (*Hyalella azteca*), a midge (*Chironomus dilutes*), a mussel (*Villosa iris*), and an oligochaete (*Lumbriculus variegates*). The benthic invertebrates were exposed to sonicated or nonsonicated MWCNTs from two different sources and to a nitric acid-modified MWCNT. The amphipod *H. azteca* was also exposed to nonsonicated MWCNTs with or without the addition of EDTA or a nickel solution. Results showed decreased survival (in all species except *L. variegates*), growth (evaluated in *V. iris* only), and biomass (not evaluated in *V. iris*) of the test organisms. The authors concluded that acid treatment, sonication, and type and source of MWCNT influenced survival, growth, and biomass in a species-dependent manner. The authors also reported that the nickel solubilized from MWCNTs and the MWCNTs themselves contributed to toxicity. See Section 6.3.4.3 for more discussion from recently identified evidence on factors influencing toxicity to aquatic receptors and the lack of mechanistic data.

The effects of MWCNTs on marine algae, sediment macrophytes, and water-dwelling invertebrates have not been extensively studied; only four published studies were initially identified (Li and Huang, 2011; Velzeboer et al., 2011; Wei et al., 2010; Kennedy et al., 2008). Because MWCNTs are likely to partition to sediment, benthic organisms are expected to be primary receptors (Christian et al., 2008). Initially, no studies that investigated the effects of MWCNTs on benthic invertebrates, however, were identified. See Additional Information Highlight Box 17 and Section 6.3.4.3 for information on studies that were identified after the collective judgment prioritization process.

In a study on macrophyte growth, experimental plots were cleared of all living organisms and MWCNTs were added to the sediment. After three months, researchers observed that the density of macrophytes that had recolonized the plots was positively correlated with MWCNT levels (Velzeboer et al., 2011). This result was counter to the authors' initial hypothesis based on previous laboratory experiments that macrophyte growth and species composition would be negatively affected by MWCNTs, indicating a level of complexity in community-level effects of MWCNTs in real-environment situations that is not well understood (Velzeboer et al., 2011).

Unicellular green algae (*Dunaliella tertiolecta*) exposed to carboxylated MWCNTs in sea water did not exhibit inhibited growth until concentrations reached 1 mg/L and above (Wei et al., 2010). Growth lagged up to 23 days behind the control, and exponential growth rates were reduced by 35% when exposure was 10 mg/L, indicating mid-exponential growth phase cytotoxicity at high exposures (Wei et al., 2010).

Two studies provided a wide variety of data for *Ceriodaphnia dubia*, a species of water flea (Li and Huang, 2011; Kennedy et al., 2008). The MWCNT studies describe an acute median lethal concentration in the mg/L range, the variation of which might be due to differences in functionalization treatment and diameter size of the MWCNTs (Li and Huang, 2011) (see Table F-15 in Appendix F for study-specific details and Text Box 5-1 for discussion of how physicochemical properties affect toxicity). Subchronic and chronic growth and reproduction tests show that MWCNTs that had been treated to increase dispersal and limit bundling (a common treatment in MWCNTs—see Section 2.2.3.1) are not likely to cause significant, population-level effects until high doses (1- to 100-mg/L range) are reached (Li and Huang, 2011). Even though MWCNTs are expected to partition to sediment, functionalization and suspension in natural organic matter could improve dispersion and solubility of MWCNTs in aqueous media and might increase the exposure levels of MWCNTs to water-dwelling aquatic organisms (ODriscoll et al., 2010; Kennedy et al., 2008).

5.2.1.2. Aquatic Vertebrates

Table 5-3 provides a comparison of key reference values identified for the effects of decaBDE and MWCNTs on aquatic vertebrates. Additional information on decaBDE is available in Appendix H. Table F-13, Table F-16, and Table F-17, in Appendix F summarize details of the MWCNT studies identified and reviewed for this section.

Table 5-3. Effects of decaBDE and MWCNTs on aquatic receptors: aquatic vertebrates.

Organism	Exposure	Effect	Effect level	Citation
MWCNTs				
Zebrafish	Water	Reduced blood circulation	70 µg/mL	Asharani et al. (2008)
	Water	Developmental effects	60 µg/mL	Asharani et al. (2008)
	Water	Increased mortality LOAEL	60 µg/mL	Asharani et al. (2008)
	Microinjection	Developmental effects NOEL	>2 ng/embryo	Cheng et al. (2009)
	Microinjection	Second-generation reduced survival	2 ng/embryo	Cheng et al. (2009)
Japanese medaka	Water	Developmental effects LOAEL	1,500 µg/mL	Kim et al. (2012)
DecaBDE				
African clawed frog	Water	Thyroid effects LOAEL	1 ng/L	Qin et al. (2010)
Lake trout	Diet, chronic	Decreased thyroid hormones LOAEL	2.5 ng/gram	Tomy et al. (2004)
Rainbow trout	Diet, chronic	Increased liver weight LOAEL	7.5 ng/kg	Kierkegaard et al. (1999)
	NR	Vitellogenin production	NR	Nakari and Pesala (2005)
Lake whitefish	Diet, chronic	Decreased growth LOAEL	2 µg/gram	Kuo et al. (2010)
Chinese rare minnow	Water, chronic	Decreased growth LOAEL	10 µg/L	Li et al. (In Press)
	Water, chronic	Spermatogenesis inhibition LOAEL	10 µg/L	Li et al. (In Press)
	Water, chronic	Upregulation of thyroid hormones	Variably occurred at 0.1–10 µg/L	Li et al. (In Press)

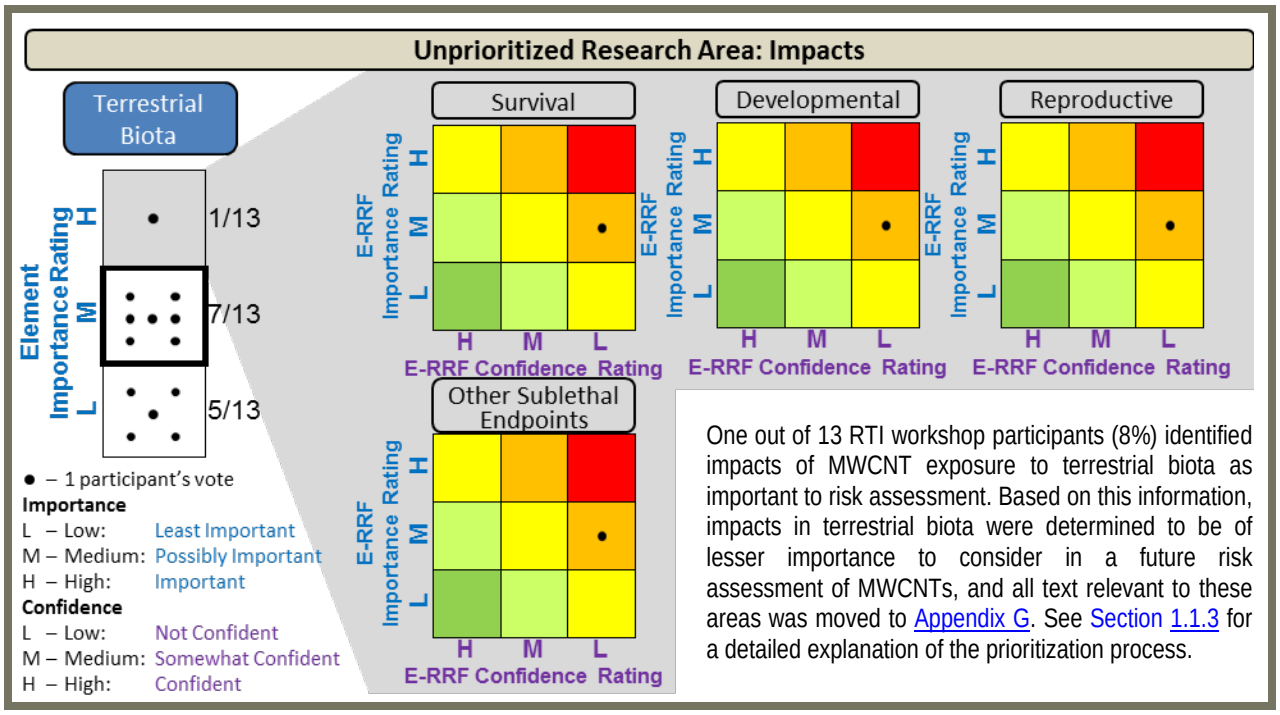
NR = Not reported, NOAEL = No-observed-adverse-effect level, LOAEL = Lowest-observed-adverse-effect level

Four studies were identified that investigated the effects of MWCNTs on fish; three of these studies used common laboratory species—zebrafish (*Danio rerio*) and Japanese medaka (*Oryzias latipes*), while one used rainbow trout (*Oncorhynchus mykiss*).

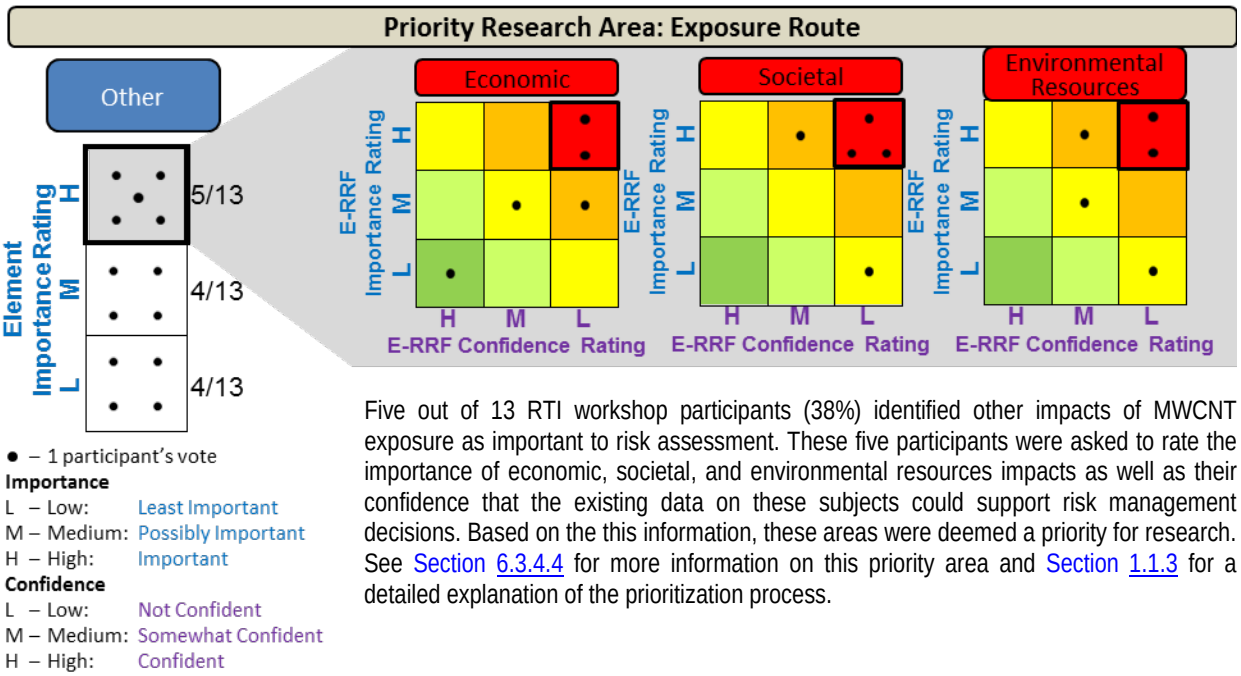
In one zebrafish study, embryos acutely exposed to MWCNTs showed dose-dependent increased mortality rates, reduced blood circulation, and delayed development (hatching), and developmental defects (bent notochord) starting at 60 µg/mL (Asharani et al., 2008). The other zebrafish study (Cheng et al., 2009) examined embryos following a smaller yet more direct exposure—a single microinjection of MWCNTs—and observed changes in enzyme expression signifying an immune response. Although no increase in mortality or developmental defects were observed in the exposed zebrafish through adulthood, survival in the second generation was significantly decreased. Similarly, Kim et al. (2012) observed a statistically significant increase in heart abnormalities, absence of swim bladders, caudal fin malformation, and pericardial and peritoneal edemas in Japanese medaka embryos following 4 days of continual exposure to 2,000 µg/L functionalized MWCNTs in the water. Increased mortality also occurred in response to exposures to 1,500 and 2,000 µg/L, and exposure to 1,500 µg/L resulted in a hatching delay.

Klaper et al. (2010) further investigated the possibility of an immune response in fish with an in vitro study of rainbow trout. In this study, MWCNTs did not elicit an antiviral response at sublethal doses up to 10 µg/mL; regardless of various types of functionalization. Investigators did, however, observe expression of IL-1beta, evident of macrophage stimulation, at 5 and 10 µg/mL (Klaper et al., 2010).

5.2.2. Terrestrial Receptors



5.3. Other Impacts



Five out of 13 RTI workshop participants (38%) identified other impacts of MWCNT exposure as important to risk assessment. These five participants were asked to rate the importance of economic, societal, and environmental resources impacts as well as their confidence that the existing data on these subjects could support risk management decisions. Based on the this information, these areas were deemed a priority for research. See Section 6.3.4.4 for more information on this priority area and Section 1.1.3 for a detailed explanation of the prioritization process.

As stated in Chapter 1, the CEA framework considers not only human and ecological health impacts, but also aesthetic, environmental, social, legal, ethical, and economic impacts. Such impacts might be associated with impacts on specific socioeconomic sectors (e.g., disparate impacts on environmental justice communities), the environment as a whole (e.g., climate change, depletion of natural resources, energy demand), or the built environment (e.g., damage to building facades).

Apart from the impacts discussed in Sections 5.1 and 5.2, the only other impacts considered in this case study are those for which a plausible premise can be developed to support assumptions that a discernible impact might occur as a result of the life cycle of MWCNTs flame-retardant upholstery textile coatings. Data from MWCNTs on each of these impacts would be required for a thorough comparison; however, in all cases where other impacts were identified as being of concern for either decaBDE or MWCNTs, no data were available for the comparison material. For example, for decaBDE, empirical data have revealed a correlation between decaBDE body burdens and socioeconomic status, indicating that effects having environmental justice implications are plausible for decaBDE. No such empirical data exist relating MWCNTs to other impacts, but the background literature on processes involved in manufacturing similar materials (e.g., carbon nanofibers [CNFs] and SWCNTs) provides some basis for concerns regarding potential impacts of MWCNTs on energy demand, resource depletion, climate change, and economics.

5.3.1. Environmental Justice

Environmental justice is defined by EPA as the "fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies."[18] The goal of environmental justice is to give all people "…the same degree of protection from environmental and health hazards and equal access to the decision-making process…"[19] As a result, environmental justice impacts include those in which a particular group or geographic area experiences a disproportionate share of the impacts associated with an environmental contaminant.

DecaBDE Can Inform MWCNT Assessment

Releases of decaBDE throughout the life cycle of a flame-retardant upholstery coating product could have greater impacts on racial and ethnic minorities and populations of lower socioeconomic status, as studies have found higher body burdens of BDE-209, the single isomer of decaBDE, among these populations. The causal pathway of this disproportionate exposure is not well understood, but certain characteristics of living environments (e.g., smaller size, poor ventilation, older age) might contribute to increased exposure levels for lower income families or individuals. Research planning to inform the societal impacts of MWCNTs in future risk assessments could consider: Are certain populations at greater risk of negative MWCNT impacts because of social, economic, or cultural differences? See Appendix H for more information about unintended societal impacts of decaBDE.

No information was identified that examined the relationship between MWCNT exposures and socioeconomic status.

5.3.2. Energy Demand and Natural Resource Depletion

DecaBDE Can Inform MWCNT Assessment

No information was identified that examined impacts on energy demand and natural resource depletion associated with the production of decaBDE flame-retardant textile coatings. Therefore, decaBDE does not provide information on environmental resource demands that could be applicable to research for future risk assessment of MWCNTs.

No information was identified that examined impacts on energy demand and natural resource depletion associated with the production of MWCNT flame-retardant textile coatings. Various studies, however, have calculated a large range of minimum energy requirements for synthesis of CNTs (Khanna et al., 2008; Cipiriano et al., 2007; Smalley et al., 2007). Table 5-4 presents an overview of some estimated minimum energy requirements and process rates for CNT synthesis.

The differences in energy requirements are largely attributable to different synthesis processes, different process rates, different feedstocks, and process improvements as synthesis of CNTs has been

[18]U.S. EPA Compliance and Enforcement. Environmental Justice. http://www.epa.gov/environmentaljustice/
[19]ibid

optimized (Gutowski et al., 2010; Kushnir and Sandén, 2008). Additionally, these energy requirements represent only the minimum for synthesis and do not consider the energy required for purification, additional infrastructure (e.g., equipment needed to regulate environmental conditions during synthesis and processing), and other related processes. Including these additional energy requirements, Gutowski et al. (2010) estimated that CNTs could be one of the most energy-intensive materials of all time. Although information regarding the energy requirements for MWCNT synthesis is limited, such energy requirements likely also would be sizeable and span a large range as synthesis processes are continually optimized.

One environmental impact assessment examined the water inputs required for two methods of continuous synthesis of SWCNTs via chemical vapor deposition (CVD) (Kolosnjaj-Tabi et al., 2010). These results indicated that production of SWCNTs can require significant amounts of water (almost 65,000 kg/hour at a manufacturing rate of about 595 kg/hour of SWCNTs). The relationship between water requirements for SWCNT synthesis and MWCNT synthesis, however, is unclear.

Table 5-4. Estimated minimum energy requirements and process rates for synthesis of CNTs.

Synthesis process	Material	Process rate (kg/hr)	Synthesis energy requirements (J/kg)	Estimated energy per hour (J/hr)	Reference
CVD	CNF (methane-based) CNF (ethylene-based)	1.30×10^{-2} 1.80×10^{-2}	3.13×10^{9} 2.22×10^{9}	4.07×10^{7} 3.96×10^{7}	Khanna et al. (2008)
Arc discharge	SWCNT	8.10×10^{-5}	8.73×10^{10}	7.07×10^{6}	Healy et al. (2008)
HiPCO®	SWCNT	4.50×10^{-4}	2.41×10^{10}	1.08×10^{7}	Smalley et al. (2007)
HiPCO®	SWCNT	4.50×10^{-4}	3.18×10^{10}	1.43×10^{7}	Healy et al. (2007)
Floating catalyst CVD[1]	MWCNT	NR	2.95×10^{8} (thermal) 1.87×10^{8} (electric)	NR	Kushnir and Sanden (2008)
Laser ablation[2]	MWCNT	NR	2.11×10^{8} (thermal) 9.4×10^{9} (electric)	NR	Kushnir and Sanden (2008)[3]

[1]Benzene gas feedstock.

[2]Graphite feedstock.

[3]Authors report both baseline (shown above) and "efficient" estimates (not shown).

CVD = chemical vapor deposition; CNF = carbon nanofiber; HiPCO® = a high pressure carbon monoxide synthesis process; NR = not reported.

Source: Gutowski et al. (2010).

A life-cycle assessment of CNF production via CVD calculated potential impacts on acidification, eutrophication, and ozone layer depletion (Khanna et al., 2008). The results of this analysis are presented in Table 5-5. The authors found that CNF production of both methane-based and ethylene-based CNFs has minor impacts on acidification, eutrophication, and ozone layer depletion. This study did not incorporate CNF emissions into its calculations, however, due to a lack of data on fate, transport, and impacts of CNFs (Khanna et al., 2008). The authors noted that the lack of models to predict endpoint effects of some emissions (e.g., CNF emissions) renders these calculations uncertain. Plata et al. (2009) found that release of gases such as methane, volatile organic compounds, and polycyclic aromatic hydrocarbons from MWCNT synthesis is possible. Methane release would likely have a negligible impact on local air pollution and ozone depletion compared to existing methane sources; however, release of volatile organic compounds such as 1,3-butadiene and benzene, could be significant on a local scale (Plata et al., 2009).

Table 5-5. Environmental assessment of production of 1 kilogram (kg) of carbon nanofibers.[1]

Impact category	Impact[2]		Unit
	Methane-based CNF	Ethylene-based CNF	
Acidification	5.5	4.0	Kg SO_2 Equivalent
Eutrophication	4.0	3.0	Kg PO_4 Equivalent
Ozone layer depletion potential	2.8×10^{-5}	2.8×10^{-5}	Kg CFC-11 Equivalent

[1]Environmental impacts of production of 1 kg of carbon nanofibers (CNFs) using chemical vapor deposition calculated by SimaPro® Eco-Indicator 1999 (EI99) method, hierarchist perspective (long-term; substances included if there is consensus regarding their effect; damages avoidable by good management; fossil fuels assumed not easily substituted).

[2]Normalized and weighted impacts.

Source: Khanna et al. (2008).

Eckelman et al. (2012) developed a life-cycle framework to compare the impact on ecological (and specifically aquatic) organisms of CNT production versus CNT releases to environmental media during the product life cycle. This assessment used existing data and a recently established consensus model for life-cycle impact assessments, USEtox, to estimate ecotoxicity from emissions during CNT production and CNT releases during product use and disposal for "realistic" and "worst case" scenarios. They calculated the potentially affected fraction of aquatic organisms per unit mass of CNTs released and "comparative toxic units for ecosystems" for different methods of synthesis and projected scale-up results. The theoretical framework was useful for comparing the relative impacts of different synthesis methods, what proportion of potential ecotoxicity is due to the synthesis process compared to required

purification methods, and also made projections based on future increased scale of production. The authors concluded that the greatest ecotoxicity impacts do not result from release of CNTs during the product life cycle or from unused reagents or synthesis products during production, but rather from the emission of metals due to the combustion of fossil fuels necessary to generate electricity for CNT synthesis or production of various inputs.

Another study analyzed a broad range of environmental impacts from the production of one SWCNT polymer mesh (a transistor/electromagnetic interference-shielding application) (Dahlben and Isaacs, 2009). The study examined both the energy requirements for raw material extraction and manufacturing and emissions from these processes (excluding SWCNT emissions due to the current lack of consensus on its effects). The authors found that manufacturing this CNT application could damage ecosystems and resource quality, as shown in Table 5-6. Damage to ecosystems (due to acidification/eutrophication and land use) was expressed as the loss of species over a certain area in a given time. Damage to resource quality was expressed as the surplus energy needed for future extractions of minerals and fossil fuels (due to the resources needed to extract these materials for SWCNT polymer mesh production).

Table 5-6. Environmental assessment of production of one SWCNT polymer mesh.

Impact category[1]	Impact[2]	Unit
Acidification/Eutrophication	1.229×10^{-2}	PDF*m^{2}yr
Land use	4.440×10^{-3}	PDF*m^{2}yr
Minerals	1.117×10^{-3}	MJ Surplus
Fossil fuels	7.531×10^{-1}	MJ Surplus

[1]Environmental impacts of production of one SWCNT polymer mesh by high-pressure carbon monoxide synthesis (a form of chemical vapor deposition) calculated by SimaPro® Eco-Indicator 1999 (EI99) method, hierarchist perspective (long-term; substances included if there is consensus regarding their effect; damages avoidable by good management; fossil fuels assumed not easily substituted).

[2]Normalized and weighted impacts.

PDF*m^{2}yr = potentially disappeared fraction per area (m^2) per year;
MJ Surplus = Additional megajoules of energy required for future extraction of the resource.

Source: Dahlben and Isaacs (2009).

The authors found that production of SWCNT polymer mesh generated larger fossil fuel impacts relative to other measured environmental impacts. The authors also found that fossil fuel impacts were dominated by processes requiring energy-intensive equipment (e.g., furnace for synthesis, wet bench for cleaning, and spinner for coating). Although the impact measures were reported to be low for all categories, they represent the resource impacts of producing a single SWCNT polymer mesh. The level of aggregation required to compile these metrics, however, coupled with the lack of models to predict

endpoint effects of some emissions (e.g., from nanotubes), render these metrics highly uncertain (Khanna et al., 2008). Additionally, this study did not include impacts of SWCNT emissions in its overall calculations of environmental impact. How the environmental impacts of SWCNT polymer mesh production differ from the impacts of flame-retardant textiles using MWCNTs or other alternative materials, such as decaBDE, is unclear.

5.3.3. Climate Change

No information was identified that directly examined climate change impacts due to MWCNT flame-retardant coatings. Empirical data suggest, however, that release of greenhouse gases such as methane, volatile organic compounds, and polycyclic aromatic hydrocarbons from MWCNT synthesis is possible (Plata, 2009; Plata et al., 2009). The authors concluded, however, that for commercial-scale production the contribution of MWCNT synthesis to atmospheric methane will be negligible compared to existing methane sources, and that volatile organic compound emissions might be significant only on the local scale (Plata et al., 2009). Singh et al. (2009) calculated emissions of 4 kg CO_2/kg SWCNT from one method of CVD synthesis. Altering CNT synthesis methods might minimize formation of these or other hazardous by-products. For example, Plata (2009) found that by identifying select thermally generated compounds correlated with CNT growth rate, such compounds could be delivered to the catalyst without thermal treatment and thereby eliminate the need to heat reactant gases.

On the other hand, a life-cycle assessment of CNF production calculated that manufacture of 1 kg of methane-based CNFs equals at least 700 kg of CO_2 equivalents, and 1 kg of ethylene-based CNFs equals at least 400 kg of CO_2 equivalents (Khanna et al., 2008). In other words, the authors calculated that production of 1 kg of methane-based CNFs is equivalent to CO_2 emissions from 78.5 gallons of gasoline consumed, while production of 1 kg of ethylene-based CNFs is equivalent to CO_2 emissions from 44.8 gallons of gasoline consumed.[20] The relationship between climate change effects due to synthesis of SWCNTs, CNFs, and MWCNTs is unclear.

[20]EPA GHG Calculator available at http://www.epa.gov/cleanenergy/energy-resources/calculator.html .

5.3.4. Economics

No information was identified that calculated the cost of manufacturing MWCNTs or MWCNT flame-retardant textiles. Isaacs et al. (2010) estimated, however, that the cost of manufacturing 1 gram of SWCNTs by arc discharge, CVD, and HiPCO® (a type of CVD commonly used to manufacture SWCNTs) is roughly $1,906; $1,706; and $485; respectively. These estimates include all materials, labor, and equipment necessary for synthesis, dispersion, filtration, inspection, and packaging of SWCNTs. MWCNTs are generally thought to be less expensive to produce than SWCNTs, and further optimization of MWCNT manufacturing is likely to decrease manufacturing costs further.

DecaBDE Can Inform MWCNT Assessment

No information was identified that calculated the cost of manufacturing decaBDE or decaBDE flame-retardant textiles. Therefore, decaBDE does not provide economic impact information that could be applicable to research for future risk assessment of MWCNTs.

Chapter 6. Identifying and Prioritizing Research Needs to Support Risk Assessment and Risk Management

6.1. Context for Identifying and Prioritizing Research

Previous chapters in this case study represent the assembly of information through the vertical continuum of the comprehensive environmental assessment (CEA) framework (see Figure 1-1) as introduced in Chapter 1; however, this step is merely the first in the CEA process (see Figure 1-2). The second step is for a diverse group of expert stakeholders to consider the information compiled in the framework in the context of their own knowledge of multiwalled carbon nanotubes (MWCNTs) and flame-retardant materials. This second step serves to identify and prioritize research needs for future risk assessment efforts that inform risk management practices for MWCNTs in flame-retardant textile coatings. The outcomes of this step are the focus of the current document and are intended to support subsequent efforts within the CEA process to facilitate an iterative communication flow across the horizontal spectrum of research, risk assessment, and risk management (see Figure 6-1).

Figure 6-1. Iterative communication flow in the CEA framework.

Recently, the National Research Council and others in the scientific community have made several recommendations to improve risk assessment and risk management approaches. Recommendations include calls for greater transparency and increased stakeholder engagement in assessment efforts for evaluating options to mitigate the exposures or hazard(s) associated with an agent (NRC, 2009). Greater transparency and broader stakeholder input promote informed evaluations of the various trade-offs between individual risk management options (NRC, 2009). More recently, the need to

consider longer term consequences of alternative options in a broader context has been recognized, which would encompass social, environmental, and economic indicators (NRC, 2011). All of these recommendations indicate the need for risk assessments to address cumulative effects from multiple exposures to one or more stressors, vulnerability of susceptible populations, and potential for impacts throughout the product life cycle (NRC, 2011, 2009). A shift toward this more holistic, systems-based approach would provide more complete information to risk assessors to better inform risk managers in making decisions that support long-term, sustainable management practices (NRC, 2011).

Many efforts are underway to gather information and develop approaches that support the implementation of such recommendations [e.g., (Anastas, 2012; Lavoie et al., 2010; Rossi et al., 2006)]. The CEA approach represents one such effort by recognizing that research supporting risk assessment must be transparently planned and executed if risk assessments are to be used effectively and efficiently for evaluating risk management options and understanding the longer term consequences of a broad scope of complex information (e.g., cumulative risk, life-cycle analyses). The External Review Draft of this document was used in the collective judgment step of the CEA process as part of an effort to plan such research for MWCNTs in flame-retardant textile coatings. Specifically, a group of expert stakeholders representing a variety of technical backgrounds (e.g., analytical chemistry, toxicology, polymer science) and sectors (e.g., industry, academia, nongovernmental organizations) used this document as a starting point for identifying and prioritizing research needs to support assessments that inform near-term risk management goals (see Section 1.1.3).

In planning research to support assessments, it is useful to review risk management goals to understand the types of analyses and assessments that would inform management efforts. Such a review is consistent with the connections highlighted in the CEA process diagram (see Figure 1-2). Research outcomes in the form of data from single studies or assessment reports [which have compiled information across multiple studies (e.g., risk assessments, life-cycle assessments, meta-analyses)], feed back into the CEA framework to provide additional information necessary for assessing risk-related trade-offs. This additional information is subsequently used in developing adaptive risk management plans. Such future evaluations of risk-related trade-offs could focus on informing one of a variety of risk management goals for the application of MWCNTs in flame-retardant textile coatings. As discussed in Chapter 1, the selection of any one goal for a comparative CEA would depend on the needs of risk managers at the time. One particular scenario, however, based on what might occur for this specific nanoenabled product, is described below as an example that might inform research planning for the research priorities identified in this application of CEA. The use of this scenario is not meant to imply actual assessment or risk management recommendations, but rather to illustrate the type of context in which the research priorities

identified here could inform future evaluations of MWCNTs. Additional considerations and examples of risk assessment and risk management decisions are discussed in Section 6.2.

As outlined in Chapter 1, the use of MWCNTs in flame-retardant textile coatings is not common, although evidence suggests that they could be used more extensively in the future as conventional flame-retardants such as decaBDE are phased out due to concerns surrounding environmental persistence and human health effects (see Additional Information Highlight Box 1and Section 1.1.3). Should a flame-retardant textile coating containing MWCNTs be developed for use in the United States, the manufacturer or importer likely would submit a premanufacturing notice (PMN) (U.S. EPA, 2008c). Information in a PMN includes the identity of the chemical (i.e., name and structure), anticipated production volume, use and disposal methods, human exposure estimates, and any readily available test data (U.S. EPA, 2010g). Thus, one of the first risk management decisions for MWCNT flame-retardant textile coatings could be to determine whether the material should be (1) produced without restriction or regulations, (2) imported, produced, or used with limitations, or (3) prohibited from import, production, or use (U.S. EPA, 2010f). The third outcome, prohibition, could result from several determinations, including insufficient information on potential impacts of the material (U.S. EPA, 2010f).

To support this and other risk management decisions about the use of MWCNTs in flame-retardant textile coatings, information must be readily available to decision-makers to enable a considered determination within the relevant time constraints. Ideally, the research objectives identified and prioritized in this CEA application would provide such information within 3 to 5 years of initiating the research. Notably, completion of all research is not feasible within this time frame due to practical constraints. Thus, the collective judgment step of the CEA approach emphasizes the prioritization of information gaps (see Figure 1-2).

6.2. Identification and Prioritization of Research Needs

With the above context for identifying and prioritizing research needs to support future assessments and risk management decisions for MWCNT, the lingering question is: How? As discussed in the previous section and in Chapter 1, a group of expert stakeholders representing diverse technical (e.g., toxicology, ecology, material science) and sector (e.g, industry, academia, government) perspectives participated in a structured collective judgment process that supported equal representation of each individual's input. Specifically, participants used a more detailed view of the CEA framework (see Figure 1-3) to consider each element of the framework (e.g., stages of the product life cycle or spatial zones in the environment) in relation to potentially relevant risk factors (e.g., mobility in air) associated with the life cycle of a MWCNT flame-retardant textile coating product. Stakeholders used an online software-

based tool that supported their consideration of each area of the CEA framework remotely. They used the tool in a series of exercises to qualify the: (1) importance of CEA framework components for future assessments, and (2) current state of the science of the components for supporting risk management initiatives (see Figure 1-3). These exercises were intended to actively engage stakeholders in identifying critical research needs based on each stakeholder's: (1) perception of the information presented in the case study, (2) individual experience, and (3) expert opinion. Based on previous applications of CEA, this approach is thought to be an improvement over one that would simply ask stakeholders to review and prioritize a predetermined list of data gaps, which could exclude important data gaps a priori. This collective judgment exercise, coupled with a subsequent structured, face-to-face workshop, provided a set of specific research needs (see Section 6.3).

As discussed in the previous section, planning and conducting research to fill the priority areas discussed below (see Section 6.3) is facilitated by having an understanding of assessment and risk management approaches. To help facilitate the transition from reviewing the case study to identifying and prioritizing specific research needs, experts participating in the collective judgment exercise were encouraged to consider the first step of conducting an assessment—problem formulation. Considering problem formulation can similarly help plan research to fill the gaps that experts identified as priorities (see Section 6.3). Placing a greater focus on problem formulation is recognized as an important step toward improving risk assessment (NRC, 2009), but the preceding step—anticipating what information to research to support problem formulation—has received less attention. The CEA approach places greater emphasis on problem formulation during the research planning stage by engaging stakeholders to prioritize areas for research mangers to consider in allocating research resources. In doing so, it ensures that (1) major factors important to stakeholders are included early in the planning process, and (2) risk assessors and managers have the information they need to develop risk assessments and management plans that include those considerations. This approach is consistent with recent National Academy of Science recommendations (NRC, 2011, 2009). Similarly, the inclusion of long-term, broad environmental impacts in the CEA framework supports identifying research gaps in these areas, which are increasingly recognized as essential to assessments but are often more difficult to incorporate because of insufficient data or knowledge on how to include such information (NRC, 2011).

Thus, in planning research to support future assessments and risk management efforts, it is essential to have a clear understanding of problem formulation. This early step in the risk assessment process establishes the goals, scope, focus, and potential options to consider in decision-making (NRC, 2009; Van Leeuwen et al., 1998). The problem formulation step helps establish the type of analyses, and associated uncertainty and variability, which will be useful to a risk manager in making a decision about the material, chemical, or technology of focus (NRC, 2009; Van Leeuwen et al., 1998). It is important

then to establish the type of research that will be useful for the analyses that inform a risk manager about a particular material, such as MWCNT. Notably, it is necessary to plan for a variety of types of risk management decisions, as shown in Table 6-1. Although this particular CEA case study was not developed with a specific risk management objective in mind, the identification of key research gaps within the CEA framework can inform research planning that supports multiple assessment objectives identified during the problem formulation stage of each respective assessment. These future assessments can then supply new information in the CEA framework for MWCNTs, which could subsequently be evaluated in collective judgment prioritization of risk-related trade-offs to inform specific risk management decisions.

Table 6-1. Examples of risk management decisions.

Area of Decision-Making	Directed At	Example Decisions
Product environmental health and safety	• New chemicals • Existing chemicals • Biotechnology	• Pre-manufacturing notices • Pesticide re-evaluations • Permits to release genetically modified organisms
Site management	• Risk avoidance • Risk mitigation • Site location	• Accidental releases • Cleanup of hazardous waste landfills • Degree of contamination, presence of endangered species
Natural Resource Use	• Habitat integrity • Species introductions	• Land use (e.g., road construction, mining, agriculture, logging) • Integrated pest management

Adapted from Van Leeuwen et al. (1998).

The External Review Draft of this document used the CEA framework to lay out the technical aspects related to MWCNTs in flame-retardant textile coatings so that expert stakeholders could determine (1) what types of risk management decisions are likely to be needed and (2) what information would support assessments that inform those decisions. Stakeholder input was incorporated into this final version of the case study document to emphasize areas of the CEA framework that stakeholders felt were research priorities for risk assessment and risk management. The questions in Table 6-2 are examples of those that could be asked during the problem formulation phase of an assessment to evaluate whether data are available and useful (e.g., consider relevant endpoints, relevant exposure routes, doses and timing, acceptable levels of uncertainty in assays selected, data variability) to support each component of an assessment. The answers to these questions can help formulate an appropriate assessment approach or facilitate the identification of additional data gaps that must be filled before the assessment can proceed.

In the context of this case study, the extent to which these questions, along with other questions identified by stakeholders, could be answered indicates whether specific research initiatives should be pursued in certain areas of the CEA framework.

Table 6-2. Example questions for problem formulation.

General Areas	Specific Questions
What are the characteristics of the stressor of concern?	Is the stressor of concern chemical, physical, or biological?
	What are the physicochemical characteristics of the stressor?
	What are the locations and quantities of releases of the stressor to different media?
What are the characteristics of the exposure setting?	What are the known concentrations of the stressor in different media?
	What processes move the stressor through the environment?
	How does the stressor change as it moves through the environment?
	What is the spatial scale over which exposures to the stressor are likely to occur?
What are the characteristics of the exposed populations?	Which individuals, populations, or population segments are expected to be exposed?
	Which species and trophic-level relationships are present in exposed ecosystems?
	What are the probable exposure routes and pathways for the population(s) of interest?
	Is exposure to the stressor expected to occur only during a single event or will exposures be episodic or continuous?
	What is the time scale over which exposures to the stressor are likely to occur?
What are the assessment endpoints?	What adverse effects have been observed in the population(s) of interest?
	What are the most sensitive species and measured endpoints?
	What processes affect the behavior of the stressor within the receptor?
	How does the stressor change as it moves through the receptor?
	What biological mechanisms are involved in the formation of adverse effects?
	What social conditions or impacts might result from the stressor?
	What economic conditions or impacts might result from the stressor?
	What natural resources might be affected and how?
	What ecosystem services might be altered and how?

6.3. Research Priorities Identified through Collective Judgment in this Application of CEA

The collective judgment process to engage expert stakeholders, which was summarized in Section 6.2 and in Chapter 1, is described in detail in a separate report, which was prepared by the contractor that independently conducted the EPA-funded workshop (RTI, 2012). The areas of the CEA framework that experts most commonly identified as "important to consider in a risk assessment" (presented in Chapter 2 through Chapter 5) are discussed here in the context of supporting research planning and future assessment and risk management of MWCNTs in flame-retardant textile coatings.

For each area, the reasons why the experts rated certain research areas as priorities, is first discussed. When participants individually rated the importance of an area and their confidence that the current data could support risk management, they had the option of completing a checklist of "influential factors." These factors (Table 6-3) represent various aspects of MWCNT science that could play a role in determining, inducing, or otherwise influencing the potential risks associated with the particular area in question and are listed after the rationales provided by participants. As this portion of the prioritization process was voluntary, not all participants chose to identify influential factors and omission of an influential factor does not necessarily imply that the factor is unimportant. Nevertheless, identification of the influential factors for each area provides some additional insight as to why a particular area might be a priority, and what particular aspects of that area might warrant further research.

Next, other relevant literature, which was not included in the External Review Draft of the case study, is discussed in terms of whether that literature might improve confidence in the ability of the data to support risk management decisions, or how it might support research planning. Finally, for those areas that expert stakeholders discussed at the workshop, the potential risk scenario that they identified for the area is outlined along with the types of risk management decisions they noted might be made to mitigate or avoid the potential risk. The type(s) of assessments that could inform these types of risk management decisions that participants noted are laid out, followed by a table detailing the key research questions or areas that experts identified along with their estimates of the financial and time resources needed to carry out the research.[21] For those Research Priority Areas not discussed at the workshop due to time constraints, potential research directions are listed in the text. Research Priority Areas are presented below

[21] Note that time and financial estimates were generated by experts participating in the independently conducted RTI workshop. They are based on participants' experience with planning and conducting scientific research and are included here with the intention of providing a general indication of the level of resources that would support carrying out the identified priority research questions.

in the order in which they appear in the CEA framework and in Chapter 2 through Chapter 5 of this document.

Table 6-3. Influential Factors options for all areas.

Influential Factors	Methods, Techniques	Analytical techniques, control technologies, MWCNT processing methods, MWCNT purity, MWCNT synthesis methods, personal protective equipment, other (specify other)
	Engineered Nano Material Characteristics	Adsorption/desorption ability, aggregation/agglomeration state, applied coatings, biodegradability, catalytic activity, charge, conductive or magnetic properties, crystalline phase, lipophilicity, matrix bound vs. free form, morphology, persistence, redox potential, size/size distribution, specific surface area, structural formula/molecular structure, surface chemistry, water solubility/dispersibility, other (specify other)
	Surrounding Media	Air, groundwater, sediment, soil, surface water, wastewater, other (specify other)
	Physical Conditions	Flow regime, light availability, soil porosity, soil/sediment fractionation, temperature, wind, other (specify other)
	Chemical Conditions	Conductivity, dispersing agents, dissolved oxygen content, exposure to sunlight, heavy metals in environment, ionic strength in environment, ligand concentrations in environment, natural organic matter, other contaminants in environment, pH, protein concentration in environment, salinity, surfactant (in lab) other (specify other)
	Biological Conditions	ADME, bioaccumulation, biomagnification, microbial communities, organism health, species/individual developmental behavior, species/individual feeding behavior, species/individual reproductive behavior, other (specify other)
	Social Conditions	Acute exposure, chronic exposure, exposure route, geographic location, habitat structure, human activity, individual activity level, life stage, occupation, subchronic exposure, susceptible populations/individuals, other (specify other)

6.3.1. Product Life Cycle

Multiple areas of the product life cycle were considered to be Priority Research Areas according to workshop participants. Material synthesis and processing as well as product manufacturing were noted to be particularly important by workshop participants, in part because these areas of the CEA framework play a key role in determining all other parts of the CEA framework, including fate and transport in various environmental media, bioavailability and potential exposure, as well as ecological and human toxicological impacts. In a recent publication, Nowack et al. (2012) similarly note the importance of characterizing engineered nanomaterials throughout the life cycle: how the starting material is intentionally modified through functionalization (see Figure 2-2) and unintentionally modified by environmental factors (see Figure 3-1) determines how it will behave in the environment, how organisms can be exposed, and the extent to which it will adversely impact ecological and human receptors [(Nowack et al., 2012); see Additional Information Highlight Box 6]. While the chemical alterations to nanomaterials are important for potential release and toxicity, the properties of the product matrix and the manner in which nanomaterials are incorporated into a matrix are equally important (Nowack et al.,

2012). Nowack et al. (2012) also note that a key research question is whether different modifications to nanomaterials and incorporation into different product matrices will have increased or decreased reactivity or toxicity relative to their pristine counterparts. There is also a lack of available data on the emissions of nanomaterials from products and releases to the environment, particularly under realistic conditions (Nowack et al., 2012). This is due in part to the absence of robust analytical techniques and instrumentation for accurately detecting and quantifying both emissions and environmental concentrations of nanomaterials (Nowack et al., 2012) (see Additional Information Highlight Box 10).

In each product life cycle stage in the CEA framework, "volume" and "release rate" are risk relevance factors that might be considered in risk assessments and risk management efforts of a material. While these might be considered separately during future assessment and risk management efforts they are discussed together for each area below. In general, workshop participants rated release rate more highly than volume in terms of importance to consider in future risk assessments of MWCNTs. Experts noted during the workshop that this is partially due to the fact that while production volume is important for understanding the potential scale of impact (see Table 2-2 for information on current scale and projected growth of MWCNTs production), release rate is what will ultimately determine the extent of exposure. In other words, a large production volume might not cause concern if release rate is relatively small, but a smaller production volume could still cause concern if release rate is particularly high. Given that very little information is available for either topic and that each product life cycle area has such a large influence on all other CEA areas, volume and release rate are particularly important to consider in future risk assessment and risk management of MWCNTs.

6.3.1.1. Material Synthesis: Volume and Release Rate

The workshop participants identified MWCNT material synthesis as important to risk assessment. Risk relevance factors that might be considered in future assessment or risk management efforts for this or other stages of the product life cycle include volume and release rate. Participants most commonly identified both of these factors as important to risk assessment. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 2.2.2). Below are examples of experts' rationale for rating these areas as research priorities.

- **Material synthesis—Volume:** Reporting from material synthesis is voluntary at this point, so little is known about MWCNT synthesis volume.
- **Material synthesis—Release rate:** No universal reporting mechanism is available, so little is known about MWCNT release rates. In addition, there is currently uncertainty about manufacturing factors that could have ecological consequences (e.g., surfactants,

not just active ingredients, should be tested to make experiments more realistic to real-world scenarios.)

The overarching influential factors identified by multiple experts for both volume and release rate characteristics included a variety of methods and techniques (e.g., control technologies, personal protective equipment, MWCNT synthesis and purity), ENM characteristics, factors associated with the surrounding media, as well as physical (e.g., flow regime, temperature, wind), chemical, and social conditions (e.g., acute, subchronic, and chronic exposure).

No studies were identified regarding the volume of MWCNTs produced for use in flame-retardant textiles or the release rate during synthesis of MWCNTs for flame-retardant formulations (see Table 2-2 for general information on production volume). As noted in Section 2.2.2.2, there are several potential release scenarios during material synthesis, including recovery of the synthesized substance, handling/packaging, equipment cleaning, and accidental release (e.g., fugitive leaks, equipment malfunction, malfunctioning ventilation systems, exposure to fire and heat). In particular, during handling and mixing of raw materials, CNTs might become airborne under conditions where powder is being handled, weighed, or mixed, although this will largely depend on the synthesis methods and use of control technologies (SAFENANO, 2012); see Sections 2.2.2.2 and 6.3.3.1). In one study for example, Dahm et al. (2011a) found that some facilities typically handling large quantities (40 grams to 1 kg of MWCNTs handled per day in powder form and aqueous form), still had measured releases above the NIOSH REL of 7 $\mu g/m^3$ of concern, despite the use of enclosed processes or other forms of control technologies. The authors note, however, that their measurements were collected as inhalable mass concentration of elemental carbon while the NIOSH REL is based on the respirable mass concentration of elemental carbon, suggesting that measurements at primary facilities might not be appropriately characterized in reference to this standard (see Section 6.3.3.1 for information regarding occupational exposure and use of control technologies).

Though time did not allow for expert stakeholders participating in the CEA collective judgment workshop on MWCNTs to develop specific research questions for material synthesis, the existing information described above and in Chapter 2 point to several research areas that could support future risk assessment and risk management efforts, including:

- What is the median volume of MWCNT produced at manufacturing facilities?
- What volume of metal catalysts and support materials (e.g., aluminum, silica) are required for manufacturing MWCNTs in current production facilities?
- What volume of water is used by MWCNT production facilities to clean equipment?
- Does release rate vary during MWCNT synthesis using chemical vapor deposition, fluidized bed chemical vapor deposition, arc discharge or other methods?

- Are metal catalyst or support materials released during MWCNT synthesis?

6.3.1.2. Material Processing: Volume and Release Rate

The workshop participants identified MWCNT material processing as important to risk assessment, and subsequently processing volume and release rate were both most commonly identified as important risk relevance factors. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 2.2.3). Below are examples of experts' rationale for rating these areas as research priorities.

- **Material processing--Volume:** While processing volume information may be available to manufacturers and EPA regulators, and volume figures for decaBDE could be used to calculate potential worst case release scenarios, little information is available for scientists and the general public. Depending on the application of the product, there is great opportunity for exposure.

- **Material processing--Release rate:** There is not enough data on releases from material processing, yet it is critical to determine release rate and exposure. Fabric coating operations, for example, are resulting in releases to the environment, so there is a need to understand the form of release (e.g., matrix bound, aggregate, etc.) and develop better analytical methods for carbon nanotube quantification.

The overarching influential factors identified by multiple experts for both material processing volume and release rate characteristics included: methods and techniques (e.g., control technologies and MWCNT purity), ENM characteristics, factors associated with the surrounding media (e.g., air, sediment, soil, wastewater), as well as physical, chemical, biological and social conditions.

No additional data were identified for this area in revising the External Review Draft; however to extend upon available data for MWCNT material processing, research planning efforts might consider input from the CEA collective judgment workshop. Expert stakeholders discussed release rate during material processing to identify potential risk scenarios that might occur during this stage of the product life cycle along with specific research questions that, if pursued, might inform future assessment and risk management efforts in this area (RTI, 2012). Based on those discussions, potential risk scenarios include: (1) release into the air that results in worker exposure, and (2) MWCNT release into sewage treatment plants (STP) that results in environmental exposures. To mitigate or avoid these potential risk scenarios experts noted that risk management decisions could include the use of controls to minimize MWCNT concentrations in occupational air or waste water. Experts noted that quantifying release rates in these scenarios could inform the selection of appropriate control technologies. This type of quantification might be carried out as part of an environmental or occupational assessment, according to experts. To support

these types of measurements the following research questions were developed by expert participants along with an estimate of the resources and time to carry out the research:

Table 6-4. Research Identified by RTI Workshop Participants: MWCNT Material Processing.

Research	Estimated Finances ($)	Estimated Time Frame
What is occupational exposure at current MWCNT processing facilities? [Evaluate exposure to workers at manufacturing facilities to identify key steps in exposure. Evaluate control or personal protective equipment measures for reducing exposure].[1]	100,000	1 year
What is release rate in wastewater from current MWCNT processing facilities? [Evaluate release rates based on different technologies for: synthesis, filtration, remediation.]	100,000	1 year
Develop Method (instrument) to characterize and quantify in waste liquid for monitoring.	500,000	5 years
What is the best method to capture/destroy CNT in waste liquid?	300,000	3 years
Can CNT synthesis techniques reduce potential releases through control of initial raw CNT form?	300,000	3 years
What air handling technologies can be used to reduce occupational exposure?	200,000	2 years

[1]Note: Information in brackets [ ] denotes details extracted from responses experts provided along with the question or research area.

6.3.1.3. Product Manufacturing: Volume and Release Rate

The workshop participants identified MWCNT product manufacturing as important to risk assessment, and subsequently volume and release rate at this stage were most commonly identified as important risk relevance factors. Participants were generally not confident or only somewhat confident in the ability of data to support risk management decisions related to either volume or release rate at this stage of the product life cycle (see Priority Research Area Highlight Box in Section 2.2.4). Below are examples of experts' rationale[22] for rating these areas as research priorities.

- **Product manufacturing—Volume:** No universal reporting mechanism is currently available to capture product manufacturing volume of MWCNTs, thus the magnitude for potential for release is not known (we currently assume decaBDE-product volumes to calculate worst case scenarios). While confidential business information may be known to manufacturers and available to EPA regulators, little information is available for scientists and the general public. Development of methods to quantify and detect ENMs is needed.

[22] Note that rationales are taken directly from participants' responses in the RTI workshop process.

- **Product manufacturing—Release rate:** There has not been enough study of manufacturing release rates, which are critical for determining exposure. Better analytical methods are needed for carbon nanotube quantification. There is a disconnect between EHS research and real-world ENM toxicity, characterizations, etc.

The overarching influential factors identified by multiple experts for both product manufacturing volume and manufacturing release rate characteristics included: methods techniques (e.g., processing methods, personal protective equipment), ENM characteristics, factors associated with the surrounding media, as well as physical, chemical, biological and social conditions.

Of all the stages in the product life cycle, workshop participants placed the most importance on product manufacturing, with 12 of 13 participants (92%) identifying it as being important to consider in future risk assessments of MWCNTs. No studies were identified regarding the volume of MWCNT flame retardant textiles produced, although Additional Information Highlight Box 2 notes that the scale is relatively small and is primarily associated with the research and development stage.

Chaudhry et al. (2009) provides the most relevant information available regarding the material synthesis (see Section 6.3.1) and product manufacturing stages of CNT textiles. The authors note that the production of such textiles involves the use of fibers, yarn, fabrics, or finished products where the CNTs will be embedded in the matrix via melting, mixing, co-extruding, granulating, or fixing/curing. Further, CNTs could be released during these stages when powders are handled or CNTs are dispersed in polymers (Chaudhry et al., 2009); see Section 2.2.3.2. Similarly, SAFENANO (2012) noted that when fibers are coated with CNTs, a suspension containing CNTs is likely to be applied to a textile either through dipping or spraying. Dipping activities would be less likely to result in airborne CNTs and therefore have less potential for exposure than spray applications. During spinning of fibers or weaving, SAFENANO (2012) noted that CNTs could be released due to the high-energy mechanical abrasion of the filaments as they are drawn, spun, and wound, but that released CNTs are not likely to be "free" in this scenario. This premise is also supported by the results of Takaya et al. (2012). Yarn coated with MWCNTs was released during the weaving process without evidence of free MWCNTs in the respirable dust (see Section 6.3.3.1 for more information regarding occupational exposure and use of control technologies in the industry).

To build upon available data for product manufacturing of MWCNT flame retardant textiles, research planning efforts might consider input from the CEA collective judgment workshop. Expert stakeholders participating in the workshop discussed release rate during product manufacturing to identify potential risk scenarios that might occur during this stage of the product life cycle along with specific research questions that, if pursued, might inform future assessment and risk management efforts in this area (RTI, 2012). Similar to the material processing product life cycle stage, for product manufacturing, workshop participants noted the possibility of release to air and subsequent worker exposure, as well as

MWCNT release to sewage treatment plants that could result in environmental exposures (see Section 6.3.2.2 for discussion on the Research Priority of the environmental transport, transformation and fate of MWCNTs in waste water). The following research questions related to these potential scenarios were developed by expert participants, along with an estimate of the resources and time to carry out the research:

Table 6-5. Research Identified by RTI Workshop Participants: MWCNT Product Manufacturing.

Research	Estimated Finances ($)	Estimated Time Frame
What is the step in manufacturing that presents most risk of release to the environment? [Evaluate potential release rates (e.g., grams/day) based on the manufacturing technique(s) used for: functionalization, dispersion, coating. Evaluate how manufacturing techniques influence released particle characteristics.][1]	100,000	1 year
What is the step in manufacturing that presents most risk of occupational exposure? [Evaluate potential release rate (e.g., mass / m^3, surface area/ m^3, number/ m^3) to occupational air based on manufacturing technique during: functionalization, dispersion, coating. Evaluate how manufacturing technique influences released particle characteristics.]	100,000	1 year
How does MWCNT functionalization affect the filtration efficiency and size distribution?	100,000	2 years
How does the dispersion technique affect the filtration efficiency and size distribution?	100,000	2 years

[1]Note: Information in brackets [ ] denotes details extracted from responses experts provided along with the question or research area.

6.3.1.4. Use: Volume and Release Rate

The workshop participants identified MWCNT use as important to risk assessment, and subsequently use volume and release rate were most commonly identified as important risk relevance factors. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 2.4). Below are examples of experts' rationale for rating these areas as research priorities.

- **Use—Volume:** No universal reporting mechanism is currently available to capture volume of use of MWCNTs, thus the magnitude for potential for release is not known (we currently assume decaBDE-product volumes to calculate worst case scenarios). While confidential business information may be known to manufacturers and available to EPA regulators, little information is available for scientists and the general public.

- **Use—Release rate:** Better analytical methods are needed for carbon nanotube quantification, particularly for measuring consumer exposure to releases from furniture and other products, as well as quantifying and detecting ENMs in the environment.

The overarching influential factors identified by multiple experts for both use volume and use release rate characteristics included: methods and techniques (e.g., MWCNT processing), ENM characteristics (e.g., applied coatings, matrix bound vs. free, morphology, surface chemistry), factors associated with the surrounding media, as well as chemical, biological and social conditions (e.g., chronic exposure, life stage).

No studies were identified regarding the volume of MWCNT use in flame-retardant textiles, as this application is not widespread (see Additional Information Highlight Box 2). In the absence of data, predictions must be made using known information about decaBDE flame-retardant textiles and textiles in general. Release during use is primarily expected to be caused by the degradation of the product matrix. For example, garments typically have 10% weight loss over the course of the life cycle due to washing, ironing, weathering, thermal degradation, and wear and tear (SAFENANO, 2012; Chaudhry et al., 2009). Other non-clothing textiles have been reported to lose between 5% and 20% of their weight during normal use due to washing, exposure to heat, aging, and abrasion (Greßler et al., 2010). Very little information is available regarding the likelihood of MWCNTs being released from textiles during normal use, particularly in the specific application of flame-retardant textiles, but some evidence exists that MWCNTs could become airborne after the textile is burned and the char residue is mechanically disturbed (Uddin and Nyden, 2011a; Nyden et al., 2010) or during washing (Gonçalves et al., 2012).

Experts at the workshop noted that the release rate during product use was a particularly important area for further investigation and in need of better analytical techniques due to its direct influence on human exposure (RTI, 2012). Similar to material processing and product manufacturing, workshop participants also noted that potential risk might arise in this product life cycle stage from release of MWCNTs in indoor air or the environment (e.g., wastewater treatment), resulting in exposure to consumers (see Sections 6.3.3.2 and 6.3.2.2 for discussion on Priority Research Areas: Consumer Exposure and Wastewater, respectively). For this product life cycle stage they noted that regulations pertaining to the type of matrix used with MWCNT flame retardants might be used to avoid or mitigate potential risk. Based on their input, human health and ecological risk assessments could inform this type of risk management decision. Research questions that experts identified to support conducting these types of assessments, along with estimates of the resources and time to carry out the research, include:

Table 6-6. Research Identified by RTI Workshop Participants: MWCNT Product Use.

Research	Estimated Finances ($)	Estimated Time Frame
How does particle functionalization and matrix affect aging and release to air (use accelerated weathering test), measure quantities (number and concentration) and characterize (size distribution)?	300,000	2–3years
How does particle functionalization and matrix affect release in washing MWCNT textile products (use mini washing machines, measure quantities (number and concentration) and characterize (size distribution))?	300,000	2–3 years

6.3.1.5. Disposal/ Recycling: Volume and Release Rate

The workshop participants identified MWCNT disposal and recycling as important to risk assessment. Subsequently, the risk relevance factors of MWCNT disposal and recycling volume and release rate were both most commonly identified as important. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 2.5). Below are examples of experts' rationale for rating areas as research priorities.

- **Disposal/recycling--Volume:** It is unclear to what extent products containing MWCNTs will be recycled. This information is not available yet and may not be until the products are on the market. The potential for release from disposal and recycling operations and processes is unknown. Currently estimates are based on decaBDE data. There is currently no system like a national registry, however this step will be less critical for exposure and risk assessment than previous steps.
- **Disposal/recycling—Release rate:** Releases to air from incineration and to water from landfills are possible. Better analytical methods are needed for MWCNT quantification. Release rate will depend on specific recycling methods, which are still evolving, and there is the potential for secondary products to emerge. Understanding release rate is critical to estimating exposures. Large volumes of waste may accumulate and increase the potential for a release event. Currently, no system like a national registry exists. However, this step will be less critical for exposure/risk assessment than previous steps. Research is needed on how companies can dispose of ENMs in an environmentally conscious way.

The overarching influential factors identified by multiple experts for both disposal and recycling volume and use release rate characteristics included: methods and techniques, ENM characteristics, factors associated with the surrounding media (e.g., air, wastewater, surface water), as well as physical, chemical, biological and social conditions.

As noted above, one reason experts rated disposal and recycling as important is that very little information is available about the release from textiles during these processes. Similarly, no information is available on the byproducts, metals, and other waste products that could result during these processes. Workshop participants noted that MWCNTs could be released into the environment during disposal and recycling, and that potential release could lead to exposures (e.g., release to wastewater that ends up in the environment; release to air resulting in potential occupational exposure).

During recycling, textiles undergo various mechanical, thermal, and chemical treatments that could result in CNT release from the product matrix (SAFENANO, 2012). Industrial textiles are often reclaimed and recycled in specialized facilities while other types of textiles might be shredded and repurposed as a part of the recycling process (e.g., polyester is often shredded, granulated into pellets, and processed to recover the monomers and re-polymerized and processed by extruding, melting, spinning, etc., into new fibers) (Chaudhry et al., 2009). How MWCNT-treated flame retardant upholstery would be recycled, and how the MWCNTs might be released from the product matrix as a result of the recycling process, is unclear.

During disposal, textiles are expected either to be sent to a landfill or incinerated (SAFENANO, 2012; Chaudhry et al., 2009). Although no information regarding the current or predicted volume of disposed MWCNT textiles was available, general quantities of disposed textiles were reported in Chaudhry et al. (2009). For example, approximately 5.5 kg of textiles per person per year are disposed of and burned in Switzerland; in the UK, 75% of "fashion textiles" are landfilled. This information suggests that the likelihood of disposal of MWCNT flame-retardant textiles through landfill or incineration will vary by country, but could be relatively high. The likelihood of CNTs being released from the product matrix during these processes partially depends on which disposal method is used. For example, uncontrolled incineration could result in CNT release if the resulting char is mechanically disturbed (SAFENANO, 2012; Uddin and Nyden, 2011a; Nyden et al., 2010), whereas under controlled conditions (>850°C), CNTs are likely to be destroyed and not released (SAFENANO, 2012; Nyden et al., 2010). However, no data are currently available to corroborate these predictions.

In building upon existing literature discussed above and in Chapter 2, research planning efforts might consider research questions identified by expert stakeholders participating in the CEA collective judgment workshop for MWCNTs (RTI, 2012). Based on their input, potential risk scenarios for the disposal/ recycling stage of the product life cycle might include: (1) unknown or relatively large volumes of materials at the end of life the product life cycle (e.g., incineration, recycling, reuse, litter, landfill disposal), (2) release during recycling for reuse (e.g., industrial shredding), resulting in release to the environment (e.g., waste water) and subsequent environmental exposure, (3) occupational exposure from MWCNTs released in air during recycling, and (4) release during sludge application to land that results in

exposure to humans or other biota on the surface. To mitigate or avoid these potential risk scenarios, experts noted that risk managers might use a reclaim system to return upholstery and upholstered products to manufacturers at the end of the product life, or limit MWCNT production and use. Further, risk managers might need to evaluate the use of controls in occupational settings or regulation of sludge waste disposal. Life cycle analysis, and occupational exposure and/or environmental risk assessments could inform these types of risk management decisions. Research questions that participants identified to inform these types of assessments, along with estimates of the resources and time to carry out the research, include:

Table 6-7. Research Identified by RTI Workshop Participants: MWCNT Disposal / Recyling.

Research	Estimated Finances ($)	Estimated Time Frame
How much volume of CNTs is used in upholstery? How much volume of CNTs is lost from upholstery during life span? How much volume of CNTs is lost via destruction (e.g., burning), recycling, reuse, litter, or disposal in landfill?	100,000	1 year
What is the airborne release rate of MWCNTs during shredding (e.g., form, size distribution, number & mass concentration)?	100,000	1 year
Survey the nanotechnology industry and municipal STP to gather mass of sludge/year applied to land: Is sufficient sludge being applied that uptake from plants, or exposure to farmers is possible?	50,000	1 year

6.3.2. Environmental Transport, Transformation, & Fate

The sections below discuss areas within environmental transport, transformation, and fate that were considered to be Priority Research Areas by workshop participants. Relevant to this priority area, OECD (2012) noted that research needed to inform risk assessment includes more robust data regarding how nanomaterials move through different environmental and biological media, particularly in relation to variation in physical-chemical properties (i.e., morphology, surface chemistry, size, functionalization). OECD (2012) also identified mechanisms of bioaccumulation and predictive models for bioaccumulation of nanomaterials as important to informing risk assessment, particularly because evidence suggests that traditional relationships between octanol water partition coefficient (Kow) and bioaccumulation or bioconcentration factors (BAF/BCFs) may not be applicable to carbon nanotubes (OECD, 2012; Petersen et al., 2011b).

6.3.2.1. Air: Mobility, Persistence, and Bioavailability

The workshop participants identified MWCNT air issues as important to risk assessment, and subsequently the risk relevance factors of MWCNT mobility, persistence, and bioavailability were most commonly identified as important. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 3.2). Below are examples of experts' rationale for rating these areas as research priorities.

- **Mobility in air:** Mobility in air is a primary route of exposure and existing data are insufficient.
- **Persistence in air:** MWCNTs may persist in air, yet data are currently insufficient. More data are needed on persistence and degradation of carbon nanotubes in air and the availability of MWCNTs in air for inhalation by humans and ecological receptors. Indirect effects of decaBDE need to be considered.[23]
- **Bioavailability in air:** While absorption across epithelial tissues has not been observed in other organisms, data on the bioavailability of MWCNTs are currently insufficient.

Participants at the workshop who identified fate and transport in air to be important also voluntarily listed influential factors to include in developing research plans for this area, such as: analytical techniques, MWCNT characteristics (e.g., aggregation state, persistence, surface chemistry), and a variety of physical and chemical conditions.

To date, there is very little information available regarding the mobility, persistence, and bioavailability of MWCNTs in air. From an ecological toxicology perspective, Petersen et al. (2011b) note that while a few studies estimate the release of CNTs to air (and other environmental media), as well as the potential risks to ecological receptors, such models are limited by the lack of analytical techniques needed to accurately detect and quantify CNTs in environmental matrices.

The issue of MWCNT bioavailability and characterization in air is also pertinent to human health, as was noted by the workshop participants. Laboratory studies have often been hindered by the inability to generate aerosolized MWCNT particles. Ahn et al. (2011) have used heat and sonication prior to atomization to generate untangled MWCNTs in aerosol without the use of surfactants. These untangled MWCNTs could then be used in in vivo toxicity models, unlike those often produced in previous studies that also had tangled or clumped structures. While no data was identified on the mobility, persistence, or bioavailability of MWCNTs in air under normal environmental conditions, these studies may provide insight as to which physicochemical properties of MWCNT increase and decrease aerosolization

[23] Assumed to mean that indirect effects of decaBDE can inform research planning for MWCNTs.

potential. Aersolization potential could in turn influence mobility, persistence, or bioavailability. Information gaps persist, however, regarding the influence of environmentally relevant conditions on aerosolization potential and other aspects of MWCNT behavior in air.

In extending upon existing data for mobility, persistence and bioavailability of MWCNTs in air, research planning efforts might consider input from the CEA collective judgment workshop on MWCNTs. Expert stakeholders participating in the workshop discussed persistence and mobility in air to identify potential risk scenarios that might occur in this environmental spatial zone, along with specific research questions that, if pursued, might inform future assessment and risk management efforts in this area (RTI, 2012). Based on their input, potential risk might arise from the persistence of CNTs released to occupational or ambient air resulting in longer residence times that increase the probability of exposure. Similarly, mobility dictates the extent of potential MWCNT exposure in ambient air, and thus can influence risk. To mitigate or avoid potential exposure in occupational or ambient air, experts noted that risk mangers might reduce MWCNT residence time in air (e.g., by increasing aggregation potential or decreasing mobility and retainment), or limit MWCNT production and use. To inform these types of risk management decisions, experts suggested carrying out human health risk assessments, exposure assessments quantifying MWCNTs in air, and cost benefit analyses. To support conducting these types of assessments expert stakeholders recommended the following research areas, along with estimates of the resources and time to carry out the research:

Table 6-8. Research Identified by RTI Workshop Participants: MWCNT Mobility & Persistence in Air.

Research	Estimated Finances ($)	Estimated Time Frame
Develop a model to predict atmospheric residence time as a function of CNT particle characteristics (QSAR).	500, 000	3 years
Determine CNT properties and meteorological properties that increase aggregation rate and decrease residence time.	>1 million	5 years
Develop new methods or instruments to improve CNT quantification in air (determine number or mass of CNT/m^3).	2 million	3 years
Apply conventional Benefit/Cost Analysis Procedures to determine the economic consequences of limiting MWCNT product and use.	200,000	1 year
Develop model to predict extent of mobility as a function of CNT particle characteristics (QSAR) for near-field and long-distance transport.	1 million	3 years
Alter CNT properties or meteorological properties to increase aggregation and decrease mobility.	>1 million	5 years

6.3.2.2. Wastewater: Mobility, Persistence, and Bioavailability

The workshop participants identified the environmental transport, transformation, and fate of MWCNTs in wastewater as important to risk assessment. Subsequently, the risk relevance factors of mobility, persistence, and bioavailability in wastewater were each most commonly identified as important to risk assessment. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 3.3.3). Below are some examples of experts' rationale for rating these areas as research priorities.

- **Mobility in wastewater**: The extent to which MWCNTs move in wastewater determines which environmental compartments will be exposed (e.g., water, soil, sediment). Waste water is the most likely route into the environment; more research is needed on how ENMs get out of the waste water stream and how to prevent this.
- **Persistence in wastewater**: MWCNTs might be persistent in wastewater and the potential for MWCNT transformation and subsequent effects of transformation are unknown.
- **Bioavailability in wastewater**: MWCNTs are potentially persistent and likely to interact with activated sludge given results from studies with other organisms.

The overarching influential factors identified by multiple experts for all three characteristics included: analytical techniques, control technologies, MWCNT purity, a variety of MWNCT characteristics (including but not limited to aggregation/agglomeration state, applied coatings, size distribution, surface chemistry, water solubility/dispersibility), factors associated with the surrounding media (particularly wastewater and sediment), chemical conditions (ionic strength, natural organic matter, other contaminants in the environment, and salinity), and biological conditions (microbial communities in the environment).

In the introduction to a recent special *Environmental Science and Technology* issue on Transformations of Nanomaterials in the Environment, Plata et al. (2012a) outlined some of the challenges involved in characterizing nanomaterials (in particular, CNTs) in water and sediment and some promising analytical techniques that would help increase understanding of MWCNT mobility, persistence, and bioavailability in wastewater. Some of the advances in analytical methods to detect MWCNTs in aqueous systems, such as wastewater, are mentioned in Additional Information Highlight Box 10. Research on analytical methods serves as a basis to begin to assess MWCNT mobility, persistence, and bioavailability in wastewater (and in other environmental matrices).

Recent studies of MWCNT transport in water-saturated porous media might help inform understanding of MWCNT mobility in wastewater. Wang et al. (2012) observed that 75% of functionalized MWCNTs delivered through a water-saturated sand system were detected in effluent. The authors also concluded that MWCNTs with lengths greater than 8 μm were more likely to be deposited than smaller MWCNTs. Although wastewater systems are unique, they often involve the use of

filters such as sand. These results suggest that functionalized MWCNTs might be mobile during wastewater treatment processes, with longer MWCNTs exhibiting less mobility than shorter MWCNTs.

With respect to the potential transformation of MWCNTs in wastewater, a recent paper by Nowack et al. (2012) concluded that released CNTs could enter wastewater (and other environmental compartments) where they could be transformed by photochemistry, oxidation, adsorption of natural organic matter and other organic colloids, biotransformation, and continued abrasive forces (Nowack et al., 2012). The authors also noted that transformations could change CNT aggregation, dispersibility, and interaction with biota in the environment (Nowack et al., 2012). These conclusions highlight the importance of studying not only MWCNTs, but also potential environmental transformations of MWCNTs to understand the dynamics driving mobility, persistence, and bioavailability in wastewater.

To that end, expert stakeholders at the workshop discussed MWCNT persistence and mobility in wastewater to identify the type of risks that might arise in this area of the environment and develop specific research questions that could support future assessment and risk management efforts of the material (RTI, 2012). They noted that MWCNTs could be released in either pulse industrial discharges or sewers, or in semi-continuous loadings from industrial, commercial, and residential wastewater with flame-retardant materials. To mitigate or avoid potential risks from these scenarios, experts identified several types of decisions risk managers might consider, including: utilizing pretreatment controls to prevent MWCNT discharge from industrial facilities, or regulating efficiencies of control technologies to mitigate MWCNT release into the environment. Information to support making these types of risk management decisions might include analytical measurements made during ecological risk assessments, or evaluations completed during life cycle analyses.

According to expert participants, research that could inform these and other types of assessments in this area might include the following, along with resource and time estimates to carryout the research:

Table 6-9. Research Identified by RTI Workshop Participants: MWCNT Mobility & Persistence in Waste Water.

Research	Estimated Finances ($)	Estimated Time Frame
How does the degree of functionalization and changes in wastewater treatment processes (e.g., activated sludge, disinfection processes) affect the rate of transformation? [Evaluate the rate of transformation of MWCNTs alone and in a product matrix.]	400,000	3 years
How to extract and characterize MWCNTs from suspended and fixed biomass or treated effluent with minimal modifications to surface group, functionalization, impregnated metals, and coatings.	400,000	3 years
What are the transformation byproducts from MWCNT and flame resistant fibers?	300,000	3 years
To what extent does MWCNT surface properties and incorporation into fibers affect distribution of MWCNTs between treated effluent and biosolids for different wastewater treatment plant configurations? [Evaluate using batch or OECD experiments using pilot tests with two or more MWCNT materials. Distribution coefficients for some nanomaterials are available which could be used with existing WWTP models to crudely predict MWCNT removals.]	250,000 600,000 with pilot plant	2.5 years 4 years with pilot plant
Develop extraction and/or analytical techniques to quantify MWCNTs, of diverse origin, at environmentally relevant levels in raw sewage, treated effluent and biosolids. [Detection limits of several methods exist, and may be relevant to apply given current acute toxicity test results.]	300,000 600,000	3 years 4 years for new methods

[1]Note: Information in brackets [ ] denotes details extracted from responses experts provided along with the question or research area.

6.3.2.3. Sediment: Mobility, Persistence, and Bioavailability

The workshop participants identified environmental transport, transformation and fate of MWCNTs as important to risk assessment. Subsequently, the risk relevance factors of mobility, persistence, and bioavailability in sediment were each most commonly identified as important to risk assessment. Participants were generally not confident or only somewhat confident in the ability of data on each factor to support risk management decisions (see Priority Research Area Highlight Box in Section 3.3.1). Below are some examples of experts' rationale for rating these areas as research priorities.

- **Mobility in sediment:** Sediment is a likely ultimate repository for MWCNTs and the extent to which MWCNTs can be redistributed to the water column through sediment disruption is unclear.
- **Persistence in sediment:** Degradation of MWCNTs is likely to be slow, if it occurs at all. More research is needed on transformations in the environment and interactions between microbes and soil.
- **Bioavailability in sediment:** MWCNTs are potentially persistent, however uptake was not observed in several recent studies.

The overarching influential factors identified by multiple experts for all three characteristics of MWCNTs in sediment included: a variety of MWNCT characteristics (e.g., aggregation/agglomeration state and surface chemistry) and chemical conditions (particularly natural organic matter).

In a recent review paper, Petersen et al. (2011b) noted that MWCNTs sorb more readily to sediments in seawater, but will tend to stay in the water column in aquatic systems with high concentrations of dissolved organic matter (DOM). The authors concluded that future studies of the subsurface mobility of CNTs (including mobility in sediment) should examine a larger range of porous media size, mineralogy, aqueous chemistry (including DOM), and natural soils (e.g., clays, silts, peats). The authors also stressed that the influence of CNT functionalization and surface properties on transport are critical research areas.

Some workshop participants stated that MWCNTs are likely to persist in sediment. While previous studies indicated that carboxylated SWCNTs (but not pristine SWCNTs) can be transformed by soil enzymes (Allen et al., 2009; Allen et al., 2008a), which suggest that similar processes could occur in sediment, more updated and sediment-specific research needs to be conducted to confirm that MWCNTs could biodegrade in sediment.

In a recent paper examining the effect of MWCNTs on bioaccumulation of polycyclic aromatic hydrocarbons (PAHs) by *Chironomus plumosus* larvae in sediment, Shen et al. (2012) concluded that MWCNT-associated PAHs may have been absorbed by larvae and hypothesized that CNTs could increase the exposure risk of PAHs to benthic organisms due to their unique structure. These results suggest that uptake of MWCNT by organisms could potentially occur in sediment. Some previous research, however, has not found substantial uptake of CNTs by sediment-dwelling earthworms (Petersen et al., 2008) or soil-dwelling earthworms (Petersen et al., 2011a; Petersen et al., 2009)**.** These differing conclusions support the designation of MWCNT bioavailability in sediment as a research priority.

While time did not allow for expert stakeholders at the workshop to specifically discuss bioavailability in sediment, they did consider persistence in sediment (RTI, 2012). From this discussion, the relative persistence of MWCNTs could influence the potential risk associated with instances when there is continuous deposition and burial of fiber or polymers containing MWCNTs from multiple sources

(e.g., air, waste water discharge, release from products, storm water). To mitigate or avoid potential risks influenced by the persistence of MWCNTs in sediment, experts noted that risk managers might consider regulating the efficiencies of control technologies that can minimize MWCNT concentrations in the environment, or regulating loadings of CNTs in fabrics. While specific assessments that could inform these types of risk management decisions were not identified by experts, such information might include: measurements of MWCNTs in environmental compartments in ecological risks assessments, as well as measurements to quantify release of MWCNTs from textile production. Experts identified the following research directions, which might support conducting these and other types of assessments,along with estimates of the resources and time to carry out the research:

Table 6-10. Research Identified by RTI Workshop Participants: MWCNT Persistence in Sediment.

Research	Estimated Finances ($)	Estimated Time Frame
How does the degree of functionalization or changes in sediment affect the rate of transformation? Is there long term persistence? Are MWCNT released from fabrics and sediments? [Evaluate both the rate of release from fibers as well as the transformation of MWCNT alone and combined in a matrix.][1]	300,000–600,000	3–5 years
How to extract and characterize MWCNT from sediment with minimal modifications to surface group, functionalization, impregnated metals, and coatings.	400,000	3 years
What are the transformation byproducts from MWCNT and flame resistant fibers? What byproducts could be formed during degradation processes and would this be impacted by the MWCNT concentration in the fabrics?	Not provided	Not provided

[1]Note: Information in brackets [ ] denotes details extracted from responses experts provided along with the question or research area.

6.3.3. Exposure Route and Dose (Kinetics)

The following exposure routes and dose/kinetic topics were considered to be Priority Research Areas according to workshop participants.

6.3.3.1. Exposure Route – Human Occupational: Ingestion, Inhalation, Dermal

Human occupational exposure was identified as important to risk assessment by the workshop participants. Risk relevance factors that might be considered in risk assessment or management of occupational exposure include: ingestion, inhalation, and dermal routes of exposure. Although experts strongly agreed that occupational exposure is important, the way they rated the importance of each risk

relevance factor, varied. Overall, they were not confident or only somewhat confident that the current data could support risk management decisions for each factor (see Priority Research Area Highlight Box in Section 4.2.1). Below are some examples of why experts' rated these areas with varying levels of importance and confidence.

- **Human occupational exposure—Ingestion:** Experts do not see much concern from ingestion of MCs[24] based on data; there will likely be good controls to limit exposure via ingestion. From the exposure amount perspective, the relative amount of CNT intake in the form of ingestion would be much lower than inhalation in occupational settings and there are some studies presenting our luminal surfaces of GI tracks are resistant to the passage of CNTs.
- **Human occupational exposure—Inhalation**: Inhalation is thought to be a likely first type and some say the most important type of human occupational exposure; inhalation exposure must be controlled as it can cause effects, including indirect effects in children. Some animal studies have been conducted but exposure routes and administration techniques have been criticized.
- **Human occupational exposure—Dermal:** Dermal exposure is less likely an issue based on the known physicochemical properties of CNTs. A low dermal absorption rate is expected and there would likely be controls to limit dermal exposure, however some studies in insects have shown some systematic effects (however other routes, inhalation and ingestion, were not completely blocked).

The overarching influential factors identified by multiple experts for human occupational exposure characteristics included: methods and techniques (e.g., processing and synthesis methods, personal protective equipment), ENM characteristics (e.g., applied coatings, morphology, persistence), factors associated with the surrounding media (e.g., air), as well as physical, chemical, biological and social conditions (e.g., chronic exposure, occupation).

MWCNTs are found in facilities ranging from research laboratories and production plants to those where they are processed, used, disposed, and recycled, and the limited literature available suggests potential for worker exposure in at least some of these types of facilities [(Dahm et al., 2011a; Johnson et al., 2010; Lee et al., 2010; Han et al., 2008); see Sections 4.1.2.4, 4.2.1, and 4.2.5)]. The extent of worker exposure to MWCNTs, however, is not well understood. No published literature was available investigating occupational exposure to MWCNTs in flame-retardant textiles specifically and no more recent literature regarding exposure potential was identified after the CEA workshop process. OECD (2012) noted that research needed to inform risk assessment includes obtaining robust data on the exposure of workers at all stages of the life cycle from material synthesis to disposal and recycling facilities.

[24]Word choice of expert; assumed to mean multiwalled carbon nanotubes

While no information was identified specific to MWCNTs in flame retardant textiles, literature pertaining to similar applications is available. For example, Takaya et al. (2012) reported that occupational workers could be exposed to respirable particles of yarn coated with MWCNTs during the weaving process of the production of a conductive fabric. The authors concluded that the mechanical force of weaving with the MWCNT-coated yarn was sufficient to break the coating and release yarn fibers still embedded with MWCNT, but is not likely to provide sufficient mechanical action to release individual MWCNTs from the coating layer [(Takaya et al., 2012); see Additional Information Highlight Box 4]. Similar exposure scenarios can be imagined with MWCNTs in flame retardant upholstery textiles, but how use of MWCNTs as coatings on upholstery textiles compared to yarns would affect the release and subsequent exposure is unclear.

Several publications by Schubauer-Berigan et al. (2011) (see Table 2-2) and Dahm et al. (2011b; 2011a) examined the current industry of engineered carbonaceous nanomaterial to better characterize potential occupational exposure and use of engineering controls. While little information was provided specific to MWCNT and no information was provided specific to flame-retardant textiles, the data indicate that many companies employ various engineering controls (including use of LEV, HEPA filters, enclosed production processes and safety cabinets) for production, laboratory procedures, and research and development operations (Dahm et al., 2011b). Many companies also use health and safety training, good hygiene practices, and other practice or administrative methods to reduce occupational exposure. However, nearly one in four companies surveyed either did not report using respiratory protection or were using an ineffective form of respiratory protection (Dahm et al., 2011b). Similarly, one in seven companies not reporting respiratory protection stated that such protection was not needed because operations were fully enclosed; however, the authors note that NIOSH recently recommended the use of respirators even when processes are enclosed if measurement data suggest that the nanomaterial release is not well controlled (Dahm et al., 2011b). Results of these studies suggest that while many companies employ several forms of protective measures, there is still room for improvement to better characterize and mitigate potential occupational exposure. There is a great need for recommended exposure limits for different formulations of MWCNTs and evaluation criteria for assessing the release possibilities of individual MWCNTs. In 2010 NIOSH suggested an 8-hour REL of 7 $\mu g/m^3$ for carbon nanotubes and nanofibers but that value has not yet been finalized (NIOSH, 2010). Similarly, OECD is currently developing standard test methods for MWCNT, but this process is complicated by the lack of an accepted "representative" MWCNT that could be broadly applicable to other MWCNT formulations (Takaya et al., 2012).

To develop a better understanding of human occupational exposures, research planning efforts could incorporate input from the CEA collective judgment workshop on MWCNTs. Expert stakeholders

participating in the workshop discussed inhalation exposure in occupational settings to identify the type of risks that might arise in this area of the environment and develop specific research questions that could support future assessment and risk management efforts of the material (RTI, 2012). Based on their discussion, potential risks could arise due to inhalation of the material (pristine MWCNTs, functionalized MWCNTs, or otherwise modified MWCNTs) during any part of the manufacturing process. To mitigate or avoid potential risk associated with occupational inhalation exposures, experts noted that risk managers might consider the use of engineering controls, personal protective equipment, or if necessary, banning the material outright. Experts noted that information from assessments that might inform these types of risk management decisions include a NOEL or LOEL for the relevant material and other data from occupational exposure assessments. To carry out these types of assessments, experts recommended the following research areas, along with financial and time estimates:

Table 6-11. Research Identified by RTI Workshop Participants: MWCNT Occupational Exposure via Inhalation.

Research	Estimated Finances ($)	Estimated Time Frame
Acute and chronic rodent bioassay studies after inhalation exposure at relevant doses of well-characterized material.	2 million	3 years (2 year rodent bioassay & an additional year for setup and anlaysis)
Analytical and rodent studies to examine effect of co-factors (e.g., solvents, resins) on particles size, deposition, translocation, and removal.	2 million	3 years (2 year rodent bioassay & an additional year for setup and anlaysis)

6.3.3.2. Exposure Route – Human Consumer: Ingestion, Inhalation, Dermal

Human Consumer exposure was identified as important to risk assessment by the workshop participants. Risk relevance factors that might be considered in risk assessments or management efforts in this area include: ingestion, inhalation, and dermal routes of exposure. Participants rated the importance of each of these risk relevance factors differently, but were generally not confident or only somewhat confident in the ability of data on each route to support risk management decisions (see Priority Research Area Highlight Box in Section 4.2.2). Below are examples of why experts rated these topics at varying levels of importance and confidence.

- **Human consumer exposure—Ingestion:** Currently there is not much concern from ingestion based on data; however, more analytics are needed to determine risk of human consumer exposure via ingestion.
- **Human consumer exposure—Inhalation:** The risk of human consumer exposure via inhalation depends on release rate; if it is high enough it could become an issue. There is a need to understand persistence and how upholstery exposure affects consumers.
- **Human consumer exposure--Dermal:** The risk of human consumer exposure via a dermal route depends on dermal absorption rates. Need to understand potential exposure to children, especially potential impacts from crawling around on floor.

The overarching influential factors identified by multiple experts for all three exposure routes included: analytical techniques, control technologies, MWCNT purity, personal protective equipment, a variety of MWNCT characteristics (e.g., aggregation/agglomeration state, applied coatings, persistence, size distribution, surface chemistry, water solubility/dispersibility), factors associated with the surrounding media (particularly air and wastewater), chemical conditions (dispersing agents, ionic strength, salinity, other contaminants in the environment, surfactants in a lab study), and social conditions (exposure duration, human activity, life stage, susceptible populations).

Similarly, OECD (2012) noted that research needs to inform risk assessment include improved characterization of consumer exposure, including the concentration in and release from consumer products. Although the likelihood of MWCNT release from polymers, textiles, and other product matrices during normal product use is not well understood, Nyden et al. (2010) provides some information on the potential release of nanoparticulate additives during incineration of polyurethane foam (PUF)—which is relevant in the context of MWCNT use as flame-retardant additives because behavior during incineration is an important consideration for potential consumer exposure. This study specifically investigated the release of carbon nanofibers (CNFs), but identifies mechanisms of release that might be applicable to MWCNTs. In a controlled well-ventilated flame test, the authors found evidence of CNFs in the char on the surface of the foam after burning but not in the smoke content, indicating that CNFs were not released into the air during this process. The researchers noted that CNF release to the environment might still be possible under different combustion conditions (e.g., under-ventilated conditions that might decrease the destructive forces of the flame on the CNFs). The authors also identified released submicron particles when the char residue was mechanically disturbed, but could not definitively attribute the particles to the CNFs (Nyden et al., 2010). A later publication by the same authors suggested that the aerosolized particles from the disturbed char were likely CNF bundles partially encapsulated in a thin layer of charred PUF after spectroscopic measurements (Uddin and Nyden, 2011a). The authors concluded that the major potential hazard for CNF exposure during well-ventilated combustion resulted from the disturbance of residual char rather than from aerosolized CNF in smoke (Uddin and Nyden, 2011a).

Many of the available MWCNTs studies involve polymer matrices in which the MWCNTs are embedded, but in this specific application of flame-retardant textiles, MWCNTs likely would be incorporated through dipping, dyeing, thermal fixation, and other methods (as described in Chapter 1). Nevertheless data show that, in addition to the polymer matrix and the application technique, the chemical properties of MWCNTs will be important in determining the likelihood that MWCNTs leave the product matrix during washing. Goncalves et al. (2012) investigated the extent to which acidic or basic MWCNTs were "washed out" of polyester and cotton textiles. The results indicated that the more acidic MWCNTs were less likely to be removed from the matrix, particularly in the polyester textile. Although removal from the textile under realistic conditions (e.g., the washing machine) might not present much opportunity for consumer exposure given that upholstery textiles are unlikely to washed frequently, these data do suggest that acidic MWCNTs might be preferable to incorporate in flame-retardant textiles to reduce potential release (see Section 2.4.2).

While expert stakeholders participating in the CEA collective judgment workshop did not focus on consumer exposure due to time constraints, the results from recently identified literature do point to several questions that are currently not addressed by the available literature. For example, if MWCNTs can be removed from the textile matrix during washing, how frequently are MWCNT flame-retardant textiles likely laundered or hand washed? Could consumers be dermally exposed to MWCNT particles from handling the laundered textiles or be exposed to airborne MWCNTs after drying of the textiles? How do differences in surface chemistry and textile type influence this exposure potential? How do differences in cleaning practices (e.g., machine washing versus hand washing versus spot cleaning of upholstery) influence potential exposure? To what extent do other activities (e.g., chewing on textiles) lead to consumer exposures?

6.3.3.3. Dose (Kinetics) – Human: Absorption, Distribution, Metabolism, and Excretion

Human dose/kinetics was identified as important to risk assessment by workshop participants. Factors that risk assessors or managers might consider in this area include absorption, distribution, metabolism, and excretion. Expert workshop participants identified each factor as important, with the exception of distribution, which they identified as possibly important. Participants were generally not confident or only somewhat confident in the ability of data to support risk management decisions related to each factor (see Priority Research Area Highlight Box in Section 4.2.6). Below are examples of experts' rationale for rating these areas as research priorities.

- **Dose (Kinetics)—Human Absorption:** Except for the inhalation route, absorption needs to occur to have an effect; need to know if ENMs are bioavailable. Concern is significantly reduced if oral or dermal absorption does not occur after exposure; data are currently insufficient.
- **Dose (Kinetics)—Human Distribution:** Distribution within tissues and specific organs could be important to determine risk; data are currently insufficient.
- **Dose (Kinetics)—Human Metabolism:** Data are currently insufficient.
- **Dose (Kinetics)—Human Excretion:** Data are currently insufficient.

As note above, at least one participant recognized that this area is a priority for research because currently available data on all four components of human toxicokinetics are insufficient. Importantly, concerns for risk through routes other than inhalation would be significantly reduced if it was determined that oral and dermal absorption does not occur. Experts developing specific research questions related to MWCNT absorption noted that although little evidence is available demonstrating dermal absorption (via abraded skin), additional work should be considered due to the potential for high exposure, especially in children. Additionally, distribution within tissues and organ, in conjunction with data on mode of action and toxicity, could play a key role in increasing or limiting risk.

There was agreement among experts that methods/techniques were influential to understanding toxicokinetics of MWCNTs, including analytical techniques, MWCNT purification methods, processing and synthesis methods, and control technologies and personal protective equipment. Several characteristics of the MWCNT formulation were also deemed by multiple experts as influential factors for all toxicokinetic components, including aggregation/agglomeration state, matrix bound vs. free form, persistence, size/size distribution, and surface chemistry. Several experts also noted the importance of applied coatings, morphology, and adsorption/desorption ability for adsorption and distribution, as well as the importance of water solubility/dispersibility for distribution and elimination. Finally, several experts noted the importance of social conditions on toxicokinetics: Exposure length (acute, subchronic, chronic), exposure route, human activity, life stage, and individual susceptibility can all influence the human toxicokinetic processes for MWCNTs.

Generally, inhaled nanomaterials—including CNTs—are assumed to be more toxic than conventional-sized materials, in part because they can be inhaled more deeply into the lung (resulting in longer residence times and greater particle-cell interactions), have a smaller size distribution (so are more readily internalized by individual cells and more easily migrate through the body), and have large surface area-to-mass ratios resulting in more reactivity (Bakand et al., 2012). Absorption, distribution, metabolism, and excretion are key processes that determine how the administered or received dose of MWCNTs differs from the internal dose that reaches a target organ or tissue. Toxicokinetic processes thus play a key role in determining toxic potential.

Yet, little is currently known about the specifics of absorption, distribution, metabolism, and excretion of MWCNTs (see Section 4.2.6 and Additional Information Highlight Box 9). Pathways of CNT uptake into cells, intercellular trafficking, and distribution are not well characterized despite multiple studies on the subject (Al-Jamal et al., 2011). Additionally, toxicokinetics could vary with different MWCNT formulations or cell type. For example, Al-Jamal et al. (2011) recently showed that MWCNTs functionalized with an ammonium group and positive charge (NH_3^+) could be internalized by human lung epithelial cells by three different mechanisms (membrane wrapping, direct membrane translocation, and clustering within vesicular compartment), whereas Zhang et al. (2012) showed that uptake of oxidized MWCNTs by human epithelial cervical cancer cells occurred through nonspecific cellular uptake. Jain et al. (2011) found that biodistribution of acid-oxidized MWCNTs (which contain surface carboxyl groups) in mice was dependent on the density of functionalization, and this physicochemical characteristic particularly influenced clearance of MWCNTs from reticuloendothelial systems such as liver, spleen, and lungs. MWCNTs with shorter lengths and higher degrees of oxidation (therefore greater density of functionalization) quickly partitioned to the kidney but were rapidly excreted through the renal system; longer, less functionalized MWCNTs and pristine MWCNTs preferentially accumulated in the liver rather than the kidney and were more likely to be excreted in the feces through biliary pathways. The authors suggest that this functionalization-dependent distribution between organs and excretion patterns might also explain why pristine and less-oxidized MWCNTs do not demonstrate nephrotoxicity in subchronic studies.

A greater understanding of physicochemical properties influencing internal dose (i.e., particle kinetics in biological systems) and therefore biopersistence and bioaccumulation was also noted by OECD (2012) as particularly important research needed to inform risk assessment since this information is useful in interpreting toxicological results. Similarly, additional research on appropriate dose metrics is needed to inform risk assessment based on evidence suggesting that particle surface area or number concentration, rather than standard mass concentration, may be more appropriate for nanomaterials (OECD, 2012).

To continue building upon existing literature for human toxicokinetics summarized in Chapter 4, as well as the newly identified the sources discussed above, research planning efforts might consider input from the CEA collective judgment workshop on MWCNTs. Experts participating in the workshop discussed human absorption, metabolism, and excretion to identify potential risk scenarios and specific research questions that could inform future assessment and risk management efforts (RTI, 2012). Based on their discussion, potential risks related to MWCNT toxicokinetics might include the potential for absorption in the lungs or GI tract, degradation into a more toxic metabolite, and bioaccumulation of the material due to lack of excretion. To mitigate or avoid potential risks related to MWCNT toxicokinetics in

humans, experts noted that risk managers might consider: implementing appropriate control technologies to minimize exposures, minimizing the absorption potential of MWCNTs, or limiting MWCNT production or use. Information to inform these types of risk management efforts could come from: human health risk assessment, occupational exposure assessment, and a cost benefit analysis. To support conducting these and other types of assessments, experts recommended the following areas of research, along with estimates of the resources and time to carry out the research:

Table 6-12. Research Identified by RTI Workshop Participants: Human Absorption, Metabolism and Excretion of MWCNTs

Research	Estimated Finances ($)	Estimated Time Frame
Determine particle properties that influence extent and rate of absorption across mammalian lung epithelial tissue, GI luminal epithelia, and dermal layers. Quantify extent and rate of absorption across mammalian lung epithelial tissue, GI luminal epithelia, and dermal layers (if answer is yes, maximize particle properties that decrease absorption while maintaining beneficial uses). [Examining all three absorption processes increases the potential for discovery of unique interactions among systems.][1]	5 million	5 years
Develop analytical techniques for measuring the original MWCNT or metabolites in cells. [Evaluate the degradability of the relevant MWCNT material compared to original MWCNT. Determine of the half-life of relevant MWCNT material in biological systems.]	275,000	2 years
Measuring the original MWCNT or metabolites in tissues after whole body inhalation exposures.	500,000	2 years
Perform experiments in rodents after exposure to determine fate and clearance of MWCNT.: [Compare of the fate of relevant MWCNT material compared to original MWCNT in rodents. Measure of the half-life of MWCNT material in biological systems.]	500,000	3 years
Develop tracer methodology to detect excretion by-products of the relevant MWCNT material to enable: [Quantify levels of by-products in the body.]	300,000	2 years

[1]Note: Information in brackets [ ] denotes details extracted from responses experts provided along with the question or research area.

6.3.4. Impacts

The following impact areas were considered to be Priority Research Areas according to workshop participants.

6.3.4.1. Human: Cancer and Non-Cancer

Experts in the workshop generally rated human health impacts as important to consider in future risk assessments of MWCNTs. Participants most commonly identified human cancer impacts as important and generally somewhat confident in the availability and utility of current data to support risk management decisions; however, those who identified human non-cancer impacts as important were generally not confident in the current data. Listed below are examples of experts' reasons for choosing these topics as Research Priority Areas.

- **Human Cancer:** Data are currently insufficient. There is a lack of cancer studies done on inhalation exposure, particularly occupational inhalation exposure.
- **Human Non-cancer:** Data are currently insufficient.

Those who chose to note influential factors generally agreed that MWCNT characteristics (e.g., surface coatings, size, morphology) and social conditions (e.g., exposure duration, exposure route, occupation, individual or population susceptibility) were of particular importance for future assessments of human cancer and non-cancer effects.

OECD (2012) similarly identified topics pertaining to human impacts as important for risk assessment. These topics include the identification of toxicological endpoints specific to nanoparticles to ensure that risk assessors identify all appropriate biological responses potentially leading to adverse outcomes. Better characterization of mode of action in mammalian systems and interspecies variation were also identified as important research to inform risk assessment.

In addition to effects described in Section 5.1, MWCNTs have been shown to generate reactive oxygen species, increase cell permeability in human microvascular endothelial cells (HMVEC), promote cell migration in HMVEC (Pacurari et al., 2012), and cause inflammation (see Additional Information Highlight Box 16). MWCNTs have also been shown to demonstrate subpleural deposition and pleural translocation (Mercer et al., 2010; Ryman-Rasmussen et al., 2009a), which has important implications for carcinogenicity. In particular, as noted in Additional Information Highlight Box 13, MWCNTs have structural similarities to asbestos, raising concern over the potential for asbestos-like effects (e.g., mesotheliomas).

In a review of the available literature, Donaldson et al. (2010) concluded that long MWCNT fibers are retained in the stomata of the parietal pleura, which is normally responsible for particle

clearance; therefore, this is the site of inflammation and pathogenic effects. Schinwald et al. (2012) investigated this mechanism further and reported a clear threshold where MWCNTs greater than 4 µm were pathogenic to the pleura. To elucidate the molecular mechanism of pathogenic action, Murphy et al. (2012) investigated the pro-inflammatory response of mesothelial cells and macrophages. The results indicated that CNTs indirectly resulted in an increase in cytokine release from mesothelial cells, as a result of frustrated phagocytosis of the macrophages. The authors concluded that the response in the pleura is first initiated by the macrophages, which in turn stimulate a pro-inflammatory response from the adjacent mesothelial cells (Murphy et al., 2012).

To extend upon the existing research described above and in Chapter 5, research planning efforts might consider input related to human health effects from the CEA collective judgment workshop. While time did not allow for experts participating in the workshop to discuss carcinogenic effects in humans, they did develop specific research questions to further investigate non-cancer effects in humans. Based on their discussion, potential risks of non-cancer effects result from chronic or non-chronic exposures to coated or functionalized MWCNT in upholstery textiles. To mitigate or avoid potential risks related to non-cancer effects in humans, experts noted that risk managers might consider banning the material outright; however, assessments would be necessary to inform this or other types of risk management decisions. Experts did not specify the types of assessments that would inform these decisions, but they did note that a NOEL or LOEL should be identified for materials in consumer or occupational exposure scenarios. Such information could be used in a human health hazard assessment. To support this type of assessment, experts recommended the following research areas, along with estimates of the resources and time to carry out the research:

Table 6-13. Research Identified by RTI Workshop Participants: Non-Cancer Human Health Impacts of MWCNTs.

Research	Estimated Finances ($)	Estimated Time Frame
Conduct acute and chronic rodent bioassay studies after inhalation exposure at relevant doses using well-characterized material.	2 million	3 years
Perform experiments to test impacts of exposure on immune compromised individuals.	1 million	3 years

6.3.4.2. Human: Reproductive/Developmental

The workshop participants who rated human health impacts as important most commonly rated reproductive and developmental effects as possibly important. They were generally not confident in the availability and utility of current data to support risk management decisions related to these effects (see Priority Research Area Highlight Box in Section 5.1). Listed below are examples of experts' rationale for rating this area as a research priority.

- **Human Health Impacts—Reproductive/ Developmental:** Data are currently insufficient. There is concern about the long-term effects of ENMs due to large effects on reproduction shown in animal populations.

Experts who chose to note influential factors commonly selected the following considerations to take into account in planning research on human reproductive or developmental impacts: MWCNT purity, applied coatings, persistence, surface chemistry, matrix bound versus free form, morphology, exposure route, and life stage.

The External Review Draft of this document did not contain information regarding reproductive toxicity of MWCNTs, but two studies investigating developmental toxicity in rodents were described (Fujitani et al., 2012; Lim et al., 2011b). An expert involved in the collective judgment prioritization process identified, one study of MWCNT reproductive toxicity in mice (Bai et al., 2010) and a targeted literature search identified a study of developmental toxicity in rats (Lim et al., 2011a). The findings presented by Lim et al. (2011a) appear to be from the same group of experiments described by Lim et al. (2011b) and discussed in Section 5.1.7; the conclusions of the two reports are the same: no differences in gestation index, fetal death, fetal and placental weights, or sex ratio were observed as a result of maternal MWCNT exposure at 1,000 mg/kg-day. Thus, the study by Lim et al. (2011a) is not described in further detail here.

Bai et al. (2010) conducted a reproductive toxicity assay using intravenous injection of water-soluble amine and carboxylate-functionalized MWCNTs in male mice (single injection or 5 doses over 13 days of 5 mg/kg). Results indicated that MWCNTs accumulated in the testes, generated oxidative stress, and reduced the thickness of the seminiferous epithelium (authors reported that this damage was reversible) without producing any significant effects on sperm parameters, sex hormones, fertility, pregnancy rate, or delivery success of female mice mated with treated males (Bai et al., 2010). Although this study used an exposure method that is not typically considered to be relevant, it is useful in that it indicates that if MWCNTs were absorbed into the bloodstream via inhalation or oral exposure they would not likely cause male reproductive effects. Therefore, use of resources to further investigate reproductive and developmental toxicity might be better allocated toward characterizing female reproductive endpoints or developmental effects during various critical windows of development.

Due to time constraints, expert stakeholders participating in the CEA collective judgment workshop did not discuss potential human reproductive or developmental effects; however, the limited available data suggest several remaining research questions that might inform future risk assessment and management efforts of MWCNTs. For instance, does gestational exposure to MWCNTs result in behavioral or other subtle neurodevelopmental effects in offspring observed through adolescence? Does comparing different formulations of MWCNTs within the same experiment indicate certain physicochemical characteristics that influence reproductive or developmental effects?

6.3.4.3. Aquatic Biota: Survival, Developmental, Reproductive, and Other Sublethal

Workshop participants identified impacts on aquatic biota as important to risk assessment. Risk relevance factors that might be considered in risk assessments and management efforts for this element are: survival, developmental, reproductive, and other sublethal effects. Although there was some variation in the way experts rated the importance of the "aquatic impacts" category and each risk relevance factor, there was overall strong agreement among those who found aquatic impacts important that they were "not confident" or only "somewhat confident" in the availability and utility of the current data to support risk management decisions (see Priority Research Area Highlight Box in Section 5.1). Listed below are examples of experts' rationale for why these topics were chosen as Research Priority Areas.

- **Impacts to Aquatic Biota—Survival:** Data does not indicate acute toxicity
- **Impacts to Aquatic Biota—Developmental:** As seen with endocrine disrupting chemicals, aquatic species are very sensitive and low exposures can lead to developmental effects. A few studies could go a long way toward understanding chronic effects.
- **Impacts to Aquatic Biota—Reproductive:** As seen with endocrine disrupting chemicals, aquatic species are very sensitive and low exposures can lead to reproductive effects.
- **Impacts to Aquatic Biota—Other Sublethal Effects:** These effects are not typically studied until environmental problems occur, need to give adequate attention.

The most commonly selected influential factors identified across all three areas included the following: analytical techniques; a variety of MWCNT characteristics (e.g., adsorption/desorption ability, aggregation/agglomeration state, lipophilicity, persistence, redox potential, surface chemistry); physical and chemical conditions associated with the surrounding media (particularly groundwater, sediment, surface water, and wastewater); biological conditions (ADME, bioaccumulation, biomagnification, microbial communities, organism health, developmental behavior, feeding behavior, reproductive behavior); exposure route; habitat structure; and geographic location. The discussion below provides more detailed information relating to aquatic toxicity, particularly in terms of aspects relevant to these

identified influential factors. This information was gathered from literature identified after the workshop process.

OECD (2012) similarly noted that a better understanding of the absorption, distribution, metabolism, and excretion of nanomaterials in ecological receptors is needed to evaluate the utility and appropriateness of standard ecotoxicological assessments for nanomaterials. OECD (2012) also recommended research of environmentally relevant conditions that could influence MWCNT toxicity.

As described in a recent review by Petersen et al. (2011b), the aquatic toxicity of CNTs has been investigated in a variety of organisms including fish, algae, daphnia, copepods, amphibians (larvae), protozoans, and bacteria. Toxicity depends on the bioavailability of MWCNTs to aquatic organisms (see Additional Information Highlight Box G1), which is thought to be influenced by specific surface chemistry and functionalization; but, conflicting evidence makes this relationship difficult to elucidate. Petersen et al. (2010) reported that acid-treated MWCNTs, which were expected to be more bioavailable than pure MWCNTs, did not actually accumulate at greater rates in the oligochaete *L. variegatus*. Similarly, different surface coatings and charges had no apparent impact on accumulation or elimination of MWCNTs in *D. magna* (Petersen et al., 2011a; Petersen et al., 2011b), but a clear increase in MWCNT toxicity to *C. dubia* was observed with the addition of positively charged functional groups (Kennedy et al., 2009).

Another potentially important factor is the presence of metallic impurities. Mwangi et al. (2012) found conflicting evidence: The removal of such impurities by acid pre-treatment decreased the lethal effects of MWCNTs to mussels (*V. iris*), midges (*C. dilutes*), and amphipods (*H. azteca*) but did not mitigate biomass reduction for *H. azteca*, *C. dilutes*, and *L. variegates*, indicating that metal impurities are responsible for some, but not all, of the effects observed (see Additional Information Highlight Box 17). Abiotic factors, such as pH and natural organic matter (NOM), are also expected to influence the bioavailability and toxicity of MWCNTs; however, Edgington et al. (2010) found no impact on toxicity to *D. magna* with a range of dissolved organic carbon content in NOM (although some variation was reported based on the source of NOM). Clearly, MWCNTs do not conform to classic theoretical predictions of chemical behavior in aquatic media, which is further complicated by incomplete information or conflicting data.

Another important factor in aquatic toxicity of MWCNTs is their potential interaction with other contaminants. For example, Shen et al. (2012) showed that the presence of MWCNTs in sediment or soil can complicate the toxicity of a system by altering the bioavailability of hydrophobic organic contaminants like polycyclic aromatic hydrocarbons.

Available evidence indicates that MWCNTs are not absorbed in the gut. For example, Edgington et al. (2010) observed MWCNTs in the gut of *D. magna* without evidence of nanotube uptake into the

microvilli. Similarly, several studies conducted by Mouchet et al. (2011; 2010; 2008) showed DWCNT in the gut lumen but not in the blood, liver, or interstitial cells of *X. laevis* larvae, and there was no evidence that DWCNT passed across the intestinal barrier. Because current evidence shows a lack of CNT absorption across epithelial membranes, any observed toxic effects are likely due to interactions with epithelial surfaces. For example, *O. mykiss* exposed to SWCNTs showed signs consistent with impaired gill function (e.g., dilation of blood vessels in the brain, other signs of oxidative stress), suggesting that SWCNT accumulation on the gill surface results in impaired respiration (Petersen et al., 2011b; Smith et al., 2007). Indeed, authors observed elevated mucous secretion with SWCNT deposits associated with mucoproteins in the gills. Although SWCNTs were observed in the gut of exposed fish, likely as a result of drinking water with SWCNTs, no histological changes after were observed, with the exception of increased lipid peroxidation at one time point in the 6-week experiment (Petersen et al., 2011b; Smith et al., 2007). Similarly, Mwangi et al. (2012) found no evidence of MWCNT penetration through cell membranes in *C. dilutus* and *H. azteca.* Nevertheless, authors observed MWCNT accumulation in the gut of these organisms, which they speculated, along with lack of depuration after transfer into clean water, contributed to decreased survival and biomass (Mwangi et al., 2012). Evidence supporting the possibility of MWCNT accumulation in the gut of aquatic organisms is found in studies in water fleas showing that elimination of MWCNTs from the gut of *C. dubia* (Kennedy et al., 2008) and *D. magna* (Petersen et al., 2011a; Petersen et al., 2009) was possible only with the addition of algae as a food source. Edgington et al. (2010) also attributed the toxicity of MWCNTs in *D. magna* to blockage in the gut. MWCNT aggregation behavior has also been shown to be an influential factor in toxicity as evidenced by increased lethality in *C. dubia* with greater aggregation (Kennedy et al., 2009; Kennedy et al., 2008), which might also support the influence of digestive tract blockage. Together, these studies demonstrate the potential of MWCNTs to have toxic impacts on growth and survival of benthic invertebrates and other aquatic biota; however, the mechanism of that toxicity and influence of environmental factors remains unclear.

Due to time constraints, expert stakeholders participating in the CEA collective judgment workshop did not discuss potential impacts in aquatic biota; however, based on the literature described above, remaining questions related to potential impacts in aquatic receptors include the following:

- What modifications to MWCNTs might decrease interaction of the material with epithelial surfaces in aquatic biota?
- Are there population level effects in aquatic biota?

6.3.4.4. Other: Economic, Societal, and Environmental Resources

Workshop participants identified “other impacts” as important to risk assessment. Economic, societal, and environmental resource considerations are all included as risk relevance factors within this

element of the CEA framework. Although there was some variation in the way experts rated the importance of the "other impacts" category and each risk relevance factor, there was generally strong agreement among the experts who found other impacts to be important that they were "not confident" in the ability of the current data to support risk management decisions. Listed below are examples of reasons that experts chose these topics as Research Priority Areas.

- **Other Impacts—Economic:** There may be consequences of nanotechnology that are not yet known.
- **Other Impacts—Societal:** There may be consequences of nanotechnology that are not yet known.
- **Other Impacts—Environmental Resources:** There may be consequences of nanotechnology that are not yet known.

While there was some variation in the influential factors identified within each area (i.e., economic, societal, environmental), there was a great deal of overlap in influential factors identified for all three areas, including analytical techniques, control technologies, geographic location, human activity, occupation, subchronic exposure, and susceptible populations. Additional influential factors selected for at least one but not all three areas included acute exposure, chronic exposure, and life stage.

Newly identified information on potential economic, societal, and environmental impacts reveals several ongoing efforts to balance societal needs with potential risks. For instance, according to Safe Work Australia's *Human Health Hazard Assessment and Classification of Carbon Nanotubes* (NICNAS, 2012), carbon nanotubes have garnered much attention in recent years due to unique physical and chemical properties that show promise for a wide variety of advanced applications across many diverse fields. Unique challenges to risk communicators result from the uncertainty surrounding these new applications and the implication that the rapid innovation has for development of a wide variety of MWCNT formulations. Risk assessors and risk communicators need to strike a difficult balance between mitigating potential risk and unintended consequences of novel technology (Priest, 2012; Siegrist et al., 2011) without stifling much needed scientific innovation to meet the demands of a growing global economy, the global population, and the ever-shrinking availability of natural resources (Klaine et al., 2012; OECD, 2009). Nanotechnology has been praised for its potential to offer solutions for many of today's environmental concerns, including pollution, drinking water filtration, climate change, and energy efficiency, while also fueling economic growth by promoting new technologically advanced industries. However, as a rapidly growing and evolving field, there is a great deal of uncertainty regarding potential trade-offs and unintended consequences (IPEN, 2012; Siegrist et al., 2011; OECD, 2009; Sass, 2007). For this reason, emphasis has been placed on interdisciplinary participation and collaboration, including government, stakeholders, researchers, academics, and the public, throughout all stages of the risk

assessment process to fully understand and effectively communicate potential risks while continuing to invest in technologically advanced solutions to everyday problems and to manage public perception (Klaine et al., 2012; Siegrist et al., 2011; OECD, 2009; Sass, 2007).

The OECD Working Party on Nanotechnology (OECD, 2012) noted that the ability to evaluate the economic impacts of nanotechnology depends on the development of valuation models specific to nanotechnology. Two valuation models described in the OECD report are the Defra model, which is based on a comparative valuation of an existing product and a nanoenabled "replacement," and the STAR METRICS approach, which uses an input/output method to analyze data between industries (OECD, 2012). The Defra model offers some useful insight for this particular case study because a non-nanoenabled product, decaBDE, has already been identified for comparison. Although no information was identified regarding the energy and resource demands for decaBDE, some economic assumptions could be made for MWCNT in flame-retardant textiles based on how decaBDE diffused and performed in the market. For example, as noted in Table 1-10, global demand for decaBDE was quite high between 2001 and 2007, driven in part by its use in textile applications for flame retardancy. Because flammability performance and ability to meet stringent regulations is important for a variety of industries with textile applications (see Section 1.2.1), the possibility exists for the demand for MWCNT in this application to be on the same scale (i.e., similar percentage of total production). As discussed in Chapter 1, considerations related to efficacy and production scale remain to be seen for MWCNT flame-retardant coatings (see Additional Information Highlight Box 1 and Additional Information Highlight Box 2). Although two valuation models are available to begin to inform economic impacts of MWCNTs, these are limited because the development and commercial success of products containing MWCNTs face unique challenges compared to non-nanoenabled products (OECD, 2012). For example, the research and development stage for nanotechnologies often requires a very high level of investment and is accompanied by a long lag period before any potential payoff is realized. With such a large number of MWCNT-enabled products in this stage and relatively few products that have moved past it, estimating when and how that payoff might take place is difficult. Similarly, additional risks are associated with consumer perception or acceptance of nanoenabled products.

Considerations raised in the literature on potential economic, societal, and environmental impacts suggest several remaining research questions, including the following:

- What is the relative impact on environmental resources (e.g., water, energy) of MWCNT production compared to other flame-retardant materials (non-nanoenabled or nanoenabled)?
- What are the economic implications of producing MWCNTs and MWCNT products (e.g., jobs created, infrastructure development)?

- What lessons from GMOs and other emerging technologies can be applied when communicating the potential risks and benefits of MWCNTs?

Workshop participants discussed societal impacts within this category to identify a potential risk scenario and to develop research questions that could inform future assessment and risk management efforts for MWCNTs (RTI, 2012). They noted that unintended consequences of MWCNTs could arise, which might lead to concerns in government and industry, fear in the public, and abandonment of future applications of the material. To manage or avoid these risks, experts suggested that risk managers might consider efforts "to build capacity and enable informed consent," or ban the material if necessary. They further suggested a socioeconomic assessment to inform these types of risk management decisions. To support this type of assessment, experts recommended the following research areas, along with estimates of the resources and time to carry out the research:

Table 6-14. Research Identified by RTI Workshop Participants: Societial Impacts of MWCNTs.

Research	Estimated Finances ($)	Estimated Time Frame
Evaluate the capacity of the institutions to meaningfully engage the public on nanotechnology.	50,000	0.5 year
Characterize the public's understanding of the benefits and risks of nanotechnology and their potential for participating in decision-making.	150,000	1.5 year
Capacity building to improve understanding of benefits and risks of nanotechnology. Development of a more effective systems approach to examine interrelated consequences (good and bad) of new technologies. Development of new methods of facilitating communication amongst stakeholders on complex issues like nanotechnology.	500,000	2 year

6.4. Moving From "Assessment" to "Management" in the CEA Process

Compiling information in the CEA framework and the subsequent collective judgment and prioritization process represent the steps of the "assessment" phase of the CEA process (see Figure 1-2). The "management" stage of the process involves moving the results of these steps into research plans or risk management plans. The outcome of identifying and prioritizing information gaps in the collective judgment step of CEA applied to MWCNTs is a list of topics in the CEA framework rated on the basis of each topic's importance to risk assessment efforts and the level of confidence the experts have in the information available for that topic to support risk management decisions. Areas collectively deemed of

high importance to risk assessment, but least understood based on available information, were high priorities for developing specific research questions in the final stage of the prioritization process, a face-to-face workshop. If these research questions are pursued, the knowledge gained could support a variety of risk assessments and other analyses that could then be used to update the CEA framework, and subsequently carry out a collective judgment prioritization of risk-related trade-offs to inform risk management decisions.

Such research fits within the overall research paradigm at EPA, the principles of which include sustainability; systems thinking; integrated transdisciplinary research; and relevant, responsive, and rapid research (Anastas, 2012). Within this research paradigm, known as the "Path Forward," are six national research programs (Anastas, 2012). Research specific to nanomaterials falls within the Chemical Safety for Sustainability program, which has several themes (e.g., Life Cycle Considerations, Systems Models), and thus this Program is oriented toward addressing some of the priority research areas identified through the CEA process for MWCNTs. For example, questions related to physicochemical properties might be investigated under the Program's theme on inherent chemical properties. Yet, the integrated transdisciplinary nature of CEA and the Path Forward suggest that some research questions could be addressed by multiple national programs working collaboratively. Notably, some of the identified research objectives might best be addressed by other government agencies, academic institutions, or others in the scientific community. The research priorities identified in the CEA process are thus intended not only to inform EPA research, but also to serve as a resource for the broader scientific community.

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Appendix A: Case Study Candidate Evaluation and Selection Process

Appendix A. Case Study Candidate Evaluation and Selection Process

Appendix A describes the process of evaluating and selecting carbon-based nanomaterials in specific applications as candidates on which to focus in the current case study. Specifically, it outlines the process by which the candidate carbon-based nanomaterial applications were identified and highlights factors relevant to the suitability of each candidate for a Nanomaterial Case Study. This information was used to support an informed selection of the nanomaterial and application for this case study by U.S. Environmental Protection Agency (EPA) program offices, labs, and centers in the Office of Research and Development, and regional offices during September 2011.

A.1. Background

As discussed in Chapter 1, the EPA (2007) Nanotechnology White Paper called for the use of nanomaterial case studies and multidisciplinary expert workshops as a means to inform research planning to support the risk assessment process for nanomaterials. In response to the recommendations of the Nanotechnology White Paper, EPA has been developing case studies of selected nanomaterials in specific applications, including *Nanoscale Titanium Dioxide in Water Treatment and Topical Sunscreen* (U.S. EPA, 2010c) and *Nanoscale Silver in Disinfectant Spray* (U.S. EPA, 2012b). To continue this series of case studies, five carbon-based nanomaterial applications were identified as candidates for the next Nanomaterial Case Study (presented in alphabetical order by material and application):

- Carbon nanofibers in cement/concrete
- Carbon nanotubes (multi-walled) in flame-retardant coatings and composites
- Carbon nanotubes (multi-walled) in rubber tires
- Carbon nanotubes (single-walled) in textiles
- Nanocrystalline cellulose in biodegradable packaging

This appendix provides further detail on the process by which the candidate carbon-based nanomaterial applications were identified, briefly summarizes the state of the science for each of the identified candidates, and highlights factors relevant to the suitability of each candidate for a Nanomaterial Case Study. The following criteria were used as guides in judging the candidates:

- "Nano-ness" of the material (i.e., whether the material is intentionally engineered at the nanoscale and has properties that distinguish it from conventional forms of the material);
- Potential for exposure throughout the product life cycle (in humans, both occupational and general public, as well as in other biota);
- Availability of data (whether directly related or inferred from other materials/products);
- Feasibility of comparing the nano-enabled application to a non-nano-enabled application; and
- Relevance to EPA programs.

Despite the wealth of information on carbon-based nanomaterials, EPA had previously encountered difficulties in identifying an appropriate carbon-based nanomaterial application as a candidate for a case study. These difficulties arose in part due to the following factors:

- Few data are available on the actual commercial use of carbon-based nanomaterials in products.
- Little to no information is available on release of carbon-based nanomaterials from applications during normal use.
- Small loadings (<5% by weight or volume) of carbon-based nanomaterials are generally required to confer desirable properties.
- Compared to other types of nanomaterials, the applications for carbon-based nanomaterials appear to have a smaller exposure potential outside of occupational and disposal scenarios.

Although these challenges are still present, the recent increase in carbon-based nanomaterial research has produced new data, and new applications have been proposed that offer greater potential for widespread exposure. As a result, the selection of a carbon-based nanomaterial application for the next in the Nanomaterial Case Study series appears to be feasible.

A.2. Candidate Identification Process

The process by which the five nanomaterial application candidates were identified is summarized in Figure A-1. As noted in Section 1.1, the process began with a systematic approach to the identification of nanomaterials and applications for investigation. This preliminary phase of the process utilized strategic literature and Internet searches to identify supporting scientific literature, relevant news reports, and nanomaterial information aggregation websites. Certain basic literature search statistics (e.g., number

of total hits, number of hits in scientific databases) were then evaluated to provide a preliminary metric of interest within the nanotechnology community for each candidate nanomaterial/application combination and general data availability. After the "long list" of material/application combinations was identified and narrowed down using this systematic approach, a more judgment-based approach was used to evaluate the suitability of a "medium list" of potential candidates and identify the most feasible candidates for a case study. In this phase of the process, a list of suitability questions was used to step through the life cycle of a specific nano-enabled product and evaluate the characteristics of that product that might affect release, exposure, environmental fate, and impact on humans, ecological receptors, and the environment.

A professional judgment as to whether a case study feasibly could be conducted for each candidate then was determined based on the answers to the suitability questions, and a "short list" of five feasible candidates was developed based on professional judgment of suitability.

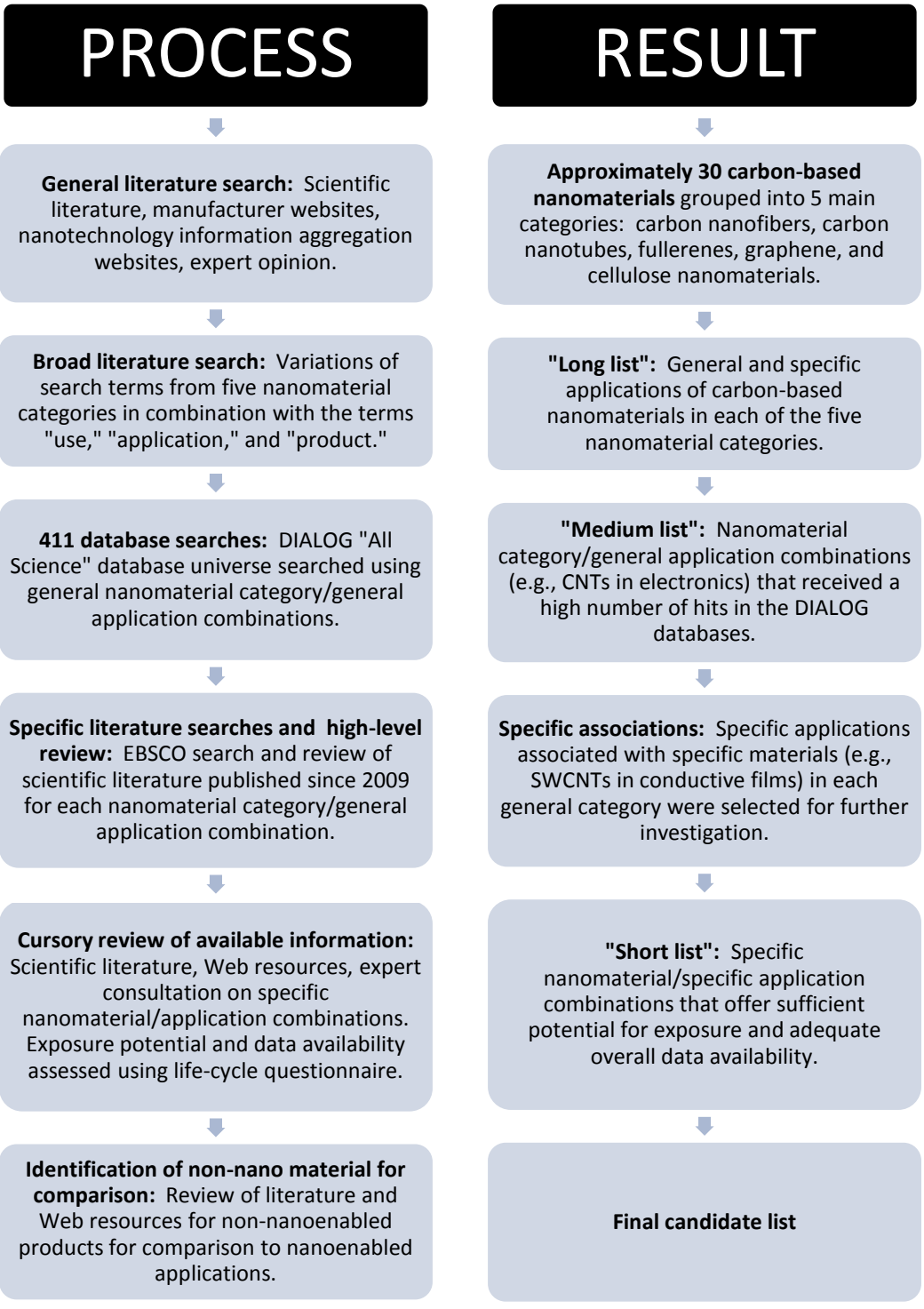

Figure A-1: Candidate identification process.

A.3. Nanomaterial Application Candidates

The candidate identification process yielded five nanomaterial applications for consideration as the subject of a new case study. The nanomaterial application candidates and proposed non-nanoenabled products for comparison are presented in Table A-1 below. As discussed in Chapter 1, the non-nanoenabled product is intended to provide a frame of reference against which the ecological, human health, and other implications of the selected nanomaterial application can be compared.

Table A-1. Nanomaterial application candidates and non-nano-enabled products for comparison in a case study.

Nanomaterial	Application	Proposed Non-Nano-Enabled Product for Comparison
Carbon nanofiber (CNF)	Cement/concrete (CNF-reinforced)	Steel- or glass-fiber reinforced cement/concrete
Multi-walled carbon nanotubes (MWCNTs)	Flame-retardant coatings and composites	Polybrominated diphenyl ether (PBDE) flame-retardant materials
MWCNT	Rubber tires (MWCNT as filler)	Carbon black and silica filler in tires
Single-walled CNTs (SWCNTs)	Textiles (SWCNT-reinforced/impregnated)	Traditional textiles reinforced with carbon fiber polymer composites
Nanocrystalline cellulose (NCC)	Biodegradable packaging (NCC-polymer composite)	Packaging containing polylactic acid (PLA) resin alone

A.4. Summary of Factors Affecting Suitability

Key considerations of the suitability of each candidate for development into a case study were summarized in a suitability chart (Table A-2). Based on the initial findings of this analysis (which should not be considered exhaustive or comprehensive), four of five applications appeared to still be in the research stage and unavailable for the commercial market in the United States or internationally. Although carbon nanotubes have been incorporated into military textiles, carbon nanotube flame-retardant coating is the only application identified as being currently available on the consumer market.

Table A-2. Factors for consideration in selecting a candidate for case study.

	Selection Factors	Candidates				
		CNF Cement/Concrete	MWCNT Flame-Retardant Coatings and Composites	MWCNT Rubber Tires	SWCNT Textiles	NCC Biodegradable Packaging
	■ = High ▣ = Medium □ = Low					
Data Availability	Nanomaterial production volume	▣	▣	▣	▣	▣
	Nanomaterial manufacturing processes	■	■	■	■	▣
	Nanomaterial characterization	■	▣	▣	▣	▣
	Nanomaterial release from application	□	□	□	▣	□
	Nanomaterial fate and transport in the environment	□	▣	▣	□	□
	Human exposure to nanomaterial	□	▣	▣	▣	□
	Ecological exposure to nanomaterial	□	▣	▣	▣	□
	Human health effects of nanomaterial	□	■	■	■	□
	Ecological effects of nanomaterial	□	▣	▣	▣	□
	Nano-product data (i.e., nanomaterial application data)	▣	▣	□	□	□
	Conventional (i.e., non-nano) product data for comparison	■	■	■	■	■

Data Availability Qualifiers.
High (■) = The database appears to contain a large quantity of good quality, diverse literature on the topic.
Medium (▣) = The database contains some literature specific to the topic, but substantial data gaps were observed.
Low (□) = Little to no information was identified on the topic.

		● = Yes	◉ = Possibly	○ = No		
Suitability Questions	Is there presumptive potential for exposure: During manufacturing?	◉	◉	◉	◉	◉
	During use?	●	◉	◉	◉	●
	At end of life?	◉	◉	◉	◉	◉
	Will extrapolation from other applications/materials be necessary?	●	●	●	◉	◉
	Is the nanomaterial currently produced in quantities >5 tons/year?	●	●	●	◉	○
	Is material production expected to increase in the near future?	●	●	●	◉	●
	Will the nanomaterial be used in the product at levels >5% by weight?	○	○	●	◉	◉
	Is the product already on the market?	○	●	○	○	○
	Is there evidence that the nanomaterial is hazardous: To humans?	●	●	●	●	○
	To eco receptors?	◉	◉	◉	◉	○

Answers to Suitability Questions.
Yes (●) = Initial findings suggest that an affirmative answer can be given with relatively high confidence.
Possibly (◉) = Initial findings from the preliminary literature review were conflicting.
No (○) = Initial findings suggest that a negative answer can be given with relatively high confidence.

A.5. U.S. EPA Program Involvement in Final Selection

As noted in Chapter 1, the selection of which of the five nano-carbon product candidates to use in this case study document involved representatives from EPA program offices, labs and centers within the Office of Research and Development, and regional offices. To facilitate distributing and discussing information relevant to the selection, an internal online forum was developed using a commercially available product (www.IdeaScale.com). The forum included brief introductory material on this nanomaterial case study series, instructions on using the website to nominate nano-carbon product candidates, links to tables summarizing life-cycle information on five candidate nano-carbon products (i.e., the applications in Table A-2), and a more detailed report summarizing the state of the science for each candidate.

A link to the forum was sent to EPA representatives along with a request to share the link with colleagues in their organization. Representatives and others in the Agency could then use the forum to discuss the candidates informally and nominate candidates for selection. Representatives were asked to submit a formal vote that reflected input from their colleagues through the IdeaScale forum and other communication channels they wished to use, as well as consideration of their own knowledge, the information provided on the forum, and the consideration of the criteria listed in Section A.1.

The candidates receiving the most votes were SWCNTs in textiles and MWCNTs in flame-retardant coatings and composites; thus, a hybrid option (MWCNTs in flame-retardant coatings applied to textiles) was selected. This choice reflected comments that, although the textile application was preferable, MWCNTs were perhaps of greater interest based on indications that they will contain a higher level of contaminants and are currently more widely produced.

Appendix A References

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Appendix B. Analytical Methods for Detecting, Measuring, and Characterizing BDE-209 and Multiwalled Carbon Nanotubes

Appendix B. Analytical Methods for Detecting, Measuring, and Characterizing BDE-209 and Multiwalled Carbon Nanotubes

This appendix provides a brief overview of some of the available techniques to detect, quantify, and characterize polybrominated diphenyl ethers (PBDEs; specifically BDE-209 [decaBDE]) and multiwalled carbon nanotubes (MWCNTs) in laboratory, biological, and environmental settings, along with current challenges to making such measurements. This information is not intended to be exhaustive in reporting every applicable method and associated challenges or to be comprehensive in describing available methods; rather, it is a summary of relatively common or known methods for characterizing BDE-209 and MWCNTs based on information available at the time this case study was developed.

B.1. Measuring and Characterizing PBDEs and MWCNTs

Accurately measuring BDE-209 or MWCNTs in relevant biological or environmental media is critical for evaluating any potential impacts of either material on human health, ecological populations, or environmental resources (Alcock et al., 2011; Lehman et al., 2011). The choice of which measurement technique to use for either BDE-209 or MWCNT samples will ultimately involve a consideration of trade-offs related to cost, time, selectivity, and sensitivity (Alcock et al., 2011; Lehman et al., 2011; Stapleton, 2006). In evaluating which analytical technique(s) to use, having an understanding of the challenges related to quantifying and characterizing BDE-209 and MWCNTs is useful. For both materials, multiple techniques might be required to characterize all of the physicochemical properties of interest in a single sample (e.g., molecular composition, purity, shape, surface charge) (Alcock et al., 2011; Lehman et al., 2011). Moreover, the training of personnel and the capital cost associated with some of these tools can impede the analysis of materials by multiple laboratories (Alcock et al., 2011). In addition, the standardization and validation of methods, availability of material standards, and the consistent reporting of material characteristics in peer-reviewed literature have proven difficult for both BDE-209 and MWCNTs (Alcock et al., 2011; Lehman et al., 2011). Distinguishing the sample from background concentrations or other materials of similar composition (e.g., nonaBDE congeners versus decaBDE, single-walled CNTs versus MWCNTs) is also a challenge for both materials (Lehman et al., 2011; Stapleton, 2006).

For BDE-209, gas chromatography coupled with mass spectrometry is the most prevalently used method; however, a number of variations in this approach exist (Stapleton, 2006). Even small differences in analytical techniques can result in significant variation in results (Alcock et al., 2011; Stapleton, 2006). Recent efforts to standardize methods and develop techniques that minimize material degradation have improved interlaboratory variation, but continue to be the subject of study, particularly for measuring samples in complex milieus (Stapleton, 2006). Detection and characterization of BDE-209 has proven more difficult than lower brominated compounds due in part to degradation at high temperatures and with ultraviolet light exposure (Stapleton, 2006).

For MWCNTs, transmission electron microscopy is generally used to characterize structural properties of the material, which is the first step in differentiating between MWCNTs, SWCNTs, or other materials; however, using this tool in tandem with others is necessary to characterize the material (Lehman et al., 2011) more completely. Challenges related to characterizing and quantifying MWCNTs include their propensity to agglomerate or otherwise transform (e.g., surface oxidize) during the process of production, purification, or exposure, as well as interference from experimental artifacts (e.g., metal catalysts used in material production) (Petersen and Henry, 2012; Lehman et al., 2011). The challenge of combining multiple techniques (e.g., gas chromatography and mass spectrometry) for BDE-209 analyses is amplified for MWCNTs in that a multitude of measurements and sampling techniques are generally required to fully characterize nanomaterials (Lehman et al., 2011).

B.2. Summary Tables

The tables below highlight techniques for detecting, measuring, and characterizing PBDEs and MWCNTs. Table B-1 briefly outlines advantages and disadvantages of individual approaches to gas chromatography and spectrometry, as well as a few alternative techniques that are available for studying PBDEs. Table B-2 provides a brief overview of available methods to characterize a range of MWCNT properties. More detail on each approach can be found in the references listed at the end of this appendix, particularly the recent review by Lehman et al. (2011).

Table B-1. Analytical techniques for detecting, measuring, and characterizing PBDEs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Stapleton (2006)	Atmospheric pressure photoionization (APPI)-coupled liquid chromatography (LC)/MS-MS[2,3]	• Determination of congener ratios in environmental and biological media	• Relatively soft ionization technique compared to electrospray ionization	• Limited chromatographic resolution relative to gas chromatography
Stapleton (2006)	Gas chromatography (GC)/electron capture detection[3]	• Determination of congener ratios in environmental media	• Inexpensive • Ability to detect halogenated organic compounds	• Relative imprecision compared to GC/ECNI
Stapleton (2006) La Guardia et al. (2006)	GC/electron capture negative ionization mass spectrometry (ECNI-MS)[1,2,3]	• Determination of congener ratios in environmental and biological media	• Low limit of detection	• Selectivity
Stapleton (2006) La Guardia et al. (2006)	GC/electron ionization (EI) MS[1,2,3]	• Determination of congener ratios in environmental and biological media	• Selectivity	• Interference may occur with methoxylated PBDEs
Stapleton (2006)	GC/high resolution mass spectrometry (HRMS)[2,3]	• Determination of congener ratios in environmental and biological media	• Selectivity • Sensitivity • Can detect relatively high molecular weight analytes	• Necessary equipment is not commonly found in laboratories • Expensive
Stapleton (2006)	GC/HR time of flight (TOF) MS[1,2,3]	• Determination of congener ratios in environmental media	• Spectral data can be obtained over a wide mass range with little sacrifice in sensitivity	• Expensive • Low sample concentration required for accuracy
Stapleton (2006)	On-column injection GC[1,3]	• Separation and detection of PBDE congeners • Determination of molecular weight	• Necessary equipment commonly present in laboratories • Precise discrimination, particularly of BDE-209	• Small injection volume • Sample must be free of impurities

Table B-1, cont.: Analytical techniques for detecting, measuring, and characterizing PBDEs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Stapleton (2006)	Programmable temperature vaporization (PTV) injection GC[2,3,4]	• Separation and detection of PBDE congeners • Determination of molecular weight	• Relatively large injection volume compared to other GC techniques • Separation can be performed on human serum	• Requires significant optimization to perform separation
Stapleton (2006)	Split/splitless injection gas chromatography (GC)[2,4]	• Separation and detection of PBDE congeners • Determination of molecular weight	• Can be used on environmental samples • Necessary equipment commonly present in laboratories	• Injection volume must be small • High injection temperature

[1]Techniques listed in alphabetical order
[2]Used for chemical (in vitro) analysis as reported in reference document
[3]Used to analyze in vivo samples as reported in reference document
[4]Used to analyze environmental samples as reported in reference document

Table B-2. Analytical techniques for detecting, measuring, and characterizing MWCNTs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Petersen and Henry (2012)	Atomic force microscopy[2]	• Size (diameter and length) and shape		• Limited to samples in aqueous phase
Lehman et al. (2011) Johnston et al. (2010) Petersen and Henry (2012)	Centrifugation[2]	• Dispersion in solution • Length distribution • Size of nanoparticle aggregates	• Centrifugation equipment commonly present in laboratories	• Dispersion difficult; requires extensive sonication • Accuracy may be affected by dispersion
Petersen and Henry (2012)	Chemothermal oxidation[4] (at 375 °C)	• Measurement of MWCNT concentration in environmental samples	• Allows for quantitative determination of MWCNT concentration	• Inaccurate
Petersen and Henry (2012)	Cryotransmission electron microscopy (CEM)[2]	• Properties of MWCNTs in aqueous phase		• Limited to samples in aqueous phase
Petersen and Henry (2012)	Fluorescence microscopy (FLM)[3,4]	• Detection of MWCNT in environmental media or tissue from biological specimens	• Can detect single MWCNTs	• Necessary equipment is not common in laboratories

Table B-2, cont.: Analytical techniques for detecting, measuring, and characterizing MWCNTs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Lehman et al. (2011)	Fourier transform infrared spectroscopy (FTIR)[2]	• Nanoparticle functionalization • CNT orientation (parallel or perpendicular to beam)	• Reliable detector of carboxylic acids	• Sample preparation may result in water contamination or altered surface functionalization
Petersen and Henry (2012)	Dynamic light scattering (DLS)[2]	• Size of aggregates in aqueous phase	• Useful for detecting changes in MWCNT size at various points during synthesis or experimentation	• Estimation of size by DLS based on spherical molecular structure and cannot be used for absolute calculation of aggregate size
Lehman et al. (2011)	Gas pycnometry[2]	• Density	• Can be used to determine both bulk and skeletal densities	• Sample must be powder
Lehman et al. (2011) Johnston et al. (2010) Petersen and Henry (2012) Revel and Ayrault (2000)	ICP mass spectrometry (ICP-MS)[3, 4]	• Metal concentration in environmental samples	• Can be used to study health effects of MWCNT exposure by detecting changes in protein expression or structure • Faster than instrumental neutron activation analysis	• Necessary equipment is not commonly found in laboratories
Petersen and Henry (2012) Revel and Ayrault (2000)	Instrumental neutron activation analysis[2,3,4]	• Metal concentrations	• Can be more accurate than ICP-MS	• Safety risk associated with radioactivity • Lower sample throughput than ICP-MS • Requires equipment not commonly found in laboratories
Petersen and Henry (2012) Johnston et al. (2010)	Light microscopy[2,3,4]	• Identification of large MWCNT aggregates	• Necessary equipment is common in laboratories	• Technique provides qualitative, non-specific information • Detection limited to large aggregates

Table B-2, cont.: Analytical techniques for detecting, measuring, and characterizing MWCNTs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Lehman et al. (2011)	N_2 gas adsorption[2,4]	• Surface area determination		• Permanent quadrupole inhibits N_2 adsorption to some substrates • Model of N_2 adsorption based on homogeneity across adsorption surface • May not be suitable for characterization of ecotoxicity
Lehman et al. (2011) Johnston et al. (2010)	Nitrogen and phosphorous doping[2,3]	• Structural defects	• Can detect non-carbon atoms present in MWCNT • Can differentiate between pentagonal and hexagonal structure	• Interaction between donor molecules and pentagonal and hexagonal structures on nanoparticle surface have not yet been quantified
Lehman et al. (2011) Petersen and Henry (2012) Johnston et al. (2010)	Optical density (UV-vis absorbance)[2,3,4]	• MWCNT concentration in solution	• Necessary equipment is common in laboratories	• Results sensitive to presence of other compounds in solution
Petersen and Henry (2012) Johnston et al. (2010)	Radioactive labeling[3,4]	• Detection of MWCNTs in environmental media	• Quantitative • Versatile (can be used in many forms of environmental media)	• Expensive • Inherent danger of radioactivity
Lehman et al. (2011) Johnston et al. (2010)	Raman spectroscopy[2,3,4]	• Analysis of MWNCNT purity • Detection of defects in MWNCT structure • Tube alignment • Tube diameter	• Relatively high resolution information about structure	• Complex interpretation of spectra for MWCNT
Lehman et al. (2011)	Scanning electron microscopy (SEM)[2]	• Surface morphology • Surface purity	• Repeatable	• Does not provide information on internal morphology

Table B-2, cont.: Analytical techniques for detecting, measuring, and characterizing MWCNTs.

Citation(s)	Technique[1]	Application(s)	Advantages	Disadvantages
Petersen and Henry (2012)	Thermal optical transmittance[4]	• Loss of mass at various temperatures	• Samples can contain dissolved environmental material	• Only useful for MWCNTs in aqueous phase • Necessary equipment is uncommon in laboratories
Lehman et al. (2011)	Thermogravimetric analysis (TGA)[2]	• MWCNT purity analysis	• Necessary equipment is common in laboratories	• Sample size requirements may be large for certain applications (3-10 mg) • Multiple measurements needed to ensure accuracy of data
Lehman et al. (2011) Petersen and Henry (2012) Johnston et al. (2010)	Transmission Electron Microscopy (TEM)[2,3,4]	• Surface morphology • Crystallinity	• Provides high resolution information about nanotube structure	• Difficult sample preparation; preparation may damage sample • requires expert personnel • Images susceptible to excessive beam exposure • Difficult to analyze large volumes in timely manner
Lehman et al. (2011)	X-ray diffraction[2]	• Skeletal density		• Cannot be used to determine bulk density
Lehman et al. (2011) Echlin (1998)	X-ray microanalysis[2,3]	• Purity	• Narrowing of incident beam allows greater resolution	
Lehman et al. (2011) Petersen and Henry (2012)	X-ray photoelectron spectroscopy (XPS)[2]	• Surface chemical composition • Presence of functional groups		• May be inaccurate without fluorine tagging

[1]Techniques listed in alphabetical order
[2]Used for chemical (in vitro) analysis as reported in reference document
[3]Used to analyze in vivo samples as reported in reference document
[4]Used to analyze environmental samples as reported in reference document

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Appendix C. Efficacy of Various Methods of Carbon Nanotube Purification

Appendix C. Efficacy of Various Methods of Carbon Nanotube Purification

Appendix C provides a comparative overview of various purifications methods for carbon nanotubes reported in the literature, and as summarized by Hou et al. (2008). This information is organized to demonstrate the relative effectiveness of each method at removing each of the specified carbonaceous or metallic impurities. Each method is ranked as effective, partially effective, or not effective (✓= effective; O= partially effective; ✖= not effective) for removing each impurity specified in Table C-1 below.

Table C-1. Purification methods for carbon nanotubes.

Purification methods			Yield (wt%)	Carbonaceous impurities				Metallic impurities		
				Amorphous carbon	Graphite	Carbon impurity on walls	Soluble carbon in solution	Exposed metal	Metal covered in polyhedral carbon	Metal encapsulated by CNT
Chemical methods	Gas phase	Air (Plus HCl)	~2-35	✓[1]	✗	O	✗	✓	O	O
		Cl_2, H_2O, HCl	~15	✓	✗	O	✗	✓	O	O
		H_2O, Ar, O_2 (Plus HCl)	~30	✓	✗	O	✗	✓	O	O
		O_2, $C_2H_2F_4$, SF_6	25-48	✓	✗	O	✗	✓	✓	O
	Liquid phase	HNO_3	~30-50	✓	✗	O	✗	✓	O	O
		H_2O_2, HCl	10-75	✓	✗	O	✗	✓	O	O
		Mixture of acid or $KMnO_4$	30-75	✓	O	O	✗	✓	✓	O
		Microwave in inorganic acid	10-60	O	✗	O	✗	✓	O	O
	Electrochemical	Alkali or acid solution (Plus HCl)	~80	O	✗	✗	✗	✓	✗	O
Physical methods	Filtration		~30-84	O	O	✗	✓	O	O	✗
	Centrifugation		~10-40	O	O	✗	✓	O	O	✗
	Solubilization with functional groups		~17-50	O	O	✗	✓	✗	O	✗
	High temperature annealing		~70-90	✗	✗	✗	✗	✓	✓	✓
	Other physical techniques		~10-	✗	✗	✗	✗	✓	✓	✓
	Chromatography, electrophoresis, FFF[2]		?	✓	✓	✗	✗	O	O	✗
Multistep methods	HIDE[3], wet grinding, filtration, oxidation, sonication, centrifugation		~2	✓	✓	O	✓	✓	O	O
	Filtration/magnetic filtration, oxidation, annealing		~9-20	✓	✗	✓	✓	✓	✓	O
	Sonication in H_2O_2, HNO_3/HF/SDS, filtration		~25	✓	O	O	✓	✓	O	O
	High temperature annealing extraction		~90	O	O	✓	✓	✓	✓	✓

[1]✓= effective; O= partially effective; ✗= not effective

[2]Field-flow fractionation

[3]Hydrothermally initiated dynamic extraction

Source: Hou et al. (2008). Purification of carbon nanotubes. Carbon 46: 2003-2025. http://dx.doi.org/10.1016/j.carbon.2008.09.009.

Appendix C References

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Appendix D: Study Summaries on the Transport, Transformation, and Fate of Decabromodiphenyl Ether and Multiwalled Carbon Nanotubes in Environmental Systems

Appendix D. Study Summaries on the Transport, Transformation, and Fate of BDE-209 and MWCNTs in Environmental Systems

The following tables provide details from studies related to fate, transport, or transformation of decabromodiphenyl ether [(decaBDE) specifically the single isomer of decaBDE, BDE-209] or multiwalled carbon nanotubes (MWCNTs) in environmental media. Study information that provides support for the transformation (debromination) of BDE-209 in environmental media is included in Table D-1. Table D-2 provides study summaries related to the behavior of MWCNTs in aqueous media. Table D-3 and Table D-4 present information from studies conducted in terrestrial ecosystems for BDE-209 and MWCNTs, respectively.

Table D-1. Relevant studies of transformation (debromination) of BDE-209.

Citation	Relevant Study Information[1]
Biotic Debromination	
Deng et al. (2011)	• Used aerobic bacterium *Lysinibacillus fusiformis* strain DB-1 to determine its capability to debrominate BDE-209 in sediments of the Lianjiang River, China; DB-1 is an indigenous bacterium in PBDE-contaminated sediments. • DB-1 efficiently transformed BDE-209 to lower-brominated BDEs using lactate, pyruvate, and acetate as carbon sources, and this debromination was an aerobic (oxygen-consuming) process.
He et al. (2006)	• Studied degradation of BDE-209 in various microbial cultures. • Debromination of BDE-209 was observed with anaerobic bacteria including *Sulfurospirillum multivorans* and *Dehaloccoides* species.
Huang et al. (2010)	• Studied behavior of BDE-209 in soil-plant system; transportation of BDE-209 within plants was examined using six plant species. • OH-metabolized and debrominated products of BDE-209 were measured in plants and soil; higher proportions of penta- through diBDE congeners in plant tissues than in the soil suggest either further debromination of PBDEs within plants or lower PBDEs are more readily taken up by plants; significant negative correlation between residual BDE-209 concentration and soil microbial biomass, suggesting microbial metabolism and degradation of BDE-209.

Table D-1, cont.: Relevant studies of transformation (debromination) of BDE-209.

Citation	Relevant Study Information[1]
Biotic Debromination	
Tokarz et al. (2008)	• Studied reductive debromination in an anaerobic sediment microcosm experiment. • BDE-209 debrominated slowly; its half-life ranged from 6 to 50 years, and averaged about 14 years; formation of nona-, octa-, hepta-, and hexaBDEs and 9 new congeners, including lower brominated congeners that are greater environmental concern (more bioavailable); experiments suggested anaerobic reductive debromination of BDE-209; authors noted competing influences of hydrophobicity and reactivity that can significantly retard rate of debromination.
Wang et al. (2011)	• Examined microbial degradation of BDE-209 in the rhizosphere of ryegrass using arbuscular mycorrhizae. • 12 lower brominated congeners were detected in soil samples and 24 were detected in plant samples; there was evidence of debromination in soil and within plants based on higher proportion of di- through hepta-BDEs.
Abiotic Debromination (Photolysis)	
Ahn et al. (2006)	• Characterized photodegradation of BDE-209 adsorbed on clay, metal oxides, and sediment using sunlight and artificial UV light. • Photodegradation rates were likely dependent on the chemical and physical properties of the sorbent; however, degradation product distribution was not believed to be dependent on sorbent type. • Enhanced photolytic transformation rates observed when BDE-209 was adsorbed to clay minerals; no significant BDE-209 degradation of BDE-209 observed on metal oxides; very slow degradation rates of BDE-209 sorbed to carbon-rich sediment; results indicated stepwise (sequential) debromination. • Suggested that organic matter has inhibitory effect on photodegradation possibly by shielding BDE-209 from the light or by satisfying excited states of the BDE-209 before they can form products.
An et al. (2008)	• Characterized photolytic activity on BDE-209 degradation using a TiO_2 photocatalyst. • TiO_2 was an effective photocatalyst for degrading BDE-209; results suggested sequential debromination occurred in the formation of products during BDE-209 transformation; products were hexa-, penta, and tetraBDEs.
Bezares-Cruz (2004)	• Examined BDE-209 photochemical transformation using a hexane solvent and solar light. • Reaction rate of photolysis was dependent on solar intensity and what the BDE-209 was adsorbed to; 43 PBDEs were detected, including BDE-47.
Christiansson et al. (2009)	• Examined BDE-209 photochemical transformation in the laboratory using various solvents and UV irradiation. • BDE-202 was identified as a marker of BDE-209 photolysis; PBDEs accounted for about 90% of products formed (primarily heptaBDEs to nonaBDEs); Poly brominated dibenzofurans (PBDFs) accounted for approximately 10% of products formed; authors noted the formation of BDE-183 and BDE-153 as important environmental congeners.
Hua et al. (2003)	• Measured photochemical reactions of BDE-209 on artificial surfaces—quartz glass, silica particles, humic acid-coated silica particles—using UV light and natural sunlight. • Transformation occurred more slowly using sunlight irradiation; presence of humic acid slowed transformation; tetraBDE and pentaBDE were not found at detectable levels.

Table D-1, cont. Relevant studies of transformation (debromination) of BDE-209.

Citation	Relevant Study Information[1]
Abiotic Debromination (Photolysis)	
Raff and Hites (2007)	• Examined the role of photolysis in the atmospheric removal of BDE-209. • Determined that photolysis is minor removal process; removal of particle-bound BDE-209 more likely due to wet (primarily) and dry deposition.
Schenker et al. (2008)	• Used multimedia model that incorporated photolysis to predict fate of BDE-209 in environmental compartments. • Model estimated that about 13% of pentaBDE and 2% of tetraBDE in the environment occurs from degradation of BDE-209; model-predicted degradation in the atmosphere (e.g., by photolysis) represents 45% of BDE-209 loss; loss to deposition estimated at 30%.
Shih and Wang (2009)	• Examined solar and UV-lamp degradation of BDE-209. • Observed that photodegradation of BDE-209 was not affected by initial BDE-209 concentrations; photodegradation rate increases with increasing light intensity; photodegradation of higher brominated congeners faster than for lower brominated congeners; photodegradation of BDE-209 is a sequential dehalogenation mechanism with stepwise bromine losses.
Söderstrom et al. (2004)	• Studied photodegradation of BDE-209 in toluene, on silica gel, and in sand, soil, sediment using artificial UV light and natural outdoor sunlight. • Debromination rates were strongly dependent on matrix type; half-lives were shorter using artificial matrices (<15 min); longer half-lives observed on more complex natural matrices (40–200 hours) ; no matrix-related or light intensity-related differences in the debromination pattern of the BDE congeners formed; formation of lower brominated BDEs (nona-hexaBDEs) occurred, including BDE-154 and BDE-183; PBDFs were also formed.
Stapleton and Dodder (2008)	• Studied photodegradation of BDE-209 in house dust exposed to natural sunlight. • Initial BDE-209 concentration decreased by about 38%, 35% of which believed to be due to debromination.

[1]Additional information obtained from U.S. EPA (2010a).

Table D-2. Relevant studies of MWCNTs in aqueous media.

Citation	Relevant Study Information
Chae et al. (2011)	• Studied photochemical reactivity of CNT aggregates and compared with other fullerene nanoparticles. • After photosensitization from ultraviolet irradiation, the primary mode of oxidation of chemical compounds by CNTs is singlet oxygen production; this reactivity appeared to be correlated with the surface area of colloidal aggregates in solution.
Chappell et al. (2009)	• Examined the mechanism by which humic substances stabilize MWCNT dispersions in aqueous media. • Adding humic substances to MWCNTs in solution enhanced stability, decreased particle diameter, and decreased polydispersivity; presence of surfactive domains in the structure of the humic substances directly impacts CNT dispersal in solution.
Christian et al. (2008)	• Studied aggregation of nanoparticles and effects of humic acid and cations on CNT stability. • Cations, in particular divalent cations (e.g., Ca^{2+} and Mg^{2+}), were found to reduce the stability of CNT with or without NOM surface coating.
Desai et al. (2012)	• Investigated antisolvent precipitation of functionalized MWCNTs and aggregation behavior in the aqueous media. • Organic-soluble MWCNTs functionalized to be hydrophobic by addition of octadecylamine were shown to form stable dispersions in water/solvent systems even after antisolvent precipitation via aggregation; stability was shown to be long term, and particle aggregation increased with the addition of electrolytes.
Han et al. (2008b)	• Investigated the influence of clay minerals on the stability of surfactant-facilitated MWCNTs. • Solutions of MWCNTs facilitated by three surfactants reacted differently to addition of two minerals—kaolinite and montmorillonite; stability of the solutions after mineral addition depended on the surfactant and the mineral; two mechanisms by which minerals were shown to affect the stability of MWCNT solution were by mineral adsorption to surfactants and bridging between mineral and MWCNTs by surfactant.
He et al. (2012)	• Studied the behavior of stabilized MWCNTs in a ferric chloride coagulation system and the structure characteristics of the produced flocs. • MWCNTs stabilized by humic acid were effectively removed from solution by coagulation after application of relatively large amounts of ferric chloride.
Holbrook et al. (2010)	• Examined surface water constituents that affect MWCNT coagulation. • Higher influent concentrations of kaolin and alginate increased MWCNT removal by coagulation; higher concentrations of NOM reduced MWCNT removal by coagulation.
Hyung et al. (2007)	• Studied the aqueous stability of MWCNTs in the presence of NOM. • For the same initial MWCNT concentrations, suspended MWCNT concentrations were considerably higher in solutions of synthetic modeled Suwannee River NOM and actual river water than in solutions of sodium dodecyl sulfate, a common surfactant; the mechanism for CNT-NOM interactions are dependent on the characteristics of the MWCNTs and the NOM.

Table D-2, cont.: Relevant studies of MWCNTs in aqueous media.

Citation	Relevant Study Information
Hyung and Kim (2008)	• Investigated the effect of NOM characteristics and water quality parameters on NOM adsorption to MWCNTs. • Adsorption capacity was directly proportional to NOM aromatic carbon content and the ionic strength of the solution; adsorption capacity was indirectly proportional to pH; adsorption strength was indirectly proportional to ionic strength and not significantly changed by pH.
Kennedy et al. (2008)	• Investigated factors that influence the partitioning of CNTs (raw versus functionalized [either engineered or natural]) in the aquatic environment. • Pure CNTs had limited potential for aqueous transport; instead, aggregation and adsorption to sediment particles; no ionic strength influences on aggregate size; hydrophobicity of CNTs likely increased affinity for particles and enhanced aggregation; aqueous destabilization by van der Waals attractions and rapid sedimentation; sedimentation rate might accelerate with increased concentration; dispersion was enhanced by surface modifications (engineered or NOM)—increased residency time in surface water, aggregate size/structure changes.
Kennedy et al. (2009)	• Examined influence of surface modifications and various dispersal methods on MWCNT fate and toxicity. • Dissolved organic matter, humic acid, and fulvic acid were shown to be dispersing agents of MWCNTs; humic acid was a more effective dispersant than fulvic acid; sonication treatment of MWCNTs was shown to increase fragmentation of the particles relative to magnetic stirring; functionalization and laboratory methods of dispersal of MWCNTs affect their behavior in aqueous solutions in the presence of NOM.
Kummerer et al. (2011)	• Investigated biodegradability of functionalized and nonfunctionalized MWCNTs in aqueous media. • MWCNTs were not biodegradable under the conditions tested. Surface modification resulted in better solubility, but not better biodegradability.
Lin et al. (2009b)	• Studied the influence of solution pH and ionic strength on the interaction between tannic acid-facilitated MWCNTs of various diameters. • Suspension of MWCNTs in tannic acid solution greatly improved with tannic acid concentration until a plateau concentration was reached; suspension was greatest for particles of 40 nm diameter, followed by 60 nm, 20 nm, 100 nm, and 10 nm, respectively; MWCNTs stabilized in tannic acid were stable at pH > 5, and precipitated at pH < 5; presence of ions Na^{+}, Mg^{2+}, Ca^{2+}, and La^{3+} caused tannic acid-stabilized MWCNTs to aggregate, in a manner exponentially correlated to ionic valence.
Lin et al. (2010)	• Described stabilities of MWCNTs in forms of particulate aggregates and surfactant-facilitated suspensions in various fresh surface waters. • Nonfunctionalized MWCNTs could not stabilize in eight samples of natural surface waters by shaking, but stabilized in one sample with high dissolved organic content after sonication; nonfunctionalized MWCNTs did not stabilize in one surface water sample that also had a high NOM content, suggesting that other characteristics of the sample affected MWCNT stabilization; MWCNTs stabilized with CTAB surfactant were destabilized in all surface water samples, TX100- and SDBS- facilitated MWCNT suspensions remained stable in all eight surface water samples; addition of cations to solutions were shown to destabilize surfactant-facilitated MWCNT suspensions.

Table D-2, cont.: Relevant studies of MWCNTs in aqueous media.

Citation	Relevant Study Information
Liu et al. (2009)	• Examined the mobility of MWCNTs in porous media using column experiments. • At low flow rates similar to those found in natural subsurface aqueous environments, OH- and COOH-functionalized MWCNTs were retained in porous media to a significant extent; at high flow rates, OH- and COOH-functionalized MWCNTs were very mobile; a medium with a large number of small pores was shown to retain the functionalized MWCNTs better than media with fewer wider pores.
Petersen et al. (2008a)	• Studied ecological uptake in sediment spiked with MWCNTs by sediment-burrowing *Lumbriculus variegatus*. • Study showed that CNTs did not readily absorb into organism tissues; sizes of MWCNTs could have been a factor in the lack of absorption by organisms.
Saleh et al. (2008)	• Examined aggregation kinetics of MWCNTs in aquatic media with varying solution pH and salt concentrations and presence of organic matter. • Increasing monovalent and divalent salt concentration in aqueous solution and increasing solution pH from acidic to basic in aqueous solution reduced aggregation of sonicated MWCNTs; addition of humic acid to solution also reduced aggregation rate and enhanced sonicated MWCNT stability; these results show that sonicated MWCNTs are relatively stable in solution chemistries with electrolyte and pH levels typical of natural aquatic environments.
Wang et al. (2009)	• Investigated sorption of humic acid and aromatic compounds by MWCNTs. • With increasing concentration of humic acid in solution, MWCNTs increasingly sorbed humic acid until a plateau was reached; maximum humic acid sorption capacity of MWCNTs depended on π–π interactions, surface area of MWCNTs, and dispersion of MWCNTs; sorption of hydrophobic organic compounds decreased with increasing humic acid concentrations, suggesting that sorption of hydrophobic organic compounds would be suppressed in the presence of NOM.
Zhang et al. (2010)	• Investigated NOM, pH, and ionic strength effects on adsorption of SOCs by MWCNTs in natural waters. • NOM showed a more significant effect on sorption of SOCs by MWCNTs than pH or ionic strength of solution, which had negligible impacts on SOC sorption; surface functionalization of MWCNTs with hydroxyl and carboxyl groups slightly suppressed the effects of NOM on SOC sorption by MWCNTs, and this suppression decreased with increasing hydrophobicity of the SOC.
Zhang et al. (2011a)	• Examined interactions (phase distribution) between MWCNTs and aqueous systems containing peat under various conditions (ionic strength and pH). • Presence of DOM greatly increased the stability of MWCNTs in aqueous solution in a way similar to surfactant stabilization; solid peat did not adsorb MWCNTs except with the increasing concentration of sodium cations.

CNT = carbon nanotube; MWCNT = multiwalled carbon nanotube; CTAB = cetyl trimethyl ammonium bromide; NOM = natural organic matter, DOM = dissolved organic matter; SDBS = sodium dodecyl benzene sulfonate; SOC = synthetic organic chemicals

Table D-3. Relevant studies of BDE-209 in soils and plants.

Citation	Relevant Study Information
Soils	
Li et al. (2010)	• Collected wet and dry particle deposition samples at the urban sites of Guangzhou and Hong Kong, South China. • Depositional fluxes of BDE-209 ranged from 273 to 6,000 (mean 2,220) ng/m^2-day in Guangzhou and from 29.1 to 1,100 (mean 259) ng/m^2-day in Hong Kong. • BDE-209 was most abundant PBDE congener; distinct seasonal patterns were observed—higher depositional fluxes during winter; lower fluxes during the summer; seasonal variation associated with local usage and meteorological factors.
Liu et al. (2011a)	• Studied the effects of BDE-209 on soil microbial activities and function using soil enzymatic activity analysis. • Bacterial counts were suppressed as BDE-209 concentration increased; BDE-209 inhibited microbial diversity and altered soil microbial community structure.
Yu et al. (2010)	• Studied the effects of humic acids (HA) and microorganisms on the migration of BDE-209 in soils using soil enzymatic activity analysis. • Distribution of BDE-209 in the colloidal fraction related to the HA and microorganism concentration; HA acted as surface modifier and microorganisms acted as biosurfactants; BDE-209 transported by soil colloids along with water currents especially in the presence of HA and microorganisms.
Zhu et al. (2010)	• Studied the response of bacterial communities in soils spiked with BDE-209; soil microbial activities and composition were affected by BDE-209. • BDE-209, although expected to be of low bioavailability, had an adverse impact on the structure and function of the soil microbial community and microbial processes; high doses of BDE-209 were toxic, inhibiting growth for some microorganisms.
Zou et al. (2007)	• Investigated the distribution and fate of BDE-209 in soils, Pearl River Delta, China. • Concentrations of BDE-209 generally decreased with increasing soil depth; BDE-209 in soil was significantly correlated with total organic carbon levels; sorption of BDE-209 on organic matter influences its distribution, transportation, and fate in the environment.

Table D-3, cont.: Relevant studies of BDE-209 in soils and plants.

Citation	Relevant Study Information
Plants	
Huang et al. (2010)	• Described the uptake, translocation, and metabolism of BDE-209 in six plant species—ryegrass, alfalfa, pumpkin, summer squash, maize, and radish. • Accumulation of BDE-209 occurred in the roots and shoots of all plants. • Root lipid content was positively correlated with BDE-209 uptake. • Translocation factor ($Concentration_{shoot}/Concentration_{root}$) of BDE-209 was inversely related to BDE-209 concentration in the roots, suggesting root lipids restrict translocation of BDE-209 from roots to shoots because of its partitioning to root lipids.
Salamova and Hites (2010)	• Evaluated air samples and tree bark for levels of PBDEs. • BDE-209 concentration in tree bark was strongly correlated with concentrations of these compounds in the air and precipitation; highest air and tree bark concentrations occurred at urban sites.
Vrkoslavova et al. (2010)	• Studied the ability of plants (tobacco and nightshade) to accumulate and translocate PBDEs from contaminated sewage sludge. • BDE-209 was accumulated via roots into tobacco tissue at 116.8 ng/gram dry wt; BDE-209 was not detected in nightshade; PBDEs detected in aboveground plant biomass provided evidence of translocation by plants.

Table D-4. Relevant studies of carbon nanotubes (CNTs) in soils.

Citation	Relevant Study Information
Jaisi and Elimelech (2009)	• Investigated the transport behavior of functionalized single-walled CNTs in columns of natural soil. • Single-walled CNT mobility in soils is likely limited because of its irregular shape, large aspect ratio, and bundled (aggregated) state—these properties would promote soil retention. • Natural soil environments that are more heterogeneous and contain "open soil structures" could promote CNT mobility in soil. Dissolved organic molecules in soil pore water could also enhance the colloidal stability of CNTs and increase their mobility.
Petersen et al. (2011a)	• Studied the effects of modifying ^{14}C-labeled MWCNTs with polyethyleneimine surface coatings—making them more stable in solution and modifying surface charges. Tested MWCNT sorption by soils and uptake and elimination behaviors by earthworms. • Nearly linear sorption isotherms for regular MWCNTs and nonlinear isotherms for modified MWCNTs, indicating that the PEI coatings influenced MWCNT interactions with soils; little difference in sorption results among the different soils tested; soil type might not be as important as the MWCNT characteristics in predicting soil sorption behaviors.

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Appendix E: Environmental Contaminant Concentrations

Appendix E. Environmental Contaminant Concentrations

Appendix E provides information available from the literature regarding reported environmental concentrations of decaBDE (BDE-209) and multiwalled carbon nanotubes (MWCNTs) in environmental media (dust, indoor and outdoor air, aquatic systems, sewage, and soil) (Section E.1), and biota (Section E.2). Literature was identified primarily using review articles published in the past two years. Targeted literature searches were carried out as needed.

E.1. Concentrations in Environmental Media

The following tables provide details from studies that measured BDE-209 in dust, air, water, sediment, soil, and sewage effluent/sludge. No data were identified on MWCNT concentrations in environmental media.

Table E-1. BDE-209 concentrations in building dust.

Citation	Relevant study info	BDE-209 levels (ng/gram)
United States		
Stapleton et al. (2005)	• Washington, DC • Dust samples from 16 homes	Mean (dry wt): 2,090
Sharp and Lunder (2004) as cited in U.S. EPA (2010a)	• Throughout United States • 10 homes	Mean (dry wt): 2,394
Sjodin et al. (2008)	• Atlanta, GA • Dust in vacuum cleaner bags analyzed from 10 homes • BDE-209 was the dominant congener in dust samples	Median (range): 2,000 (120–21,000)
Charles et al. (2005)	• Computer labs, CA • 2 carpet dust samples • BDE-209 was the dominant congener in carpet dust	Mean: 5,180
Schecter et al. (2005)	• Dallas, TX • 9 vacuum samples • BDE-209 was the dominant congener in 7 samples	Mean (Median) (dry wt): 8,567 (665)

Table E–1, cont.: BDE-209 concentrations in building dust.

Citation	Relevant study info	BDE-209 levels
United States		
Allen et al. (2008)	• Boston, MA • 20 homes; 3 locations/home: living room, bedroom, vacuum • One sample contained highest concentration of BDE-209 in house dust reported to date (527,000 ng/gram)	Geometric means: 4,502 (main living area); 1,703 (bedroom); 1,811 (vacuum)
Wu et al. (2007) [levels reported by U.S. EPA (2010a)]	• Boston, MA area • 46 women; 11samples above detection limits	Median: ND; 9,020
Harrad et al. (2008b)	• Amarillo, Austin, TX carpet dust from 17 homes	Mean (geometric mean): 1,600 (1,300)
Johnson-Restrepo and Kannan (2009)	• Albany, NY • Vacuum dust from 12 homes	Mean (median) (dry wt): 2,810 (903)
Batterman et al. (2010)	• Southeast Michigan (Ann Arbor area) • Vacuum dust from 10 office buildings	Mean: 6,930
Watkins et al. (2011)	• Boston, MA area • Vacuum dust from 8 office buildings	Geometric Mean: 4,204
International		
Muenhor et al. (2010)	• Thailand: 5 electronic/ electrical waste storage facilities • Dust, 25 samples	Mean: 33,000
Harrad et al. (2008b)	• Canada: carpet dust from 7 homes • U.K.: carpet dust from 16 homes • Concentrations of BDE-209 in 2 UK samples were highest recorded to date in a domestic (or office) indoor dust sample (520,000 and 100,000 ng/gram)	Mean (geometric mean): 670 (590) (Canada); 45,000 (3,800) (U.K.)
Harrad et al. (2008a)	• Birmingham, UK • 30 homes, 18 offices, 20 cars • BDE-209 concentrations (ng/gram) in three samples were highest to date at 2,600,000 (car), 2,200,000 (home), 1,400,000 (home)	Mean (median): 260,000 (8,100) (homes); 30,000 (6,200) (offices); 410,000 (100,000) (cars)
Ma et al. (2009)	• Taizhou, China • 5 dust samples from electronic waste recycling workshop floor • BDE-209 accounted for major proportion of total PBDEs in dust	Mean (range) (dry wt): 29,800 (5,560–80,600)
Sjodin et al. (2008)	• Household dust in vacuum cleaner bags from 10 homes in each country: 6 cities in Germany, 2 cities in Australia, and 1 city in the United Kingdom (total n=30) • BDE-209 dominant congener	Median (range): 63 (<6–410) (Germany); 730 (23–13,000) (Australia); 10,000 (910-54,000) (U.K.)

Note: Additional information obtained from U.S. EPA (2010a); Acronyms: dry wt = Dry weight; ND = Not detected

Table E-2. BDE-209 air concentrations in outdoor and indoor air.

Citation	Relevant study info	BDE-209 levels
United States		
Hoh and Hites (2005) as cited in U.S. EPA (2010a)	• Outdoor sampling at 5 locations; sampling every 12 days (August 2003–January 2004) • Chicago (urban), remote locations in Michigan and Louisiana, agricultural site in Arkansas, and small college town of Bloomington, Indiana • BDE-209 dominant congener at all sites	Means (pg/m^3) 60.1 (Chicago) 1.4 (Michigan) 2.6 (Louisiana) 9.0 (Arkansas) 2.2 (Indiana)
Hoh et al. (2005)	• Outdoor sampling at 5 locations; sampling every 12 days (September 2002–December 2003 or throughout 2003 [Chicago only]) • Chicago (urban), remote locations in Michigan and Louisiana, agricultural site in Arkansas, and small college town of Bloomington, Indiana	Values at different sampling dates (pg/m^3) 15, 16, 17, 65 (Chicago) 9.7, 12 (Louisiana) 20, 22 (Arkansas) 0.2, 7.3 (Indiana)
Strandberg et al. (2001)	• Outdoor sampling at 4 locations; 4 samples/year at each location, May–October (1997–1999) • 1 urban (Chicago), 1 remote (Michigan), 2 rural (Michigan, New York)	Means (pg/m^3) 0.3 (Chicago) ND (rural/remote sites)
Charles et al. (2005)	• Indoor and outdoor sampling at industrial and office sites, outdoors at UC Davis (2004) • Control – outdoors at UC Davis • Indoors at computer facility measured concentrations with computers on and off. Concentrations higher when computers turned on compared to when computers turned off.	Mean (range) (pg/m^3) 10.6 (4.44–17.8) (control) 58 (50.2–65.3) (indoors, computer facility) 140–11,400 (range for outdoors surrounding electronics recycling facility) 79,700–833,000 (range for indoors at electronics recycling facility) 45.5–1,940 (range for outdoors at auto shredder facility)
CADAMP [(Cal/EPA, 2006); as cited in U.S. EPA (2010a)	• 7 outdoor sampling sites in California: 4 Bay Area sites, 3 South Coast sites (2003–2004) • 6 monthly samples in 2003; 12 monthly samples in 2004	25 pg/m^3
Allen et al. (2007)	• Indoor air at 20 urban residences, Boston, MA area (January-March 2006) • Personal air (within 30 cm of breathing zone), bedroom, and main living area • Total personal air concentrations for BDE-209 was significantly higher than bedroom and main living room concentrations • Inhalation may account for up to 22% of the total BDE-209 exposure in U.S. adults.	Geometric means (pg/m^3) 173.6 (personal air) 94.8 (bedroom) 94.2 (living room)

Table E–2, cont.: BDE-209 concentrations in outdoor and indoor air.

Citation	Relevant study info	BDE-209 levels
United States		
Johnson-Restrepo and Kannan (2009)	• Indoor air in 12 homes, Albany, NY (December 2007–January 2008)	ND (ng/m^3)
Salamova and Hites (2011)	• Vapor, particle, and precipitation samples collected at 2 urban sites, 1 rural site, 2 remote sites) around the Great Lakes (2005–2009; part of the Integrated Atmospheric Deposition Network) • Statistical analysis indicated that levels of BDE-209 have not changed between 2005 and 2009	Means (pg/m^3) Vapor: 3.4, 1.8 (urban); 0.7 (rural); 0.5, 0.8 (remote) Particle: 13, 56 (urban); 1.9 (rural); 1.3, 2.5 (remote) Precipitation (ng/L): 2.1, 4.1 (urban); 0.6 (rural); 0.4, 0.5 (remote)
Batterman et al. (2010)	• Airborne particulate matter and vapor samples collected at 10 office buildings in southeast Michigan (Ann Arbor area)	Means and medians were all below the limit of detection
International		
Su et al. (2007)	• Air samples collected in the Canadian High Arctic (Alert, Nunavut); PBDEs quantified in 104 samples (2002–2004) • Lack of seasonality effects for BDE-209; BDE-209 likely particle-bound and experiences LRT	Mean (range) (pg/m^3) 1.6 (0.091–9.8)
Chang et al. (2009)	• Characterized airborne exposure of students to BDE-209 and other PBDEs inside and outside a computer classroom with 61 computers, southern Taiwan college • BDE-209 was one of the five highest indoor concentrations • Mean BDE-209 concentration outdoors significantly higher than the mean in indoor air	Means (pg/m^3) 23.0 (inside classroom) 53.3 (outside, open space in front of teacher building)
Agrell et al. (2004)	• Atmospheric concentrations (gaseous and particulate) of BDE-209 measured at solid waste incineration plant in Sweden • Particulate concentrations at MSW significantly higher	Medians (pg/m^3) 10.4 (MSW) 6.5 (reference site)
Gouin et al. (2006)	• Examined particle bound air transport of BDE-209, Southern Ontario, Canada (2002) • Nearly all BDE-209 sorbed to aerosol particles • LRT of BDE-209 might be controlled by transport characteristics of aerosols to which they sorb	Mean (range) (pg/m^3) 19 (ND–105)

Note: Additional information obtained from U.S. EPA (2010a)

LRT = Long range transport; MSW = Municipal solid waste; ND = Not detected

Table E-3. BDE-209 concentrations in aquatic systems.

Citation	Relevant study info	BDE-209 levels
United States		
Oros et al. (2005)	• San Francisco estuary (2002) • 48 sediment samples; 33 water samples	Range (pg/L) ND–191 (surface water) ND (sediment)
Hun Yun et al. (2008)	• Saginaw River Watershed, Michigan (2004) • 53 surficial sediment samples • BDE-209 was the predominant congener (79% and 90% of the total PBDE in the Shiawassee and Saginaw Rivers, respectively)	Means (ng/gram dry wt) 2.28 (Shiawassee River) 4.76 (Saginaw River) 1.98 (Saginaw Bay)
Song et al. (2005b; 2005a; 2004)	• Great Lakes • 16 total sediment sampling stations	Range (ng/gram): 4.3–242 (surficial sediment)
Raff and Hites (2004)	• Mississippi and tributaries • Suspended sediment samples from 31 sites (2002–2003) • BDE-209 was the dominant congener (96.8% of total concentration)	Range of 15 PBDEs (ng/gram dry wt): 29–1,548
Ashley et al. (2006)	• Delaware River • 4 sediment samples • BDE-209 was the dominant congener (49% of total concentration)	Range (ng/gram dry wt): 0.16–14.79
Dodder et al. (2002)	• Lake Hadley, Indiana • 4 surficial sediment samples • BDE-209 was the dominant congener	Range (ng/gram dry wt): 19–36
La Guardia et al. (2007)	• Downstream of WWTP of plastics manufacturer, North Carolina • 8 sediment sample locations downstream of outfall (2002 and 2005); 2 sludge samples, 1 for each year • BDE-209 was the dominant congener in sediment (>89% of total concentration)	Range 2002 SD: 300–3,150 ng/gram 2005 SD: 181–2,390 ng/gram
International		
Toms et al. (2006) as cited in U.S. EPA (2010a)	• Estuarine, freshwater, marine sediments, Australia • 90 sediment samples from remote and industrial areas (2002–2003 and 2005) • BDE-209 was the dominant congener in 86% of samples	Mean (range) (ng/gram dry wt) 4.7(ND–60.9) (all PBDEs)
Christensen and Platz (2001)	• Danish marine coastal areas, freshwater lakes, river (2000) • BDE-209 was the dominant congener in marine and freshwater sediments • Highest BDEs detected in urban sediments	Range (ng/gram dry wt) <0.9–3.9 (marine) <1.3–8.1 (freshwater)

Table E–3, cont.: BDE-209 concentrations in aquatic systems.

Citation	Relevant study info	BDE-209 levels
International		
Eljarrat et al. (2005)	• Coastal areas, Spain • 13 marine sediment samples • BDE-209 was the dominant congener (50–99% of total concentration)	Range (ng/gram dry wt) 2.46–132.10
Eljarrat et al. (2007)	• Spanish River Vero, samples collected up- and downstream from an industrial park (2004, 2005) • 6 sediment and 3 effluent samples • Maximum BDE-209 in sediment downstream of industrial park (that includes textile industry)	Maximum (ng/gram dry wt) 5,395 (2004) 12,459 (2005) (collected 5 meters downstream of textile industry effluent discharge)
Qiu et al. (2007)	• Lake Ontario • Sediment core study	Mean (ng/gram dry wt): 14 (surficial)
Zhu and Hites (2005)	• Lake Michigan and Lake Erie • Sediment core study • BDE-209 was the dominant congener in both sediment cores (95–99% of total concentration)	Surface concentrations (ng/gram) 315 (Lake Michigan) 39 (Lake Erie)
De Boer et al. (2003)	• Various locations, The Netherlands • Collected 44 SPM samples at 18 locations • Collected 22 sediment samples at 17 locations • SPM identified as an important carrier for BDE-209 in aquatic environment. Maximum of 4,600 mg/kg dry wt likely related to spills from textile industries; maximum of 510 mg/kg dry wt in sediment at same location of maximum SPM	Median (Range) (µg/kg dry wt) 71 (<9–4,600) (SPM) 22 (<4–510) (sediment)
Eljarrat et al. (2004) [also reported in Law et al. (2006b) review article]	• BDE-209 determined in 5 riverine and 8 marine sediments, Spain	Range (ng/kg dry wt) 2.06–39.89 (river) 2.95–132.11 (marine)
Sawal et al. (2004) [also reported in Law et al. (2006b) review article]	• BDE-209 determined in 29 surface sediment from River Elbe, Germany and Czech Republic • BDE-209 represented 80% of total BDEs	Range (µg/kg dry wt): 0.5–17.4
From Law et al. (2006b) review article	• BDE-209 determined in sediments from Lake Mjosa, Norway (Schlabach et al., 2004) • In some parts of the lake, BDE-209 represented 50–90% of total BDEs	Range total BDE (µg/kg dry wt): 0.6 – 27
Voorspoels et al. (2004) [also reported in Law et al. (2006b) review article]	• Analyzed sediments from Belgian North Sea, Western Scheldt Estuary • BDE209 was detected in 83% of samples from the Belgian North Sea and in 100% of samples from the Scheldt Estuary	Maximum (ng/kg dry wt): 1,200 (at estuary)

Table E–3, cont.: BDE-209 concentrations in aquatic systems.

Citation	Relevant study info	BDE-209 levels
International		
Ricklund et al. (2010)	• Measured levels of BDE-209 in 11 lake sediment samples and 7 marine sediment samples in Sweden • No known point sources of BDE-209 exist; presence in sediments was presumed to be evidence of long-range atmospheric transport and deposition	Range (ng/gram dry wt) 0.48–11 (lake) 1.0–88 (marine)
Mai et al. (2005)	• Examined 66 surface sediment samples from the Pearl River Delta and South China Sea, China • Sources of PBDEs in the area: waste discharges from urban centers; regional growth of electronic manufacturing • BDE-209 dominated congener compositions in sediments; PBDE composition analysis provided possible evidence of debromination of BDE-209	Range (ng/gram dry wt): 0.4–7,340
Chen et al. (2007b)	• Examined 3 sediment cores from the Pearl River Estuary, South China • Increased BDE-209 flux in the upper sediment cores attributed to rapid regional growth of electronics and other industry	Range (ng/gram):13.5–30.3
Guzzella et al. (2008)	• PBDEs measured in sediment cores (2005) from Lake Maggiore and tributary grab samples, Italy and Switzerland • BDE-209 was the dominate congener (>95% of total PBDEs) • Increase in BDE-209 attributed to textile industries	Range (ng/gram dry wt): 1.6–15.3
Zhao et al. (2011)	• Measured concentrations of PBDEs in sediments of the Daliao River Estuary, China • BDE209 was the dominating congener in all samples • Intrusion of sea waters accelerated deposition of the colloid-associated PBDEs; significantly negative correlations observed between PBDE concentration and both pH and salinity in bottom waters; higher river flow in the flood season (summer) accelerated transport of PBDEs to the ocean; TOC and PBDE distributions indicated that TOC controlled distributions of PBDEs in sediments of the estuary	Range of all PBDEs (ng/gram dry wt): 0.13–1.98 (BDE-209 levels stated to be about 1 order of magnitude higher)

Note: Additional information obtained from U.S. EPA (2010a)

dry wt = Dry weight; ND = Not detected; SPM = Suspended particulate matter; TOC = Total organic carbon; WWTP = Waste water treatment plant

Table E-4. BDE-209 concentrations in sewage effluent and sludge.

Citation	Relevant study info	BDE-209 levels	
		STP effluent	Sewage sludge
United States			
Hale et al. (2001)	• Mid-Atlantic biosolids • Northeast biosolids • Gulf biosolids • West biosolids	–	Ranges(µg/kg dry wt) 84.8–1,460 1,940–4,890 368 (single site) 340–450
Hale et al. (2003)	• Lake Superior watershed communities • Lake Michigan watershed communities	–	Mean (µg/gram dry wt) 510 466
North (2004)	• Samples analyzed for 41 BDE congeners in CA • STP discharges effluent into San Francisco estuary • In sludge, BDE-209 was 35% of total BDEs • Estimated that 96% of PBDEs that enter the STP adsorb to sludge; 4% in effluent	1,730 (pg/L)	Mean (µg/kg dry wt) 1,183
La Guardia (2007)	• Downstream of WWTP of plastics manufacturer, North Carolina • 2 sludge samples, one taken in 2002 and the other in 2005 • BDE-209 was the dominant congener in sludge		58,800 µg/kg dry wt (2002 measurement) 37,400 µg/gram dry wt (2005 measurement)
U.S. EPA (2009)	• National Sewage Sludge Survey • Evaluated 74 STPs in 35 states (2006-2007) • Nationally, BDE-209 was the dominant congener	–	Mean (µg/kg dry wt) 2,181
International			
De Boer et al. (2003)	• Various locations, The Netherlands • Collected 13 sewage treatment plant (STP) influent/effluent samples at 9 locations (measured filtering out particulate matter); 3 sludge samples	Median (range) (µg/kg dry wt) 24 (<0.5–330) (influent) 350 (310–920) (effluent)	<180, 190, 8.6 (µg/kg dry wt)
Knoth et al. (2007)	• Sewage sludge from 11 STPs in Germany (2002-2003) • BDE-209 was the dominant congener in sludges; no PBDEs with fewer than 7 bromines observed • Estimated 350 kg/acre BDE-209 applied to land in Germany in 2001	–	Mean (ng/ g dry wt) 429

Table E–4, cont.: BDE-209 concentrations in sewage effluent and sludge.

Citation	Relevant study info	BDE-209 levels	
		STP effluent	Sewage sludge
International			
Wang et al. (2007)	• Sewage sludge from 31 STPs in 26 cities in China • BDE-209 was dominant congener in most samples	–	Mean (ng/gram dry wt) 68.5
Clarke et al. (2008)	• Australian sewage sludge survey; 16 WWTPs (2006) • Presented urban mean, rural mean, and overall mean of BDE-209 in sludge samples	–	Mean (µg/kg dry wt) 880 (urban); 490 (rural) 720 (overall)
Kupper et al. (2008)	• Switzerland, monitoring network • 16 WWTPs	–	Mean (µg/kg dry wt) 310
Eljarrat et al. (2007)	• Spanish River Vero, samples collected up- and downstream from an industrial park (2004, 2005) • 6 sediment and 3 effluent samples	1,170 ng/L (2005 effluent maximum)	–
Ricklund et al. (2009)	• Stockholm, Sweden • WWTP (2006, 2007)	–	800 Mean (ng/gram dry wt)

Note: Additional information obtained from U.S. EPA (2010a)
dry wt = Dry weight; STP = sewage treatment plant; WWTP = Waste water treatment plant

Table E-5. BDE-209 concentration data in soil.

Citation	Relevant study info	BDE-209 levels
United States		
Offenberg et al. (2006) as cited in U.S. EPA (2010a)	• 33 surface soil samples, 15 states • BDE-209 detected in 24/33 samples	Mean (ng/gram dry wt): 15.3
Yun et al. (2008)	• Saginaw River Watershed, Michigan • 26 floodplain surface soil samples (2004)	Mean (ng/gram dry wt) 10.8 (Shiawassee River) 2.77 (Saginaw River) 0.6 (Saginaw Bay)

Table E–5, cont.: BDE-209 concentration data in soil.

Citation	Relevant study info	BDE-209 levels
International		
Sellström et al. (2005)	• 5 sites in Sweden • Evaluated sewage sludge amended soils and earthworms	Range (ng/gram dry wt) 0.028–2,220
Luo et al. (2009)	• Southern China • Analyzed road and farmland soils from e-waste recycling region • BDE-209 contributions averaged 84% in samples from the e-waste region higher than 97% in samples from the industrial and reference sites	Mean (range) (ng/gram dry wt) 19.7 (rural farmland soil) 59.8 (farmland soil near industrial) E-waste region 1,539.3 (69.1–6,319.6) (road soil) 32.2 (farmland soil near dismantling workshop) 29.9 (farmland soil near open burning site)
Zou et al. (2007)	• Pearl River, China • 33 surface soil samples; 3 point source samples	Mean (range) (ng/gram dry wt) 13.8 (2.38–66.6) (SS) 70.5 (25.7–102)(PS contaminated)

Note: Additional information obtained from U.S. EPA (2010a)
dry wt = Dry weight; SS = Surface soil; PS = Point source

Table E-6. Proxy data for estimating MWCNT concentrations in occupational air.

Citation	Relevant study info	Proxy data and CNT counts
United States		
Bello et al. (2008)	• Personal breathing zone and area air sampling and real-time monitoring in a CNT research laboratory synthesizing and handling CNTs • Fast mobility particle sizer measured number concentration for particles sized 5.6–560 nm. Personal breathing zone and area air samples near the emission source were collected and analyzed for respirable dust and respirable fiber concentrations, and electron microscopy characterized particles and fibers on filters.	No increase in total particle number concentration or in particle number in any size range compared to background No individual or bundled CNTs detected
Bello et al. (2009)	• Personal breathing zone and area air sampling and real-time monitoring during machining of carbon, alumina, CNT-carbon, and CNT-alumina composites at a research laboratory • Fast mobility particle sizer and aerodynamic particle sizer measured number concentrations of particles sized 5.6–560 nm and 0.5–20 μm, respectively, and condensation particle counter counted all particles 10 nm–1 μm. Total dust mass was measured in real time using TSI Dust Trak®. Personal breathing zone and area air samples near the emission source were collected and analyzed for respirable dust and respirable fiber concentrations, and electron microscopy characterized particles and fibers on filters • No engineering controls were employed • Dry cutting of all composites produced significant numbers of nanoscale particles, and particle sizes were similar for all composites. • The thinnest CNT-alumina composite released fewer nanoscale particle than the other composites during dry cutting • No discernible difference between the number of respirable particles and fibers produced during dry cutting of CNT-composites versus base composites	No individual CNT structures or bundles were observed in the samples No CNT structures or bundles were observed in the composite particle dust

Table E–6, cont.: Proxy data for estimating MWCNT concentrations in occupational air.

Citation	Relevant study info	Proxy data and CNT counts
United States		
Dahm et al. (2011)	• Task based area air, full-shift personal breathing zone (PBZ), and outdoor background sampling at 6 CNT/CNF primary and secondary manufacturing facilities • PBZ samples collected for inhalable fraction and area air samples collected for inhalable and respirable fractions of elemental carbon mass. Electron microscopy characterized CNT structures (both single CNTs and bundles) on filters • PBZ samples collected during dry powder handling tasks at two secondary MWCNT facilities exceeded the National Institute of Occupational Safety and Health recommended exposure limit (7 μg/m^3 elemental carbon) in the presence of controls • CNT/CNF structure were identified on filters at all sites and correlation between filter mass and CNT structure count was statistically significant (p = 0.01) after exclusion of single outlier value	Elemental carbon mass (μg/m^3) and CNT structure count at primary MWCNT facilities Outdoor background: not detected MWCNT production and harvesting: 1.6–2.74 (PBZ),0.49–4.62 (area: inhalable), not detected to 0.78 (area: respirable), 0.090–0.399 CNTs/cm^3 (PBZ), 0.026–0.134 CNTs/cm^3 (area: inhalable) MWCNT sonication, sieving, and spray coating: 1.13 (PBZ), not detected (area: inhalable), not detected to 0.7 (area: respirable),0.010 CNTs/cm^3 (PBZ),0.002 CNTs/cm^3 (area: inhalable) Elemental carbon mass (μg/m^3) and CNT structure count at secondary MWCNT facilities Outdoor background: not detected Office work and waste collection: 0.8–1.06 (PBZ),0.001–0.214 CNTs/cm^3 (PBZ) Weighing, mixing, sonication, extruding, transferring MWCNTs: not detected to 7.86 (PBZ),not detected to 1.01 (area: inhalable), not detected to 2.76 (area: respirable), not detected to 0.242 CNTs/cm^3 (PBZ), not detected to 0.008 CNTs/cm^3 (area: inhalable) Milling MWCNT composite: not detected

Table E–6, cont.: Proxy data for estimating MWCNT concentrations in occupational air.

Citation	Relevant study info	Proxy data and CNT counts
United States		
Johnson et al. (2010)	• Area air sampling and real-time monitoring of MWCNT and hydroxylated MWCNT (MWCNT-OH) emissions during weighing, transferring, and sonicating with water and natural organic matter • HHPC-6 particle counter measured particle number per liter air for 6 size cuts: 300, 500, 1,000, 3,000, 5,000, and 10,000 nm. Condensation particle counter measured total particle numbers10–1,000 nm. Electron microscopy characterized MWCNT structures on filters. • Area air sample collected prior to tasks was used as background concentration and subtracted from samples taken during performance of tasks	Adjusted number concentration (particles/L) Raw MWCNT weighing, transferring, and mixing without ventilation: 123,403 (300 nm: above limit of quantitation), 34,446 (500 nm), 4,338 (1,000 nm), 50 (3,000 nm), 0 (5,000 and 10,000 nm). MWCNT-OH weighing, transferring, and mixing without ventilation: 0 (300 and 10,000 nm), 3,065 (500 nm), 1,699 (1,000 nm), 280 (3,000 nm), 4 (5,000 nm). Raw MWCNT sonication: 42,796 (300 nm), 23,777 (500 nm), 2,184 (1,000 nm), 86 (3,000 nm), 0 (5,000 and 10,000 nm). MWCNT-OH sonication: 144,623 (300 nm: above limit of quantitation), 65,402 (500 nm), 6,205 (1,000 nm), 0 (3,000, 5,000, and 10,000 nm). Total adjusted number concentration 10–1,000 nm (particles/cm^3) Raw MWCNT weighing, transferring, and mixing without ventilation: 1,576 MWCNT-OH weighing, transferring, and mixing without ventilation: 676 Raw MWCNT sonication: 2,776 MWCNT-OH sonication: 726

Table E–6, cont.: Proxy data for estimating MWCNT concentrations in occupational air.

Citation	Relevant study info	Proxy data and CNT counts
United States		
Methner et al. (2010)	• Area air sampling and real-time monitoring of 2 MWCNT research and development laboratories during specific handling tasks • Condensation particle counters (CPC) counted particles sized 10–1,000 nm and optical particle counters (OPC) counted particle sized 300–500 nm and 500–1,000 nm. Electron microscopy characterized MWCNT structures on filters and energy-dispersive X-ray analysis confirmed chemical identity. • MWCNT structures on microscopy grids were not quantified, but were detected in samples taken during weighing and sonication of both raw and functionalized MWCNTs. No MWCNT structures were observed on filters sampling background. Filters were not analyzed by electron microscopy for samples taken during opening of the growth chamber. • Measured particle number concentrations are background adjusted	CPC particle number concentrations (particles/cm^3); 10–1,000 nm fraction Opening MWCNT growth chamber: 300 (with exhaust), 42,400 (without exhaust) Handling raw MWCNTs: 1,480–1,580 (weighing); 2,200–2,800 (sonicating) Handling functionalized MWCNTs: 680 (weighing); 730 (sonicating) OPC particle number concentrations (particles/L): 300–500 nm fraction; 500–1,000 nm fraction Opening MWCNT growth chamber: 0; 0 (with exhaust), 350; 400 (without exhaust) Handling raw MWCNTs: 53,1,000–123,400 (above limit of quantitation); 3,900–34,400 (weighing); 23,900–42,800; 6,500–23,800 (sonicating) Handling functionalized MWCNTs: 0; 3,100 (weighing); 144,600 (above limit of quantitation); 65,400 (sonicating)
International		
Han et al. (2008a)	• Personal and area air sampling and real-time aerosol monitoring conducted at MWCNT research facility • Scanning mobility particle sizer with ultrafine condensation particle counter and aerodynamic particle sizer monitored particle size distribution 14–630 nm and 0.5–20 μm, respectively, and aethalometer characterized mass exposure to carbon black. Electron microscopy characterized MWCNT structures on filters and energy-dispersive X-ray analysis confirmed chemical identity. • Exposure controls included installation of a fan, cleaning, and equipment rearrangement (i.e., isolation) • No values exceeded ACGIH TLVs or Korean Ministry of Labor OELs for carbon black or particles not otherwise specified, but fiber counts exceeded limits for asbestos and other fiber or tube-like materials	Total dust concentration (μg/m^3) No control measures: 210–430 With control measures: not detected MWCNT counts (MWCNTs/cm^3) No control measures: 172.9–193.6 With control measures: 0.018–0.05

Table E–6, cont.: Proxy data for estimating MWCNT concentrations in occupational air.

Citation	Relevant study info	Proxy data and CNT counts
International		
Lee et al. (2010)	• Personal air sampling, area sampling, and real-time aerosol monitoring conducted at 7 MWCNT handling facilities (3 manufacturing plants, 4 research laboratories) • Scanning mobility particle sizer, dust monitor, and aethalometer characterized particle number, size distribution, and mass exposures. Electron microscopy characterized MWCNT structures on filters. • No values exceeded American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLVs) or Korean Ministry of Labor occupational exposure levels (OELs) for carbon black, particles not otherwise specified, or asbestos. • Nanoscale particles most often released during opening of chemical vapor deposition (CVD) reactor and catalyst preparation. • Nanoscale particles assumed to be primarily metal catalysts, not MWCNTs	One filter sample detected MWCNTs at 0.00312 tubes/cm^3; all others were non-detects Total suspended particulate matter Personal air: 7.8 – 320 μg/m^3 Area air: 12.6–187 μg/m^3 Particle number count for mode particle sizes (particles/ cm^3) – by task Catalyst preparation (mode diameter 20–30nm): 18,600–75,000 CVD opening (mode diameter 20 or 50 nm): 6,974–16,857 Other operations (no mode diameters reported): 5,276–6,399
Takaya et al.(2010) (English translation available only for abstract)	• Real-time aerosol monitoring and personal air sampling in two MWCNT packing facilities (automated packing versus manual packing) • Nanoscale and submicron-/micron-scale particles measured using scanning mobility particle sizer and optical particle counter, respectively • Submicron scale particles (not nanoparticles) released during bagging	Airborne dust (both facilities): 240 μg/m^3 Personal air at manual facility: 2,390 μg/m^3 (total dust); 390 μg/m^3 (respirable dust) Personal air at automated facility: 290 μg/m^3 (total dust); 80 μg/m^3 (respirable dust)

E.2. Concentrations in Biota

The following tables provide details from studies that measured BDE-209 in different types of biota. No data were identified on MWCNT concentrations in biota.

Table E-7. Measured concentrations of PBDEs in biota.

Species	Location	Year	Tissue	PBDE burden (ng/gram)[1]	Common congener(s)	Source
Terrestrial birds						
Peregrine falcon	Chesapeake Bay	1993-2002	Eggs	Median: 201[2]	BDE-153: 26%	Potter et al. (2009)
	CT, MA, ME, NH, VT	1996, 1999–2006		Median: 440[2]	BDE-153, BDE-99	Chen et al. (2008)
Common blackbird	Switzerland	2003-2005	Brain	BDL	NA	Naert et al. (2007) as cited in U.S. EPA (2010a)
			Adipose	BDL	NA	
			TB	0.82	BDE-47: 100%	
Sparrow hawk	Switzerland	2003-2005	Brain	14	NR	Naert et al. (2007) as cited in U.S. EPA (2010a)
			Adipose	709	NR	
			TB	790.2	BDE-99: 40%	
	Belgium	NR	Liver	Mean: 4,900 Median: 1,300	Top 3: BDE-99, BDE-47, BDE-153	Voorspoels et al. (2006b)
			Brain	Mean: 1,200 Median: 360	NR	Voorspoels et al. (2006b)
			Adipose	Mean: 1,900	NR	Voorspoels et al. (2006b)
	NR	NR	Liver	Mean: 9,500	Top 4: BDE-99, BDE-47, BDE-100, BDE-153	Voorspoels et al. (2007) as cited in U.S. EPA (2010a)
Common buzzard	Switzerland	2003-2005	TB	34.55	BDE-153: 29% BDE-99: 23% BDE-47: 22%	Naert et al. (2007) as cited in U.S. EPA (2010a)
	Belgium	NR	Liver	Mean: 480 Median: 70	Top 3: BDE-153, BDE-47, BDE-99	Voorspoels et al. (2006b)
	Beijing, China	NR	Liver	148	BDE-209: ~43%	Chen et al. (2007a)

Table E–7, cont.: Measured concentrations of PBDEs in biota.

Species	Location	Year	Tissue	PBDE burden (ng/gram)[1]	Common congener(s)	Source
Terrestrial birds						
Common buzzard	NR	NR	Liver	Mean: 720	NR	Voorspoels et al. (2007) as cited in U.S. EPA (2010a)
Cormorant	Switzerland	2003-2005	TB	98.76	BDE-47: 42%	Naert et al. (2007) as cited in U.S. EPA (2010a)
Owls	Belgium	NR	NR	250	Top 3: BDE-153, BDE-99, BDE-47	Voorspoels et al. (2006b)
Common kestrel	Beijing, China	NR	Muscle	Mean: 12,300	NR	Chen et al. (2007a)
			Liver	Mean: 12,200	NR	
			Kidney	Mean: 5,340	NR	
Passerines	NR	NR	Adipose	160	NR	Voorspoels et al. (2007) as cited in U.S. EPA (2010a)
			Eggs	220	NR	
Marine birds						
Herring gull	Great Lakes	1981-2000	Eggs	9.4-1,544	NR	Norstrom et al. (2002)
Fulmar	Northern Canada	1975-1998	Eggs	0.212-2.37	NR	Wakeford et al. (2002) as cited in U.S. EPA (2010a)
Murre	Northern Canada	1975-1998	Eggs	0.442-2.93	NR	Wakeford et al. (2002) as cited in U.S. EPA (2010a)
Heron	British Columbia	1983-2000	Eggs	1,308-288	NR	Wakeford et al. (2002) as cited in U.S. EPA (2010a)
Mammals						
Red fox	Belgium	NR	Adipose, liver, muscle	Median range: 2.2-3.4	Liver- BDE-209: 70%	Voorspoels et al. (2006a)
Ringed seals, female	Canadian Arctic	NR	Blubber	Mean: 25.8	Tetra, pentaBDE	Alaee et al. (1999)
Ringed seals, male	Canadian Arctic	NR	Blubber	Mean: 50.0	Tetra, pentaBDE	Alaee et al. (1999)
	Arctic	1981		0.6	Tetra, pentaBDE	Ikonomou et al. (2002)
	Arctic	2000		6.0	Tetra, pentaBDE	Ikonomou et al. (2002)

Table E–7, cont.: Measured concentrations of PBDEs in biota.

Species	Location	Year	Tissue	PBDE burden (ng/gram)[1]	Common congener(s)	Source
Mammals						
Beluga whales, female	Canadian Arctic	NR	Blubber	Mean: 81.2	Tetra, pentaBDE	Alaee et al. (1999)
	St. Lawrence estuary	NR		665	NR	Lebeuf et al. (2001) as cited in U.S. EPA (2010a)
Beluga whales, male	Canadian Arctic	NR	Blubber	Mean: 160	Tetra, pentaBDE	Alaee et al. (1999)
	St. Lawrence estuary	NR		466	NR	Lebeuf et al. (2001) as cited in U.S. EPA (2010a)
	Baffin Island	1982	Blubber	2	Tri to hexaBDE	Stern and Ikonomou (2000)
		1997		15	Tri to hexaBDE	
Harbor seals	San Francisco Bay	1989-1998	Blubber	Range: 88-8,325	Tetra, penta, hexaBDE	She et al. (2002)
Harbor porpoise	Vancouver	NR	Blubber	2,269	TetraBDE: >50%	Ikonomou et al. (2000)
Fish						
Lake trout	Lake Ontario	1997	NR	434	NR	Luross et al. (2002)
	Lake Erie			117		
	Lake Superior			392		
	Lake Huron			251		
Rainbow trout	Spokane River, WA	1999	NR	297[4]	NR	Johnson and Olson (2001)
Mountain whitefish	Spokane River, WA	1999	NR	1,250[4]	NR	Johnson and Olson (2001)
	Columbia River, British Columbia	1992-2000	Muscle	Mean range 4.5-19.1	NR	Rayne et al. (2003)
Largescale sucker	Spokane River, WA	1999	NR	105[4]	NR	Johnson and Olson (2001)
Carp	Virginia	1998-1999	NR	1,140[4]	NR	Johnson and Olson (2001)

Table E–7, cont.: Measured concentrations of PBDEs in biota.

Species	Location	Year	Tissue	PBDE burden (ng/gram)[1]	Common congener(s)	Source
Lower trophic levels						
Caddisflies	Pyrenees Mountains, Spain	NR	Larva TB	Mean range: 0.65-13.00[3]	NR	Bartrons et al. (2007)
			Pupa TB	Mean range 9.32- 27[3]		
Midges	Pyrenees Mountains, Spain	NR	Larva TB	Mean range: 0-13.07	NR	Bartrons et al. (2007)
			Pupa TB	Mean range 3.9-5.2[3]		

[1] ng/gram lipid weight, unless otherwise specified.
[2] Units = ng/gram wet weight
[3] Units = ng/gram dry weight
[4] Measurement for a single fish only
BDE-47: tetraBDE; BDE-99: pentaBDE; BDE-153: hexaBDE; BDE-209: decaBDE; BDL = Below detection level; TB = Total body; NR = Not reported; NA = Not applicable

Table E-8. Mean concentration of PBDEs in media/biota in an aquatic ecosystem.

Media	Total PBDEs	BDE-47	BDE-99	BDE-100	BDE-153	BDE-209
Water (pg/L)	47.01	16.98	9.01	1.89	1.02	<MDL
Sediment (ng/gram dry wt)	1.31	0.12	0.15	0.03	0.06	0.63
Biota level 1 (mg/gram lipid wt)						
Mussels	127.32	21.11	26.41	5.7	8.13	50.84
Biota level 2 (mg/gram lipid wt)						
Zooplankton	61.57	11.71	17.79	4.89	5.81	1.21
White fish	11.1	1.82	1.48	0.6	0.43	3.61
Biota level 3 (mg/gram lipid wt)						
Emerald shiner	151.07	60.78	2.15	10.65	7.25	40.33
Goldeye	381.26	83.84	116.15	24	31.98	41.64
White sucker	150.03	71.4	1.22	16.49	12.55	12.03

Table E–8, cont.: Mean concentration of PBDEs in media/biota in an aquatic ecosystem.

Media	Total PBDEs	BDE-47	BDE-99	BDE-100	BDE-153	BDE-209
Biota level 4 (mg/gram lipid wt)						
Walleye	54.39	16.21	2.56	2.34	1.98	24.72
Burbot	240.32	44.37	20.48	10.49	12.12	98.68

<MDL = Concentration less than minimal detection limit, approximately half
Source: Law et al. (2006a)

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Appendix F. Toxicological and Ecological Effects

Appendix F. Toxicological and Ecological Effects

Appendix F comprises tables summarizing the material characteristics, study design, and results of select toxicokinetic and toxicological studies for BDE-209 and MWCNTs. Much of the relevant toxicological data for BDE-209 has been summarized in reviews, and many of the toxicological endpoints of concern have been identified and used by regulatory agencies to establish reference values for the protection of human health and the environment (see Chapter 5). Because the BDE-209 studies have been described in detail in many previous reviews, a relatively small subset of the BDE-209 studies discussed in Chapter 5 of this document are summarized in the tables of this appendix. Select BDE-209 study summary tables are generally provided only for general comparison to MWCNT study summary tables or for the primary exposure route of concern (oral).

By comparison, the toxicokinetics and toxicological effects of MWCNTs are not well understood and only one draft reference value has been established for the protection of human health (see Chapter 5). Moreover, as emphasized throughout this document, variations in certain physicochemical characteristics of MWCNTs are likely to affect their behavior in biological systems and impacts to humans and biota. Appendix F therefore provides summary tables for most of the MWCNT toxicokinetic and toxicological studies referenced in Chapter 5 of this case study. These tables supply more detailed information on material characteristics, study design, and observed effects than was presented in the text.

Appendix F provides information on the absorption, distribution, metabolism, and elimination of BDE-209 and MWCNTs from identified toxicokinetic studies (Section F.1.1). In addition, summary tables present information from select in vivo studies reporting effects other than carcinogenicity using the dermal, ocular, inhalation, and oral routes of exposure (Section F.1.2); in vitro studies including those investigating genotoxicity and mutagenicity (Section F.1.3); and carcinogenicity studies (Section F.1.4) for BDE-209 and MWCNTs.

Appendix F also provides summary tables of data from studies that investigated effects of BDE-209, other PBDEs, and MWCNTs on different types of biota. Data from studies in aquatic ecosystems are summarized in Sections F.2.1 and F.2.2; data from terrestrial ecosystems are summarized in Sections F.2.3 and F.2.4.

Literature was identified primarily using review articles published in the past two years. Targeted literature searches were carried out as needed.

F.1. Toxicological Effects

F.1.1. Toxicokinetic Studies

Table F-1. Select toxicokinetic studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Oral (diet)	Unlabeled decaBDE (92% pure) and [U-^{14}C] decaBDE (98.9% pure)	Fischer 344 rat (male)	12 days (sacrificed 24, 48, 72 hours after exposure to [U-^{14}C] on day 8)	0.0277%, 4.80% diet	Excretion results: urine 0.004–0.012%, feces 82.5–86.4% (recovery not related to dose); tissue recovery: 0.109% in liver, 0.248% in muscle, 0.136% in skin (other smaller quantities reported); for all tissues the maximum percent (%) in organs and tissues was reported in the low-dose group; for both doses percent (%) of dose remaining in the gut contents and gut tissues decreased with time after exposure	el Dareer et al. (1987)
i.v.	[U-^{14}C] decaBDE (98.9% pure)	Fischer 344 rat (male)	72 hours	1.07 mg/kg	Excretion results: urine 0.129%, feces 70.0%; tissue recovery: 4.27% in liver, 5.063% in GI, 12.9% in muscle, 7.25% in skin, 2.99% in fat (other smaller quantities reported)	el Dareer et al. (1987)
Oral (diet)	Unlabeled decaBDE (92% pure) and [U-^{14}C] decaBDE (98.9% pure)	Fischer 344 rat (male)	12 days (sacrificed 72 hours after exposure to [U-^{14}C] on day 8)	0.025, 0.0509, 0.250, 0.487, 2.49, 4.99 % diet	Recovery of radiolabeled decaBDE in feces ranged from 91.3–101% of the amount ingested; recovery was not related to dose; liver weights of rats increased as dose increased	el Dareer et al. (1987)

Table F–1, cont.: Select toxicokinetic studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Oral (diet)	[U-^{14}C] decaBDE (97.9–99.2% pure) diluted with unlabeled decaBDE	Rat	>8 days (7 days unlabeled, 1 day labeled, then returned to unlabeled diet for remainder of holding period)	250–50,000 ppm	Excretion results: feces 61%, urine 0.1%	NTP (1986)
Oral (diet)	[U-^{14}C] decaBDE (97.9–99.2% pure) diluted with unlabeled decaBDE	Rat	>8 days (7 days unlabeled, 1 day labeled, then returned to unlabeled diet for remainder of holding period)	250–50,000 ppm	Excretion results: urine 0.01%, feces >99% in 72 hours	NTP (1986)
Oral	[U-^{14}C] decaBDE (assumed to be77.4% pure based on reference description)	Sprague-Dawley rat (male and female)	16 days	1 mg/kg	Excretion results: urine <1.0%, feces 90.6% (day 1), >8.4% (day 2), >99% (at 48 hours); tissue recovery: limited absorption to GI at 1, 3, and 16 days; 0.06% in spleen, 0.01% in adrenals (no others reported) at 16 days	Norris et al. (1975)
Oral (diet)	>99.8% pure	Pregnant Wistar rat (female)	96 hours (gestation days 16–19)	2.61 mg/kg-day	>19% recovered in tissues; efficient absorption reported; highest residue concentrations in endocrine glands and the liver; most of recovered product was unchanged decaBDE with 9–27% biotransformation products (nona- and octaBDEs) in tissues and 14% in fetuses; main metabolic pathways are debromination and oxidation	Riu et al. (2008)

Table F–1, cont.: Select toxicokinetic studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Oral	77.4% decaBDE, 21.8% nonaBDE, and 0.8% octaBDE	Rat	NR	NR	Slight accumulation occurring very slowly over time in adipose tissue	Great Lakes (1976) and IRDC (1976, 1977) as cited in NRC (2000)
Oral (diet)	77.4% pure	Rat	2 years	0; 0.01; 0.1; 1 mg/kg-day	No increase in the kidney, muscle, or serum	Dow (1994) as cited in NRC (2000)
Oral (gavage)	>98% pure, specific activity 17.5 Ci/mol	Sprague-Dawley rat (male)	3, 7 days	3 µmol/kg, 15 Ci/mol, 1 mL/kg volume	>10% absorbed; 90% excreted in feces (65% metabolites); 10% excretion in bile (mostly metabolites)	Mork et al. (2003)
Oral (diet)	98.5% pure	Sprague-Dawley rat (male)	21 days followed by 21-day withdrawal period	0.3 µg/gram of diet	After 21 days 5% of decaBDE was measured as BDE-209 (<4% in feces); nona- and octaBDEs were also present; BDE-209 was highest in the liver, followed by the GI track; several lower congeners were present at higher concentrations than could be attributed directly to dose impurities as the result of debromination	Huwe and Smith (2007)
Oral (diet)	NR	Lactating cow (female)	3 months	Naturally contaminated diet (not measured)	BDE-209 was dominant congener in all tissue samples except milk (milk concentrations were generally low); dominant output route was feces; congener profiles in adipose tissue and feed differed; BDE-207, BDE-196, BDE-197, and BDE-182 accumulated to a greater extent in the fat compared to their isomers suggesting metabolic debromination of BDE-209; indicates that meat may be a more important human exposure route to higher brominated BDEs than dairy products	Kierkegaard et al. (2007)
Oral	NR	Sprague-Dawley rat (male)	90 days	100 mg/kg bw-day	Preferential accumulation of BDE-209 in the liver; BDE-209 induced hepatotoxicity (indicated by serum clinical chemistry data for AST, ALP, T-CHO, HDL-C, Cr, and TBA); significantly increased CYP2B1 expression in mRNA; metabolites of BDE-183, 196, 197, 202, 203, 206, 207, and 208 were all found in kidney and liver tissues (207 most prominent)	Wang et al. (2010a)

Table F–1, cont.: Select toxicokinetic studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
In vitro (incubation)	98 ± 1% pure	Human hepatocytes; 2 cryopreserved (1 male, 1 female), 1 fresh (male)	48-hour exposure for cryopreserved cell cultures; 1 dose per 24 hours for three days for fresh hepatocyte cultures	10 nmol/well	No hydroxylated or debrominated metabolites observed; Up-regulation of genes encoding for cytochrome P450 monooxygenase (CYP) 1A2, CYP3A4, deiodinase type 1, and glutathione S-transferase M1	Stapleton et al. (2009)
Oral	98% pure	Sprague-Dawley rat (female)	GD7 to PND4	5 µmol/kg	Increased accumulation with time in maternal blood, placenta, fetuses, and neonates; more BDE-209 found in neonate whole-body samples obtained during lactation than fetal whole-body samples during pregnancy; increased nonaBDE in maternal blood and placenta over time; slight changes observed for octaBDEs in maternal blood and placenta; significant decrease observed in the fetuses or neonates for BDE-196 and 198/203	Cai et al. (2011)
Gavage or i.v.	Unlabeled BDE-209 (>98% pure)	Sprague-Dawley rat (male)	1, 3, 6, 24, 48, 72, 96, 120, or 144 hours	2 µmol/mL	Bioavailability calculated to be >26%; 13 metabolites were identified in the plasma (octa- nona-, and hexaBDEs) at concentrations 4 times higher than the parent compound on days 3 and 7; BDE-209 was rapidly distributed to well perfused tissues (e.g., liver)	Sandholm et al. (2003)
Liver microsomal depletion	BDE-209	Harbor seal (*Phoca vitulina*) and sperm whale (*Physeter catodon*)	NR	31 µg/mL	No detectable depletion of parent BDE-209; lack of microsomal depletion consistent with persistent and accumulative nature of BDE-209	de Boer et al. (1998, 2000) as cited in Hakk and Letcher (2003)

Table F–1, cont.: Select toxicokinetic studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Oral	DecaBDE (BDE-209)	Sprague-Dawley rat (male)	72 hours	3 mg/kg	Excretion results: urine <0.05%, feces: >90%, bile: 9.5%; tissue recovery: 0.9 in liver, 3.5 in GI, 0.7 in muscle (other smaller quantities reported); rats metabolized BDE-209 to fecal metabolites (including debrominated mono-OH- and ortho-MeO-OH-BDEs) via oxidative debromination	Morck and Klasson-Wehler (2001) as cited in Hakk and Letcher (2003)
Oral (diet)	BDE-209 with detectable amounts of nona- and octaBDEs	Rainbow trout (*Oncorhynchus mykiss*) (male and female)	16, 49, 120 days	1.7–10 mg/kg-day	Low uptake efficiency; elevated levels in liver and muscle (20–40 times greater in liver, 560 ± 210 ng/gram fresh wt to 870 ± 220 ng/gram fresh wt from day 16 to day 120 for liver and 10 ± 3.2 ng/gram fresh wt to 38 ± 14 ng/gram fresh wt from day 16 to day 120 for muscle), decreased upon depuration; metabolites detected in liver and muscle tissues, not all metabolites decreased with depuration	Kierkegaard et al. (1999)

GI = Gastrointestinal tract; NR = Not reported

Table F-2. Select toxicokinetic studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Absorption									
Intratracheal instillation; i.v.; and gavage	10–20	0.01–0.6	NR	>95%	Kunming mouse (male)	Single exposure; 28-day observation	10 μg	20% of administered dose remained within the lung at 28 days (intratracheal instillation); 80% accumulate in the liver and remain at 28 days (i.v.); only levels measured in stomach, large and small intestines, 74% directly excreted (gavage)	Deng et al. (2007)
Inhalation (intratracheal instillation)	20–50	0.5–2	NR	(% w/w): 0.53 Ni, 0.08 S, <0.02 Mg, <0.01 Na, <0.01 V	Sprague-Dawley rat (male)	Single exposure; 1-, 7-, 30-, 90-, and 180-day observations and 6-month MWCNT elimination observation	1, 10, 100 μg/rat	MWCNTs did not significantly cross the pulmonary barrier; MWCNTs were evident within the lungs at 6 months	Elgrabli et al. (2008b)
Inhalation (aspiration)	Mean: 49 ± 13.4	Median: 3.86	NR	0.78%; 0.41% sodium, 0.32% iron	C57BL/6 mouse (male)	Single exposure; 1-, 7-, 28- and 56-day observations	10, 20, 40, 80 μg	MWCNTs reached the pleura and induced pleural inflammation at 56 days	Porter et al. (2010)
Oral (gavage)	10–20	0.01–0.6	NR	>95%	Kunming mouse (male)	Single exposure; 12-hour observation	10 μg	Majority of MWCNTs evident in feces, stomach, and small and large intestines; no detectable transport into the blood; MWCNTs remained unchanged suggesting biopersistence if not excreted	Deng et al. (2007)

Table F–2, cont.: Select toxicokinetic studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Distribution									
Inhalation	10–50	<0.1–10	NR	NR	C57BL6 mouse (male)	Single 6-hour exposure; 14-week observation	1, 30 mg/m^3	MWCNTs reached the subpleura; nanotubes were embedded in subpleural wall and within subpleural macrophages	Ryman-Rasmussen et al. (2009a)
Inhalation (intratracheal instillation)	NR	0.9–0.15	197	NR	Wistar albino rat (male)	Single exposure; 24 hour, 1 week, 1- and 3-month observations	0.2, 1, 5 mg/kg	MWCNTs translocated from the lung to liver and kidney (not to the heart) at 1 month	Reddy et al. (2010)
Elimination									
Inhalation (intratracheal instillation)	20–50	0.5–2	NR	(% w/w): 0.53 Ni, 0.08 S, <0.02 Mg, <0.01 Na, <0.01 V	Sprague-Dawley rat (male)	Single exposure; 1-, 7-, 30-, 90-, and 180-day observations and 6-month MWCNT elimination observation	1, 10, 100 μg/rat	Following phagocytosis of the MWCNTs, the macrophages underwent apoptosis, with no inflammatory response or other physiological and histological pathology	Elgrabli et al. (2008a)

NR = Not reported

F.1.2. In Vivo Studies (Excluding Carcinogenicity Studies)

Table F-3. Select dermal and ocular studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Irritation						
Dermal	Dry solid	New Zealand albino rabbit	24 hours, 3 days, 2 weeks	500 mg, reported by NRC (2000)	No dermal response in intact skin; no indication of bromacne	Norris et al. (1975) [also reported in NTP (1986); Norris et al. (1973); Dow (1972) and IRDC (1974) as cited in NRC (2000)]
Dermal	NR	Rabbit	Single administration 24 hours; 14 days observation	200, 2000 mg/kg	Slight erythematous and edematous response in abraded skin	IRDC (1974) and Great Lakes (1977) as cited in NRC (2000); Norris et al. (1975)
Sensitization						
Dermal	Homogenous 5% suspension in petrolatum; 77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE	Human	3 times per week for 3 weeks	NR	No skin sensitization response	Norris et al. (1975) [also reported in NTP (1986); Norris et al. (1973); Dow (1972) as cited in NRC (2000)]
Systemic effects						
Dermal	NR	Rabbit	Single administration 24 hours observation	200, 2,000 mg/kg	No treatment-related effects in body weight gain or survival	IRDC (1974) and Great Lakes (1977) as cited in NRC (2000)

Table F-3. cont.:, Select dermal and ocular studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Ocular						
Ocular	Saytex 102	Rabbit	Single application	100 mg	No primary eye irritation	Pharmakon (1981) as cited in NRC (2000)
Ocular	Dry solid	New Zealand albino rabbit	Single application	100 mg per eye	Transient irritation of conjunctival membranes in washed and unwashed eyes (not sustained past 24 hours)	Norris et al. (1975) [also reported in NTP (1986); Norris et al. (1973); IRDC (1974) Dow (1972) as cited in NRC (2000)]

NR = Not reported

Table F-4. Select dermal and ocular studies for MWCNTs.

Test substance	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Skin irritation									
1% Nikkiso-MWCNTs	44	NR	69	176 ppm Ga, 80 ppm Al, 53 ppm Fe, 16 ppm Cd, 0.5 ppm Li	Kbl:New Zealand white rabbit (male)	4-hour exposure; 1-, 24-, 48-, and 72-hour observation	0.5 gram	Exposure resulted in a primary irritation index of 0.6	Ema et al. (2011) (OECD 404 compliant; not GLP compliant)
2% Mitsui product of MWCNTs	60	NR	23	3,600 ppm Fe, 14 ppm Cr, 6 ppm Bi, 4 ppm Ni	Kbl:New Zealand white rabbit (male)	4-hour exposure; 1-, 24-, 48-, and 72-hour observation	0.5 gram	No erythema or edema was observed	Ema et al. (2011) (OECD 404 compliant; not GLP compliant)
MWCNTs	Inner: 3–8, outer: 140 ± 30	5–9	10–15	NR	New Zealand white rabbit (female)	4-hour under semi-occlusive conditions; 96-hour observation	0.5 gram	No erythema or edema at 72 hours	Kishore et al. (2009) (OECD 404 compliant)
MWCNTs	Inner: 2–6, outer: 10–15	0.1–10	30–45	NR	New Zealand white rabbit (female)	4-hour under semi-occlusive conditions; 96-hour observation	0.5 gram	No erythema or edema at 72 hours	Kishore et al. (2009) (OECD 404 compliant)

Table F–4, cont.: Select dermal and ocular studies for MWCNTs

Test substance	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Skin sensitization									
1% Nikkiso-MWCNTs	44	NR	69	176 ppm Ga, 80 ppm Al, 53 ppm Fe, 16 ppm Cd, 0.5 ppm Li	Slc:Hartley guinea pig (male)	3 doses; 6-hour challenge was conducted on day 28	0.4 gram paste	No sensitization observed	Ema et al. (2011) (OECD 406 compliant; Buehler method)
2% Mitsui product of MWCNTs	60	NR	23	3,600 ppm Fe, 14 ppm Cr, 6 ppm Bi, 4 ppm Ni	Slc:Hartley guinea pig (male)	3 doses; 6-hour challenge was conducted on day 28	0.4 gram paste	No sensitization observed	Ema et al. (2011) (OECD 406 compliant; Buehler method)
Ocular irritation									
1% Nikkiso-MWCNTs	44	NR	69	176 ppm Ga, 80 ppm Al, 53 ppm Fe, 16 ppm Cd, 0.5 ppm Li	Kbl:New Zealand white rabbit (male)	Single exposure to left eye; right eye served as control	0.1%, 0.25% (0.1 mL)	Conjunctival redness and blood vessel hyperemia at 1 hour, not at 24 hours	Ema et al. (2011) (OECD 405 compliant)
2% Mitsui product of MWCNTs	60	NR	23	3,600 ppm Fe, 14 ppm Cr, 6 ppm Bi, 4 ppm Ni	Kbl:New Zealand white rabbit (male)	Single exposure to left eye; right eye served as control	1% (0.1 mL)	No eye irritation observed	Ema et al. (2011) (OECD 405 compliant)

NR = Not reported

Table F-5. Select inhalation studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Inhalation (Intratracheal injection)	77.4% purity decabromodiphenyl oxide (DBDPO) dust, respirable size	Sprague-Dawley rat (male)	3, 10, 30, 91, 365, 416, 556 days	20 mg/mL rat serum	Slightly enlarged thoracic lymph nodes in 3/10 rats on Days 10 and 30; scattered focal aggregates of alveolar macrophages on Days 10 and 556	Dow Chemical Co. (1990b)
Inhalation	DE-83, 97% purity aerosolized dust	Spartan rat (male and female)	1 hour (observed for 14 days)	2 or 48.2 mg/L air	1 instance of marked to slight respiratory difficulty, 1 instance of ocular porphyrin discharge at 2 mg/L dose level before Day 13; eye squint, changes in motor activity (first decreased, then increased), respiratory difficulty, ocular porphyrin discharge at 48.2 mg/L dose level before Day 13. All rats normal on Days 13 and 14.	Great Lakes Chemical Corporation (1994) and IRDC (1974)

Table F-6. Select inhalation studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Acute or subacute									
Inhalation (nose only)	1,900–2,900	~≤1	253	98.6% (bulk) and 99.1% (micronized)	Wistar rat (male)	Single exposure for 6 hours; 7-,28-, 90-day observation	11, 241 mg/m^3	Deregulation of genes (inflammation, oxidative stress, and fibroses) at 241 mg/m^3; mild reversible inflammation and no fibroses at 11 mg/m^3 (LOAEC)	Ellinger-Ziegelbauer and Pauluhn (2009) (OECD 403 compliant)
Inhalation (intratracheal instillation)	50	10	280	>95%	Kunming mouse (female)	Single exposure; 8-, 16-, 24-day observation	1.7 mg/kg	Inflammation of lining of bronchi at 24 days; severe destruction of alveolar netted structure around CNT clumps	Li et al. (2007)
Inhalation	50	10	280	>95%	Kunming mouse (female)	6 hours/day; 5, 10, 15 days	32.61 mg/m^3	Thickening of alveolar wall, but alveolar structure remained	Li et al. (2007)
Inhalation (whole body)	10–20	5–15	100	0.5% Ni and Fe	C57BL/6 mouse (male)	6 hours/day; 7, 14 days	0.3, 1, 5.3 mg/m^3	No local pulmonary effects; non-monotonic systemic immune suppression	Mitchell et al. (2007)
Inhalation (whole body)	10–20	5–15	100	0.5% Ni and Fe	C57BL/6 mouse (male)	6 hours/day; 14 days	0.3, 1 mg/m^3	Systemic immune suppression, not due to systemic uptake of MWCNTs, but release of immune suppressing signals from lung	Mitchell et al. (2009)

Table F–6, cont.: Select inhalation studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Acute or subacute									
Inhalation (intratracheal instillation)	NR	NR	NR	NR	SD rat (female)	Single exposure; 3-, 15-, 28-, 60-day observation	2.2, 8.9, 22.2 mg/kg	Inflammation and fibrosis; granulomas with ground MWCNTs	Muller et al. (2005)
Inhalation (intratracheal instillation)	11.3	0.7	NR	98%; traces of Co and Fe catalysts	Wistar rat (female)	Single exposure; 3-day observation	0.5, 2, 5 mg/rat	Significant dose-dependent increase in micronucleated pneumocytes	Muller et al. (2008a)
Inhalation (intratracheal instillation)	NR	NR	NR	NR	Wistar rat (female)	Single exposure; 3- and 60-day observation	2 mg/rat	Toxicity of CNT mediated by defective sites in carbon framework; significant differences between ground MWCNTs not heated, heated to 600°C, and to 2,400°C for both short and long-term response	Muller et al. (2008b)
Intranasal injection	15.04 ± 0.47	0.5–200 (reported by supplier)	139.7	>90% carbon (as reported by supplier)	BALB/cAnNCrl mouse (female)	3 days	200, 400 μg/mouse (with 10 μg OVA per injection and 10 μg OVA booster given at 21, 22, and 23 days)	Increased IgE in serum and inflammatory cells in BALF	Nygaard et al. (2009)
Inhalation (intratracheal instillation)	11–170	5–9	12.83	>90% carbon	ICR mouse (male)	Single exposure; 1-, 3-, 7-, 14-day observation	5, 20, 50 mg/kg	Increase in immune cells and granulomas; increase in inflammatory cytokines (IL-1, TNF-α, IL-6, IL-4, IL-5, IL-10, IL-12, IFN-γ) and IgE; distribution of B cells in spleen	Park et al. (2009)

Table F–6, cont.: Select inhalation studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Inhalation (nose-only)	30–50	0.3–50	109.29	>94%	C57BL/6 mouse (male)	Single exposure; 6 hours; 1-, 14-day observation	~10 mg/kg; concentration in air was 103.6±8.34 mg/m^3 (both with and without 20 μg OVA injection given 14 and 7 days before exposure)	OVA sensitized group: significant airway fibrosis at 14 days, Elevated PDGF-AA and TGF- β1 at day 1 but not day 14; increased IL-5 mRNA levels not sensitized group: elevated PDGF-AA, but not increased levels of TGF- β 1and IL-13	Ryman-Rasmussen et al. (2009b)
Inhalation	10–15	~20	NR	95%	Sprague-Dawley rat (male)	6 hours/day; 5 days; 1 month observation	0.1, 0.34, 0.94 mg/m^3	pulmonary DNA damage initiated; a Comet assay performed on lung cells showed a significant increase in DNA damage for high dose compared to controls immediately and 1 month following the last exposure	Kim et al. (2012)
Subchronic									
Inhalation	50	10	280	>95%	Kunming mouse (female)	6 hours/day; 30, 60 days;	32.61 mg/m^3	No obvious toxicity at 30 days; severe pulmonary toxicity at 60 days	Li et al. (2009)
Inhalation (head-nose)	5–15, 500–1,300, 1,300–2,000/900–1,500, 700–800	0.1–1	250–300	90%	Wistar rat (male and female)	6 hours/day; 13 weeks	0.1, 0.4, 2.5 mg/m^3	Minimal granulomatous inflammation in lung at 0.1 mg/m^3 (LOEC); significant granulomatous inflammation <0.5 mg/m^3; no systemic toxicity; no pulmonary fibrosis	Ma-Hock et al. (2009) (OECD 413 compliant)

Table F–6, cont.: Select inhalation studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Subchronic									
Inhalation (intratracheal instillation)	67	3–30	26	99.79%	ICR mouse (male)		25, 50 μg/week/ mouse (both with and without 1 μg OVA/2 wk)	Increased total cells in BALF, infiltration of inflammatory leukocytes in airways, induction of goblet cell hyperplasia in both groups, enhanced response in sensitized group	Inoue et al. (2009)
Inhalation (nose only)	1,900–2,900	~≤1	253	98.6% (bulk) and 99.1% (micronized)	Wistar rat (male and female)	6 hours/day; 5 days/week; 13 weeks	0.1, 0.4, 1.5, 6 mg/m3	Sustained pulmonary inflammation at ≥1.5 mg/m3; granulomas and alveolar hyperplasia at ≥6 mg/m3; no systemic toxicity; 0.1 mg/m3 was NOAEC	Pauluhn (2010) (OECD 413 compliant)

NR = Not reported

Table F-7. Select oral and intragastric studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Acute						
Oral (gavage)	NR	Rat	Single dose	5,000 mg/kg	No clinical signs, toxicity, or death	LSRI (1984); Great Lakes (1984); IRDC (1974) as cited in NRC (2000)
Intragastric intubation	77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE	Sprague-Dawley rat (female)	Single dose (acute)	126, 252, 500, 1,000, 2,000 mg/kg (10% corn oil suspension)	No indications of toxicity; no detectable pathological changes	Norris et al. (1975) [also in Norris et al. (1973)]
Subchronic						
NR	97–99% pure	Rat (male and female)	28 days	0, 7.4, 75 mg/kg-day	No histology in liver or thyroid (NOAEL 74 mg/kg-day)	Great Lakes (1976); IRDC (1976) as cited in NRC (2000)
Intragastric	>98% pure	Wistar rat (female)	7–28 days	0, 10, 100, 1,000 mg/kg-day	2-fold induction of CYP1A and CYP2B at 10–1,000 mg/kg-day (not dose-dependent)	Bruchajzer et al. (2010)
Oral (diet)	94–98% pure	F344/N rat (male and female)	14 days	0, 5,000, 10,000, 20,000, 50,000, 100,000 ppm	No treatment-related clinical signs or gross pathologic effects	NTP (1986)
Oral (diet)	94–98% pure	B6C3F$_1$ mouse (male and female)	14 days	0, 50,00, 10,000, 20,000, 50,000, 100,000 ppm	No treatment-related clinical signs or gross pathologic effects	NTP (1986)

Table F–7, cont.: Select oral and intragastric studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Subchronic						
Oral (gavage)	97% pure	Wistar rat (male)	28 days	0, 1.9, 3.8, 7.5, 15, 30, 60 mg/kg	Increased weight of seminal vesicle/coagulation gland (BMDL 0.2 mg/kg-day); increased expression of hepatic CYP1A and CYP2B (BMDL 0.5–0.7 mg/kg-day)	Van der Ven et al. (2008)
Oral (gavage)	97% pure	Wistar rat (female)	28 days	0, 1.9, 3.8, 7.5, 15, 30, 60 mg/kg	Decreased activity of P450c17 (BMDL 0.18 mg/kg-day)	Van der Ven et al. (2008)
Oral (diet)	77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE	Sprague-Dawley rat (male)	30 days	0, 8, 80, 800 mg/kg-day	Decrease in packed cell volume and total red blood cell count in highest dose group; enlarged livers in mid- and high-dose groups; liver and kidney lesions at 800 mg/kg-day; thyroid hyperplasia at 80 mg/kg-day	Norris et al. (1975)
Oral (diet)	94–98% pure	F344/N rat (male and female)	13 weeks	0, 3,100; 6,200; 12,500; 25,000, 50,000 ppm	No treatment-related clinical signs or gross or microscopic pathologic effects	NTP (1986)
Oral (diet)	94–98% pure	B6C3F$_1$ mouse (male and female)	13 weeks	0, 3,100, 6,200, 12,500, 25,000, 50,000 ppm	No treatment-related clinical signs or gross or microscopic pathologic effects	NTP (1986)
Chronic						
Oral (diet)	77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE	Sprague-Dawley rat (male and female)	2 years	0, 0.01, 0.1, 1.0 mg	No differences observed in hematology or urinalysis at 1 year; no other results reported (report published before completion of study)	Norris et al. (1975)
Oral (diet)	94–98% pure	F344/N rat (male)	2 years	0, 2,500, 50,000 ppm	Increased incidence of neoplastic lesions (nodules in the liver; acinar cell adenomas, sarcoma of the spleen, hepatocellular adenomas and carcinomas, thyroid gland follicular cell adenomas or carcinomas) and nonneoplastic lesions (thrombosis and degeneration of the liver; fibrosis of the spleen, lymphoid hyperplasia)	NTP (1986)

Table F–7, cont.: Select oral and intragastric studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Chronic						
Oral (diet)	94–98% pure	F344/N rat (female)	2 years	0, 2,500, 50,000 ppm	Increased incidence of neoplastic lesions (nodules in the liver of high-dose group) and nonneoplastic lesions; degeneration of the eye in low dose group	NTP (1986)
Oral (diet)	94–98% pure	B6C3F$_1$ mouse (male)	2 years	0, 2,500, 50,000 ppm	Dose-dependent increase in thyroid follicular cell hyperplasia; centrilobular hypertrophy (indicated by enlarged hepatocytes with frothy vacuolated cytoplasm)	NTP (1986)
Oral (diet)	94–98% pure	B6C3F$_1$ mouse (female)	2 years	0, 2,500, 50,000 ppm	Increased incidence of nonneoplastic lesions	NTP (1986)
Oral (diet)	94–98% pure	F344/N rat (male)	2 years	1,120, 2,240 mg/kg (adjusted)	Increased incidences of thrombosis and degeneration of the liver in high-dose group; enzyme induction; significant increases in hepatic CYP1A mRNA, CYP2B mRNA, CYP1A1 protein, and 7-pentoxyresorufin *O*-dealkylase activity; increased 7-ethoxyresofurin *O*-deethylase activity	NTP (1986)
Oral (diet)	94–98% pure	F344/N rat (female)	2 years	1,200, 2,550 mg/kg (adjusted)	Increased 7-ethoxyresofurin *O*-deethylase activity	NTP (1986)
Oral (diet)	77.4% pure	Sprague-Dawley rat (male and female)	2 years	0, 0.01, 0.1, 1 mg/kg-day	No histology; NOAEL 1 mg/kg-day	Norris (1973); Dow (1994) and Kociba et al. (1975) as cited in NRC (2000)
Oral (metal gastric tube)	>99%	NMRI mice (male)	single dose given at age 3, 10, or 19 days	2.22, 20.1 mg/kg-day for 3 and 19 day old mice; 0, 1.34, 13.4, or 20.1 mg/kg-day for 10 day old mice	Statistically significant changes in spontaneous behavior variables (increased activity for locomotion, rearing, total activity) at 2, 4, and 6 months at highest dose when exposed on PND3 (developmental effects), but not PND10 or PND19	Viberg et al. (2003)

Table F-8. Select intubation and injection studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Acute/Subacute									
intra-peritoneal injection	15–30	15–20		>95%; functionalized (2–7% COOH)	Swiss-Webster mice	daily, 5 days	0.25, 0.5, 0.75 mg/kg-day	Dose-related increase in ROS level in liver homogenate at all doses; increase in LHPs in liver homogenate and ALT in serum at medium and high dose; increase in serum ALP at high dose; non-statistically significant, dose-dependent increase in AST/GOT at all doses.	Patlolla et al. (2011)
Developmental Studies									
Oral (gavage)	10-15	~20	NR	~95%	Sprague-Dawley rat (pregnant dams)	Single dose on GD6-GD19	of 0, 40, 200, and 1,000 mg/kg-day	Dose-dependent decrease in absolute and relative thymus weight and increase in malondialdehyde concentration (maternal effects); no other treatment-related maternal or fetal (developmental) effects were reported; 1,000 mg/kg-day was the embryo-fetal NOAEL	Lim et al. (2011)

Table F–8, cont.: Select intubation and injection studies for MWCNTs.

Route of exposure	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
Developmental Studies									
Intraperitoneal	Width distribution from 70-170 nm with the greatest frequency occurring at 90-110 nm, length distribution between 1 - 19 μm with the greatest frequency occurring between 1 - 5 μm [reported to be identical to those described by Takagi et al. (2008) and Sakamoto et al. (2009)]				ICR mice (pregnant dams)	Single dose on GD9; fetuses examined on GD18	0, 2, 3, 4, or 5 mg/kg-bw	Dose-dependent decreased maternal body weight; increased number of resorptions, decreased number of live fetuses per litter in the two highest dose groups; external and skeletal malformations (e.g., cleft palate, limb deformities, hypo/ hyperphalangia) observed more frequently (ratio of litter with malformed fetuses and percent(%) incidence at all dose levels	Fujitani et al. (2012)
Intratracheal injection	Width distribution from 70-170 nm with the greatest frequency occurring at 90-110 nm, length distribution between 1 - 19 μm with the greatest frequency occurring between 1 - 5 μm [reported to be identical to those described by Takagi et al. (2008) and Sakamoto et al. (2009)]				ICR mice (pregnant dams)	Single dose on GD9; fetuses examined on GD18	0, 3, 4, or 5 mg/kg-bw)	Decreased final body weight of dams and decreased body weight of live fetuses in 5mg/kg group; external and skeletal malformations (e.g., limb deformities, fused ribs) observed more frequently (ratio of litter with malformed fetuses and percent [%] incidence) in two highest dose groups	Fujitani et al. (2012)

F.1.3. Genotoxicity, Mutagenicity, and Other In Vitro Studies

Table F-9. Select genotoxicity, mutagenicity, and other in vitro studies for MWCNTs.

Assay	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Doses tested	Effects observed	Citation
Cytotoxicity								
Trypan blue test	110–170	5–9	22	>98%; <0.1% Fe; ~1.5% Ni; other metal catalysts	Murine macrophage cell line RAW 264.7	0.01, 0.1, 1, 10, 100 μg/mL	Significant cytotoxic effect at 10 and 100 μg/mL	Migliore et al. (2010)
Bacterial mutation								
Ames assay	110–170	5–9	130	>90%; <0.1% Fe; residual amorphous carbon; other metal contaminants	*Salmonella typhimurium* strains TA 98, TA 100; *Escherichia coli* strain WP2uvrA	0.01, 0.05, 0.13, 0.23, 0.46, 1.26, 2.30, 4.60, 9.0 μg/plate, ±S9	No significant increase in number of revertant colony with or without metabolic activation	Di Sotto et al. (2009)
Ames assay	100 to >150 (bimodal distribution)	0.2–1	NR	>95%; no free amorphous carbon	Salmonella strains TA1535, TA100, TA1537, TA98, TA102	50, 158, 500, 1,581, 5,000 μg/plate, ±S9	Not mutagenic and bacteriotoxic up to 5,000 μg/plate with or without metabolic activation	Wirnitzer et al. (2009) (OECD 471)

Table F–9, cont.: Select genotoxicity, mutagenicity, and other in vitro studies for MWCNTs.

Assay	Diameter (nm)	Length (µm)	Surface area (m^2/ gram)	Purity	Species	Doses tested	Effects observed	Citation
DNA damage and unscheduled DNA synthesis								
Chromosome aberration	88 ± 5	5 ± 4.5	NR	NR	Chinese hamster lung cells	0.078, 0.31, 1.4, 5.0, 20, 80 µg/mL, –S9	Formation of polyploidy with no structural chromosome aberration at ≥5.0 µg/mL for 24-hour test and ≥1.3 µg/mL for 48-hour test	Asakura et al. (2010)
Comet assay	110–170	5–9	22	>98%; <0.1% Fe; ~1.5% Ni; other metal catalysts	Murine macrophage cell line RAW 264.7	0.01, 0.1, 1, 10, 100 µg/mL	Significantly higher percent (%) DNA in comet tails for doses ≥1 µg/mL; significant dose-related effect overall	Migliore et al. (2010)
Comet assay	20–40	0.5–200	NR	93.37%	human lung epithelial A549 cells	5, 10, 40, 100 µg/mL	Significantly higher perrcent (%) DNA in comet tails concentration-dependent for 10, 40 µg/mL at 2 hours post exposure and 5, 10, 100 µg/mL 4 hours post exposure; corresponds with reduced cell viability	Cavallo et al. (2012)
Comet assay	15–30	15–20	NR	> 95%	normal human dermal fibroblast cells (NHDF)	40, 200, 400 µg/mL	statistically significant, dose-dependent increase in percent (%) DNA in comet tails	Patlolla et al.(2010b; 2010a).
Sister chromatid exchange; micronucleus assay	10–30	1–2	NR	95–98%	Human lymphocyte cells	1 mg/mL, –S9	No significant cytotoxic effects	Szendi and Varga (2008)
Chromosome aberration	100 to >150 (bimodal distribution)	0.2–1	NR	>95%; no free amorphous carbon	V79 cells	2.5, 5, 10 µg/mL, ±S9	No cytotoxic or clastogenic effects detected with or without metabolic activation	Wirnitzer et al. (2009) (OECD 473)

Table F–9, cont.: Select genotoxicity, mutagenicity, and other in vitro studies for MWCNTs.

Assay	Diameter (nm)	Length (µm)	Surface area (m^2/ gram)	Purity	Species	Doses tested	Effects observed	Citation
DNA damage and unscheduled DNA synthesis								
Sister chromatid exchange	>80% of particles 70–110, Gaussian peak at 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	Chinese hamster ovary AA8 cells	0.1, 1.0, 2.0 µg/mL	Significant increase in sister chromatid exchange frequency at all doses; approximately 3-fold increase over controls at 1.0 µg/mL	Kato et al. (In Press); CNT characteristics in Sakamoto et al (2009)
Comet assay (in vivo intra-tracheal instillation; 3 hours)	>80% of particles 70–110, Gaussian peak at 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	Male ICR mice (6 weeks old); lung cells	Single doses of 0.05 or 0.2 mg/animal	Significant, dose-dependent increase in DNA damage observed by significant increases in DNA tail moment and percentage of DNA in the tail compared to controls.	Kato et al. (In Press); CNT characteristics in Sakamoto et al (2009)
DNA adduct assay (in vivo intra-tracheal instillation; 3, 24, 72, 168 hours)	>80% of particles 70–110, Gaussian peak at 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	Male ICR mice (6 weeks old); lung DNA	Single dose of 0.2 mg/animal	Three (out of four analyzed) DNA adducts related to oxidative stress and lipid peroxidation significantly increased (relative to controls) in a time dependent manner up to 72 hours; a significant smaller significant increase relative to controls was observed at 168 hours.	Kato et al. (In Press); CNT characteristics in Sakamoto et al (2009)
DNA damage via Western blot	NR	NR	NR	NR	Mouse embryonic stem cells	100 µg/mL	Increased expression of two isoforms of base excision repair protein 8-oxoguanine-DNA glycosylase 1 (OGG1), double strand break repair protein Rad 51; phosphorylation of H2AX histone at serine 139; SUMO modification of XRCC4	Zhu et al. (2007)

Table F–9, cont.: Select genotoxicity, mutagenicity, and other in vitro studies for MWCNTs.

Assay	Diameter (nm)	Length (μm)	Surface area (m^2/ gram)	Purity	Species	Doses tested	Effects observed	Citation
Mutation								
Micronucleus assay	88 ± 5	5 ± 4.5	NR	NR	Chinese hamster lung cells	0.02, 0.078, 0.31, 1.3, 5.0 μg/mL, –S9	Increased bi- and multi-nucleated cells at ≥0.31 μg/mL; no micronucleus induction	Asakura et al. (2010)
Mutation at hgprt locus	88 ± 5	5 ± 4.5	NR	NR	Chinese hamster lung cells	6.3, 12.5, 25, 50, 100 μg/mL, –S9	Negative hgprt mutagenicity at all doses	Asakura et al. (2010)
Micronucleus assay	20–40	1–5	NR	>99% wt	Human blood cells	0.25–150 μL/5 mL total cell culture volume, –S9	MWCNTs acted as clastogen and aneugen agents simultaneously	Cveticanin et al. (2010)
Micronucleus assay	>80% of particles 70–110, Gaussian peak: 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	Human lung carcinoma A549 calls	20, 100, 200 μg/mL	6 hour treatment at 20 μg/mL inhibited cell growth to around 70% of control levels. Significant, dose-dependent increase in frequency of micronucleated cells at all doses (up to 8.6% at 200 μg/mL)	Kato et al. (In Press); CNT characteristics in Sakamoto et al (2009)
Mutation assay (in vivo intra-tracheal instillation; 8 – 12 weeks)	>80% of particles 70–110, Gaussian peak at 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	Male guanine phosphoribosyl-transferase (*gpt*) mice (9 weeks old)	One, two, or four single doses of 0.2 mg/animal given once, two weeks apart, and every week, respectively	No increase in *gpt* mutant frequencies following single or double dose, but significant increase (approximately 2-fold over control) after 4 doses. No increases observed in SPi– (sensitive to P2 interference) mutation frequencies.	Kato et al. (In Press); CNT characteristics in Sakamoto et al (2009)
Micronucleus assay	110–170	5–9	22	>98%; <0.1% Fe; ~1.5% Ni; other metal catalysts	Murine macrophage cell line RAW 264.7	0.01, 0.1, 1, 10, 100 μg/mL, –S9	Significantly more micronucleated cells for doses ≥1 μg/mL	Migliore et al. (2010)

Table F–9, cont.: Select genotoxicity, mutagenicity, and other in vitro studies for MWCNTs.

Assay	Diameter (nm)	Length (µm)	Surface area (m^2/gram)	Purity	Species	Doses tested	Effects observed	Citation
Mutation								
Micronucleus assay	11.3	0.7	NR	98%; traces of Co and Fe	Rat lung epithelial cells	10, 25, 50, 100, 150 µg/mL, –S9	Significant increase in micronuclei	Muller et al. (2008a)
platelet aggregation (Aggro-Link data reduction system; Chronolog)	NR	NR	NR	NR	human platelet cells	0.2–300 µg/mL; platelets isolated and resuspended in Tyrode's solution; aggregation was studied for 8 min post-addition of MWCNTs	concentration-dependent increase in platelet aggregation; activation of GPIIb/IIIa	Radomski et al. (2005)
T-cell viability; Trypan Blue exclusion assay	20–40	1–5	NR	95%	Jurkat T lymphocyte (leukemia) cells from healthy human blood donors	1, 10 ng/cell (40, 400 µg/mL); Cell aliquots collected at 0, 24, 48, 72, 96, 120 hours post-exposure; stained for 5 min with Trypan Blue to determine cell proliferation and percentage of apoptotic Jurkat or peripheral blood lymphocytes (PBL) determined using annexin V-FITC	time-dependent decrease in the viability of Jurkat T leukemia cells; increased number of cells staining with annexin V indicating increased apoptosis	Bottini et al. (2006)

NR = Not reported

F.1.4. Carcinogenicity Studies

Table F-10. Select carcinogenicity studies for decaBDE.

Route of exposure	Description of decaBDE	Species	Exposure duration	Doses tested	Effects observed	Citation
Oral	94–98% pure	F344/N rat (male)	2 years	1,120, 2,240 mg/kg-day (adjusted)	Some evidence of carcinogenicity; increased incidences of neoplastic nodules of the liver (low dose 7/50, high dose 15/49, control 1/50)	NTP (1986)
Oral	94–98% pure	F344/N rat (female)	2 years	1,120, 2,550 mg/kg-day (adjusted)	Some evidence of carcinogenicity; increased incidences of neoplastic nodules of the liver (low dose 3/49, high dose 9/50, control 1/50)	NTP (1986)
Oral	94–98% pure	B6C3F$_1$ mouse (male)	2 years	25,000, 50,000 ppm	Equivocal evidence of carcinogenicity; increased incidences of hepatocellular adenomas or carcinomas (combined) in both dose groups	NTP (1986)
Oral	94–98% pure	B6C3F$_1$ mouse (female)	2 years	25,000, 50,000 ppm	No evidence of carcinogenicity	NTP (1986)
Oral	77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE	Sprague-Dawley rat (male and female)	2 years	0, 0.01, 0.1, 1.0 mg/kg-day	No alterations in appearance, behavior, bodyweight, feed consumption, hematologic analyses, urinalysis, clinical chemistry, organ weights, survival, or tumor incidence	Kociba et al. (1975) as reported in NTP (1986) and NRC (2000)

Table F-11. Select carcinogenicity studies for MWCNT.

Test substance	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
MWCNTs with structural defects	11.3 ± 3.9	~0.7	299	1.97% Al, 0.49% Fe, 0.48% Co	Wistar rat (male)	Single injection, 24-month observation	2, 20 mg/rat	2 mesotheliomas at low dose (1 at 20 months and 1 at terminal sacrifice); 1 other peritoneal tumor at low dose at 16.6 months; no mesotheliomas at high dose; 3 other peritoneal tumors (1 lipoma at 13.8 months, 1 angiosarcoma and 1 liposarcoma at terminal sacrifice) at high dose; no significant difference in body weight or survival rates	Muller et al. (2009)
MWCNTs without structural defects	11.3 ± 3.9	~0.7	190	0.37% Al, <0.01% Fe, <0.01% Co	Wistar rat (male)	Single injection, 24- month observation	2, 20 mg/rat	No tumors observed at low dose; 3 mesotheliomas (at 10.7, 18.9, and 19.8 months) and 3 lipomas (at terminal sacrifice) at high dose; no significant difference in body weight or survival rates	Muller et al. (2009)
Short MWCNTs	14.84 ± 0.50	1–5	NR	7.9% Fe, 5.1% Cu, 9.7% Ni, 5.5% Zn, 3.7% Co	C57BL/6 mouse (female)	Single injection, 24-hour, 7-day observations	100 μg/mL	No significant effects	Poland et al. (2008)
Short MWCNTs	10.40 ± 0.32	5–20	NR	(μg/gram) 13.4 Fe, 1 Cu, 5 Ni, 7.5 Zn	C57BL/6 mouse (female)	Single injection, 24-hour, 7-day observations	100 μg/mL	No significant effects	Poland et al. (2008)
Long MWCNTs	165.02 ± 4.68	Maximum 56	NR	(μg/gram) 37.3 Fe, 1.2 Cu, 6.2 Ni, 3.4 Co	C57BL/6 mouse (female)	Single injection, 24-hour, 7-day observations	100 μg/mL	Inflammatory responses; formation of granulomas on peritoneal surface of the diaphragm; foreign body giant cells comparable to long-fiber amosite asbestos	Poland et al. (2008)

Table F–11, cont.: Select carcinogenicity studies for MWCNTs.

Test substance	Diameter (nm)	Length (μm)	Surface area (m^2/gram)	Purity	Species	Exposure duration	Doses tested	Effects observed	Citation
MWCNTs	70–110, peak at 90	72.5% within 1–4, peak at 2	NR	(ppm) 3,500 Fe, 470 S, 20 Cl, <5 Br, <40 F	p53 (+/-) mouse (male)	Single injection, 25-week observation	3 mg/mL	100% mortality by week 25; mesothelioma incidence 14/16 (87.5%, 11 as cause of death, 3 incidental); moderate to severe fibrous peritoneal adhesion with slight ascites; fibrous peritoneal thickening with black-colored depositions; high incidence of macroscopic peritoneal tumors; peritoneal mesothelial lesions	Takagi et al. (2008)
MWCNTs	10–30	1–2	NR	95–98%	F344 rat	Single exposure; 12-month observation	10 mg/rat	Granulomatous reactions of foreign body type with multinucleated giant cells in liver; abdominal cavities dispersed carbon on the adjacent organs (omentum, peritoneum), resulting in partial expansion of the gastric wall and residual carbon in peritoneal envelope of liver; no signs of mesothelioma	Varga and Szendi (2010)
MWCNTs	>80% of particles 70–110, Gaussian peak at 90	>70% of particles 1–4, peak: 2	NR	3,500, 470, and 20 ppm iron, sulfur, and chlorine contaminants	F344 rat (male)	single intrascrotal injection; observed at 52 weeks	1 mg/kg	85.7% mortality by 37-40 weeks; intraperitoneally disseminated hypertrophic mesothelioma (cause of death in 6/7 animals); nodular and papillary lesions of mesothelioma; mesotheliomas invasive to adjacent organs and metastasized into pleura	Sakamoto et al. (2009)

NR = Not reported

F.2. Ecological Effects

F.2.1. Effects of DecaBDE and Other PBDEs on Aquatic Receptors

Table F-12. Effects of exposure to PBDEs in aquatic invertebrates.

Life stage	Number/ group	Test type / duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Algae[1]								
NR	NR	Semi-chronic/ 96 hours	Commercial decaBDE	NR	NR	EC_{50}	>1 mg/L	Marine algae; review article, study-specific details were not provided
NR	NR	Semi-chronic/ 96 hours	Commercial pentaBDE	NR	NR	NOEC	>water solubility	Freshwater algae; review article, study-specific details were not provided
Zebra mussels (*Dreissena polymorpha*)[2]								
Post-spawn	150	Comet assay/ 48, 96, 168 hours; micronucleus (MN) assay/ 48, 96 hours	Technical grade decaBDE, 98% pure	Water	0.1, 2, 10 µg/L	Mortality, hemocyte viability	NOE	None
						DNA damage, chromosomal aberrations	All tested doses	Increasing trend over time @ 0.1, 2 µg/L; damage increased until 96hr then decreased at 168 hours @10 µg/L
Freshwater oligochaete (*Lumbriculus variegates*)[3]								
NR	NR	Chronic/28 days	Commercial decaBDE	Sediment	NR	EC_{50}	>5,000 mg/kg	Review article, endpoints not specified
						NOEC	≥5,000 mg/kg	Review article, endpoints not specified

Table F-12, cont.: Effects of exposure to PBDEs in aquatic invertebrates.

Life stage	Number/ group	Test type/ duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Freshwater oligochaete (*Lumbriculus variegates*)[3]								
NR	NR	Chronic/28 days	Commercial pentaBDE	Sediment	NR	EC_{50}	>50 mg/kg	Review article, endpoints not specified
Adult	80	Chronic/28 days	55%pentaBDE, 36% tetraBDE, 8.5% hexaBDE	Sediment	0, 3.1, 6.3, 13, 25, 50 mg/kg	EC_{50}, survival, reproduction	>50 mg/kg	Review article, study-specific details were not provided
						LOEC, survival, reproduction	6.3 mg/kg	Review article, study-specific details were not provided
Adult	80	Chronic/28 days	Mixture, 97% decaBDE	Sediment	0, 313, 625, 1,250, 2,500, 5,000 mg/kg	NOEC, survival, reproduction	>5,000 mg/kg (mean measured 3,841 mg/kg)	Review article, doses listed are minimal measured conc.
Water fleas (*Daphnia magna*)[4]								
24 hours old at test start	40	Acute/96 hours	55%pentaBDE, 34% tetraBDE, 12% hexaBDE	NR	0, 1.4, 2.6, 5.3, 9.8, 20 µg/L	EC_{50} mortality, immobility	17 µg/L	Review article, study-specific details were not provided
24 hours old at test start	40	Chronic/21 days	55%pentaBDE, 34% tetraBDE, 12% hexaBDE	Water	0, 1.4, 2.6, 5.3, 9.8, 20 µg/L	EC_{50} mortality, immobility	14 µg/L	Review article, study-specific details were not provided
						EC_{50} reproduction	14 µg/L	Review article, study-specific details were not provided
						LOEC mortality, immobility	20 µg/L	Review article, study-specific details were not provided
						LOEC growth	9.8 µg/L	Review article, study-specific details were not provided

Table F-12, cont.: Effects of exposure to PBDEs in aquatic invertebrates.

Life stage	Number/ group	Test type/ duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Water fleas (*Daphnia magna*)[4]								
24 hours old at test start	20	Chronic/21 days	42% heptaBDE, 36% octaBDE, 14% nonaBDE, 6% hexaBDE, 2% decaBDE	Water	0, 0.13, 0.25, 0.54, 0.83, 1.7 µg/L	NOEC survival, reproduction, growth	>1.7 µg/L	Review article, study-specific details were not provided
						EC_{50}, LOEC survival, reproduction, growth	>2.0 µg/L	
NR	NR	Chronic/21 days	Commercial octaBDE	NR	NR	EC_{50}, NOEC	>water solubility	Review article, study-specific details were not provided
NR	NR	Acute/48 hours	Commercial pentaBDE	NR	NR	EC_{50}	14 µg/L	Review article, study-specific details were not provided
NR	NR	Chronic/21 days	Commercial pentaBDE	NR	NR	LOEC	9.8 µg/L	Review article, endpoints not specified

[1]Source: Hardy (2002a)

[2]Source: Riva et al. (2007)

[3]Source: Rows 1–3: Hardy (2002a); rows 4–6: Environment Canada (2006)

[4]Source: Rows 1–7: Environment Canada (2006); rows 8–10: Hardy (2002a)

EC_{50} = Median effective dose; LOEC = Lowest observed effect concentration; NR: Not reported; NOE: No observed effects at tested doses; NOEC = Maximum no observed effect concentration

Table F-13. Effects of exposure to PBDEs in fish and frogs.

Duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Juvenile rainbow trout (*Oncorhynchus mykiss*)[1]						
16 days	Dow FR-300-BA[2]	Diet	7.5–10 mg/kg-day[3]	Increased liver weight, increased blood lactate concentrations, decreased lymphocyte count	NOE	None
49 days					NOE	Saw effects in group after 71 days of depuration (non-exposure). indicating potential delayed chronic effects
120 days					7.5 mg/kg-day	None
96 hours	Commercial pentaBDE	NR	NR	LC_{50}	≥water solubility	Review article, study-specific details were not provided
NR	PentaBDE, tetraBDE mix	Injection	NR	Egg mortality	≥12 µg/egg	Review article, study-specific details were not provided
72 hours	Tetra-, penta-, and octaBDE	Cell culture	0–264 µg/l	Vitellogenin production	10–50 µg/l	In vitro hepatocyte assay; intensity of response increased with increasing number of bromine atoms
Juvenile lake whitefish (*Coregonus clupeaformis*)[4]						
30 days	DecaBDE; 97.5–99.25% pure	Diet	0, 0.1, 1, 2 µg/gram	Negative growth effects	2 µg/gram	Otolith increment widths narrowed starting day 1

Table F-13, cont.: Effects of exposure to PBDEs in fish and frogs.

Duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Juvenile lake trout (*Salvelinus namaycush*)[5]						
56 days	DecaBDE, >96% pure	Diet	0, 2.5, 25 ng/gram	Mortality, whole body growth rate	NOE	No effects observed during exposure period and up to 112 days depuration
				Phase I EROD activity in liver microsomes	NOE	Measured on days 14, 56 of uptake and 14, 56 of depuration
				Liver somatic index changes (liver weight ÷ whole fish weight × 100)	NOE	No effects observed during exposure period and up to 112 days depuration
				Decreased free thyroxine (T_4) concentrations	2.5, 25 ng/gram	Level significantly decreased at both doses (greater decrease at 25 ng/gram) at 56 days, no effects at earlier time points; levels remain decreased in high dose but not low dose after 112 days depuration
				Decreased free tri-iodothyronine (T_3) concentrations	2.5 ng/gram	Level significantly decreased at 2.5 ng/gram at 56 days, no effects at earlier time points; no effects at 25 ng/gram at any time; author states "no consistent differences related to PBDE exposure level were evident"
Adult Chinese rare minnow (*Gobiocypris rarus*)[6]						
21 days	DecaBDE, ≥99% pure	Water	0.01, 0.1, 1, 10 µg/L	Mortality, malformations	NOE	None
				Decreased body length, gonadosomatic index (GSI) changes	10 µg/L	GSI = Gonad weight ÷ whole fish weight × 100
				Inhibition of spermatogenesis, reduction of spermatocytes	10 µg/L	Males only
				mRNA levels of thyroid hormone related genes	Variable at all doses	Upregulation of *nis* at all doses; *tr-a* in all male groups but not female; *ttr* in all female groups but not male; *dio2* in females at 0.01 µg/L, females + males at 0.1 µg/L.

Table F-13, cont.: Effects of exposure to PBDEs in fish and frogs.

Duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Adult Chinese rare minnow (*Gobiocypris rarus*)[6]						
21 days	DecaBDE, ≥99% pure	Water	0.01, 0.1, 1, 10 µg/L	Liver degeneration, hepatocyte swelling	10 µg/L	Females only
Unspecified/general fish[7]						
48 hours	Commercial decaBDE	NR	NR	LC_{50}	>500 mg/L	Review article, study-specific details were not provided
48 hours	Commercial octaBDE	NR	NR	LC_{50}	>500 mg/L	Review article, study-specific details were not provided
48 hours	Commercial pentaBDE	NR	NR	LC_{50}	≥500 mg/L	Review article based value on data for *Oryzias latipes*, details were not provided
NR	Commercial pentaBDE	Diet	NR	Reproduction (spawning success)	NOE	Review article based value on data for *Gasterpsteis aculeatus,* details were not provided

Table F-13, cont.: Effects of exposure to PBDEs in fish and frogs.

Duration	Test substance	Medium	Doses tested	Effect	Effect dose	Notes
Tadpoles (*Xenopus laevis*)[8]						
51 days	DE-83R	Water	1, 10, 100, 1,000 ng/L	Physical malformation, abnormal behavior, increased mortality	NOE	None
				Delayed time to metamorphosis	1,000 ng/L	Statistically significant at 1,000 ng/L; concentration-dependent trend of metamorphic delay in all groups
				Histological alterations in thyroid glands (epithelial cell height, follicle size, colloid depletion, colloid vacuolation)	All doses	Statistically significant increase in mean epithelial cell height at 100 and 1,000 ng/L; multilayer follicular epithelial cells at all doses
				Decrease in TR-β-A mRNA expression (thyroid hormone) in tail tissue	All doses	None

[1]Source: Rows 1–3: Kierkegaard et al. (1999); row 4: Hardy (2002a); row 5, Nakari and Pesala (2005); individuals per group not reported

[2]Commercial mixture contains 77.4% decaBDE, 21.8% nonaBDE, 0.8% octaBDE as reported in Hardy (2002a)

[3]One dose administered, dose was minimum 7.5 mg/kg-day, maximum 10 mg/kg-day

[4]Source: Kuo et al. (2010); 75 individuals per test group

[5]Source: Tomy et al. (2004); 70 individuals per test group

[6]Source: Li et al. (2011); individuals per group not reported

[7]Source: Hardy (2002a) (Review article)

[8]Source: Qin et al. (2010); free swimming larvae 5 days post-fertilization (stage 46/47) through forelimbs emergence (FLE, stage 57/58); n = 70 in rows 1–2; n = 10–12 in row 3, n = 8 in row 4

EROD = Ethoxyresorunfin-*O*-deethylase enzyme; LC_{50} = Median lethal concentration; LOEC = Lowest observed effect concentration; NOE: No observed effects at tested doses; NOEC = Maximum no observed effect concentration tested; NR: Not reported

F.2.2. Effects of MWCNTs on Aquatic Receptors

Table F-14. Effects of exposure to MWCNTs in algae, macrophytes, and aquatic macroinvertebrates.

Organism	Test substance	Dimensions	Test duration	Medium	Doses tested	Effect	Effect dose	Notes
Unicellular green algae (*Dunaliella tertiolecta*)[1]	Carboxylated MWCNT	OD: 20–30 nm L: 50 µm	96 hours	Water	0.1, 0.5, 1, 2.5, 5, 10 mg/L	Inhibited growth	LOEL 1 mg/L, NOEL 0.5 mg/L	Growth lagged up to 23 days at 10 mg/L, 36% reduction in exponential growth rate
Aquatic macrophytes (*Chara*, *Elodea nuttallii*, *Potamogeton obtusifulius*, *Glycera*, *Alisma plantagoaquatica*)[2]	Pure MWCNT	OD: 20–30 nm ID: 5–10 nm L:10–30 µm	3 months	Stream bed sediment	0.002, 0.2, 2 grams/kg	Changes in macrophyte density	LOEL 0.002 grams/kg	Density increased compared to control at all levels; significant at 0.002 and 2 grams/kg
Macroinvertebrates (Gastropoda, Crustacea, Oligochaeta, Hirundinea, Bivalvia, Arachnida, Diptera)[2]	Pure MWCNT	OD: 20–30 nm ID: 5–10 nm L:10–30 µm	3 months	Stream bed sediment	0.002, 0.2, 2 grams/kg	Recolonization rates	LOEL 0.002 grams/kg	Dose-dependent increase in recolonization (# of taxa and individuals) compared to control
						Biodiversity	NOEL >2 grams/kg	No observed effect
Amphipods (*Leptocheirus plumulosus*)[3]	Pure MWCNT	OD: 10–30 nm L: 10–30 µm	10 days	Sediment	4, 10, 33, 99, 300 grams/kg	Death	LOEL 99 grams/kg, LC_{50} 68 grams/kg	Mortality 30 ± 10% at 99 grams/kg, 30 ± 0% at 300 grams/kg
Amphipods (*Hyalella azteca*)[3]	Pure MWCNT	OD: 10–30 nm L: 10–30 µm	10 days	Sediment	3, 9, 29, 87, 264 grams/kg	Death	LOEL 264 grams/kg	Mortality 53 ± 25%

[1]Source: Wei et al. (2010); microwave assisted acid oxidation was used to carboxylate pristine nonfunctionalized MWCNT resulting in functionalized MWCNTs with 7.61% carboxylation, 1% residual cobalt by weight, elemental composition 948:51:1 carbon:oxygen:cobalt

[2]Source: Velzeboer et al. (2011); MWCNTs nonfunctionalized, purity 95% wt

[3]Source: Kennedy et al. (2008); authors note that mortality increased as particle size decreased

L = Length; LC_{50} = Median lethal concentration; ID = Inner diameter; LOEL = Lowest observed effect level; NOEL = Maximum no observed effect level; NR: Not reported; OD= Outer diameter

Table F-15. Effects of exposure to MWCNTs via water on *Ceriodaphnia dubia*.

Individuals per test group	Outer diameter (nm)[3]	Functionalization	Concentrations tested (mg/L)	Effect	Effect dose
Acute (24 hours)[1]					
20	10–20	NF	1–200	LC_{50}	17 mg/L
20	30–40	NF	1–200	LC_{50}	8 mg/L
20	50–70	NF	1–200	LC_{50}	20 mg/L
20	10–20	Ozone-treated	1–200	LC_{50}	100 mg/L
20	30–40	Ozone-treated	1–200	$LC5_0$	100 mg/L
20	50–70	Ozone-treated	1–200	LC_{50}	100 mg/L
20	10–20	Ultrasound-probe treated	1–200	LC_{50}	8 mg/L
20	30–40	Ultrasound-probe treated	1–200	LC_{50}	7 mg/L
20	50–70	Ultrasound-probe treated	1–200	LC_{50}	2 mg/L
Subchronic (48 hours)[2]					
NR	10–30	NF	25.1, 39.5, 59.6	EC_{50}	50.9 mg/L
NR	20–30	MWCNT-OH	120.2	mortality increase	No effects
NR	20–30	MWCNT-COOH	88.9	mortality increase	No effects
>12	50–70	Ozone-treated	5, 10, 20, 50, 100	Body length decrease[4]	LOEC 5 mg/L; 73% of control at 100 mg/L
>12	50–70	Ultrasound-probe treated	1, 2, 3, 5, 10	Body length decrease[4]	NOEC 1 mg/L; LOEL 2 mg/L; 75% of control at 10 mg/L

Table F–15, cont.: Effects of exposure to MWCNTs via water on *Ceriodaphnia dubia.*

Individuals per test group	Outer diameter (nm)[3]	Functionalization	Concentrations tested (mg/L)	Effect	Effect dose
Chronic (8 days)[1]					
>8	50–70	Ozone-treated	5 concentrations, 0.5 to >30	EC_{50} decreased reproduction[5]	17 mg/L
>8	50–70	Ultrasound-probe treated	5 concentrations, 0.5 to >30	EC_{50} decreased reproduction[5]	4 mg/L

[1]Source: Li and Huang (2011)

[2]Source: Rows 1–3: Kennedy et al. (2008); rows 4–5: Li and Huang (2011)

[3]Other properties not reported in Li and Huang (2011), Kennedy et al. (2008) reported length 10–30 µm and purity 95%

[4]Dose-response growth assay

[5]Three generation reproductive test

EC_{50} = Median effective concentration; LC_{50} = Median lethal concentration; LOEC = Lowest observed effect concentration; NF= Not Functionalized; NOE: No observed effects at tested doses; NOEC = Maximum no observed effect concentration tested; NR = Not reported

Table F-16. Effects of exposure to MWCNTs on zebrafish and medaka embryos.

Number per group	Outer diameter (nm)	Test substance	Exposure medium	Doses tested	Effect	Effect dose	Notes
Zebrafish, 72 hours post fertilization[1]							
75	30–40	MWCNT	Microinjection at 8-cell stage	2.5, 5, 10, 20, 30, 40, 50, 60, 70, 100, 200, 300 µg/mL	Heart rate decrease	NOEC 10 µg/mL, LOEC 20 µg/mL	Measured at 24, 48, 72 hpf; dose-dependent drop at 48 and 72 hpf
					Reduced blood circulation	NOEC 60 µg/mL, LOEC 70 µg/mL	Observed at 24, 48, and 72 hpf
60	30–40	MWCNT	Water	2.5, 5, 10, 20, 30, 40, 50, 60, 70, 100, 200, 300 µg/mL	Delayed hatching	NOEC 50 µg/mL[3], LOEC 60 µg/mL	8% at 60 µg/mL, 60% at 100 mg/mL
					Increased mortality	NOEC 50 µg/mL, LOEC 60 µg/mL	10% at 60 µg/mL, 80% at 100 µg/mL, 97% at 200 µg/mL

Table F–16, cont.: Effects of exposure to MWCNTs on zebrafish and medaka embryos.

Number per group	Outer diameter (nm)	Test substance	Exposure medium	Doses tested	Effect	Effect dose	Notes
Zebrafish, 96 hours post injection[2]							
NR	19.9	BSA-MWCNT	Microinjection at 1-cell stage	2 ng/ embryo	Developmental defects	NOE	Through adult stage
					Immune response	2 ng	Observed at 24 hpf
Medaka, 96 hours continual exposure[3]							
12	NR	oxidized MWCNT	Water	500, 1,000, 1,500, 2,000 µg/mL	Increased mortality	NOEC 1,000 µg/mL, LOEC 1,500 µg/mL	MWCNTs were functionalized by acid treatment
Medaka, 10 days following 4 days of continual exposure[4]							
12	NR	oxidized MWCNT	Water	500, 1,000, 1,500, 2,000 µg/mL	Increased malformations	NOEC 1,000 µg/mL, LOEC 1,500 µg/mL	MWCNTs were functionalized by acid treatment
12	NR	oxidized MWCNT	Water	500, 1,000, 1,500, 2,000 µg/mL	Hatching delay	NOEC 1,000 µg/mL, LOEC 1,500 µg/mL	MWCNTs were functionalized by acid treatment
Zebrafish, 56 days post injection[2]							
NR	19.9	BSA-MWCNT	Microinjection at 1-cell stage	2ng/ embryo	Reduced survival of 2nd generation	2 ng	Measured at day 14 of 2nd generation lifecycle

[1]Source: Asharani et al. (2008)

[2]Source: Cheng et al. (2009)

[3]Source: Kim et al. (2012)

[4]Authors state NOEC of 40 µg/mL and LOEC of 60 µg/mL but do not provide the effect level at 50 µg/mL.

BSA = bovine serum albumin; hpf = hours post fertilization; LOEC = Lowest observed effect concentration; NOE: No observed effects at tested doses; NOEC = Maximum no observed effect concentration tested; NR: Not reported

Table F-17. Immune responses in rainbow trout (*Oncorhynchus mykiss*) head kidney cells following MWCNT exposure.

Endpoint	Measured as	Pure MWCNT[1]	Anionic MWCNT[1]
Antiviral response	IFNa expression observed after 6 hours incubation	NOE	NOE
Macrophage stimulation	IL-1b expression observed after 24 hours incubation	LOEL 5 µg/mL	LOEL 0.1 µg/mL (dose-dependent)
Cytotoxicity	Measured after 24 hours incubation	NOE	NOE

[1]Pure MWCNTs: >95% pure; Anionic MWCNTs: functionalized with sulfonate groups, centrifuged and ultrafiltered to purify. Both had diameter 10–20nm, length 1–2 µm

Note: Testing protocol: head kidney cells of adult fish were collect and incubated 5 days prior to experiment; doses tested: 0.1, 0.5, 1, 5, and 10 µg/mL MWCNTs diluted in water solution; 8 replicates for antiviral response/ macrophage stimulation, duplicate for cytotoxicity

LOEL = Lowest observed effect level; NOE: No observed effects at tested

Source: Klaper et al. (2010)

F.2.3. Effects of DecaBDE and Other PBDEs on Terrestrial Receptors

Table F-18. Effects of exposure to decaBDE in soil microbes, terrestrial invertebrates, and plants.

Test duration	Test substance	Doses tested (mg/kg dry weight soil)	Effect	Effect dose (mg/kg)	Notes
Soil microbes[1]					
180 days	DecaBDE	1, 10, 100	Altered community structure	All doses	Control shows increase in Shannon-Weaver index at each checkpoint from 15 days to 180 days; index number decreased compared to control (continues to increase over time) at all doses beginning at ~90 days, indicating less diversity over time
			Cytotoxicity	100	Total bacteria count was ~50%; dose-dependent decrease observed at all doses; alpha, beta, gamma-proteobacteria groups were decreased to 74.7–84.7% at 100 mg/kg; decreases not observed at lower doses
180 days	DecaBDE	1, 10, 100	Changes in alkaline phosphatase (APA) enzyme activity	All doses	Increased activity from 60–120 days at 10, 100 mg/kg then decreased activity (inhibition) at 180 days; increased activity through full study at 1 mg/kg
			Changes in urease enzyme activity	All doses	Increased activity through 150 days at 1 mg/kg; activity increased at 10 mg/kg from 15 days to 120 days, and at 100 mg/kg at every checkpoint except 150 days
Nitrifying bacteria[2]					
4 weeks	DecaBDE	15.1, 230, 2,274	Change in behavior	NOE	Measured by change in nitrate/nitrite content
Red clover (*Trifolium pratense*)[3]					
21 days	DecaBDE	15.1, 230, 2,274	Early life growth	NOE	Measured by mean fresh weight of seedlings per soil plot for 15–17 days post seedling emergence

Table F-18, cont.: Effects of exposure to decaBDE in soil microbes, terrestrial invertebrates, and plants.

Test duration	Test substance	Doses tested (mg/kg dry weight soil)	Effect	Effect dose (mg/kg)	Notes
Corn (*Zea mays*)[4]					
21 days	55% pentaBDE, 36% tetraBDE, 8.6% hexaBDE	62.5, 125, 250, 500, 1,000	Germination	NOE	None
			LOEL reduced shoot height	250	None
			LOEL reduced shoot height	62.5	None
Soil invertebrate (*Enchytraeus crypticus*)[5]					
21 days	DecaBDE	15.1, 230, 2,274	Reproductive effects	NOE	Measured as number of juveniles per soil plot
Earthworms (*Eisenia fetida*)[6]					
7 days	DecaBDE	0.01, 0.1, 1, 5, 10, 50, 100	Hydroxyl free radical generation	All doses	Dose-dependent increase starting at lowest dose, reached level 2× control at highest dose
56 days	DecaBDE, 98% pure	320, 668, 1,240, 2,480, 4,910	Reproductive effects	NOE	Also observed at 28 days (no effects seen)
56 days	Commercial octaBDE	84.9, 166, 361, 698, 1,470	Mortality	NOE	None
			Reproductive effects	NOE	None

[1]Source: Liu et al. (2011a); 3 replicates per group
[2]Source: Sverdrup et al. (2006); number of replicates per group not reported
[3]Source: Sverdrup et al. (2006); 20 seeds per test group
[4]Source: Environment Canada (2006); 40 seeds per test group
[5]Source: Sverdrup et al. (2006); 40 adult worms per test group
[6]Source: Row 1: Xie et al. (2011), 60 worms per test group; row 2–4: Environment Canada (2006), 80 worms per test group
NOE = No observed effects

F.2.4. Effects of MWCNTs on Terrestrial Receptors

Table F-19. Effects of exposure to MWCNTs in bacteria.

Test substance	Properties	Test duration	Exposure protocol	Medium	Doses tested	Effect	Effect dose	Notes
General soil microorganisms[1]								
MWCNT	OD: 15.1 nm, L: 10-20 µm, SA: 237.1 m^2/gram, V: 0.86 cm^3/gram, P: 96%	11 days	MWCNTs suspended in water, suspension applied to soil	Soil	50, 500, 5,000 µg/gram	LOEL decreased microbial activity	500 µg/gram	Indicated by enzyme presence; nonsignificant tendency to be repressed at 500 µg/gram; activity decreased by 34.2–60.5% at 5,000 µg/gram
		20 days	MWCNTs suspended in water, suspension applied to soil	Soil	50, 500, 5,000 µg/gram	LOEL decreased biomass	5,000 µg/gram	C decreased by 36.9–43.4%, N decreased n by 27.8–30.4%
Gram negative *Escherichia coli*[2]								
MWCNT	OD: 44.0 nm, L: 1.5 µm, SA: 42 m^2/gram, 0.08%wt Fe	24 hours	Exposure to aqueous suspensions of MWCNT at room temp, gentle stirring; strain: MG1655	Water	10, 100 mg/mL	LOEL cytotoxicity	100 mg/mL	~ 50% loss in viability
MWCNT-Fe	OD: 44.0 nm, L: 1.5 µm, SA: 42 m^2/gram, 4.24%wt Fe	24 hours	Exposure to aqueous suspensions of MWCNT at room temp, gentle stirring; strain: MG1655	Water	10, 100 mg/mL	LOEL cytotoxicity	100 mg/mL	~ 60% loss in viability
MWCNT	OD: 17.4 ± 6.1 nm, L: 77 ± 31 µm	1 hour	Incubation exposure to MWCNT-coated filter in 0.9% NaCl solution	Filter in culture	CNQ	cytotoxicity	Effect seen	~32% inactivated cells

Table F-19, cont.: Effects of exposure to MWCNTs in bacteria.

Test substance	Properties	Test duration	Exposure protocol	Medium	Doses tested	Effect	Effect dose	Notes
Gram negative *Escherichia coli*[2]								
MWCNT	OD: 30 nm, L: 70 µm, 0.62%wt metal catalysts	1 hour	5×10^7 cells/mL incubated with MWCNTs in saline for 1 hour at 37 °C; strain: K12	Cell culture	5 µg/mL	Cytotoxicity	5 µg/mL	~3× reduction in viability compared to controls
			Incubation exposure to MWCNT-coated filter in 0.9% NaCl solution; strain: K12	Filter in culture	CNQ	Cytotoxicity	Effect seen	~3.8× reduction in viability compared to controls
						Reduced metabolic activity	Effect seen	30% metabolic activity compared to 74% in control
Metallic-pollutant resistant *Cupriavididus metallidurans* CH34[3]								
MWCNT	OD: 44.0 nm, L: 1.5 µm, SA: 42 m^2/gram, 0.08%wt Fe	24 hours	Exposure to aqueous suspensions of MWCNT at room temp, gentle stirring	Water	10, 100 mg/mL	NOEL cytotoxicity	NOE	NOE
MWCNT-Fe	OD: 44.0 nm, L: 1.5 µm, SA: 42 m^2/gram, 4.24%wt Fe	24 hours	Exposure to aqueous suspensions of MWCNT at room temp, gentle stirring	Water	10, 100 mg/mL	NOEL cytotoxicity	NOE	NOE
Gram negative *Pseudomonas aeruginosa*[4]								
MWCNT	OD: 17.4 ± 6.1 nm, L: 77 ± 31 µm	1 hour	Incubation exposure to MWCNT-coated filter in 0.9% NaCl solution	Filter in culture	CNQ	Cytotoxicity	Effect seen	~25% inactivated cells

Table F-19, cont.: Effects of exposure to MWCNTs in bacteria.

Test substance	Properties	Test duration	Exposure protocol	Medium	Doses tested	Effect	Effect dose	Notes
Gram positive *Staphylococcus epidermidis*[4]								
MWCNT	OD: 17.4 ± 6.1 nm, L: 77 ± 31 µm	1 hour	Incubation exposure to MWCNT-coated filter in 0.9% NaCl solution	Filter in culture	CNQ	Cytotoxicity	Effect seen	~50% inactivated cells
Gram positive *Bacillus subtilis*[5]								
MWCNT	OD: 17.4 ± 6.1 nm, L: 77 ± 31 µm	1 hour	Incubation in 0.9% NaCl solution	Filter in culture	CNQ	Cytotoxicity	NOE	None
OH-MWCNT	OD: 15–30 nm, L: 1–5 µm	1 hour	Cells suspended in 1 mL of solution	Water, culture	100 µg/mL	Delayed growth	CNQ	NOE in solutions of DI water, PBS, BHI, or 0.9% NaCl
COOH-MWCNT	OD: 15–30 nm, L: 1–5 µm	1 hour	Cells suspended in 1 mL of solution	Water, culture	100 µg/mL	Delayed growth	NOE	NOE in solutions of DI water, PBS, BHI, or 0.9% NaCl
NH_2-MWCNT	OD: 15–30 nm, L: 1–5 µm	1 hour	Cells suspended in 1 mL of solution	Water, culture	100 µg/mL	Delayed growth	NOE	NOE in solutions of DI water, PBS, BHI, or 0.9% NaCl

Table F-19, cont.: Effects of exposure to MWCNTs in bacteria.

Test substance	Properties	Test duration	Exposure protocol	Medium	Doses tested	Effect	Effect dose	Notes
Gram negative *Salmonella typhimurium*[6]								
OH-MWCNT	OD: 15–30 nm L: 1–5 µm	1 hour	Cells suspended in 1 mL of water	Water	100, 170, 290, 375, 500 µg/mL	Delayed growth	NOE	Nonsignificant reductions in viability at all doses
			Cells suspended in 1 mL of solution	Culture	100, 170, 290, 375, 500 µg/mL	Delayed growth	NOE	NOE up to 500 µg/L in BHI broth, PBS, or 0.9% NaCl
COOH-MWCNT	OD: 15–30 nm L: 1–5 µm	1 hour	Cells suspended in 1 mL of solution	Water, culture	100, 170, 290, 375, 500 µg/mL	Delayed growth	NOE	NOE up to 500 µg/L in DI water, BHI broth, PBS, or 0.9% NaCl
NH_2-MWCNT	OD: 15–30 nm L: 1–5 µm	1 hour	Cells suspended in 1 mL of solution	water, culture	100, 170, 290, 375, 500 µg/mL	Delayed growth	NOE	NOE up to 500 µg/L in water, BHI broth, PBS, or 0.9% NaCl

[1]Source: Chung et al. (2011)

[2]Source: Rows 1–2 Simon-Deckers et al. (2009), created with aerosol-assisted catalytic chemical vapor deposition using Fe as catalyst, heat purified; row 3, Kang et al. (2009), purified with hydrochloric acid then dispersed in 0.1 µg/mL ethanol sonicated for 10 min in a bath sonicator; rows 4–6: Kang et al. (2008)

[3]Source: Simon-Deckers et al. (2009), details same as footnote b

[4]Source: Kang et al. (2009), details same as footnote b

[5]Source: Row 1: Kang et al. (2009), details same as footnote b; rows 2–4: Arias and Yang (2009), no details provided

[6]Source: Arias and Yang (2009), no details provided; OH-MWCNT: Functionalized with OH groups derived directly from the surface of CNTs

BHI = Brain heart infusion broth; COOH-MWCNT= Carboxylated, acid treated with COOH groups derived from the surface of CNTs by acid treatment; DI = deionized water; NH_2-MWCNT=Functionalized with NH_2 groups by activation of carboxyl moieties with thionyl chloride and subsequent reaction with $CH_3(CH_2)_{16}CH_2$-NH_2; CNQ= Could not quantify; L = Length; LOEL = Lowest observed effect level; NOE = No observed effect; NOEL = Maximum no observed effects level; ND = Not determined; OD = Outer diameter; P = Purity; PBS = Phosphate buffers saline; SA = Surface area; V = Volume

Table F-20. Effects of exposure to MWCNTs on plants.

MWCNT properties	Exposure protocol	Plant	Doses tested	Effect dose	Notes
Decreased germination rates[1]					
SA: 126 m^2/gram, OD: 10–20 nm, L: 1–2 µm	30 seeds in water, 5 days	Rapeseed	2,000 mg/L	NOE	Non-significant decrease
		Radish	2,000 mg/L	NOE	Non-significant decrease
		Ryegrass	2,000 mg/L	NOE	None
		Corn	2,000 mg/L	NOE	Non-significant decrease
		Lettuce	2,000 mg/L	NOE	No observed effect
		Cucumber	2,000 mg/L	NOE	Non-significant decrease
SA: 73 m^2/gram, OD: 40–60 nm, L: NR	10 seeds in sewage sludge, 3 days	Garden cress	0.01, 0.1, 0.5% wt	LOEL 0.01%	50–70% inhibition (compared to 10% in control)
SA: 357 m^2/gram, OD: <10 nm, L: NR	10 seeds in sewage sludge, 3 days	Garden cress	0.01, 0.1, 0.5% wt	LOEL 0.1%	60% inhibition at 0.1%, 40% inhibition at 0.5% (compared to 10% in control)
SA: NR, OD: 110–170 nm, L: 5–9 µm	60 seeds in water, 4 days	Mustard	10, 20, 40 µg/mL	NOE	None
		Urad bean	10, 20, 40 µg/mL	NOE	None
Changes in root growth[1]					
>95% pure, SA: 126 m^2/gram, OD: 10–20 nm, L: 1–2 µm	30 seeds in water, 5 days	Rapeseed	2,000 mg/L	NOE	None
		Radish	2,000 mg/L	NOE	None
		Ryegrass	2,000 mg/L	NOE	Non-significant total root growth decrease; root length increase
		Corn	20,00 mg/L	NOE	None
		Lettuce	2,000 mg/L	NOE	None
		Cucumber	2,000 mg/L	NOE	None

Table F–20, cont.: Effects of exposure to MWCNTs on plants.

MWCNT properties	Exposure protocol	Plant	Doses tested	Effect dose	Notes
Changes in root growth[1]					
SA: 357 m^2/gram, OD: <10 nm, L: NR	10 seeds in sewage sludge, 3 days	Garden cress	0.01, 0.1, 0.5% wt	LOEL 0.01%	Root length inhibition ~30% greater than control at all doses
SA: 73 m^2/gram, OD: 40–60 nm, L: NR	10 seeds in sewage sludge, 3 days	Garden cress	0.01, 0.1, 0.5% wt	NOE	None
SA: NR, OD: 110–170 nm, L: 5–9 µm	60 seeds in water, 4 days	Mustard	10, 20, 40 µg/mL	LOEL10 µg/mL	138% increase in root length at 10 µg/mL, 202% increase at 20 µg/mL, 135% increase at 40 µg/mL
		Urad bean	10, 20, 40 µg/mL	NOE	None
Cytotoxicity[2]					
SA: 250–300 m^2/gram, OD: 9.5 nm, L: 1.5 µm	T87 cells in suspension, 7 days (in exponential growth phase on day 3)	Thale cress	10 mg/L	LOEL 10 mg/L	Began on day 2; dose-dependent inhibition observed; poor linearity of curves; more severe with fine MWCNT agglomerates than loose MWCNT agglomerates

[1]Source: Rows 1–6: Lin and Xing (2007)- MWCNT purity >95%; rows 7–8: Oleszczuk et al. (2011)- MWCNT purity >95%; rows 9–10: Ghodake et al. (2010)- MWCNT purity 90%

[2]Source: Lin et al. (2009a), MWCNT carbon purity 90%; MWCNT properties reported for loose agglomerates, fine agglomerates had same average diameter but other dimensions not analyzed

L = Length; LOEL = Lowest observed effect level; NOE = No observed effect; NR = Not reported; OD = Outer diameter; SA = Surface area; V = Volume

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Appendix G.
Unprioritized Areas of the CEA Framework for MWCNTs

Appendix G. Unprioritized Areas of the CEA Framework for MWCNTs

G.1. Introduction to this Appendix

As described in Chapter 1, the Peer Review Draft of the case study has been streamlined to clearly reflect the outcomes of the collective judgment step of the CEA process. Certain topics within the CEA framework (Figure 1-3) were designated priorities for research, based on high importance for risk assessment and low confidence that the current data could support risk management decisions. All detailed information on multiwalled carbon nanotubes (MWCNTs) that was not identified as a priority research area during the collective judgment step of the CEA process has been moved to this appendix. The designation of certain areas as "unprioritized" is not intended to imply that the topics are unimportant or that continued research is not needed; it simply implies that the topic was determined to be of lesser importance for risk assessment.

G.2. Product Life Cycle

G.2.1. Feedstocks

G.2.1.1. Life-Cycle Processes

A wide variety of hydrocarbons and catalysts are used to synthesize MWCNTs. The raw materials required for MWCNT synthesis include a precursor carbon material, an inert gas, and metal catalysts, with other specific materials depending on the particular synthetic pathway used (as described in Section 2.2) (Moisala et al., 2003). Support materials such as aluminum, manganese oxide, or silica are also used during synthesis of MWCNTs (Gustavsson et al., 2011).

No quantitative data were found on the total magnitude of feedstocks that are or might be used in commercial synthesis of MWCNTs. Table G-1, however, lists the amount of inputs required to synthesize 1 gram of single-walled carbon nanotubes (SWCNTs) using two of the common forms of carbon nanotube (CNT) synthesis (both of which are discussed in Section 2.2.2): chemical vapor deposition (CVD) and fluidized bed chemical vapor deposition (FBCVD). According to Healy et al. (2008), SWCNT

Table G-1. Percent yields for agglomerated growth of SWCNTs and MWCNTs using various synthesis methods, processing temperatures, and catalysts.

SWCNTs[1]				MWCNTs[1]			
Method of Synthesis	Catalyst Used	Processing Temperature (°C)	Yield (%)	Method of Synthesis	Catalyst Used	Processing Temperature (°C)	Yield (%)
CVD	$Fe(Mo)Al_2O_3$	900	0.1–10	FBCVD	Fe/Al_2O_3	500–700	1–20
CVD	$Co/Mo/SiO_2$	600–800	0.33–1.8	FBCVD	$NiAl_2O_3$	650–800	2–17
CVD	Fe/MgO	900	5.2	CVD	$Co/Mo/Al_2O_3$	700	2–25
CVD	Fe/Co/MgO	1,000	5.5–7.6	FBCVD	Ni/SiO_2	450–850	2–145
CVD	Fe/MgO	850	8-20	CVD	Co/W/MgO	1,000	4–47
CVD	Fe/MgO	900	11	FBCVD	Fe/SiO_2	550–1,050	10–50
CVD	Fe/Mg/Al-LDH	900	17.6	FBCVD	Fe/Al_2O_3	550–750	10–70
CVD	$Fe/Mo/Al_2O_3$	850	20–60	CVD	Ni/Mo/MgO	1,000	10–100
CVD	$Fe(CO)_5$	1,200	25–44	CVD	$Fe/Co/Al_2O_3$	700	14–56
CVD	Fe/Mo/MgO	800	55	CVD	Co/Mo/MgO	1,000	16
				CVD	Fe/SiO_2	650–800	30–116
				CVD	Mo/MgO	900	33.4
				FBCVD	Fe/Mo/MgO	600–10,00	66–400
				FBCVD	$Fe(Ni)/Al_2O_3$	700–850	70–300
				CVD	Ni/Mg/Al-LDH	700	109–254
				CVD	Ni/SiO_2	680	124–426
				CVD	Ni/MgO	600	166–480
				CVD	Co/Al-LDH	700	188
				FBCVD	$Fe/Mo/Al_2O_3$	850	274
				CVD	$Co/Mo/Al_2O_3$	700	280–480
				CVD	Co/Al-LDH	850	560–625
				FBCVD	$Fe/CO/CaCO_3$	600–850	1,100
				CVD	$Ni/Fe/Al_2O_3$	600	6,000
				CVD	Co/Mn/Zn/Al	650	17,900

Source: Zhang et al. (2011b).

[1]Agglomerated growth differs from vertical and horizontal growth; however, no yield data were provided for vertical or horizontal growth of CNTs.

CVD = chemical vapor deposition; FBCVD = fluidized bed chemical vapor deposition; LDH = layered double hydroxide

synthesis requires large quantities of feedstocks, or inputs, compared to outputs. These inputs were calculated, however, assuming very low synthesis reaction yield (2.95%–4.50%), or mass of CNTs divided by the mass of carbon fed into the system. Current synthesis reaction yields can range from 1% to 17,900% depending on synthesis method, choice of catalyst, and organizational structure (i.e., vertically aligned, agglomerated, horizontally aligned; the largest synthesis yields are obtained from agglomerated MWCNT growth) (Zhang et al., 2011b). Process optimization has led to dramatically improved yields over the past few years (Zhang et al., 2011b). SWCNT reaction yields also have been reported to be typically much lower than MWCNT reaction yields (Zhang et al., 2011b) (see Table G-1).[25]

Limited information suggests that MWCNT synthesis requires more precursor material than SWCNT synthesis (Tsai et al., 2009); however, no information regarding the mass of inputs of precursor materials and catalysts was identified for MWCNTs.

G.2.1.2. Potential Releases during the Feedstock Extraction Stage

Release of MWCNTs would not occur during this initial phase of the life cycle—the feedstock extraction stage—given that synthesis does not occur until the next stage. Hazardous raw materials, however, could be released during the extraction and processing of feedstock materials. Release of CNTs also could occur if reactors are not cleaned between runs. The specific raw materials that could be released depends on the method of production; but likely would include catalyst metals and carbon precursor materials. No data quantifying the potential volume of releases during feedstock extraction for MWCNTs were identified.

G.2.2. Storage and Distribution

G.2.2.1. Life-Cycle Processes

The storage and distribution stage involves the handling and transport of (1) MWCNTs, (2) MWCNT flame-retardant formulations, and (3) MWCNT flame-retardant upholstery textiles. The principal method of transport for these materials is not known, but likely would be by truck, train, or cargo ship.

[25]An alternative method for estimating magnitude of MWCNT feedstock inputs is to consider magnitude of feedstock inputs for carbon-carbon composites. The processes to produce carbon-carbon composites and MWCNTs are the same, with the exception that producing MWCNTs requires the use of metal catalysts [Personal Communication: K. Lafdi (University of Dayton). 11/16/12].

- **MWCNTs**, if not immediately incorporated into a flame-retardant formulation, likely would be stored at the site of synthesis/processing in sealed receptacles until they are incorporated into flame-retardant formulations or transported to the sites where flame-retardant manufacture would occur.
- **MWCNT flame-retardant formulations** are typically stored at manufacturing plants in drums, tanks, or more permanent storage vessels until they are packaged and sent to textile manufacturers (U.S. EPA, 2005a).
- **MWCNT flame-retardant upholstery textiles** and end-use products likely also would be stored at the site of manufacture (or an intermediate storage site) and then transported to retail locations.

G.2.2.2. Potential Releases during Storage and Distribution

Storage and distribution of (1) MWCNTs, (2) MWCNT flame-retardant formulations, and (3) MWCNT flame-retardant upholstery textiles could result in the following releases to the environment, but all release scenarios are unlikely.

- **Releases of MWCNTs** prior to incorporation in flame-retardant formulations are likely to be negligible. Release would be due primarily to accidents, as the MWCNTs would be stored in sealed receptacles after synthesis. Exposure of the receptacles to high heat or fire could lead to the airborne release of MWCNTs (see Section 2.2.2.2 for more details).
- **Releases of flame-retardant formulations** could result in releases of MWCNTs to the environment (U.S. EPA, 2005a). The possible scenarios for release of MWCNT flame-retardant formulations during storage and distribution include damage to containers holding the flame-retardant formulation, leakage resulting from mishandling of containers, or faulty or improper stacking of cartons in transport vehicles. If the containers are sealed properly and not damaged during transport, releases of product prior to application might be limited to spills.
- **Releases of flame-retardant upholstery textiles** could result from accidental exposure to high heat or fire, off-gassing of volatile components, and infestation with pests. Exposure of the flame-retardant upholstery textiles to high heat or fire during storage and distribution could lead to the degradation of the polymer matrix and subsequent airborne release of MWCNTs (both free and matrix bound) (see Sections 2.2.2.2 and 2.4.2 for more details).
- **Off-gassing of the volatile components of MWCNT flame retardants** also could occur in poorly ventilated areas that experience high temperatures (e.g., storage units, warehouses). MWCNTs per se, however, are not highly volatile (see Table 1-9 and Table 3-1). Infestation of textile or furniture storage facilities with rodents or other pests also could lead to the release of MWCNT flame-retardant materials to the environment.

Table G-2 outlines potential release scenarios from the storage and distribution stage of (1) MWCNTs, (2) MWCNT flame-retardant formulations, and (3) MWCNT flame-retardant upholstery textiles. Parallel potential release scenarios for decaBDE are provided in the table for comparative purposes; more detailed information on release scenarios for decaBDE is provided in Appendix H

Table G-2. Potential release scenarios during storage and distribution.

	Processes included in storage and distribution life-cycle stage	Information on release	
		DecaBDE	MWCNTs
1	Storage/transport of raw materials (decaBDE and MWCNTs)	Release unlikely if properly stored	Release unlikely if properly stored
	Accidental releases of raw materials (decaBDE and MWCNTs)	Air release possible due to storage container defects	Air release possible due to storage container defects
2	Storage/transport of flame-retardant formulation	Release unlikely if properly stored	Release unlikely if properly stored
	Accidental releases of flame-retardant formulation	Water release possible due to spills from mishandling or faulty packaging	Water release possible due to spills from mishandling or faulty packaging
3	Storage/transport of treated textiles	Small air release possible if properly stored	Small air release possible if properly stored
	Accidental releases of treated textiles	Air release possible due to exposure to high heat, pest infestation, etc.	Release possible due to pest infestation; preliminary evidence suggests that release due to high heat is unlikely

G.3. Transport, Transformation, and Fate

G.3.1. Transport, Transformation, and Fate in Water and Sediment

G.3.1.1. Surface Water and Sediment (Inland and Coastal)

Although the transport, transformation, and fate of MWCNTs in surface water was not identified as a priority area, the transport, transformation, and fate of MWCNTs in sediment was. Because of the limited available data, which overlaps between surface water and sediment, however, these topics are discussed together in the main body of the document (Section 3.3.1) and therefore the surface water discussion was not extracted and presented here as a separate area.

G.3.1.2. Ground Water

MWCNTs in soil could leach into subsoil and ground water and migrate to surface water; however, no data were found on concentrations of MWCNTs in ground water.

G.3.2. Transport, Transformation, and Fate in Soil

MWCNTs released from textile products can enter terrestrial ecosystems and be transported in several ways. Early reviews speculated that the propensity of MWCNTs to adsorb to soil surfaces could make them less mobile (Borm et al., 2006; Wiesner et al., 2006). Recently, researchers showed that MWCNTs modified with surface coatings to enhance their aqueous stability or change their surface charge behave in the environment differently than pure MWCNTs (Petersen et al., 2011a).

Petersen et al. (2011a) examined sorption profiles of pure MWCNTs and MWCNTs functionalized with a polyethyleneimine surface coating and determined that sorption isotherms for pure MWCNTs were nearly linear, whereas isotherms for modified MWCNTs were nonlinear, indicating that surface coating can influence MWCNT interactions with soils. The authors also suggested that MWCNT characteristics (such as presence of surface coating) are better predictors of sorption behavior than soil type (and organic carbon content).

Properties of the soil environment (e.g., soil type, soil organic matter, pH, ionic strength, presence of other pollutants) also could affect particle transport. General information on how those properties affect nanoparticles (not specific to MWCNTs) is available in the literature (Navarro et al., 2008; U.S. EPA, 2007).

If MWCNTs are present in soils, plant roots could interact with those associated with soil material and in soil pore water (Navarro et al., 2008). Plants could also be exposed to MWCNTs in air and water. Airborne MWCNTs could attach to leaves and other aerial parts of plants and be translocated to different tissues of the plant, in which case plants also might act as transfer vectors for MWCNTs in the food chain. Additionally, bioaccumulation might be possible for carbon-based nanomaterials (Navarro et al., 2008).

Studies relevant to the fate and transport of CNTs in soil are provided in Appendix D, Table D-4. Studies that examined MWCNT uptake, translocation, and transformation in plants were not found. Literature that presents soil concentrations of MWCNTs has not been identified.

G.4. Exposure-Dose

G.4.1. Human Exposure and Kinetics Leading to Dose

G.4.1.1. General Public Exposure Pathway Scenarios through Environmental Media

No information was found on exposure to MWCNTs in the general public from environmental media (e.g., air, water, soil). See Section 4.1.2 for model estimates of MWCNT concentrations in environmental media that could be used with the exposure pathway and scenario characteristics below to estimate potential exposures.

G.4.1.1.1 Outdoor Air

Releases of MWCNTs to outdoor air throughout the product life cycle of the flame-retardant textile coatings are possible (see Chapter 2 and Section G.2). Once MWCNTs are released to air, they might sorb or attach, depending on the surface coating and functionalization, to particulate matter and be subject to long-range transport to areas distant from their source (see Section 3.2). Although this phenomenon has not been observed for MWCNTs, it has been observed for other compounds and no evidence yet exists to preclude the possibility that it would occur for MWCNTs. No data are available on MWCNT concentrations in ambient air, but general public exposure pathways could be similar to those observed for particulate-phase decaBDE (see Appendix H).

Other product constituents of flame-retardant textiles (e.g., pieces of the polymer matrix or the textile fabric) also can be released. As discussed in Section 3.2, the physicochemical properties of MWCNTs released to air might change over time as a result of aging, which could result in exposure of the general public to different MWCNTs than those that were first synthesized or released.

G.4.1.1.2 Water

Releases of MWCNTs and other product constituents to wastewater and ambient water bodies are possible throughout the product life cycle of flame-retardant textile coatings (see Section G.2). Once released to water, MWCNTs are expected to sorb to particulate matter in the water column or to sediments, which might limit their mobility (see Section 3.3). This behavior implies that MWCNTs also primarily will be removed to sludge during wastewater treatment. No data are available on MWCNT concentrations in surface waters (see Section 4.1.2.2), but general public exposure pathways could be similar to those observed for particulate-phase decaBDE (see Appendix H). MWCNT surface functionalization, however, might affect stability of free MWCNTs in water and efficacy of water

treatment methods in removal of MWCNTs (see Section 3.3.3), which could result in more or less exposure to MWCNTs in surface and drinking water, depending on the type of functionalization.

G.4.1.1.3 Soil

Releases to ambient air and water throughout the product life cycle of flame-retardant textile coatings will result in deposition of MWCNT particles and other product constituents (see Section G.2) to soil. Once deposited, MWCNTs are expected to sorb strongly to soil, which might limit their mobility (see Section 3.4). No data are available on MWCNT concentrations in surface soils (see Section 4.1.2.3), but general public exposure pathways could be similar to those observed for particulate-phase decaBDE (see Appendix H).

G.4.2. Ecological Exposure and Kinetics Leading to Dose

G.4.2.1. Factors Impacting Ecological Exposure

In biota, potential exposure routes for MWCNTs include ingestion, inhalation, or direct contact. The potential for exposure via each route along with subsequent uptake and dose depends on several factors, including properties of the environmental media and physiological and behavioral characteristics of aquatic and terrestrial organisms. These factors can, in turn, influence the bioavailability of MWCNTs. As discussed in Chapter 3 and Section H.3, the physicochemical properties of MWCNTs dictate their partitioning in the environment. This partitioning drives the exposure potentials for water-dwelling, sediment-dwelling, and terrestrial organisms. For example, CNTs without functionalizing surfactants are hydrophobic and will interact with other CNTs and organic matter in aquatic systems, resulting in stable suspensions and bundling followed by sedimentation (Koelmans et al., 2009; Hyung et al., 2007). Stable suspensions and settling allow for exposure of both water-column and benthic organisms to MWCNTs in aquatic systems (Velzeboer et al., 2011).

Properties of the environmental media also can influence exposure potential for MWCNTs by affecting bioavailability and MWCNT form. For example, the presence of dissolved organic matter in an aquatic system can cause MWCNTs to debundle. Bacterial studies have shown that debundling of MWCNTs can result in greater cytotoxicity (Kang et al., 2009). Changes in properties such as ionic strength or the pH of a solution might influence sorption behaviors of CNTs (Petersen et al., 2011a), which could differentially alter exposure levels of benthic and water-column organisms.

G.4.2.2. Absorption, Distribution, Metabolism and Excretion in Ecological Receptors

As discussed in Section 4.2.6, an understanding of absorption, distribution, metabolism and excretion (ADME) processes can be used to relate exposure concentrations to the concentration, or dose, of material that reaches the tissues of an organism. Elucidation of organism-specific ADME processes can help explain observations of high body burdens that were not predicted based on environmental fate and partitioning alone. ADME processes influence whether and for how long a material is retained in a tissue (i.e., whether the material will bioaccumulate) and how such retention rates might differ among trophic levels (i.e., whether concentrations of the material will biomagnify in a food web). Bioaccumulation and biomagnification have been shown to influence ecological exposures and might similarly influence uptake of, and exposure of ecological receptors to, MWCNTs.

Ecological receptors are likely to be exposed to MWCNTs through treated products or scraps and debris from products generated during end-of-life stages of the product life cycle (see Section 2.5). The materials released during these processes can contain components other than the contaminant of concern (e.g., textile material, glue, composite ingredients). As discussed at the beginning of Chapter 4 and throughout Section 4.2, studies are lacking on the matrix-bound state of MWCNTs and how exposure characteristics and dose implications differ for free versus matrix-bound forms. Like the situation with human exposures discussed in Section 4.2, exposure considerations for ecological receptors are informed by data on MWCNTs not embedded in a polymer matrix or associated with other product ingredients (e.g., textile fibers, coating ingredients). No data are currently available regarding leachability or environmental release of free MWCNTs from their source products in the environment.

Additional Information Highlight Box G1:
Uptake and Absorption in Aquatic Foodwebs

The bioavailability of MWCNTs in aquatic systems is greatly influenced by the extent of uptake and absorption across epithelial barriers of aquatic organisms. Uptake and absorption are in turn influenced by the aggregation or dispersal state of MWCNTs (see Section 3.1). Evidence to date for a variety of aquatic species does not indicate absorption of MWCNTs or SWCNTs across epithelial membranes (Petersen et al., 2011b). This evidence includes studies using surface-modified MWCNTs to enhance bioavailability by altering the octanol-water distribution behavior, yet greater bioaccumulation was not observed (Petersen et al., 2010). Similarly, MWCNTs surface modified with polyethyleneimine to increase their stability in solution did not result in increased bioaccumulation (Petersen et al., 2011a). As discussed in Section 6.3, understanding the likelihood of uptake and absorption across epithelial barriers informs the development of risk assessments and subsequent risk management decisions for MWCNTs in aquatic environments.

G.4.2.3. Exposure Pathways in Aquatic Systems

Information on ecological uptake pathways for MWCNTs in aquatic environments is limited, but existing studies indicate that some water-dwelling organisms can take up MWCNTs stabilized in organic

matter via absorption in the gut (Kennedy et al., 2008). Functionalization also could affect uptake by aquatic organisms by altering the binding between the MWCNTs and body tissues (Li and Huang, 2011).

Toxicokinetics and Body Burden in Aquatic Systems

Limited information is available on MWCNT ADME and body burdens in aquatic organisms. As mentioned in Section 3.3, CNTs are likely to attract lipophilic molecules in aqueous media (Wu et al., 2006), and association of MWCNTs with lipophilic molecules could affect uptake in aquatic ecosystems. One study exposed a species of water flea (*Ceriodaphnia dubia*) to MWCNTs stabilized in suspended natural organic matter and demonstrated that carbon materials can be present in the gut (Kennedy et al., 2008), suggesting that some water-dwelling organisms can take up MWCNTs. Surface functionalization by lipophilic molecules in the natural environment could further affect uptake by aquatic organisms by altering the binding between particles and body tissues (Li and Huang, 2011).

A few studies have shown that MWCNTs can be taken up by aquatic invertebrates, but are not bioaccumulated over time (Petersen et al., 2011a). For example, Peterson et al. (2010) determined tissue concentrations of MWCNTs in the freshwater sediment blackworm (*Lumbriculus variegatus*) exposed to MWCNTs via soil for 30 days. The authors calculated biota-sediment accumulation factors between 0.1 and 1, indicating that retention of MWCNTs by this species is approximately one-tenth the concentration in the sediment (Petersen et al., 2010). Although this suggests that MWCNTs will not continue to build up in the tissues of some aquatic invertebrates over time, the small concentrations in these species might be better retained by larger predator species, leading to net accumulation in those species through dietary sources. Additionally, suggestions have been made that current methods for measuring bioaccumulation and calculating bioconcentration factors are not sufficient for nanomaterials (Handy et al., 2012). These methods rely on an evenly dispersed aqueous solution of the compound that achieves a steady-state concentration between external media and biological tissues, which is potentially incompatible with the dynamic behavior of nanomaterials in environmental media and the challenges associated with dispersion of MWCNTs in particular. Further, traditional understanding of bioaccumulation assumes that the processes of uptake and elimination follow well-characterized kinetics and diffusive flux models, which are based on underlying biological mechanisms of solute transporter channels. Pathways of uptake and elimination for nanomaterials, including MWCNTs, are not well understood, and the degree to which the bioaccumulation pathways might differ from those of conventional materials is unclear (Handy et al., 2012).

Despite the lack of studies directly investigating uptake, absorption efficiency, and bioaccumulation of MWCNTs in aquatic food webs, the high persistence and hydrophobicity of MWCNTs are characteristics generally associated with bioaccumulative substances (Petersen et al., 2010;

Helland et al., 2007). Based on these characteristics alone, MWCNTs are expected to accumulate in aquatic food webs under some conditions. Which additional material, environmental, or biological characteristics determine whether and to what degree bioaccumulation occurs are unknown (Handy et al., 2012).

G.4.2.4. Exposure Pathways in Terrestrial Systems

Limited information is available regarding exposure pathways and ecological uptake of MWCNTs in terrestrial environments. As also discussed in Section 3.2, limited evidence exists that airborne MWCNTs can quickly (within approximately two weeks) transform to amorphous carbon (Zhu et al., 2011), thus limiting exposures to terrestrial organisms. Other data suggest that MWCNTs might stabilize in ambient conditions, however, which would serve to increase exposures (Yang et al., 2009). If MWCNTs are present in soils, plant roots could interact with those in soil or pore water (Navarro et al., 2008).

Toxicokinetics and Body Burden in Terrestrial Systems

Limited information is available on MWCNT ADME and body burdens in terrestrial organisms. MWCNTs present in soils could be absorbed or consumed by biota; MWCNTs taken up by plant roots and plant tissues also could be consumed. Few studies have attempted to measure tissue concentrations of MWCNTs in biota. One laboratory study was identified that determined tissue concentrations of MWCNTs in earthworms *(Eisenia foetida)* exposed to MWCNTs via soil for 30 days. The authors calculated biomagnification factors between 0.01 and 0.1, indicating that tissue concentrations of MWCNTs in this species is approximately 1/100th to 1/10th the concentration in the sediment (Petersen et al., 2010). In another study using ^{14}C-labeled pure MWCNTs and MWCNTs with various polyethyleneimine surface coatings, Petersen et al. (2011a) assessed the extent to which modified MWCNTs concentrate in earthworms. Results indicated that surface coating did not significantly affect MWCNT uptake or elimination rates over a 28-day period. The bioaccumulation factor remained less than 0.12 throughout the study regardless of MWCNT type (purified or modified with surface coatings), indicating that accumulation of MWCNTs from soil by earthworms is low (Petersen et al., 2011a). As discussed in Section G.4.2.1, past studies have speculated that the high persistence and hydrophobicity of MWCNTs are characteristics generally associated with bioaccumulative substances; however, recent studies have shown that MWCNTs do not behave like other bioaccumulative substances because altering the octanol-water distribution behavior does not change bioaccumulation factor values (Petersen et al., 2010; Helland et al., 2007). Also, the complexity of food web interactions that cross aquatic and terrestrial systems makes determining the source of MWCNTs in terrestrial food webs difficult.

G.5. Potential Human Health, Ecological, and Other Impacts

G.5.1. Ecological Effects

G.5.1.1. Terrestrial Receptors

Compared to other groups of organisms, a large amount of data was identified regarding toxicity of MWCNT to soil microbes and plants (see Sections G.5.1.1.1 and G.5.1.1.2). No information was identified for toxicity to terrestrial vertebrates (see Section G.5.1.1.3), but some assumptions can be made for mammals based on toxicity studies intended for human health purposes presented in Section 5.1.

Table G-3. Effects of decaBDE and MWCNTs on soil microbes and invertebrates.

	DecaBDE			MWCNTs		
Organism	Effect	Effect level	Citation	Effect	Effect level	Citation
Soil microbes	Acute NOEL	>2,274 mg/kg	Sverdrup et al. (2006)	Acute NOEL (*Cupriavidus metallidurans*)	>100 mg/L	Simon-Deckers et al. (2009)
				Acute LD_{50} (*Escherichia coli*)	100 mg/mL	Simon-Deckers et al. (2009)
	Chronic cytotoxicity LC_{50}	(6 months) 100 mg/kg	Liu et al. (2011a)	Chronic cytotoxicity NOEL; LOAEL	500 µg/gram 5,000 µg/gram	Chung et al. (2011)
Invertebrate worms	Acute NOEL *(Enchytraeus crypticus)*	>2,274 mg/kg	Sverdrup et al. (2006)	ND		
	Chronic NOEL *(Eisenia fetida)*	>4,910 mg/kg	ACC (2001) as cited in Environment Canada (2006)			
	Oxidative stress *(E. fetida)*	0.1–10 mg/kg	Xie et al. (2011)			

NOEL = No-observed-effect level, LD_{50} = Median lethal dose, LOAEL = Lowest-observed-effect level, ND = No data identified

G.5.1.1.1 Soil Microbes and Terrestrial Invertebrates

Changes in soil microbial activity result in changes to nutrient cycling; therefore, studying the impact of contaminants on soil microbes can provide insight on how those contaminants might affect ecosystem function (Chung et al., 2011). Similarly, effects on terrestrial invertebrates, such as worms, can influence health and fertility of a soil ecosystem (Xie et al., 2011). Table G-3 presents key toxicity values identified for the effects of MWCNTs on soil microbes and invertebrates. Parallel data for decaBDE are provided in the table for comparative purposes; more detailed information on decaBDE can be found in Appendix H and Appendix F, Table F-18. Appendix F (Table F-19) summarizes details of the MWCNT studies identified and reviewed for this section.

Multiple studies have shown that CNTs exhibit antimicrobial activity, suggesting that release of MWCNTs into soils might adversely affect soil microcosms. This possibility, however, has not yet been investigated outside of controlled lab experiments (Chung et al., 2011). A short, 1-hour exposure to low doses of MWCNTs (e.g., 5 µg/mL [5 ppm]) resulted in mortality rates of 20–50% in *Escherichia coli, Pseudomonas aeruginosa,* and *Staphylococcus epidermidis* cell cultures, which are 1.5–5 times higher than background mortality levels (Kang et al., 2009; Kang et al., 2008). An increase in exposure level or duration, however, does not drastically increase cytotoxicity, and species-specific responses vary. For example, exposure to 100 mg/mL (100,000 ppm) MWCNTs for 24 hours caused 50–60% cytotoxicity in *E. coli*, yet had no effect on *Cupriavidus metallidurans*, a more environmentally relevant bacterium (Simon-Deckers et al., 2009). In a chronic duration study (Chung et al., 2011), the authors showed that addition of MWCNTs at a high concentration of 5 mg/gram soil (5,000 ppm) resulted in an average of 34.2–60.5% decrease in microbial activity over 11 days; lower levels of MWCNTs (500 and 50 µg/gram [ppm]) did not cause significant cytotoxicity.

Additional Information Highlight Box G2:
Toxicity to Terrestrial Invertebrates

The impact of CNTs on terrestrial invertebrate reproduction, development, and survival has been studied in earthworms. Scott-Fordsmand et al. (2008) found that reproduction (i.e., cocoon production) of earthworms (*Eisenia veneta*) was affected by double-walled carbon nanotubes (DWCNT) administered in food at concentrations greater than 37 mg DWCNT/kg food. The authors found no effect of DWCNTs on earthworm hatchability or survival at up to 495 mg DWCNT/kg food. Uptake, bioaccumulation, and depuration—important considerations for predicting toxicity—have also been studied in earthworms. Petersen et al. (2008b) assessed uptake and depuration behaviors of MWCNTs in earthworms, determining bioaccumulation factors that indicated a lack of both absorption and equilibrium partitioning to tissues. Furthermore, absorption in earthworms was limited whether the MWCNTs were pristine or coated with polyethyleneimine (PEI), with little apparent difference in uptake among different types of MWCNTs (Petersen et al., 2011a). While these studies show limited uptake or absorption, which hint toward limited target tissue-level exposure and limited toxicity, no studies have been identified that were specifically focused on toxicity to terrestrial invertebrates.

G.5.1.1.2 Terrestrial Plants

Table G-4 describes key toxicity values identified for the effects MWCNTs on terrestrial plants. Parallel data for decaBDE are provided in the table for comparative purposes; more detailed information on decaBDE can be found in Appendix H and Appendix F, Table F-18. Appendix F (Table F-20) summarizes details of the MWCNT studies identified and reviewed for this section.

Table G-4. Effects of decaBDE and MWCNTs on plants.

	DecaBDE			MWCNTs		
Endpoint	Organism	Effect level	Citation	Organism	Effect level	Citation
Germination NOEL	Corn		Great Lakes Chemical Corporation (2000a)	Corn, rapeseed, radish, ryegrass, lettuce, cucumber	>2,000 mg/L	Lin and Xing (2007)
	Red clover	>2,274 mg/kg	Sverdrup et al. (2006)	Brown mustard, blackgram	>40 µg/mL	Ghodake et al. (2010)
				Garden cress	0.01% w/w	Oleszczuk et al. (2011)
Germination LOAEL	ND			Garden cress	0.1% w/w	Oleszczuk et al. (2011)
Root growth NOAEL	ND			Corn, rapeseed, radish, ryegrass, lettuce, cucumber	>2,000 mg/L	Lin and Xing (2007)
				Thale cress	>10 mg/L	Lin et al. (2009a)
Root growth LOAEL	ND			Garden cress	0.01% w/w	Oleszczuk et al. (2011)
Shoot height LOAEL	Corn	penta/tetraBDE mix: 250 mg/kg	Great Lakes Chemical Corporation (2000a)	ND		

ND = No data identified, w/w = weight-for-weight measurement, NOEL = No-observed-effect level, NOAEL = No-observed-adverse-effect level, LOAEL = Lowest observed adverse effect level

Both beneficial and detrimental effects of nanoparticle exposures have been reported for plants. For example, Khodakovskaya et al. (2011)) have demonstrated positive effects on seed germination and plant growth from MWCNT exposure. Other studies with MWCNTs, however, have implied that exposure to high levels could have negative effects on seed germination and plant growth, as several studies show trends and a few show statistically significant impacts. For example, Lin and Xing (2007) showed that exposure to MWCNTs with diameters 10–20 nm at a concentration of 2,000 mg/L caused no significant

differences in germination rates or root length for six different agriculturally relevant plant species, although a nonstatistically significant decrease in germination was observed in four of the species (Lin and Xing, 2007). Conversely, Oleszczuk et al. (2011) found that MWCNTs added to sewage sludge[26] at concentrations of 0.01, 0.1, and 0.5% weight-for-weight significantly inhibited garden cress (*Lepidium sativum*) seed germination. The authors observed diameter-dependent responses, as root growth was inhibited at all three concentrations for the smaller diameter MWCNTs but was not affected at any concentration for the larger diameter MWCNTs (Oleszczuk et al., 2011) (see Text Box 5-1). Finally, no physical injury to cell morphology was observed in thale cress (*Arabidopsis thaliana*) cell suspensions exposed to 10 mg/L MWCNTs, but significant loss in cell viability and growth and chlorophyll inhibition were observed after 7 days of exposure. Cytotoxicity was more severe following exposure to fine, small bundles than to loose, large bundles of MWCNTs (Lin et al., 2009a), indicating that dispersion state could play a role in toxicity (see Text Box 5-1 and Appendix F, Table F-20).

A study by Tan and Fugetsu (2007) provides some insight on the mechanism through which MWCNT exposure affects plant growth and the ecological relevance of the trend described above. Cultures of rice cells in an embryonic growth stage formed large associations with MWCNT; the cells that interacted with the MWCNTs experienced high cell death. Only some cells within the culture associated with the MWCNTs, however, and clumps formed by this initial subset of the cells in the culture continued to attract other MWCNTs, forming larger associations over the course of the 4-day exposure period. Cells that did not form these associations with MWCNTs were not adversely affected by the MWCNTs as exposure continued. The authors stated that their results illustrate how some plants might be able to tolerate low levels of MWCNTs without major population-level effects due to a self-defense response (Tan and Fugetsu, 2007).

Ghosh et al. (2011) illustrated clastogenicity in *Allium cepa* (onion) bulbs exposed to 0, 10, 20, and 50 µg/mL MWCNTs using traditional cell culture tests. Chromosomal aberrations, DNA cross-linking, and induction of apoptosis led authors to conclude that MWCNTs might have a significant impact on genomic activities of plants.

G.5.1.1.3 Terrestrial Vertebrates

The impacts of oral exposure to MWCNTs on mammals are uncertain (see Section 5.1). Testing performed in mammals for relevance to humans has focused on inhalation exposure routes; acute inhalation studies have found that MWCNTs or associated contaminants can induce oxidative stress,

[26]Sewage sludge samples, collected from four municipal industrial sewage treatment plants, were analyzed and reported to contain heavy metals (e.g., Pb, Cr, Cd, Cu, Ni) and polycyclic aromatic hydrocarbons.

pulmonary inflammation, and fibrosis. MWCNTs might cause slight skin and eye irritation. No studies were identified that specifically investigated the ecological effects of MWCNTs on terrestrial vertebrates.

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Appendix H. Compilation of CEA Framework Data for DecaBDE

Appendix H. Compilation of CEA Framework Data for DecaBDE

Chapter 2 through Chapter 5, and Appendix G, present information on multiwalled carbon nanotubes (MWCNTs) in a comprehensive environmental assessment (CEA) framework. This appendix contains detailed, parallel information on decabromodiphenyl ether (decaBDE). As noted in Chapter 1, Chapter 2 through Chapter 5, and Appendix G, also contain text boxes that highlight information about decaBDE and tables and figures with side-by-side comparisons of decaBDE and MWCNT data. These elements provide a highlight-level comparison between the two compounds as used in flame-retardant textiles to illustrate key concepts that might be helpful to risk assessors evaluating MWCNTs. Supplemental details about decaBDE are provided in this appendix, to provide more in-depth data for comparison for each CEA framework element. With the exception of Section H.1, the section numbers of this appendix are parallel to corresponding sections of the MWCNT CEA framework presented in Chapter 2 through Chapter 5. Section H.1 provides an introduction to decaBDE, which is identical to the introduction provided in Section 1.3.1of the main text. It is repeated here to remind readers of the introductory details regarding physical and chemical properties of decaBDE that set the stage for understanding the remainder of this appendix.

H.1. Introduction to DecaBDE

DecaBDE is part of a larger group of brominated flame retardants (BFRs) called polybrominated diphenyl ethers (PBDEs), a group of 209 structurally similar BFRs that differ in the number and location of bromine atoms (Table G-1) (Rahman et al., 2001; NRC, 2000). Although PBDEs are typically categorized into classes by number of bromine atoms (e.g., PBDE with two bromine atoms is a diBDE; ten bromine atoms is a decaBDE), a single class might contain several different PBDE congeners with the same number of bromine atoms in different locations (i.e., PBDE BFRs can have many isomers). As the only fully brominated PBDE, decaBDE is the exception, existing only as a single congener (BDE-209).

Table H-1. Major PBDE congeners.

PBDE Class	Congeners
DiBDE	BDE-7, BDE-8, BDE-11, BDE-12, BDE-13, BDE-15
TriBDE	BDE-17, BDE-25, BDE-28, BDE-30, BDE-32, BDE-33, BDE-35, BDE-37
TetraBDE	BDE-47, BDE-49, BDE-66, BDE-71, BDE-75, BDE-77
PentaBDE	BDE-85, BDE-99, BDE-100, BDE-105, BDE-116, BDE-118, BDE-119, BDE-126, BDE-138, BDE-140
HexaBDE	BDE-153, BDE-154, BDE-155, BDE-166
HeptaBDE	BDE-181, BDE-183, BDE-190
OctaBDE	BDE-196, BDE-197, BDE-203
NonaBDE	BDE-206, BDE-207, BDE-208
DecaBDE	BDE-209

Source: U.S. EPA (2010a).

Commercial formulations of decaBDE (see Table H-2) are generally 97–98% BDE-209 with less than 3% nonaBDE congeners present as impurities (Rahman et al., 2001; NRC, 2000) (see Appendix B, Table B-1 for analytical techniques used to distinguish PBDE congeners in samples). Although the terms decaBDE and BDE-209 often are used interchangeably, this case study primarily uses the term decaBDE to refer generally to the flame-retardant formulation and BDE-209 to refer to the specific decaBDE congener analyzed in scientific studies.

DecaBDE is the most widely used of the PBDEs and has been well studied. In 2001, decaBDE use accounted for 83% of total PBDE production worldwide (U.S. EPA, 2010a); an estimated 10–20% of decaBDE use is in the textile industry (Pure Strategies Inc., 2005). At the end of 2004, both octa- and pentaBDE were voluntarily withdrawn from the U.S. marketplace due to evidence of environmental persistence and toxicity, which left decaBDE as the sole PBDE available for use in commercial products in the United States (U.S. EPA, 2010a). Several standard physicochemical properties are used to describe traditional chemicals: melting point, boiling point, molecular weight, and others. Such values are presented for decaBDE in Table H-3.

Table H-2. Commercial formulations of PBDEs used as flame retardants.

Name	Congener Makeup and Percent Composition	
Penta formulation[1]	Tetra	BDE-47 (25–37%)
	Penta	BDE-99 (35–50%), BDE-100 (6–10%)
	Hexa	BDE-153 (5–10%), BDE-154 (1–5%)
Octa formulation	Hexa	BDE-153 (5–10%), BDE-154 (1–5%)
	Hepta	BDE-183 (40%)
	Octa	BDE-197 (21%), BDE-203 (5–35%), BDE-196 (8%)
	Nona	BDE-208 (10%), BDE-207 (7%)
Deca formulation[2]	Nona	BDE-206 (2.2%), BDE-207 (0.24%), BDE-208 (0.06%)
	Deca	BDE-209 (>97%)

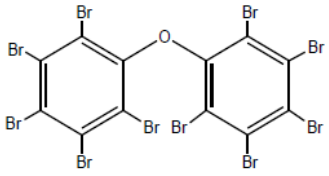
[1]Trace amounts of additional congeners might be present in commercial formulations: <0.2% triBDE congeners.

[2]Trace amounts of additional congeners might be present in commercial formulations: <0.003% heptaBDE congeners; <0.001% hexaBDE congeners; <0.002% pentaBDE congeners; <0.00003% tetraBDE congeners; <0.00001% triBDE congeners.

Source: U.S. EPA (2010a).

DecaBDE can be applied to textiles by a variety of mechanisms, but this case study focuses on the application of decaBDE as a back-coating. This application method is used most frequently for decaBDE (Pure Strategies Inc., 2005; NRC, 2000) and is most similar to the application method expected for MWCNTs used in textiles (see Section 1.3.2). The back-coating process usually involves mixing decaBDE with a copolymer or resin binder to comply with fire safety standards (Pure Strategies Inc., 2005; NRC, 2000). DecaBDE combines the flame-retardant mechanism of most BFRs (releasing halogens during combustion to compete with the availability of oxygen for the flame) with formation of a protective char barrier (NRC, 2000) that interferes with the spread of the flame and helps the material to self-extinguish (Pure Strategies Inc., 2005).

Table H-3. Physical properties and chemical identity of decaBDE.

	Physical property/chemical identity	Reference
CASRN	1163-19-5	NLM (2011)
Synonyms	2,2',3,3',4,4',5,5',6,6'-decaBDE; BDE-209; benzene, 1,1'-oxybis[2,3,4,5,6,-pentabromo]-; decabromodiphenyl oxide; decabromodiphenyl ether; decabromobiphenyl ether; ether, bis(pentabromophenyl)	NLM (2011); ATSDR (2004)
Physical state	Solid	Hardy (2002b)
Melting point,	300–310 °C	ECB (2003)
Boiling point	Decomposes at >320 °C	ECB (2003)
Vapor pressure	4.63×10^{-6} Pa at 21 °C	Hardy (2002b)
Henry's law constant	1.93×10^{-8} L atm/mol 0.04 Pa m^3/mol at 25 °C	Hardy (2002b); Cetin and Odabasi (2005)
Density	3.0 grams/cm^3	NRC (2000)
Water solubility	<0.1 µg/L at 25 °C	Hardy (2002b); ECB (2003)
Log K_{ow}	6.3–12.6	Hardy (2002b)
Log K_{oc}	6.3	Hardy (2002b)
Molecular weight	959.17	NLM (2011); ECB (2003)
Chemical formula	$C_{12}Br_{10}O$	NLM (2011)
Chemical structure		

Note: K_{ow} = Octanol/water partition coefficient, K_{oc} = Soil organic carbon/water partition coefficient.

H.2. Product Life Cycle

A product's life cycle encompasses all stages of its existence from "cradle to grave," starting with the extraction of raw materials from the earth for the manufacture of the product and continuing downstream until these materials are returned to the environment following disposal (U.S. EPA, 2006).

The components of the life cycle determine the potential for releases and possible impacts on human health, ecological populations, and the environment (Som et al., 2011), which can be evaluated systematically within the CEA framework. Potential environmental impacts of a product throughout its life cycle can be estimated using a life-cycle assessment (LCA) approach, which involves four steps: goal definition and scope, inventory analysis, impact analysis, and interpretation (U.S. EPA, 2006). The CEA

approach incorporates information from available LCAs in the "product life cycle" and "impacts" portions of the CEA framework and combines this knowledge with other analyses or qualitative indicators related to transport, transformation, and fate, exposure-dose, and additional impacts not considered in available LCAs. As discussed in Chapter 1, if a plausible reason exists to include an impact in the CEA framework, qualitative or quantitative information on that effect can be included from LCAs or other sources (if an LCA has not been completed) to evaluate that particular impact.

A generalized depiction of the life cycle for decaBDE and MWCNT coatings used to confer flame-retardant properties to upholstery textiles is presented in Chapter 2, in Figure 2-1. That figure illustrates the life cycle of these materials as five main stages: (1) acquisition and processing of feedstocks; (2) manufacturing, including research and development (R&D) processes; (3) storage and distribution; (4) use; and (5) end-of-life processes (including disposal, reuse, and recycling). These stages correspond roughly to the four primary life-cycle stages the U.S. Environmental Protection Agency (U.S. EPA, 2006) outlines: (1) raw materials acquisition, (2) manufacturing, (3) use/reuse/maintenance (with storage and distribution discussed as a distinct stage in this case study), and (4) recycle/waste management. As mentioned in Chapter 1, R&D is included in the product life-cycle portion of the CEA framework, given its importance regarding emerging materials such as MWCNTs. For such materials, R&D efforts can elucidate potential risks associated with commercial-scale manufacturing. In fact, because it often takes place when health and safety information is being developed for a material, R&D presents an ideal opportunity to gather data on a product's potential impacts and to make design adjustments if appropriate. Similarly, as discussed below, differences between R&D activities and the commercial manufacturing process (e.g., use of protective equipment, volume of material produced) could be important considerations in mitigating potential risks to individuals involved in R&D versus commercial manufacturing.

To conduct a comparative CEA, relevant information on life-cycle inventories from existing LCAs would be incorporated into the product life cycle to characterize the inputs (e.g., raw materials, energy) and outputs (e.g., emissions to air and water, co-products) associated with each material's manufacture. Impacts information from existing LCAs also would be considered (see Section H.5). Other LCA aspects also might apply, including using an appropriate functional unit, which is a quantitative measure of a product's function or a process that facilitates comparison (U.S. EPA, 2006). In the current case study, a functional unit might correspond to the degree of flame retardancy conveyed by incorporation of a certain amount of decaBDE. In general, for this case study, data that specify appropriate functional units were not identified; the reader might, however, consider how this aspect of existing or future LCAs could be incorporated into a future CEA when evaluating data gaps and needs.

This section outlines important aspects of each of the five life-cycle stages outlined in Figure 2-1 (in Chapter 2) for decaBDE used in upholstery textiles. This section also includes descriptions of the important environmental release scenarios for decaBDE and MWCNTs across the product life-cycle stages based on current knowledge. A variety of release scenarios are possible throughout the life-cycle stages described in this appendix. Figure 2-1 (in Chapter 2) also outlines potential release scenarios for decaBDE flame-retardant upholstery textile coatings throughout the life cycle along with potential forms of the released substances (i.e., free, bundled, or matrix bound). The term "free decaBDE" refers to pure, unbound materials. The term "matrix-bound decaBDE" refers to materials that are part of a polymer matrix (e.g., the flame-retardant formulation).

H.2.1. Feedstocks

H.2.1.1. Life-Cycle Processes

The raw materials used in commercial synthesis of decaBDE are phenol, bromine, and a catalyst (e.g., aluminum bromide or iron) (IPCS, 1994). Phenol is produced from cumene, which is obtained primarily from the distillation or other processing of petroleum products (Mahapatra, 2010). Commercial production of bromine involves the drying of brine, typically obtained from sea water (Kesner, 2005). No data were found on the energy and resource demands of raw material extraction for synthesis of decaBDE.

H.2.1.2. Potential Releases during the Feedstock Extraction Stage

Release of decaBDE would not occur during this initial phase of the life cycle given that its synthesis does not occur until the stage that follows extraction. Release of hazardous raw materials, however, could occur during the extraction and processing of feedstock materials. Release of decaBDE also could occur if reactors are not cleaned between runs. Specific materials that could be released include petroleum-based chemicals. No data were identified quantifying the potential volume of releases during feedstock extraction for decaBDE.

H.2.2. Manufacturing

The manufacturing stage for decaBDE flame-retardant upholstery can be viewed as a sequential process involving synthesis of decaBDE, material processing, and product manufacture (i.e., formulation of the flame-retardant mixture, application of the flame-retardant mixture to textiles, and incorporation of

the flame-retardant textile into consumer or commercial goods). Discussion of R&D also is included in this section, given the similarities to key aspects of synthesis, processing, and manufacture.

H.2.2.1. Research and Development

H.2.2.1.1 Life-Cycle Processes

Research on decaBDE and on flame-retardant coatings involving decaBDE is principally conducted in specialized laboratory environments. R&D activities are expected to be carried out by individuals rather than automated mechanisms used in commercial-scale manufacture. The processes of interest to researchers are similar to those used in commercial-scale manufacture of these materials: synthesis, purification, modification, dispersion, incorporation into flame-retardant formulations, and application to textiles. Substantially less R&D related to decaBDE flame retardants is expected to occur at the present time compared to MWCNT flame retardants, given that decaBDE flame-retardant technologies are more mature and the use of decaBDE is decreasing or being phased out due to health and ecological concerns. The following sections (material synthesis, material processing, and product manufacturing) provide detailed information on the processes of potential interest for R&D.

H.2.2.1.2 Potential Releases during the R&D Stage

Release scenarios during the R&D stage are expected to be similar to release scenarios from commercial synthesis described in the following sections, but the quantities released are anticipated to be much smaller in the R&D stage. The quantities of decaBDE handled in research laboratories are much smaller than those handled in commercial-scale manufacturing facilities. Although R&D activities are typically carried out in laboratories with specialized pollution control systems in place, including fume hoods, ventilation systems, and environmental control systems, not all facilities have standardized engineering controls. For example, these practices might not be in place for small start-up operations. Given the experimental and somewhat unpredictable nature of R&D, releases from handling of materials during synthesis, processing and purification, storage, and analysis are possible.

No information was found in the literature that describes release of decaBDE from R&D facilities. No data were found that describe how releases in academic labs compare with releases in commercial R&D labs.

H.2.2.2. Material Synthesis

H.2.2.2.1 Life-Cycle Processes

Commercial synthesis of decaBDE involves conversion of phenol to diphenyl ether via the Williamson ether synthesis [Kirk Othmer (2005) as cited in Wright et al. (2008)]. Diphenyl ether is then brominated in the presence of a catalyst (generally, aluminum bromide or iron) to produce commercial decaBDE (EU, 2002; IPCS, 1994). Commercially, decaBDE is synthesized in a batch process in enclosed vessels during both the reaction and the subsequent drying process (IPCS, 1994). DecaBDE powder is collected in bags during the recovery phase following the synthesis process (EU, 2002). Commercial formulations of decaBDE typically contain decaBDE, 97–98% weight-for-weight measurement, and other PBDEs (primarily nonaBDE), 0.3–3.0% weight-for-weight measurement (IPCS, 1994). No information was found on by-products of decaBDE synthesis.

H.2.2.2.2 Potential Releases during the Material Synthesis Stage

Synthesis of decaBDE could result in releases to air or water (U.S. EPA, 2005a). Fugitive releases of decaBDE vapor from a reactor vessel have been estimated as 1.1×10^{-5} mg/ton, and release from the bagging of synthesized PBDEs have been estimated as <70 grams/ton PBDE produced [(EU, 2002); EEC (1993) as cited in EU (2002)]. Airborne releases of decaBDE particles likely would sorb to dust (see Section 3.2), but loose dust likely would be vacuumed and the area would be washed with water, reducing airborne particles (EU, 2002). The main source of water release of decaBDE during the synthesis stage would be due to cleaning of equipment and floors after synthesis. One study found, however, that wastewater releases of decaBDE are unlikely to exceed 0.5 kg/ton if equipment is washed after every batch (EU, 2002). Releases directly to skin could occur through handling of bags containing solid decaBDE (U.S. EPA, 2005a). Large manufacturing facilities, however, likely would have exhaust ventilation in place to minimize air release into the general environment. Engineering controls that regulate temperature and pressure to minimize the potential for release also would likely be in place (U.S. EPA, 2005a). As a result, air and water releases of decaBDE to the environment during the synthesis stage are not expected to be large.

Accidental releases through fugitive equipment leaks, malfunctioning ventilation systems, and exposure to fire or high heat could occur at all stages of manufacturing (material synthesis, material processing, and product manufacture). A fugitive equipment leak or ventilation malfunction could lead to the airborne releases of decaBDE, as could exposure to fire or high heat. If exposed to high heat, decaBDE can form polybrominated dibenzofurans (PBDFs), polychlorinated dibenzo-p-dioxins, and nonhalogenated substances such as polycyclic aromatic compounds, which could be released into the

environment (EU, 2002). Such accidental events could result in larger releases of decaBDE to the environment than normal release scenarios due to the lack of control mechanisms compared to those in place to mitigate anticipated releases. Table 2-3 in Chapter 2 summarizes the anticipated potential release scenarios from the material synthesis stage of decaBDE and MWCNTs.

H.2.2.3. Material Processing

H.2.2.3.1 Life-Cycle Processes

Material processing includes any modification of decaBDE after synthesis and before incorporation into a flame-retardant formulation. These modifications can include purification, functionalization, and dispersal in solvents. After synthesis, decaBDE does not require further processing before incorporation into the flame-retardant formulation.

H.2.2.3.2 Potential Releases from the Material Processing Stage

No release scenarios for decaBDE are summarized here because the activities specified for this stage are not anticipated to occur for decaBDE.

H.2.2.4. Product Manufacturing

In this section, product manufacturing for decaBDE is described. This life-cycle stage is considered to include the manufacture of flame-retardant formulations, the manufacture of textiles containing decaBDE-based flame retardants, and the manufacture of end-use products containing flame-retardant materials, such as furniture.

H.2.2.4.1 Life-Cycle Processes

In a typical decaBDE flame-retardant formulation, decaBDE and antimony trioxide (a synergist used to enhance the activity of decaBDE) are first mixed as a dispersion in water (EU, 2002). This mix is stored in tanks and then piped directly into a closed vessel (EU, 2002). The decaBDE-antimony trioxide-water dispersion is added to emulsion polymers and mixed in this closed vessel to formulate the flame retardant (EU, 2002). One analysis found trace amounts of polybrominated dibenzo-p-dioxins (PBDDs) and PBDFs as impurities in commercial mixtures of decaBDE (Ren et al., 2011). No data were found that describe other characteristics of decaBDE flame-retardant formulations or the by-products of their manufacture.

During application, the decaBDE flame-retardant formulation is typically back-coated, or applied as a resin to the reverse surface of textiles along with a binding agent, such as latex or a copolymer (see

Section 1.2.2.2). Due to the high efficiency of decaBDE flame retardants, they can be used in formulations with low loadings compared to other brominated flame retardants (Pure Strategies Inc., 2005). Typical loadings of decaBDE in textiles range from 30 to 40% by dry weight of the dry coating with different loadings applied to different types of fabrics (30–40 grams/m^3 in cotton to 70–80 grams/m^3 for velour fabrics) (EU, 2002). After application, the decaBDE flame-retardant upholstery textile is cut, shaped, and glued or stapled to furniture.

H.2.2.4.2 Potential Releases during Product Manufacture

Release scenarios for product manufacturing are likely to be similar to those in the material synthesis and processing stages, but release amounts are probably lower (U.S. EPA, 2005a; EU, 2002). Additionally, releases from this stage likely will not be decaBDE, but rather decaBDE in a polymer matrix. As discussed, decaBDE generally is synthesized as a powder and then mixed into solution when the flame retardant is formulated, minimizing releases of decaBDE to dust (U.S. EPA, 2005a). Nevertheless, manufacture of decaBDE flame-retardant coatings could release vapors if mixing and handling of raw decaBDE occurs in an open system (U.S. EPA, 2005a). One study found that environmental release was most likely to occur during the mixing of decaBDE powder and cleaning operations of the flame-retardant formulation stage (EU, 2002). Formulation of flame retardants, however, generally occurs in closed systems with engineering controls that regulate temperature and pressure to minimize potential releases (U.S. EPA, 2005a; EU, 2002). Releases of decaBDE in this stage also can contain the impurities listed in Section H.2.2.4.1.

The application of decaBDE flame-retardant coatings to upholstery textiles could result in the release of aerosolized decaBDE due to thermal processing, but release would occur only if the manufacturing plant does not have engineering controls in place to prevent such releases. Cutting, sewing, shaping, stapling, and other textile finishing processes could result in the airborne release of free decaBDE or decaBDE in a polymer matrix through abrasion. Equipment cleaning also could lead to the release of decaBDE in wastewater during the processing stages of product manufacture.

The accidental release scenarios for decaBDE during product manufacture are similar to those in the material synthesis stage (see Section H.2.2.2.2). Additionally, in this stage, spills could lead to release of decaBDE flame-retardant formulations in wastewater. Volatilization is unlikely due to the low volatility of decaBDE (see Table H-3). Table 2-6 in Chapter 2 outlines potential release scenarios from the product manufacturing stage of decaBDE and MWCNT flame-retardant textiles.

H.2.3. Storage and Distribution

H.2.3.1. Life-Cycle Processes

The storage and distribution stage concerns the handling and transport of (1) decaBDE, (2) decaBDE flame-retardant formulations, and (3) decaBDE flame-retardant upholstery textiles. The main method of transport for these materials is not known, but likely would be by truck, train, or cargo ship.

DecaBDE, if not immediately incorporated into a flame-retardant formulation, likely would be stored at the site of synthesis/processing in sealed receptacles until it is incorporated into flame-retardant formulations or transported to sites where manufacture of the flame retardant occurs.

DecaBDE flame-retardant formulations are typically stored at manufacturing plants in drums, tanks, or more permanent storage vessels until they are packaged and sent to textile manufacturers (U.S. EPA, 2005a).

DecaBDE flame-retardant upholstery textiles and end-use products likely also would be stored at the site of manufacture (or an intermediate storage site) and then transported to retail locations.

H.2.3.2. Potential Releases during Storage and Distribution

Storage and distribution of (1) decaBDE, (2) decaBDE flame-retardant formulations, and (3) flame-retardant textiles could result in releases to the environment, but all release scenarios are unlikely.

Releases of decaBDE separate from flame-retardant formulations are likely to be negligible. Release would be due primarily to accidents, as the materials would be stored in sealed receptacles after synthesis. Exposure of the receptacles to high heat or fire could lead to the airborne release of decaBDE (see Section H.2.2.2.2 for more details).

Releases from flame-retardant formulations could result in releases of decaBDE to the environment (U.S. EPA, 2005a). The possible scenarios for release of decaBDE flame-retardant formulations during storage and distribution include damage to containers holding the flame-retardant formulation, leakage resulting from mishandling of containers, or faulty or improper stacking of cartons in transport vehicles. If the containers are sealed properly and not damaged during transport, releases of product prior to application might be limited to spills.

Releases from flame-retardant upholstery textiles could result from accidental exposure to high heat or fire, off-gassing of volatile components, and infestation with pests. Exposure of the flame-retardant upholstery textiles to high heat or fire during storage and distribution could lead to the

degradation of the polymer matrix and subsequent airborne release of decaBDE (both free and matrix bound) (see Sections H.2.2.2.2 and H.2.4 for more details). Off-gassing of the volatile components of decaBDE flame retardants also could occur in poorly ventilated areas that experience high temperatures (e.g., storage units, warehouses). DecaBDE itself, however, is not highly volatile (see Table 1-8 and Table 1-9, both in Chapter 1; and Table 3-1, in Chapter 3). Infestation of textile or furniture storage facilities with rodents or other pests also could lead to the release of decaBDE flame=retardant materials to the environment.

Table 2-7 in Chapter 2 outlines potential release scenarios from the storage and distribution stage of (1) decaBDE and MWCNTs, (2) decaBDE and MWCNT flame-retardant formulations, and (3) decaBDE and MWCNT flame-retardant upholstery textiles.

H.2.4. Use

H.2.4.1. Life-Cycle Processes

A wide variety of textiles contain flame-retardant coatings (see Section 1.2). Upholstery textiles are expected to be used in public places where people of all ages will sit, lie, or walk on them. Some unintended uses of upholstery textiles include outdoor use, repurposing for use in other products, burning as kindling, or mouthing by children. Repurposing for use in other products and burning as kindling are covered in Section H.2.5. In general, upholstery textiles are likely to have a lifespan of at least 10 years (EU, 2002).

H.2.4.2. Potential Releases during the Use Stage

Environmental releases from upholstery textiles coated with flame retardants are expected due to (1) the potential use scenarios for the upholstery textiles and (2) the physicochemical properties of decaBDE. The anticipated long lifespan of upholstery textiles (>10 years) suggests that releases in this stage could occur over several years (EU, 2002). Indeed, environmental concentrations of decaBDE in buildings with products containing decaBDE can be high, especially in dust (see Sections H.4.1.2.5 and H.4.1.2.6). One of the most important pathways for these high environmental concentrations is the airborne release of decaBDE sorbed to dust in the environment (see Section H.3.2). The following characteristics of flame-retardant upholstery textiles, however, are expected to reduce releases of decaBDE (EU, 2002):

- Flame-retardant coatings must meet durability requirements to comply with regulations (see Section 1.2.1);

- Flame retardant often is applied to the back of the fabric, minimizing wear and tear; and
- Upholstery textiles are unlikely to be washed frequently.

The integrity of the flame-retardant coating depends on the strength of the formulation that bonds it to the textile surface (Som et al., 2011; NRC, 2000). The decaBDE flame-retardant textile coatings considered in this case study are additive, suggesting that release from upholstery textiles could occur during the use stage. DecaBDE/antimony trioxide flame-retardant formulations are considered relatively durable, however, due to the copolymer resin that bonds to the textile fibers (Pure Strategies Inc., 2005). Even if migration of decaBDE through the polymer were to occur, it would be expected to be very slow due to the high molecular weight of decaBDE (Lassen et al., 1999). In a substance flow analysis of plastics containing decaBDE, however, Lassen et al. (1999) found that release of decaBDE was expected to be greatest during the use stage.

Regular use of upholstered furniture (e.g., sitting, walking, lying) could abrade the textile surface and release small amounts of free or matrix-bound decaBDE either into the air or onto the skin of users. Washing of textiles also could lead to water release of matrix-bound decaBDE. By some estimates, the principal source of decaBDE release in wastewater is due to textile washing (EU, 2002). Most flame-retardant upholstery textiles will be used indoors, minimizing exposure to UV light and weathering. Upholstery textiles that are back-coated with decaBDE flame retardant likely will not be subject to significant abrasion, washing, or UV light. Additionally, most releases of decaBDE initially will be to the indoor environment, but they could spread outdoors through environmental transport mechanisms (see Section H.3) (U.S. EPA, 2010a; Lassen et al., 1999). These processes could result in airborne release of decaBDE or releases in wastewater (U.S. EPA, 2010a).

Unintended uses also could lead to the release of decaBDE from flame-retardant textiles. Use of flame-retardant upholstery textiles outdoors could lead to weathering, which could degrade the polymer matrix and release decaBDE. Mouthing by small children, pets, or rodents on flame-retardant textiles could lead to the release of decaBDE directly into children's, pets', or rodents' mouths if the back-coating is exposed and the integrity of the fabric is compromised. Accidental contact of flame-retardant textiles with fire and high heat also could occur and could lead to airborne releases of decaBDE (see Section H.2.2.2.2] for more details). No data were found, however, that describe the likelihood of these releases from this application. Table 2-8 in Chapter 2 outlines potential release scenarios from the use stage of decaBDE and MWCNT flame-retardant textiles.

H.2.5. Reuse, Recycling, and End of Life

The reuse, recycling, and end-of-life stage encompasses a variety of different transformation and disposal processes for (1) decaBDE, (2) decaBDE flame-retardant formulations, and (3) decaBDE flame-retardant upholstery textiles. What the primary reuse, recycling, and end-of-life treatments are for decaBDE and decaBDE flame-retardant formulations are unclear.

H.2.5.1. Reuse and Recycling

H.2.5.1.1 Life-Cycle Processes

Reuse or recycling of decaBDE or decaBDE flame-retardant formulations is unlikely. On the other hand, textile waste often is recovered and reused or recycled (Köhler et al., 2008); upholstered furniture is sometimes reused, but is rarely recycled (CalRecycle, 2002). Upholstery could be donated to charitable organizations and resold for residential use. Additionally, upholstery textiles could be informally repurposed into clothing, blankets, and other textile products. Due to the difficulty of recycling furniture and flame-retardant materials, flame-retardant furniture is typically land-filled (CalRecycle, 2002; Lassen et al., 1999). Of the small portion of upholstered furniture that is recycled, about 60% of the material is recycled and 25–30% is composted (CalRecycle, 2002). No data were found that describe the proportion of other upholstery textiles (e.g., mattress ticking or curtains) that are typically recycled.

The main types of textile recycling processes are fiber-to-fiber recycling and polymer reduction recycling. During the fiber-to-fiber process, textiles are shredded and blended with other fibers to create a new mixture ready for spinning (Köhler et al., 2008). During the polymer reduction process, textiles are cut and granulated to form pellets that are processed to break down the polymer to the molecular level to be reused as raw material (Köhler et al., 2008). No data were found that describe the prevalence of each recycling process.

H.2.5.1.2 Potential Releases during the Reuse/Recycling Stage

Release of decaBDE beyond releases described in the use stage is unlikely to occur during reuse of flame-retardant upholstery textiles. Older textiles could release greater levels of decaBDE, however, due to increased degradation of the material. Informal repurposing of flame-retardant textiles likely would require cutting and shredding, resulting in possible air release of decaBDE. Airborne releases of decaBDE could occur during recycling of flame-retardant textiles. Recycling subjects textiles to a variety of mechanical, thermal, and chemical treatments that could result in the airborne releases of additive flame retardants from fibers (Köhler et al., 2008). One analysis found airborne releases of decaBDE at a plastic recycling plant with the highest concentrations of airborne particles measured near the shredder (Sjödin et

al., 2001). Although releases from recycling of upholstery textiles containing decaBDE flame retardant might be similar to those of plastics, the processing of plastics is likely to differ from that of textiles. Release of decaBDE to water also could occur during chemical treatment and processing. Although release of decaBDE is possible during recycling of flame-retardant textiles, no data were found that indicate the likelihood of release from recycling processes.

Table 2-9 in Chapter 2 outlines potential release scenarios from the reuse/recycling stage of decaBDE and MWCNT flame-retardant textiles.

H.2.5.2. Incineration

H.2.5.2.1 Life-Cycle Processes

The incineration of decaBDE or decaBDE flame-retardant formulations is unlikely, but any incineration likely would occur in a hazardous waste incinerator. Upholstery textiles treated with decaBDE flame-retardant coatings might be sent to municipal incinerators for processing. Municipal incinerators generally provide a well-controlled environment with pollution control mechanisms and sufficiently high temperatures (850 °C) to destroy most materials (Köhler et al., 2008). Processing in municipal facilities is likely to result in complete incineration of the upholstery textiles. Alternatively, upholstery textiles also might be incinerated in less well-controlled facilities or burned in open fires as a rudimentary form of waste management or as kindling. These incineration methods are likely to result in incomplete incineration of the upholstery textiles. No data were found that describe the prevalence of incineration as a form of disposal for upholstery textiles or what proportion of incinerated textiles is processed at well-controlled incineration facilities.

H.2.5.2.2 Potential Releases during the Incineration Stage

Airborne releases of decaBDE from well-controlled incineration are expected to be negligible, but incomplete incineration (e.g., open fires) could lead to some airborne release. Little empirical data exist that describe the prevalence of decaBDE in incinerator residues, but decaBDE is expected to be destroyed by the high-temperature incineration used at most municipal incineration facilities (Palm et al., 2002; Lassen et al., 1999). These temperatures also are sufficiently high to prevent the formation of PBDFs and PBDDs during incineration of decaBDE (see Section H.2.2.2.2). In one study of atmospheric concentrations of PBDEs near solid-waste incinerators, the authors found that incineration facilities do not give rise to a substantial proportion of atmospheric releases of decaBDE (Agrell et al., 2004). Incomplete incineration, however, could lead to the airborne release of decaBDE and the formation of PBDFs, PBDDs, polychlorinated dibenzo-p-dioxins, and nonhalogenated substances such as polycyclic

aromatic compounds (see Section H.2.2.2.2). Current pollution control technologies for municipal incinerators are expected to effectively filter these emissions and prevent their release to the environment (EU, 2002).

Due to the high temperatures and pollution control mechanisms at municipal incinerators, decaBDE in flame-retardant textiles are expected to be destroyed during well-controlled incineration. Incineration by open flame in uncontrolled environments, however, might lead to airborne releases of decaBDE and harmful by-products.

Table 2-10 in Chapter 2 outlines potential release scenarios from the incineration stage of decaBDE and MWCNT flame-retardant textiles.

H.2.5.3. Land-Filling

H.2.5.3.1 General Processes

Land-filling of decaBDE or decaBDE flame-retardant formulations is unlikely, except in the case of floor sweepings from manufacturing facilities. Upholstered furniture and textiles generally are disposed of in municipal landfills (Köhler et al., 2008). Remaining parts from recycled furniture, such as cover cloth materials, also are sent to the landfill (CalRecycle, 2002). Additionally, some textiles might be disposed of in uncontrolled landfills or open dumping sites that have no pollution control mechanisms in place. No data were found that describe the proportion of upholstery textiles disposed of in landfills or any further processing that might occur at the landfill.

H.2.5.3.2 Potential Releases during the Land-filling Stage

Land-filling of decaBDE flame-retardant textiles could lead to water and air releases due to mechanical processes such as mixing and compacting. DecaBDE also could leach from land-filled textiles and migrate into the underlying soil or ground water (Rahman et al., 2001; Lassen et al., 1999), however, no evidence of decaBDE in land-fill leachate has been found [Kim et al. (2006) as cited in Wright et al. (2008)]. Additionally, this release scenario is unlikely due to the low leaching potential of decaBDE (see Table 1-8). Flame retardants containing decaBDE could volatilize to the atmosphere over time (Rahman et al., 2001), but volatilization of decaBDE is expected to be negligible due to low volatility of decaBDE (Palm et al., 2002) (see Table 3-1 in Chapter 3).

Few data were identified that measure releases of decaBDE from land-filling of flame-retardant textiles, but the physicochemical characteristics of these materials suggest that such releases likely would be small. Table 2-11 in Chapter 2 outlines potential release scenarios from the land-filling stage of decaBDE and MWCNT flame-retardant textiles.

H.2.5.4. Wastewater Treatment Plants

H.2.5.4.1 Life-Cycle Processes

The wastewater treatment process consists of filtering and treating wastewater to remove solids and contaminants. Large facilities that manufacture decaBDE and decaBDE flame retardants might divert their wastewater to an on-site wastewater treatment plant. Alternatively, some wastewater from these facilities might be directly processed by municipal wastewater treatment plants. Water releases of decaBDE that occur during the storage and distribution, use, and reuse/recycling/end-of-life stages also would be treated in municipal wastewater treatment plants.

H.2.5.4.2 Potential Releases during the Wastewater Treatment Stage

Release of decaBDE or decaBDE flame-retardant formulations into wastewater could occur throughout the life cycle. Primary releases to wastewater during manufacturing stages are due to equipment cleaning, formulation and application of the flame retardant, and accidental spills. Washing processes (which can involve abrasion, detergents, and water), particularly in the product manufacturing stages, are likely to result in the release of additive flame retardants from textiles to wastewater (Som et al., 2011). Due to the physicochemical characteristics of decaBDE flame retardants (see Table 1-8 and Table 1-9 in Section 1.3), the material is likely to sorb onto particles during water treatment and be removed in sludge (Som et al., 2011; Lassen et al., 1999). The potential nonetheless exists for releases from filter backwash and other wastewater treatment plant equipment (EU, 2002). Additionally, some of this removed sludge is deposited in landfills or spread on agricultural soil (EU, 2002; Lassen et al., 1999). This activity represents one of the most significant potential releases to soil of decaBDE flame-retardant coatings (Ciparis and Hale, 2005; Lassen et al., 1999). The releases of decaBDE from wastewater treatment facilities are expected to be small. The removal efficiency of wastewater treatment plants is not well characterized for decaBDE and the spread of sewage sludge onto agricultural soil could represent a significant source of decaBDE to soil. See Section H.3.3.3 for information regarding decaBDE removal efficiency of wastewater treatment plants.

Table 2-11 in Chapter 2 outlines potential release scenarios from the wastewater treatment stage of decaBDE and MWCNT flame-retardant textiles.

H.3. Transport, Transformation, and Fate

Releases throughout the product life cycles of upholstery textile coatings containing decaBDE flame retardant will, to some extent, lead to occurrence of primary and secondary contaminants in air, soil, and aquatic media. Chapter 3 examines what might happen to these substances after their release to the environment, including transport or transformation through chemical, physical, and biological processes. Studies investigating the transport, transformation, and fate of decaBDE in the environment are summarized in Appendix D, and concentrations of BDE-209, the single isomer of deca-substituted BDE, in environmental compartments are provided in Appendix E.

DecaBDE can be released into the environment during the manufacturing, storage, distribution, use, disposal, reuse, and recycling of upholstery textiles treated with flame retardants (see Chapter 2). DecaBDE flame-retardant formulations are used primarily as additives that are mixed with, not chemically bound to, polymers in textile products. Because they are not chemically bound, these substances can escape from the material and become a source of contamination to surrounding environmental media (Yu et al., 2010; Vonderheide et al., 2008; Moniruzzaman and Winey, 2006; Song et al., 2006; Söderström et al., 2004). Although some, if not most, releases after the production stage are likely to be in the matrix-bound form, little information exists that describes the environmental behavior of decaBDE-polymer complexes. As a result, this section focuses on the transport, transformation, and fate of decaBDE not embedded in a polymer matrix.

Section H.3.1 provides a brief discussion of the chemical and physical characteristics and the processes that influence behavior (e.g., mobility, persistence, bioavailability) of decaBDE in environmental media. The sections that follow summarize the available information regarding the behavior of each substance in indoor and outdoor air (Section H.3.2), aquatic systems (Section H.3.3), and terrestrial systems (Section H.3.4). A brief discussion of models that might be used for evaluating the fate and transport of these substances in environmental media is provided in Section H.3.5.

H.3.1. Physicochemical Factors Influencing Transport, Transformation, and Fate

The environmental fate of BDE-209 will be dictated by its chemical and physical properties and its propensity for biotic and abiotic transformation. BDE-209 could transform physically, chemically, or biologically once released to the environment, leading to substances that present a very different hazard than the hazard of the untransformed material originally released. BDE-209 has been shown to biologically and photolytically debrominate (lose a bromine atom) to form lower brominated congeners

that are more readily bioavailable [U.S. EPA (2010a); Vonderheide et al. (2008); Song et al. (2006); Watanabe and Sakai (2003); Darnerud et al. (2001); see Text Box H.3-1 and additional sources in Appendix D, Table D-1]. Because the chemical properties associated with transformation products of decaBDE influence their transport, transformation, and fate in the environment, degradation processes of decaBDE are introduced in this section. A summary of key physicochemical factors that are likely to affect partitioning[27] and fate of BDE-209 and related PBDEs in the environment is presented in Table H-4. Values for key physicochemical properties of BDE-209 are provided in Section H.1 (see Table H-3).

Biotic debromination is the breakdown of BDE-209 into lower brominated compounds by aerobic and anaerobic microorganisms. Biotic transformation processes for BDE-209 that occur in soil, sediment, or sewage sludge have been described in recent literature (see Appendix D, Table D-1). These processes result in dehalogenation through microbe catalysis reactions that stimulate the replacement of a halogen atom (e.g., bromine, chlorine, fluorine) with a hydrogen atom (Kuivikko et al., 2010; Kim et al., 2007).

Photolysis or photodegradation is a chemical (abiotic) process by which molecules are broken down through the absorption of light. PBDEs are vulnerable to photolysis, which induces reductive debromination causing higher brominated congeners like BDE-209 to photodegrade to form lower brominated congeners. These lower brominated congeners are potentially more stable and bioavailable in the environment due to lower molecular weight and a lower octanol/water partition coefficient (K_{ow}) (Söderström et al., 2004). PBDFs also have been identified as photolysis products of BDE-209. Sunlight could degrade BDE-209 in air, surficial soils, water, and surficial sediments via photolysis (Christiansson et al., 2009; Söderström et al., 2004). This and other abiotic transformation processes for BDE-209 have been demonstrated in recent literature (see Appendix D, Table D-1).

Transformation also can occur with elevated temperatures (e.g., incineration, fire); thermal breakdown products of PBDEs include polybrominated, polychlorinated, and mixed brominated/chlorinated dibenzo-p-dioxins and dibenzofurans, and are similar to polychlorinated dibenzo-p-dioxins/polychlorinated dibenzofurans in their persistence and toxicity (Watanabe and Sakai, 2003; Darnerud et al., 2001; Rahman et al., 2001).

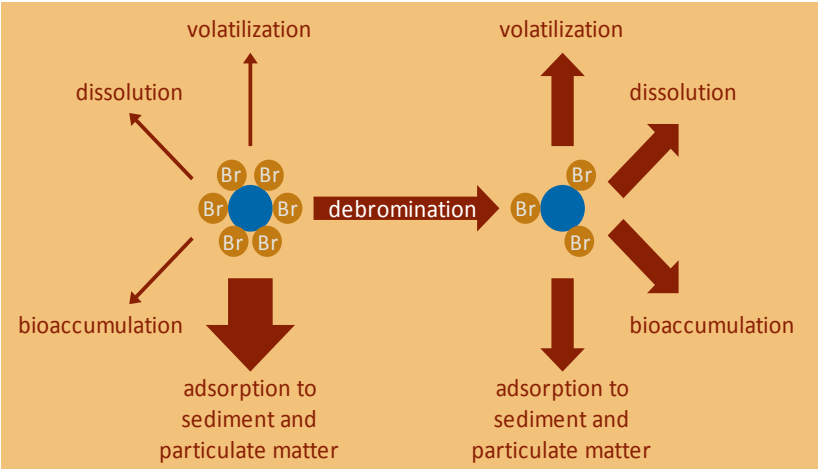
DecaBDE formulations used in textile and other products contain the fully brominated congener, which is less mobile in the environment than lower brominated congeners, probably due to low volatility, water solubility, and bioaccumulation, and the high propensity to adsorb to sediments. The lower brominated compounds are generally more volatile, water soluble, and bioaccumulative compared with higher brominated compounds (Watanabe and Sakai, 2003) and are believed to be structurally analogous to

[27]Partitioning refers to the potential for a chemical or other substance to move from one environmental medium to another (e.g., air, water, sediment) and the tendency to accumulate in one particular medium over another (U.S. EPA, 2010a).

polychlorinated biphenyls (PCBs), so their chemical properties, persistence, and behavior in the environment, are expected to follow similar patterns. PBDEs are expected to be more vulnerable to environmental degradation than PCBs, however, because their carbon-bromine bonds are weaker than the carbon-chlorine bonds of PCBs (Shih and Wang, 2009; Watanabe and Sakai, 2003; Rahman et al., 2001).

Text Box H.3-1. BDE-209 Undergoes Biotic and Abiotic Debromination

Higher brominated PBDE congeners like BDE-209 (the principal constituent in decaBDE) have lower bioaccumulation potential, water solubility, and volatility, and therefore have been considered relatively safe (Watanabe and Sakai, 2003). Lower brominated congeners (including degradation products of BDE-209), however, are predicted to be more volatile, water soluble, and bioaccumulative than the higher brominated congeners, and these degradation products are therefore likely to be more bioavailable in the environment than BDE-209. Soils and sediments are major sinks for higher brominated compounds, and other pathways are relatively minor (see the illustration below; the thickness of the arrows is an indication of the strength of the pathway). The potential significance of other pathways increases for the lower brominated congeners.



Although higher brominated congeners primarily adsorb to solids, lower brominated congeners can readily volatilize to air, dissolve in water and interstitial spaces in soil, bioaccumulate in biota, and adsorb to solids. As a result, the fate of the parent compound BDE-209 is expected to differ substantially from that of its lower brominated transformation products.

Adapted from Watanabe and Sakai (2003).

Understanding the fate and potential toxicity of BDE-209 requires understanding the various degradation processes that dictate its persistence in the environment. Debromination of BDE-209 in the environment affects potential transport and accumulation through the food web (Huang et al., 2010) and therefore potential for human exposure through the diet. Several biotic and abiotic processes of BDE-209 degradation have been demonstrated in air, water, soil, and sediments (Vonderheide et al., 2008). Photolytic degradation by solar rays and UV light is a significant abiotic process of BDE degradation and has been studied more than other processes. Other abiotic processes include geochemical degradation by metal oxides found in certain soils and degradation by engineered nanoparticles (Vonderheide et al., 2008). Biotic degradation pathways include debromination by both aerobic and anaerobic microbes found in soil (Wang et al., 2011; Huang et al., 2010; Lee and He, 2010) and possible further degradation in plants (Huang et al., 2010). These processes proceed in a stepwise fashion, removing one bromine atom at a time, and can therefore contribute to the levels of lower brominated congeners from nona- to tetra- and even diBDEs in the environment. BDE-47 (tetraBDE) and BDE-99 (pentaBDE) are the congeners most often detected in humans and biota globally (Tokarz et al., 2008; Vonderheide et al., 2008), and debromination of BDE-209 might be an environmental source of these congeners, which are known to be toxic and face restrictions on their production (Ross et al., 2009). In accordance with the comprehensive environmental assessment approach, some consideration of the exposure, uptake, and effects of lower brominated congeners produced during the natural debromination of BDE-209 is appropriate. Several studies have described the debromination of BDE-209 (often in the laboratory) and identified ranges of the lower brominated congeners produced; however, the specific congener profiles that are expected to occur in natural environmental systems following BDE-209 debromination have not been clearly identified.

Table H-4. Summary of physicochemical properties that affect partitioning and fate of BDE-209.

Physicochemical property	How does this property affect chemical partitioning and fate?
High molecular weight	• Limits bioavailability to biota Sources: Kierkegaard et al. (2004); Huang et al. (2010)
Low water solubility; hydrophobic	• Expected to associate primarily with organic (carbon-rich) particles in soil, sediment, sewage sludge; percent total organic carbon likely plays a major role in transport and distribution of BDE-209 in these media • Less mobility, strongly sorbed to solid particles such as soils, sediments, and sewage sludge • Expected to adsorb to particles by van der Waals forces and hydrophobic attraction (Ahn et al., 2006) • Reduced bioavailability to some aquatic biota Sources: Vonderheide et al. (2008); Qui et al. (2010); U.S. EPA (2010a); Hua et al. (2003); Mikula and Svobodová (2006); Rahman et al. (2001); Zhu et al (2010); Yu et al. (2010)
Low volatility; low vapor pressure	• Vapor pressures of PBDEs are inversely related to both molecular weight (i.e., as molecular weight increases, vapor pressure decreases) and degree of bromination • Partitioning for BDE-209 is expected to be 1% vapor phase and 99% associated with airborne particles; as the degree of bromination increases, likelihood increases for BDE congeners to partition to the particle phase in air • Lower brominated PBDEs could be expected to be present primarily in the vapor phase and be more susceptible to long-range transport; however, BDE-209 could sorb to aerosol particles and can experience long-range transport Sources: U.S. EPA (2010a); Watanabe and Sakai (2003)
High octanol/water partition coefficient (K_{ow})	• PBDEs partition between water and sediment based on solubility and K_{ow} • Less mobility, strongly sorbed to soils, sediments, sludge • Not easily distributed within surface water and ground water Sources: U.S. EPA (2010a); Vonderheide et al. (2008)
Low Henry's law constant (K_H)	• PBDEs partition between water and air based on K_H; lower K_H at higher degrees of bromination; BDE-209 not expected to readily volatilize to air Source: U.S. EPA (2010a)
High octanol/air partition coefficients (K_{oa})	• Stronger propensity to adsorb to the organic matter in soils and vegetation; indicator of chemical mobility in the atmosphere; tendency for atmospheric BDE-209 to deposit on forest canopies and other vegetative biomass Sources: U.S. EPA (2010a); Wania et al. (2002); Vonderheide et al. (2008)
High lipophilicity	• Dissolves in fats, oils, lipids, and nonpolar solvents (e.g., hexane, toluene) Sources: Mikula and Svobodová (2006); Rahman et al. (2001); Vonderheide et al. (2008) • Greater tendency to bioaccumulate and biomagnify in the food chain Sources: Rahman et al. (2001); Vonderheide et al. (2008)

PBDE = polybrominated diphenyl ether; BDE-209 = single isomer of decabrominated diphenyl ether

H.3.2. Transport, Transformation, and Fate in Air

BDE-209 released from the flame-retardant upholstery textile coatings life cycle could reach indoor and outdoor air in several ways. For example:

- BDE-209 can be released directly into ambient air during all stages of the product life cycle, as previously described in Section H.2. BDE-209 that remains in the particle phase can disperse through air away from the source of release.
- Particulate BDE-209 can become suspended in the surrounding indoor or outdoor air during multiple stages of the product life cycle.
- Particulate BDE-209 might remain suspended and be transported through the atmosphere or deposited onto surfaces. Particles that have been deposited on surfaces could become resuspended in the air and redeposited elsewhere.

If released indoors, BDE-209 can distribute indoors to air, dust, vacuums, and air filter systems. If the source of BDE-209 is inside a building, levels of BDE-209 in indoor air can be much higher than in outdoor air (Hale et al., 2006). Indoor air sources also could contribute to outdoor air concentrations. Variability in the indoor air and dust levels of BDE-209 can be influenced by indoor/outdoor exchange rates, building ventilation rates, and the number and age of all PBDE-treated products (e.g., electronics, mattresses, draperies, furniture) present in the building (Hazrati and Harrad, 2006).

As mentioned earlier, BDE-209 has very low vapor pressure and a high octanol/water partition coefficient and is therefore more likely to be transported on particles in the air than as a vapor (see Table H-4) (Breivik et al., 2006). Approximately 99% of BDE-209 in ambient air is expected to be present in the particle phase (U.S. EPA, 2010a). Particles could remain suspended in air or deposit on surfaces with the potential for resuspension. Because nonvolatile compounds like BDE-209 tend to sorb to particles, they likely would be concentrated in household dust and could experience an extended indoor lifetime (Kemmlein et al., 2003).

When attached to particles, BDE-209 can have an extended residence time and persistence in the atmosphere. Longer residence time in the atmosphere allows more time for the particles to be mobilized by wind and other forces and makes long-range atmospheric transport (LRT) in the atmosphere possible (Gouin et al., 2006; Wania and Dugani, 2003). Evidence exists for LRT of PBDEs to remote ecosystems, including the Arctic (de Wit et al., 2010; Su et al., 2009; Agrell et al., 2004); some literature suggests that PBDEs in remote Arctic regions originated in urban areas in North America (Breivik et al., 2006).

LRT has been considered by some to be the reason for PBDE occurrence in rural and more remote sites. Some evidence has shown LRT of BDE-209 adsorbed to airborne particulate matter at regional and global scales (Vonderheide et al., 2008), although other researchers have suggested that the

potential for LRT of BDE-209 is low. Atmospheric deposition of BDE-209 and other PBDEs is thought to be a main source of these contaminants in background waters and soils (Vonderheide et al., 2008).

Understanding of BDE-209 LRT behavior is limited. As stated previously, BDE-209 in the air is primarily attached to particles (U.S. EPA, 2010a; Su et al., 2009). Efforts by Mueller and Nowack (2008) to model atmospheric transport of engineered nanoparticles can be used to infer that materials, such as BDE-209, adsorbed to particles will eventually deposit or wash out (wet deposition) in aquatic or terrestrial systems. In turn, the fate of BDE-209 in air is likely dictated by the characteristics of the particles to which it adsorbs.

Plants exposed to BDE-209 from air can accumulate BDE-209 and act as transfer vectors in the food chain. Airborne BDE-209-laden particles could attach to leaves and other aboveground parts of plants and translocate to different tissues of the plant. Salamova and Hites (2010) evaluated PBDE levels in air samples and tree bark and determined that BDE-209 concentrations in tree bark were strongly correlated with concentrations in the air and in precipitation. The highest air and tree bark concentrations occurred at urban sites.

Breakdown and transformation of BDE-209 in the air by photolysis also can occur (see Section H.3.1 and Text Box H.3-1), and studies that evaluated this phenomenon in air are presented in Appendix D, Table D-1. Temperature variability could be an important factor that explains seasonal patterns of BDE-209 burdens in air because changes in temperature affect gas-solid partitioning coefficients and subsequently the transfer and retention of BDE-209 in air (Vonderheide et al., 2008).

Section H.4.1.2 and Section E.1 of Appendix E provide summaries of studies with BDE-209 concentration data in building dust and indoor/ambient air.

H.3.3. Transport, Transformation, and Fate in Water and Sediment

BDE-209 released from the flame-retardant upholstery textile coating life cycle could enter aquatic systems in several ways. For example:

- BDE-209 in ambient air subsequently could be deposited or washed out to aquatic systems.
- Erosion of contaminated soil could release BDE-209 to surface waters.
- Runoff flowing along the ground surface could transfer BDE-209 in contaminated soil to nearby waterways.
- Wastewater effluents containing BDE-209 could be a source of contamination to receiving water bodies near the discharge location.
- BDE-209 could leach from land-filled sewage sludge into subsoil and ground water and migrate to surface water or sediment.

H.3.3.1. Surface Water and Sediment (Inland and Coastal)

Water solubility and K_{ow} are important physicochemical factors for predicting behavior of BDE-209 in the aqueous phase—and these parameters predict that BDE-209 will partition to the particulate phase (e.g., sorb to suspended organic matter) in water or bind strongly to sediments (U.S. EPA, 2010a; Hale et al., 2006; Watanabe and Sakai, 2003). The lower brominated congeners are more water soluble than the higher brominated congeners and are expected to be more mobile in water (Watanabe and Sakai, 2003).

Sediment is both a sink and a reservoir for PBDEs such as BDE-209. In general, BDE-209 is the dominant congener in sediment samples (Tokarz et al., 2008); notably higher concentrations in urban and industrial areas and near outfalls of wastewater treatment plants have been measured (U.S. EPA, 2010a) (see Appendix E). Whether the higher concentration of BDE-209 in sediment samples is due to greater BDE-209 use or less environmental degradation compared with other congeners is unknown.

The physicochemical properties of BDE-209 and the characteristics of sediment both affect the bioavailability of BDE-209 in sediment. The bioavailability of BDE-209 in sediment is expected to be limited due to its strong hydrophobicity and large molecular size (Liu et al., 2011b). Due to its tendency to sink to sediments, BDE-209 might be bioavailable to benthic organisms, but generally not to water-column-dwelling organisms. Benthic organisms might, therefore, act as vectors for the transport of decaBDE through the food web (see Section H.4.3).

The amount of organic matter in the sediment is an important factor controlling the partitioning of BDE-209 in sediments (Liu et al., 2011b). In a study conducted by Liu et al. (2011b), the authors concluded that desorption of BDE-209 in sediment was more difficult as contaminant-sorbent interaction time increased, likely because of entrapment of BDE-209 molecules in the micropores of organic matter. Total desorption also decreased with increased total organic carbon in the sediments.

Physicochemical properties of PBDEs and the characteristics of sediment might not serve as perfect predictors of levels in surface waters due to microbial or photolytic degradation processes that could reduce concentrations of the material. Elevated quantities of hydroxylated PBDEs (a possible oxidation product of PBDEs) have been measured in surface waters near sewage treatment plants (Vonderheide et al., 2008). Anaerobic microbial reductive debromination is potentially a driving transformation process in sediment (see Section H.3.1 and Appendix D, Table D-1); the process, however, can be very slow.

Appendix E provides a summary of studies with BDE-209 concentration data in surface water and sediment. Most identified studies focus on sediment concentrations of BDE-209.

H.3.3.2. Ground Water

BDE-209 present in soil could leach into subsoil and ground water. Based on its physicochemical properties, BDE-209 does not dissolve in water, but could sorb to suspended organic matter in the ground water plume and migrate to surface water (U.S. EPA, 2010a). No data were found on concentrations of BDE-209 in ground water.

H.3.3.3. Wastewater

As introduced in Section H.2, manufacturers, homes, and public buildings could be significant sources of BDE-209 to wastewater treatment plants and municipal sewage treatment facilities (Hale et al., 2006). Because of its hydrophobicity and tendency to partition to solids, most BDE-209 in wastewater would be expected to sorb to settling solids (i.e., will not remain in effluent) during the sewage treatment process (Ricklund et al., 2009; North, 2004).

BDE-209 partitions strongly to particulate matter, so sewage sludge is expected to be a major sink for BDE-209, while effluent is likely dominated by the more water soluble lower brominated congeners. Sewage sludge applied to agricultural fields could be a source of BDE-209 to soils (Huang et al., 2010; Vrkoslavová et al., 2010; U.S. EPA, 2009; Vonderheide et al., 2008; Knoth et al., 2007; Hale et al., 2006; Law et al., 2006b; Sellström et al., 2005). Runoff along the surface of the ground then could transfer BDE-209 in the sewage sludge to nearby terrestrial systems or waterways. Sludge contaminated with BDE-209 could be disposed of in landfills (and possibly leach to subsoils and ground water) or be incinerated (introducing emissions to the atmosphere).

Wastewater effluents, although not dominated by the higher brominated PBDEs, might be a source of BDE-209 and transformation product contamination to receiving water bodies of local aquatic ecosystems near the discharge location (Peng et al., 2009; Song et al., 2006). Wastewater irrigation for farmlands could be a source of PBDEs in agricultural soils. The mobility of BDE-209 in the receiving soil could be enhanced if it sorbs to dissolved organic matter in the irrigation water (Wang et al., 2010b).

Recent studies that present concentrations of BDE-209 in wastewater effluent and sludge are presented in Section H.4.1.2.2 and Section E.1 of Appendix E.

H.3.4. Transport, Transformation, and Fate in Soil

BDE-209 released from the flame-retardant upholstery textile coatings life cycle could enter terrestrial ecosystems in several ways:

- BDE-209 in ambient air subsequently could be deposited on soil and plants. Some particles that deposit on soil or plants might experience secondary transport via wind and become resuspended into ambient air and redeposited into nearby terrestrial ecosystems.
- Runoff flowing along the ground surface could transfer BDE-209 in contaminated soil to nearby terrestrial ecosystems.
- Disposal products containing BDE-209 could be deposited in solid waste landfills. Sewage sludge containing BDE-209 also might be land-filled. BDE-209 in land-filled waste could leach into subsoils.

Similar to sediments, soils are a major sink for PBDEs, including BDE-209. BDE-209 released from the flame-retardant upholstery textile coating life cycle can enter terrestrial ecosystems and distribute in soil and plants.

As with sediment, water solubility (hydrophobicity) and K_{ow} are important physicochemical factors for predicting behavior of BDE-209 in soil, and these parameters predict that BDE-209 will associate primarily with organic (carbon-rich) particles in soil and experience limited mobility (U.S. EPA, 2010a; Yu et al., 2010; Zhu et al., 2010). In addition, percent total organic carbon likely plays a major role in BDE-209 transport and distribution in soil (Zou et al., 2007).

Plants exposed to BDE-209 from soil also can accumulate BDE-209 and potentially transform it to lower brominated compounds. Debromination in this context has been investigated only in the soil-plant system, however, not in plants alone; the possibility therefore remains that debromination might occur exclusively in the soil, after which plants take up the transformation products (Huang et al., 2010). If present in soils, BDE-209 could contact plant roots and partition to root lipids due to its high lipophilicity and thereby transport into plant tissues (Huang et al., 2010; Vrkoslavová et al., 2010). Huang et al. (2010) studied the uptake, translocation, and metabolism of BDE-209 in six plant species and found that root lipid content was positively correlated with BDE-209 uptake in those species. BDE-209 accumulated in the roots and shoots of all plants. The translocation factor, measured as the $Concentration_{shoot}/Concentration_{root}$ of BDE-209, however, was inversely related to BDE-209 concentration in the roots, suggesting root lipids restrict translocation of BDE-209 from roots to shoots because of its partitioning to root lipids. In contrast to Huang et al. (2010), the study conducted by Vrkoslavová et al. (2010) provided evidence of translocation of BDE-209 and other PBDEs in plants from the root lipids of tobacco plants to other plant tissues. Concentrations in soil will further depend on the amount of vegetative cover, which also could scavenge BDE-209 (U.S. EPA, 2010a).

Evidence of BDE-209 debromination (transformation) by soil microorganisms and photolysis in surface soils was presented earlier (see Section H.3.1 and Appendix D, Table D-1). Other studies relevant to the fate and transport of BDE-209 in soil and plants are provided in Appendix D, Table D-3. Evidence that BDE-209 affects soil microbial community structure and function is also available; some of these studies are also discussed in Section H.5.2.2.1 and Section F.2.3 of Appendix F.

Recent studies that present soil concentrations of BDE-209 have been identified; some of these data are presented in H.4.1.2.3 and Section E.1 of Appendix E.

H.3.5. Multimedia Models to Predict Environmental Fate and Transport

Multimedia models to predict environmental fate and transport of BDE-209 and PBDE congener profiles in environmental media have been used in recent studies. Breivik et al. (2006) used a multimedia fate and transport model to provide further understanding of how temporal variability and forest cover help control LRT distance for BDE-209 and determined that the fate of atmospheric BDE-209 is likely to be controlled by deposition. Results of their study suggested that the variability of precipitation and the occurrence of periods without precipitation and with strong winds can impact LRT of BDE-209. They determined that the "forest filter effect" might also be important to the LRT of BDE-209; scenarios with a forest yielded lower estimates of air travel distance than scenarios without a forest. Gouin et al. (2005) used a multimedia mass-balance model to assess the importance of seasonal variability (including snow pack, temperature, forest canopy) on concentrations of PBDEs in air, although results were not specific to BDE-209. The authors concluded that PBDE concentrations experience a "spring-pulse" due to particle-bound deposition of PBDEs in the snow pack during winter, followed by transfer of PBDEs to the soil surface following snow melt and volatilization back into the atmosphere as springtime temperatures increase. Emerging spring foliage then takes up PBDEs, decreasing atmospheric concentrations during the summer months and inhibiting LRT.

Bogdal et al. (2010) used PBDE measurement data for the Lake Thun catchment area, Switzerland, in air, lake water, lake sediment, and tributary water, and combined results from a multimedia fate model that used site-specific environmental parameters from the lake catchment to predict PBDE congener patterns in water and sediment. They incorporated measured loadings of PBDEs in air, tributaries, and wastewater into their model. The authors reported that their model successfully predicted general PBDE congener patterns in water and sediment, but that the model tended to underestimate concentrations in water and overestimate concentrations in sediment relative to measured concentrations. The parameter driving this discrepancy appeared to be partitioning of PBDEs between the aqueous dissolved phase and suspended particulate matter phase in the water column.

H.4. Exposure-Dose

Releases of decaBDE to the indoor and outdoor environments can occur at multiple stages of the product life cycle for flame-retardant upholstery textile coating (see Section H.2), and subsequent transport, transformation, and fate processes dictate how decaBDE distributes through various environmental media once released (see Section H.3). Exposure describes the pathways through which contact occurs between contaminants in the environment and living organisms and abiotic receptors. Toxicokinetics (i.e., ADME) describes the processes that relate exposure (or dosage) to the internal dose, which refers to the quantity of a chemical or material that is taken up and absorbed by living organisms (U.S. EPA, 2010b).[28]

Section H.4.1 introduces analytical techniques for identifying, characterizing, and measuring decaBDE in various matrices. The various metrics recommended for characterizing exposure and dose of decaBDE are also discussed, and available concentration data in various indoor and outdoor media are presented. In the absence of data quantifying decaBDE exposures at the point of contact, measured concentrations of decaBDE in surrounding media can be used to estimate exposures using a scenario evaluation approach. Sections H.4.2 and H.4.3 expand on the release scenarios presented in Section H.2 to discuss the potential human and ecological exposure pathways that link those releases to receptors. No data were identified regarding relevant exposure pathways leading to impacts on abiotic resources (e.g., the manmade environment); as a result, this CEA case study does not include a discussion of exposure scenarios that would influence abiotic receptors. Although broad potential impacts on society and the global environment are discussed in Section H.5.3, exposure is either not considered germane to the discussion of the impact (such as for economic impacts of manufacturing) or the exposure characteristics related to the impact are already included in the general discussion that follows (higher potential exposures levels related to such as for socioeconomic impacts).

Probable exposure scenarios throughout the flame-retardant upholstery textile coating life cycle are identified for workers, consumers, the general public, and highly exposed populations in

[28]The term "dose" is described generally by the EPA Integrated Risk Information System (IRIS) as "[t]he amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism." Several specific forms of dose are also described by IRIS, but the definitions of these terms are not used consistently across the risk assessment community. The following definitions of specific forms of dose are provided by IRIS: "The POTENTIAL DOSE is the amount ingested, inhaled, or applied to the skin. The APPLIED DOSE is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The ABSORBED DOSE is the amount crossing a specific absorption barrier (e.g. The exchange boundaries of the skin, lung, and digestive tract) through uptake processes. INTERNAL DOSE is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by any particular organ or cell is termed the DELIVERED or BIOLOGICALLY EFFECTIVE DOSE for that organ or cell."

Section H.4.2 and for aquatic and terrestrial biota in Section H.4.3. These scenarios describe the conditions under which exposures might occur; this information can be used in combination with measured or modeled concentrations in environmental media from Section H.4.1 and exposure factors to estimate exposures. Kinetic information then can be used to determine or estimate the internal dose that results from external exposures. When available, point-of-contact measurements, administered dosages, tissue or body burdens, and scenario-specific exposure guidelines and recommendations are provided, and the toxicokinetics of decaBDE are described. Finally, Section H.4.4 discusses aggregate exposures to decaBDE from multiple sources and Section H.4.5 discusses cumulative exposures to multiple related stressors. Measured concentrations of decaBDE in environmental media are provided in Appendix E, and studies describing toxicokinetics of PBDEs in mammals are summarized in Appendix F.

As described in Section H.2.2.4, decaBDE is expected to be incorporated into a polymer or other type of matrix in the flame-retardant formulation applied to upholstery textiles, and both the free and matrix-bound form might be released during the product life cycle. Very little data relevant to BDE-209 exposures, however, have been generated for the matrix-bound form. This lack of data necessitates a reliance on the existing data for free BDE-209 in the discussion throughout this section. The extent to which exposure characteristics and dose implications differ between the free and matrix-bound forms of BDE-209, however, is unknown at this time.

H.4.1. Detection, Measurement, and Characterization

Exposure scenario evaluation requires information on measured, modeled, or reasonably estimated concentrations of a stressor in exposure media. As introduced in Section H.1, PBDEs represent a group of compounds encompassing substances that span a range of physicochemical characteristics and properties. As a result, developing reliable analytical techniques for detecting, measuring, and characterizing the full range and makeup of PBDEs in environmental media can present challenges. Text Box H.4-1 provides an abbreviated discussion of a few common analytical techniques and the general challenges associated with them. Appendix B summarizes common analytical techniques for each substance, and presents the strengths and limitations of each technique.

The diversity of known PBDE congeners makes the characterization of exposure to a single congener such as decaBDE difficult, as described in Text Box H.4-1. Identifying the specific source of decaBDE in environmental samples is even more difficult. DecaBDE is present in dust in many different environments, but the source of the dust could be from manufacturing, wear, or breakdown of many consumer products, including electronics, foams, and polymer textile coatings on furniture such as couches and mattresses. Some research has been conducted using forensic microscopy to characterize the

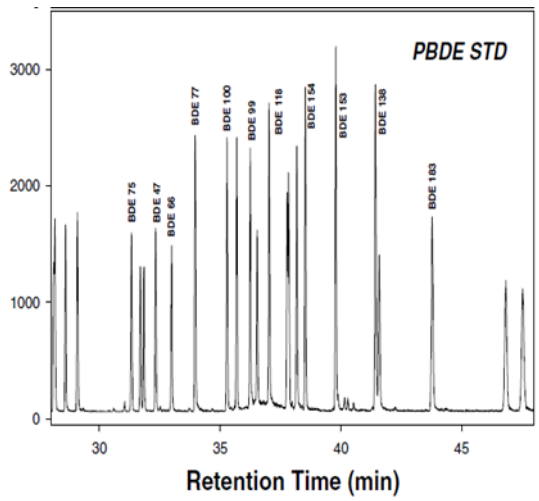
source and transfer mechanisms of BDE-209 in indoor environments, but the results are qualitative (Lagalante et al., 2011; Webster et al., 2009). PBDEs are persistent pollutants, so quantifying whether exposure and body burdens of the lower brominated PBDEs are the result of weathering and breakdown of BDE-209, or from other PBDEs such as pentaBDE and octaBDE [widely used until recently) (Stapleton, 2006)], is difficult.

Text Box H.4-1. Detecting, Measuring, and Characterizing PBDEs

Mass spectrometry is used most frequently to detect polybrominated diphenyl ethers (PBDEs), and gas chromatography (GC) is employed to measure and characterize PBDE mixtures. High-resolution mass spectrometry is the most selective method, but is also expensive and labor intensive. Low-resolution mass spectrometry is insensitive to congeners with more than six bromines (like BDE-209), but optimization of aspects like reagent gas, source temperature, and source pressure can increase sensitivity.

Accurate characterization in environmental samples has proven more problematic for BDE-209 than for lesser brominated congeners. How a GC system is set up can contribute to variation in measurements. For example, use of higher temperatures and longer column lengths can lead to degradation of higher brominated congeners and quicker evaporation of higher molecular weight congeners.

Distinguishing between certain PCBs and PBDEs is difficult with most systems, which can lead to imprecise measurements. Additionally, not all PBDE congeners are commercially available for use as standards (approximately 160 of the 209 congeners are currently available). Determining whether unidentified peaks in chromatograms (see gas chromatograph output to right) are due to these nonstandardized PBDE congeners or to other compounds can be challenging (Stapleton, 2006).



Example Gas Chromatograph Output for a PBDE Mixture with Multiple Unidentified Peaks (Stapleton, 2006)

H.4.1.1. Dose and Exposure Metrics

Environmental concentrations of decaBDE are commonly quantified in terms of mass (e.g., picograms, nanograms) per volume (e.g., m^3, L) for air and water measurements or mass per weight (e.g., grams dry weight, grams wet weight) of soil, sediment, or tissue samples (Frederiksen et al., 2009). Human exposure to decaBDE and subsequent dose has been quantified by detection of BDE-209 in the serum, breast milk, adipose tissue, and hair of humans (Darnerud et al., 2001).

H.4.1.2. Concentrations in Environmental Media and Indoor Environments

As described in the previous section, exposures can be estimated by combining knowledge of concentrations in exposure media with assumptions about contact of humans, biota, or abiotic surfaces with those media. The following sections describe the information available on concentrations of BDE-209 and related substances in environmental media (i.e., air, water, soil).

H.4.1.2.1. Outdoor Air

Research has shown that BDE-209 comprises between 6 and 31% of total PBDE concentrations in outdoor air (Frederiksen et al., 2009). Outdoor air generally has lower concentrations of total PBDEs, which can be one or two orders of magnitude lower than in indoor air (see Appendix E). This lower concentration is partly due to the dilution factor of outdoor environments, but also occurs because indoor environments contain more sources of PBDEs such as electronics, furniture, plastics, and coatings in enclosed spaces (Daso et al., 2010).

Mean levels of BDE-209 measured in outdoor air from locations throughout the United States range from 1.4 to 60.1 pg/m^3 (U.S. EPA, 2010a), and BDE-209 has been detected in the particulate phase in air near point sources (ATSDR, 2004). Sampling locations included rural, agricultural, and urban locations. The highest level detected was 65 pg/m^3 in urban Chicago, and the lowest level was 0.2 pg/m^3 at an agricultural site in Indiana (Hoh et al., 2005). International studies have reported mean BDE-209 levels ranging from 1.6 to 53.3 pg/m^3 (Chang et al., 2009). The lowest environmental concentration reported in the literature was 0.091 pg/m^3 in the Canadian High Arctic (Su et al., 2007), and the highest level reported was 105 pg/m^3 in Southern Ontario, Canada, nearly all of which was sorbed to aerosol particles (Gouin et al., 2006). Information from additional studies of concentrations in air is available in Appendix E, Table E-2.

H.4.1.2.2. Aquatic Systems – Sediment and Surface Water

PBDEs are hydrophobic and therefore are not detected in large concentrations in the water column (ATSDR, 2004). In aquatic systems (including both water and sediment), BDE-209 is the predominant PBDE congener detected (49% to nearly 97% of the total PBDEs), with most detected in sediment (ATSDR, 2004). BDE-209 has been observed in both sediments and surface waters in multiple locations in the United States, from California to Delaware and Wisconsin to Mississippi (Ashley et al., 2006; Raff and Hites, 2004). Surface water in the San Francisco Bay estuary of California was found to contain BDE-209 at concentrations below the limit of detection (reported as 20–200 pg/L for individual congeners) to 191.0 pg/L water, with all but one of the detectable concentrations ranging between 12.2 and 87.8 pg/L (Oros et al., 2005). Levels of BDE-209 observed in sediment ranged from below the level

of detection (reported as 0.1 to 1.5 ng/gram dry weight) to 3,150,000 ng/gram in sediment downstream of a wastewater treatment plant for a plastics manufacturer in North Carolina (La Guardia et al., 2007). In another study, the highest total PBDE concentration in suspended sediment from the Mississippi River and five tributaries was 1,548 ng/gram, with BDE-209 accounting for an average of 96.8% of the total observed PBDE concentration at the 31 sampling sites (Raff and Hites, 2004). Appendix E, Table E-3 provides additional information on these studies.

As detailed above, detected levels of BDE-209 in surface water are many times lower than those in sediment, which is consistent with assumptions based on the physical properties and environmental fate of BDE-209 discussed in Section H.3. The highest level of BDE-209 detected in surface water was 191 pg/L, equivalent to 191 parts per quadrillion, whereas the highest amount in sediment was 3,150,000 ng/gram, equivalent to 3,150 parts per million (ppm). These two measurements differ by a factor of approximately 165 million.

Mean levels of BDE-209 in sewage sludge in the United States have varied widely, ranging from 84.8 to 58,800 ng/gram dry weight (La Guardia et al., 2007; Hale et al., 2001). In these studies, BDE-209 was the most frequent PBDE congener detected. International studies have shown levels ranging from 68.5 to 880 ng/gram dry weight (Clarke et al., 2008; Wang et al., 2007). A mean effluent BDE-209 concentration of 1,730 pg/L was reported from a sewage treatment plant in California (North, 2004). Internationally, effluent concentrations have ranged from 310 to 1,170 ng/L (Eljarrat et al., 2007; de Boer et al., 2003). See Appendix E, Table E-4 for additional information on these studies.

H.4.1.2.3. Terrestrial Systems – Soil

Mean levels of BDE-209 observed in U.S. surface soils in two studies ranged from 0.6 to 15.3 ng/gram dry weight [(Offenberg et al., 2006) as cited in U.S. EPA (2010a); (Yun et al., 2008)]. The range of concentrations in international studies was 0.028–2,220 ng/gram dry weight (Sellström et al., 2005). Both the lowest and highest levels of BDE-209 detected were from a study in Sweden. The only other international studies examined BDE-209 levels in Chinese soil; these measurements ranged from 2.38 to 6,319.6 ng/gram dry weight (Luo et al., 2009; Zou et al., 2007). Appendix E, Table E-5 presents additional information on these studies.

H.4.1.2.4. Occupational Settings – Air

No studies were found that measured levels of BDE-209 in air in facilities where textiles containing BDE-209 are manufactured. Outdoor air at an automobile shredding facility, however, was found to have BDE-209 levels ranging from 45.5 to 1,940 pg/m^3 (Charles et al., 2005). Given that BDE-209 is used in automobile upholstery, the textiles in the automobiles could have contributed to the

observed levels. BDE-209 levels have been measured in indoor occupational settings, including e-recycling facilities, circuit-board assembly halls, and computer facilities. Reported levels in the air ranged from a median of 220 pg/m^3 in a circuit-board assembly hall to a high of 833,000 pg/m^3 in an e-recycling facility (Frederiksen et al., 2009; Charles et al., 2005). See Appendix E, Table E-2 for a summary of additional studies reporting indoor and outdoor air monitoring results.

H.4.1.2.5. Residential Settings – Air and Dust

Two U.S.-based studies evaluated residential indoor air levels of BDE-209. Levels of BDE-209 in the air ranged from below the limit of detection (limit of detection not reported) to 94 pg/m^3 for the living room and 173.6 pg/m^3 for personal air (i.e., breathing zone) (Allen et al., 2007). A study in Sweden detected BDE-209 at 257 pg/m^3 in the living room air in one of five household samples, while all other samples in the study were below the limit of detection (173 pg/m^3) (Petersen and Henry, 2012). Appendix E, Table E-2 provides a summary of additional indoor air studies.

Levels of BDE-209 in household dust are orders of magnitude higher than in other matrices by weight, and BDE-209 is the main PBDE contaminant in household dust (Daso et al., 2010). BDE-209 has been found in household dust in U.S. studies at median levels ranging from 665 to 2,000 ng/gram dry weight (Frederiksen et al., 2009). In international studies, median levels of BDE-209 in house dust ranged from 60 ng/gram dry weight (Germany) to 7,100 ng/gram dry weight (United Kingdom) (Frederiksen et al., 2009). See Appendix E, Table E-1 for additional studies that report observed levels of BDE-209 in household dust.

H.4.1.2.6. Nonresidential Settings – Air and Dust

BDE-209 is one of the main PBDE contaminants in office dust (Watkins et al., 2011; Batterman et al., 2010; Harrad et al., 2008a). One study of U.S. office buildings found a mean concentration of 6,930 ng/gram BDE-209 in office dust, but half of the sample sites had concentrations of 1 ng/gram or concentrations below the limit of detection (limit of detection not reported) (Batterman et al., 2010). Another study of dust in U.S. offices reported an average BDE-209 concentration of 4,204 ng/gram (geometric mean) with a range of concentrations between 912 and 106,204 ng/gram among sample sites (Watkins et al., 2011). In a study conducted in the United Kingdom, Harrad et al. (2008a) reported a median concentration of 6,200 ng/gram BDE-209 in office dust. See Appendix E, Table E-1 for study summaries that report observed levels of BDE-209 in office dust.

One study conducted in U.S. office buildings examined BDE-209 concentrations in airborne particulate matter and vapor; concentrations were all below the limit of detection, which was not reported (Batterman et al., 2010). Appendix E, Table E-2 provides a summary of this study.

H.4.1.2.7. Transportation, Including Automobiles and Airplanes— Air and Dust

As discussed in Section H.4.2.2.3 below, flame-retardant upholstery can be used in seats and other textiles in transportation vehicles such as automobiles and airplanes. No studies were identified that reported levels of BDE-209 in automobile or aircraft air, but several studies have investigated levels of BDE-209 in automobile or aircraft dust (Lagalante et al., 2009; Christiansson et al., 2008; Harrad et al., 2008a). Less time is generally spent in automobiles than indoors, but levels of BDE-209 in automobile dust are about 20 times higher than in household dust (Lagalante et al., 2009). In one study, the median level of BDE-209 in passenger cars was estimated as 8.12 μg/gram dust (82% of the total PBDE concentration in dust); personal automobiles generally had lower levels of decaBDE in dust than dealer vehicles (Lagalante et al., 2009). Other studies have reported median BDE-209 levels in dust from cars as high as 100 μg/gram, with a highest individual sample of 2,600 μg/gram (Harrad et al., 2008a) (see Appendix E, Table E-1 for more information). Levels of PBDE congeners in the vehicles were not statistically significantly different by vehicle manufacturer, model year, country of manufacture, seat type, or the presence of heated seats (Lagalante et al., 2009).

A study evaluating dust in aircraft during 20 international flights observed BDE-209 concentrations ranging from below the limit of detection (value not reported) to 189,882 ng/gram, with a median level of 17,262 ng/gram (Christiansson et al., 2008). No other studies were found that evaluated levels of BDE-209 in air or dust of aircraft.

H.4.2. Human Exposure and Kinetics Leading to Dose

Limited data were found that measured or quantified human exposure to BDE-209. Data on concentrations of BDE-209 measured in media such as air, soil, or dust in various settings (described in Section H.4.1.2), however, can be used in conjunction with activity pattern and other exposure factor data [such as those described in *The Exposure Factors Handbook* (U.S. EPA, 2011)] to inform estimates of potential exposure through the various exposure pathways and scenario characteristics described in this section.

The types of human exposure scenarios described here can be divided into four broad groups: occupational, consumer, general public, and highly exposed populations. For the purposes of this case study, occupational exposures include occupational exposures during synthesis, processing, or handling of decaBDE; manufacturing of flame retardants, application of the flame retardants to textiles, or textile finishing and upholstering; storage of the decaBDE, flame-retardant formulations, treated textiles, or upholstered products; disposal of decaBDE, flame-retardant formulations, treated textiles, or upholstered products; and repurposing or recycling of treated upholstery textiles and end-user products (e.g.,

furniture). Consumer exposure scenarios include the intended or unavoidable use of treated upholstery textiles in residential and nonresidential spaces, including on household or institutional/office furniture, in vehicles, and in aircraft; unintended uses of treated upholstery textiles or end-use products such as reuse or repurposing of furniture for something other than its original intended use; or recycling of upholstery textiles for new uses. General public exposure includes primary exposure to members of the community near manufacturing, disposal, or recycling facilities and secondary exposure to the general public through environmental routes such as air, soil, or water. Highly exposed refers to exposure scenarios that are expected to occur via similar pathways as outlined for consumers and the general public, but where exposure levels are expected to be higher due to key differences in population characteristics such as those described in *The Child-Specific Exposure Factors Handbook* (U.S. EPA, 2008a).

H.4.2.1. Occupational Exposure Pathway Scenarios

Limited data were found to determine the extent of occupational exposures to BDE-209 during the material synthesis, processing, and handling phases or to the flame-retardant product during formulation, application, storage, and disposal phases. See Section H.4.1.2.4 for BDE-209 concentrations measured in occupational settings, which could be applied with the exposure pathways and scenario characteristics described below to estimate potential exposures through scenario evaluation.

H.4.2.1.1. Synthesis, Processing, and Handling

As discussed in Section H.2.2.2, BDE-209 synthesis involves conversion of phenol to diphenyl ether, followed by bromination in the presence of a catalyst, typically aluminum bromide or iron (WHO, 1994). The synthesis and drying processes are carried out in enclosed vessels, so under normal circumstances exposure is unlikely to occur during this process. After synthesis, decaBDE powders are removed from the chamber and bagged. As discussed in Section H.2.2.2.2), the low vapor pressure of decaBDE results in negligible exposures to decaBDE as a vapor during synthesis or bagging, but exposures to decaBDE adsorbed to dust could occur (EU, 2002). DecaBDE adsorbed to dust is expected to settle quickly on surfaces in the occupational environment; no data were found to determine the extent of exposures to decaBDE and decaBDE adsorbed to dust during the synthesis, processing, and handling phases. The pathways through which workers might be exposed to decaBDE and decaBDE adsorbed to dust during general synthesis, processing, and handling scenarios are described below:

- **Inhalation.** Bagging and other handling of decaBDE powders might be the activities most likely to lead to exposures. Aerosol particles in the inhalable size range could be inhaled by workers if respirators are not worn.

- **Oral.** Secondary oral exposures might occur if inhaled decaBDE or decaBDE that deposits on the skin, food, or food-contact surfaces are subsequently ingested.
- **Dermal.** DecaBDE might settle on the skin if proper personal protective equipment is not worn.

H.4.2.1.2. Formulation of Flame Retardant, Application to Textiles, Upholstering

As discussed in Section H.2.2.4, decaBDE powder is mixed with other ingredients to create a paint-like flame-retardant product, after which the flame retardant is back-coated onto a textile intended for use as upholstery. No data were found on the extent of occupational exposures to decaBDE during formulation of the flame retardant, application of the flame retardant to textiles, or textile finishing and upholstering. As with exposures during the previous life-cycle stages, exposures to decaBDE vapors during the product manufacturing stages are expected to be low due to the low vapor pressure of this congener; however, exposures to decaBDE adsorbed to dust or attached to the product matrix could occur.

The first step in the product manufacturing chain is compounding (i.e., mixing) decaBDE powder with antimony trioxide in water, which typically occurs under local exhaust ventilation (EU, 2002). The mixture is then added, through a closed system, to the emulsion polymers in a sealed mixing vessel. Use of ventilation controls and a closed system in generating the flame-retardant coating is expected to greatly reduce the chance of occupational exposures during these stages under normal circumstances. Exposures might still occur to decaBDE adsorbed to dust, however, when the decaBDE powder is emptied into the mixer. Exposures also could occur during transfer of materials; equipment cleaning, maintenance, and repair; and as the result of accidental spills or releases (EU, 2002).

The potential for occupational exposure also exists when the flame-retardant polymer mixture is applied to the textile as a resin back-coating. DecaBDE flame retardant is typically not added manually, and exposures are expected to be greatest during handling and cleaning of coating equipment (EU, 2002), but accidental spills and releases also might occur. Occupational exposures to decaBDE adsorbed to dust, in the polymer matrix, or attached to textile fibers or scraps might occur as a result of cutting, sewing, and otherwise abrading the decaBDE-treated upholstery textile product during textile finishing and application to a consumer end-use product.

The pathways through which workers might be exposed to decaBDE during general formulation of the flame retardant, application of the flame retardant to the textile, and textile finishing and upholstering scenarios are expected to be comparable to those described in Section H.4.2.1.1 on exposures during synthesis, processing, and handling. Additional considerations pertaining to exposures to decaBDE in combination with polymer ingredients, textile fibers or scraps, or other product constituents during these scenarios are described below:

- **Inhalation.** Abrading textiles during tailoring and upholstering could lead to inhalation of decaBDE, other product ingredients, and textile dusts.
- **Oral.** Secondary oral exposures might occur if inhaled decaBDE and associated product constituents or decaBDE particles that deposit on the skin, food, or food-contact surfaces are subsequently ingested.
- **Dermal.** DecaBDE and associated product constituents generated during product manufacturing can land on the skin of workers if proper personal protective equipment is not worn. The liquid flame-retardant coating also can be spilled directly onto the skin.

H.4.2.1.3. Storage of DecaBDE, Flame-Retardant Formulations, Treated Textiles, and Upholstered Products

As described in Section G.2.2, decaBDE and the flame-retardant formulations to which it is added are expected to be stored in sealed receptacles that would limit potential for worker exposures to these materials during storage. Defective packaging and accidental spills or releases, however, could lead to rare exposures during storage operations.

Although no information was identified regarding procedures for storing treated upholstery textiles, these products are likely packaged to protect them from exposure to elements like water and light that could damage their aesthetics. Such packaging also is expected to limit exposures of workers to the flame-retardant coatings. Once the textiles have been applied as upholstery to end-use products, these products also are expected to be enclosed in protective packaging. Some surfaces of bulkier products (e.g., furniture), however, might remain uncovered, which could lead to worker exposures during storage operations, or exposures might occur during application and removal of packaging materials to and from the product. Dust also can accumulate in storage facilities that frequently store textiles and textile products, and decaBDE that escapes from the product matrix could sorb to dust particles. Ventilation technologies and other contamination-prevention strategies like those manufacturing facilities use are not expected to be in place in storage facilities. Dust that has settled on surfaces in storage facilities can be disturbed by worker operations, resuspended, and transported to other locations.

Although decaBDE is not expected to be highly volatile, off gassing of more volatile components of the treated textiles might occur during storage of treated textiles or upholstered products. Furthermore, due to the additive nature of decaBDE flame retardants, covalent bonding between the flame retardant and the textile does not occur, suggesting that flame-retardant coatings that are loosely attached to the textile surface might slough off during storage or handling. Because decaBDE flame retardants are generally added to the back of the textile, however, the likelihood of this detachment seems low.

No data were found on occupational exposures to decaBDE during storage throughout the product life cycle of flame-retardant upholstery textile coating. A study examining residential exposures to a range of PBDEs, however, did identify age of furniture as one of the drivers of exposure, with higher

BDE-209 body burdens in children aged 2–5 years correlating with newer furniture (e.g., couches, mattresses) (Rose et al., 2010). Whether furniture is currently treated more often with decaBDE flame retardants than previously or whether the age of the furniture influences the rate of decaBDE release (with greater amounts released from newer furniture), however, is unclear, which limits the applicability of this finding to the refinement of realistic exposure scenarios.

The pathways through which workers might be exposed to decaBDE alone or decaBDE adsorbed to dust during storage of decaBDE and decaBDE flame-retardant formulations are expected to be comparable to those described in Sections H.4.2.1.1 and H.4.2.1.2 on exposures during synthesis, processing, and handling and during formulation of the flame retardant, application to textiles, and upholstering. Additional considerations pertaining to exposures to decaBDE alone or in combination with polymer ingredients, textile fibers or scraps, or other product constituents during general treated textile of upholstered product storage scenarios are described below:

- **Inhalation.** Workers could inhale volatile components of the flame-retardant coating or decaBDE adsorbed to dust in storage facilities, particularly facilities that are not well ventilated. Furthermore, decaBDE adsorbed to dust could be resuspended in the air by worker activities, and subsequently inhaled. PBDE exposures have not been measured at textile storage facilities, but they have been measured at electronic waste storage facilities. The median estimated inhalation exposure to BDE-99 (the highest measured PBDE in air) in male workers was 0.0011 ng/kg body weight (bw) per day (Muenhor et al., 2010). Although BDE-209 exposures are likely to differ due to lower volatility and greater propensity to adsorb to particles, debromination of BDE-209 could result in worker exposures to lower brominated congeners.
- **Oral.** Higher levels of dust in textile storage facilities could lead to increased transport of decaBDE adsorbed to dust. This could result in oral exposures to decaBDE in dust transported to break rooms, homes (via clothes), and other locations where decaBDE adsorbed to dust can be unintentionally ingested while eating or due to hand-to-mouth activity. In electronic waste storage facilities, the median exposure to BDE-209 via dust ingestion was 2.89 ng/kg-bw-day for average ingestion scenarios and 7.2 ng/kg-bw-day for high-end ingestion scenarios (Muenhor et al., 2010).
- **Dermal.** DecaBDE adsorbed to dust could be resuspended by worker activities and deposit on the skin of workers if proper personal protective equipment is not worn.

H.4.2.1.4. Disposal and Recycling of DecaBDE, MWCNTs, Flame-retardant Formulations, Treated Textiles, and Upholstered Products

As described in Section H.2.5, large-scale disposal, recycling, and reuse of decaBDE, and the flame-retardant formulations to which it is added are unlikely, but containers used to store these products might enter the waste stream, and workers at disposal and recycling facilities could be exposed to product residues remaining in these containers.

Disposal and recycling of treated textiles and upholstered products, however, is prevalent. Mixing and compacting of waste for land-filling; cleaning, shredding, blending, melting, and spinning scrap

textiles for recycling; and incomplete incineration of treated upholstery textiles all could result in exposure of workers (Chaudhry et al., 2009) to decaBDE, primarily in combination with other product constituents and dusts.

No data were found on the extent of occupational exposures to decaBDE during disposal, recycling, and reuse throughout the decaBDE flame-retardant upholstery textile coating product life cycle. As discussed in Section H.4.1.2.4, BDE-209 was detected in the air outside of an automobile shredding facility (Charles et al., 2005), which suggests that exposure to BDE-209 during end-of-life operations can occur.

The pathways through which workers might be exposed to decaBDE during general disposal and recycling of decaBDE powder and flame-retardant formulations are expected to be comparable to those described in Section H.4.2.1.1 (exposures during synthesis, processing, and handling), and worker exposure pathways for decaBDE in combination with polymer ingredients, textile fibers or scraps, or other product constituents during disposal and recycling treated textiles and upholstered product are expected to be similar to those described in Sections H.4.2.1.2 (exposures during formulation of the flame retardant, application to textiles, and upholstering) and H.4.2.1.3 (exposure during storage and distribution) for these products. Additional considerations pertaining to exposures to decaBDE alone or in combination with polymer ingredients, textile fibers or scraps, or other product constituents during treated textile or upholstered product disposal and recycling scenarios are described below:

- **Inhalation.** Workers operating machines that abrade or destroy textile materials, those handling these products, and other workers in the vicinity of operations that agitate or abrade textile materials can inhale decaBDE adsorbed to dust and other product constituents, as observed by Sjodin et al. (2001) at an e-waste recycling plant where electronics are stored, dismantled, and shredded. Workers at incineration facilities also might inhale small particles comprising decaBDE and other substances in the incinerator as well as polybrominated dibenzofurans (PBDFs) and polybrominated dibenzo-p-dioxins (PBDDs) (see Section H.2.5.2.2) if treated textiles and upholstered products are not incinerated at sufficiently high temperatures.
- **Oral. No** additional considerations.
- **Dermal.** Workers at disposal and recycling facilities might come into physical contact with the decaBDE flame-retardant coating on an upholstery textile during the process of moving or handling products. DecaBDE could migrate directly to skin of workers if proper personal protective equipment is not worn.

H.4.2.2. Consumer Exposure Pathway Scenarios

BDE-209 is expected to be released from consumer products in the particulate phase. See Sections H.4.1.2.5, H.4.1.2.6, and H.4.1.2.7 for data on concentrations of BDE-209 measured in residential, nonresidential, and general public settings, which could be applied with the exposure

pathways and scenario characteristics described below to estimate potential exposures to BDE-209 through a scenario evaluation approach.

H.4.2.2.1. Intended Use – Upholstered Products in Residential Spaces

As discussed in Section H.4.1.2.5, PBDE concentration in house dust tends to be higher than in other matrices, and BDE-209 is the dominant congener in house dust. Although flame-retardant upholstery textiles typically are used in nonresidential settings (see Section H.4.2.2.2), some residential upholstered products, particularly mattresses, are known to contain decaBDE, and other upholstered furniture products, like couches, sometimes might be treated with decaBDE (Rose et al., 2010). One study has shown that body burdens of BDE-209 in children are positively associated with presence of new furniture, but are not associated with presence or use of electronics that often contain decaBDE (Rose et al., 2010). This finding suggests that decaBDE use in residential upholstery does contribute to overall decaBDE exposures related to the use of decaBDE in flame-retardant upholstery textiles. Higher body burdens of BDE-209 also have been associated with smaller living spaces, and higher concentrations of decaBDE have been measured in the main living area of the house than in the bedroom (Allen et al., 2008), indicating that variations in decaBDE exposures can be expected due to variations in housing characteristics and human behavior patterns (i.e., time spent by individuals in different rooms or outside the house). Furthermore, decaBDE released from products is suspected to debrominate to some degree to lower brominated congeners in residential settings (Allen et al., 2008), and will therefore lead to exposures to PBDEs other than decaBDE.

As introduced in Section H.2.4, upholstered products are expected to be used for many years, and contact with the textile might be frequent and prolonged, which could cause substantial wear and tear on the textile product. In addition, upholstery in residential spaces might frequently be exposed to cleaning products, sweat, food, and other substances that could affect the properties of the textile and the flame-retardant coating.

The pathways through which consumers might be exposed in residential settings to decaBDE during general consumer use scenarios for end products upholstered with decaBDE are described below:

- **Inhalation.** Chronic inhalation of particles of decaBDE in combination with other product constituents and dust could occur following release from upholstered products over time (due to wear and tear from anticipated use, aging of materials, abrasion, UV light, water, cleaning chemicals, among other factors; see Section H.2.4.2). Particulate decaBDE could settle onto surfaces, where it might be disturbed and re-entrained, after which it could be inhaled by residents. Inhalation is not expected to be a primary route of exposure for decaBDE (Johnson-Restrepo and Kannan, 2009; Allen et al., 2008), however, because the contribution of inhaled dust particles is expected to be minimal due to a lack of correlation between concentrations of decaBDE in dust and in air (Allen et al., 2008); see below.

- **Oral.** DecaBDE in combination with other product constituents and dust could be ingested after settling on food and food-contact surfaces or following hand-to-mouth activity. Ingestion of household dusts is hypothesized to be a major exposure pathway for PBDEs (Allen et al., 2008). Johnson-Restrepo and Kannan (2009) reported that most PBDE intake in toddlers, children, teenagers, and adults was attributed to the oral route of exposure via ingestion of household dust (56–77% attributed to combined oral and dermal exposure).
- **Dermal.** Dermal exposure to decaBDE in combination with other product constituents and dust might occur while touching the textile surface (particularly if the portion of the textile that has been treated with the flame-retardant coating is exposed) or touching surfaces upon which particles have settled (Frederiksen et al., 2009). Lorber (2008) estimated that dermal exposure to PBDE compounds in household dust could be a significant contributor (estimated at 16%) to the body burden of PBDEs in adults. The estimated contribution of BDE-209 to body burden from dermal contact exposure was 25.2 ng per day of a total 85.9 ng total PBDEs per day from that exposure route (Lorber, 2008). Johnson-Restrepo and Kannan (2009) similarly reported that the dermal route was a primary route of exposure for PBDEs (second to the oral route of exposure for contribution of human intake).

H.4.2.2.2. Intended Use – Upholstered Products in Nonresidential Spaces

Due to regulations requiring that upholstery textiles used in nonresidential settings pass flame-retardancy tests (see Table H-3), many upholstery textiles in public, commercial, and institutional settings are treated with decaBDE. The characteristics of the different settings in which these products are used can vary considerably. For example, flame-retardant upholstery textiles might be used in seating for airports and other transportation hubs and in waiting rooms, office buildings, penal institutions, and other nonresidential spaces that can range from very small to very large and where consumers might spend varying amounts of time. Some scenarios for nonresidential exposures are not likely to differ from those expected from residential exposures, but a few key differences do exist:

- Exposures to flame-retardant upholstery coatings in public spaces might be unavoidable. Although consumers have some control over which products they bring into their home, they have little control over the products they encounter in public spaces.
- Some nonresidential exposures might occur over long periods of time and for extended intervals (e.g., sitting in the same office chair every day over the course of several work years), while some might occur infrequently and for short periods of time (e.g., sitting in seating at the airport waiting for a flight).
- Products in public spaces might experience higher activity levels, more frequent cleaning, and less care to the textile surface, all of which could damage or weaken the textile matrix and influence releases and exposures.

With the exception of these potential differences in exposure settings and activity patterns, the pathways and scenarios through which consumers might be exposed in nonresidential settings to decaBDE during general consumer use scenarios for end products upholstered with decaBDE flame-retardant coatings are not expected to differ from those described previously in Section H.4.2.2.1 on exposures from intended use of upholstered products in residential spaces.

H.4.2.2.3. Intended Use – Aircraft and Automobile Upholstery

Flame-retardant upholstery can be used for seating, draperies, carpets, and other textiles in passenger cars and public and private transportation. Aircraft and automobile passengers, and those working in these environments (e.g., cab drivers, flight attendants), could be exposed to higher levels of BDE-209 due to the higher concentrations of PBDEs in dust in those environments as compared to home environments (Lagalante et al., 2011; Christiansson et al., 2008). Dust generated by abrasion of treated upholstery fabric is the most likely pathway for BDE-209 exposure in automobiles (Lagalante et al., 2011). No association was found, however, between time spent in automobiles and plasma PBDE levels in children aged 2–5 years in California (Rose et al., 2010); these children spent an average 7.2 hours per week (range 0–20 hours) in the car.

Photodegradation of BDE-209 is low in cars because automobile glass blocks UVB radiation, which is the region of the spectrum most strongly absorbed by BDE-209. BDE-209 adsorbed to sodium sulfate does photodegrade in automobiles, however, and has a half-life of approximately 19 days. The congeners BDE-47 and BDE-99 are environmentally and toxicologically relevant products of BDE-209 debromination (see Text Box H.3-1), but their presence in automobile dust is mainly from volatilization and weathering of products containing pentaBDE, rather than photodegradation of BDE-209 and other higher brominated congeners (Lagalante et al., 2011).

The pathways through which consumers might be exposed in vehicles (including airplanes) to decaBDE during general consumer use scenarios for end products upholstered with decaBDE flame-retardant coatings are described below:

- **Inhalation.** Inhalation of decaBDE adsorbed to dust from worn or abraded automobile upholstery is expected to occur. Inhalation exposure to photodegradation products of decaBDE could occur in automobiles if automobile textiles contain decaBDE adsorbed to sodium sulfate. The recirculation of air in aircraft cabins also might affect exposure to particulate decaBDE if filters do not adequately remove these particles.
- **Oral.** Secondary oral exposures might occur if inhaled particulate decaBDE or particulate decaBDE that deposits on the skin is subsequently ingested.
- **Dermal.** Dermal exposures to decaBDE or decaBDE photodegradates (due to worn or abraded automobile upholstery) are expected to occur, particularly when skin touches the treated part of the textile directly. Dermal exposure also can occur when particles in the air settle on the skin. Different exposure characteristics or scenarios (e.g., children sitting in safety seats) might influence whether dermal exposure occurs, or influence the extent to which exposure occurs through this pathway.

H.4.2.2.4. Unintended Use, Repurposing, or Reuse of Treated Textiles and Upholstered Products

As introduced in Section H.2.4, unintended uses of upholstery textiles treated with decaBDE flame-retardant coatings could include repurposing of treated upholstery textiles for clothing, building

insulation, other in-home or outdoor furnishings, bedding, or other purposes. The repurposing stages could introduce occupational exposures similar to those discussed in Section H.4.2.1.2 (exposures during formulation of the flame retardant, application to textiles, and upholstering) and Section H.4.2.1.3 (exposure during storage and distribution), as products that are treated with flame-retardant coatings are broken down and reprocessed into new products.

Although no information was identified that directly addresses potential consumer exposures following unintended use or reuse of flame-retardant upholstery textiles, exposure pathways and scenarios from other life-cycle stages are relevant here. Most reuse scenarios might differ little from those for anticipated consumer uses, but a few key differences might occur, particularly when products are repurposed for new uses or used in unintended ways:

- Processes similar to those involved with product manufacture (e.g., cutting, sewing) and storage of textiles also might be employed for repurposing treated textiles. In this scenario, however, these processes are not expected to occur in an occupational setting, but in the home or another private space, where no personal protective equipment is worn and limited control technologies are used. These processes, as employed for repurposing textiles, however, are not expected to occur as commonly or at the same scale as in a manufacturing facility.
- Older, more degraded textiles with weakened matrices might be handled directly and be subjected to abrasion, thereby releasing the product constituents in the vicinity of the consumer conducting the repurposing.
- Although dermal contact with products used for their intended purpose (e.g., furniture seating) might be limited by a clothing barrier between the consumer and the treated textile, should flame-retardant upholstery textiles be repurposed into clothing, direct dermal contact might occur repeatedly over long periods of time.

With the exception of these potential differences in exposure characteristics, the pathways and scenarios through which consumers might be exposed to decaBDE during repurposing, reuse, or unintended use of treated textiles and upholstered products are not expected to differ from exposure pathways associated with the cutting, tailoring, or other abrasive processes involved with product manufacturing (Section H.4.2.1.2); storage of textile products (Section H.4.2.1.3); and consumer use in residential and nonresidential spaces (Sections H.4.2.2.1 and H.4.2.2.2).

H.4.2.3. General Public Exposure Pathway Scenarios through Environmental Media

No information was found on exposure to decaBDE in the general public from environmental media (e.g., air, water, soil). See Section H.4.1.2 for concentrations of BDE-209 in environmental media that could be used with the exposure pathway and scenario characteristics below to estimate potential exposures.

H.4.2.3.1. Outdoor Air

Releases of decaBDE to outdoor air throughout the product life cycle of the flame-retardant textile coatings are possible (see Section H.2). Once released to air, decaBDE can sorb to particulate matter and experience long-range transport to areas distant from its source (see Section H.3.2). As summarized in Section H.4.1.2.1, decaBDE has been measured in outdoor air at concentrations much lower than those measured indoors. Nonetheless, general public exposures to decaBDE adsorbed to particulate matter in ambient air are expected to occur, with the primary route being inhalation.

Other product constituents of flame-retardant textiles (e.g., pieces of the polymer matrix or the textile fabric) also can be released, and in the case of decaBDE, combustion by-products (e.g., PBDDs, PBDFs) and lower brominated transformation products are expected to be present in air as a result of the flame-retardant textile coating life cycle.

H.4.2.3.2. Water

Releases of decaBDE and other product constituents to wastewater and ambient water bodies throughout the product life cycle of flame-retardant textile coatings are possible (see Section H.2). Once released to water, decaBDE is expected to sorb to particulate matter in the water column or to sediments, which might limit their mobility (see Section H.3.3). This behavior implies that decaBDE also primarily will be removed to sludge during wastewater treatment.

As summarized in Section H.4.1.2.2, decaBDE has been measured in surface waters at low concentrations [below levels of detection to 191.0 pg/L (Oros et al., 2005)]. As a result, general public exposures to decaBDE and its transformation products in water are expected to occur, with the primary routes being dermal (through bathing and swimming) and oral (drinking and incidental ingestion during bathing and swimming).

H.4.2.3.3. Soil

Releases to ambient air and water throughout the product life cycle of flame-retardant textile coatings will result in deposition of particles of decaBDE and other product constituents (see Section H.2) to soil. Once deposited, decaBDE is expected to sorb strongly to soil, which might limit mobility (see Section H.3.4).

As summarized in Section H.4.1.2.3, decaBDE has been measured in surface soils and is expected to be present in sludge applied to agricultural soils. As a result, general public exposures to decaBDE and its transformation products in soils are expected to occur, with the primary routes being dermal and oral (although in incidental amounts). Furthermore, decaBDE has been shown to translocate

from soil to plant tissues, suggesting that decaBDE can enter the food web, and dietary oral exposures also might occur.

H.4.2.4. Highly Exposed Populations

This section discusses characteristics of individuals and populations that might result in increased exposure (relative to the general population) to decaBDE released during the life cycle of flame-retardant upholstery textile coating.

The primary exposure pathway for decaBDE is likely to be ingestion of household dust, and dust levels in the home can vary by socioeconomic status or the type and condition of housing (see Section H.5.3.1). Disproportionate levels of exposure can occur in specific populations, including low-income and low-educational-attainment populations. Although race and ethnicity have not been shown to be associated with specific physiological conditions that increase susceptibility to exposure, demographic factors such as socioeconomic and educational status could cause some populations to bear a disproportionate level of the exposure burden.

Children are likely to experience higher exposures than the general population. Data suggest that breast-fed infants are potentially exposed to BDE-209 through their mother's milk [i.e., worldwide, median detected levels of BDE-209 in breast milk range from 0.1 to 2.9 ng/gram liquid weight (Frederiksen et al., 2009); maximum concentration of 7 breast milk samples containing decaBDE in the United States was 8.24 ng/gram lipid (ATSDR, 2004)]. Young children also take in more household dust than adults, with estimates for children at 100–200 mg/day compared to 50 mg/day for adults (U.S. EPA, 2008a). Increased hand-to-mouth activity contributes to increased exposures in children. Occupation also could increase exposure relative to the general population, primarily for workers involved in manufacture of decaBDE or flame retardants containing decaBDE, or textile products treated with decaBDE.

H.4.2.5. Exposure Reference Values and Recommendations

A variety of exposure standards, guidelines, or recommendations are developed by different organizations with purview over specific portions of the population or situations during which exposure might occur (e.g., occupational exposures, general population drinking water exposures). Available information on these types of values for decaBDE is presented below. Section H.5.1.1 discusses how some of these values inform quantitative toxicity assessments.

As of January 2011, no national-level environmental or occupational health standards had been established for decaBDE (DOD, 2011). EPA has derived a reference dose (RfD) for decaBDE, based on developmental neurobehavioral effects, of 0.007 mg/kg-day (U.S. EPA, 2008b) (see Section H.5.1).

An RfD is an estimate (taking into account uncertainty) of the daily exposure to the human population, including sensitive populations, that is "likely to be without an appreciable risk of deleterious effects during a lifetime" (U.S. EPA, 2008b). EPA also has derived a cancer slope factor for decaBDE based on neoplastic nodules or carcinomas (combined) in the liver of treated male rats, of 7×10^{-3} per mg/kg-day. A cancer slope factor is a plausible upper bound on the estimate of risk per mg/kg-day of oral exposure (U.S. EPA, 2008b). The Agency for Toxic Substances and Disease Registry has developed a minimal risk level (MRL) for decaBDE for intermediate duration (15–365 days) oral exposure of 10 mg/kg-day (ATSDR, 2004) based on Hardy et al. (2002). MRL values are estimates of the daily exposure to a hazardous chemical that is likely to be without appreciable risks of non-cancer health effects over a specific duration of exposure.[29] MRLs are intended as screening levels, rather than clean-up or action levels for any agency. Differences in exposure duration (chronic lifetime versus intermediate) and the key study used to derive the estimate contributed to the several-orders-of-magnitude difference between the MRL and RfD for decaBDE.

H.4.2.6. Toxicokinetics, Dose, and Body Burden

Toxicokinetics can be used to relate exposure and contact, such as those described in the scenarios above, with uptake and dose. Specifically, toxicokinetics describes how a material is absorbed, distributed, metabolized, and excreted in an organism. An understanding of the relationship between each of these concepts, which are often referred to as ADME, leads to an understanding of the concentration, or dose, of material that can reach—and potentially accumulate in—different tissues of the body.

H.4.2.6.1. Absorption, Distribution, Metabolism, Excretion

This section contains information regarding the toxicokinetic behavior of decaBDE when administered to mammals. Information regarding birds and fish is not presented in this section because, when extrapolating toxicokinetic data to humans, studies conducted with rodents (rat or mouse) or nonrodent mammals (dog or monkey) are generally used. Additionally, differences among species have been noted in numerous studies of decaBDE, and the toxicokinetic behavior in response to decaBDE differs among birds, fish, and mammals. For example, fish generally debrominate decaBDE to pentaBDE congeners, while mammals debrominate decaBDE, to a lesser degree, to heptaBDE congeners. See Section H.4.3 for toxicokinetic information relevant to ecological exposures.

Early toxicokinetic studies (el Dareer et al., 1987; NTP, 1986; Norris et al., 1975; Norris et al., 1973) were conducted on decaBDE shortly after it was developed as a flame retardant. These studies

[29]ATSDR – Minimal Risk Levels: http://www.atsdr.cdc.gov/mrls/index.asp.

demonstrated that decaBDE is poorly absorbed [0.3–1.5%; (NTP, 1986)] from the gastrointestinal tract in rats following oral exposure and eliminated in the feces as the parent congener without prior metabolism. Essentially no elimination occurred through the urine, and more than 99% of the dose was recovered in feces by 48 hours, indicating a lack of accumulation in tissues (Norris et al., 1975). The half-life of decaBDE is relatively short; the serum half-life was reported as 15 days in a human study where workers were exposed to BDE-209 (U.S. EPA, 2010a).

More recent studies, although in general agreement, have reported higher absorption rates that might be due to the solvent used to administer decaBDE. In general, BDE-209 is not expected to accumulate in terrestrial organisms. Many studies, however, have reported levels of BDE-209 in humans (breast milk, serum, and umbilical cord blood), food items (dairy, eggs, infant formula), and biota (fish, shellfish), indicating that some absorption and accumulation occur over time (Frederiksen et al., 2009). Given the high trophic levels of the organisms where accumulation has been observed (humans, predatory fish, and piscivorous birds), biomagnification appears to occur in these receptors (Environment Canada, 2010; U.S. EPA, 2010a). Bioaccumulation and biomagnification are discussed further in Section G.4.2.1.

Because of the low absorption of BDE-209, blood and tissue levels following acute (short-term) oral exposures are typically low and represent a small fraction of the total dose. More than 66% of the parent compound was excreted in the feces of rats following oral exposures to BDE-209 (Riu et al., 2008; Mörck et al., 2003). The same experiments showed that the highest concentrations of BDE-209 were found in plasma and blood-rich tissues such as liver, kidney, adrenal glands, ovaries, heart, and the intestinal wall following a single oral exposure (Mörck et al., 2003) or 4-day gavage exposure (Riu et al., 2008; Mörck et al., 2003). In these acute studies, BDE-209 was not readily distributed to adipose tissue.

In contrast, evidence shows that BDE-209 can accumulate in adipose tissue following chronic oral exposure. Studies by Norris et al. [1974; 1975, as cited in Hardy et al. (2009)] exposed Sprague-Dawley rats to a commercial product called FR-300-BA in the diet at 0.01, 0.1, and 1.0 mg/kg-day for 3, 6, or 12 months. FR-300-BA comprised 77.4% BDE-209, 21.8% nonaBDE, and 0.8% octaBDE. After 6 months of treatment, bromine concentrations (measured by neutron activation analysis) in adipose tissue were higher in treated rats (~3 μg/gram) than in controls (~1 μg/gram), but after 12 months the bromine levels in adipose tissue were similar to controls. Bromine did not accumulate in other tissues such as liver, kidney, and serum. Norris et al. [1974; 1975, as cited in (Hardy et al., 2009)] also followed the elimination of bromine from male Sprague-Dawley rats that were dosed with FR-300-BA in the diet for 90 days at 1.0 mg/kg-day and subsequently fed a control diet. After 10 days on a control diet, concentrations of bromine in the liver were similar to controls, but concentrations in adipose tissue were higher (~2.5 to 4 μg/gram) than controls (~0-2 μg/gram). Another study showed a time- and dose-dependent increase of bromine levels in adipose tissue indicating accumulation following dietary

exposure to decabromodiphenyl oxide (a synonym for decaBDE) at 0.01, 0.1, or 1 mg/kg-day, for up to 2 years (Kociba et al., 1994). Kociba et al. (1994) also reported that bromine content was not increased compared to controls in the kidney, muscle, or serum of rats in the same study.

Absorbed decaBDE is metabolized in the liver and a minor fraction of the parent compound is metabolized to lower PBDE congeners, such as tetraBDE and pentaBDE (see Text Box H.3-1). Mörck et al. (2003) reported that decaBDE was the predominant substance detected in the liver metabolites, with trace levels of nonaBDE. Similarly, a minor fraction of decaBDE (less than 3%) was debrominated to lower BDE congeners in a feeding study that exposed male Sprague-Dawley rats to DE-83R (98.5% decaBDE) (Huwe and Smith, 2007).

Metabolism of decaBDE to lower brominated congeners by oxidative debromination is indicated by some evidence in studies of rats and fish, but the mechanisms and location of metabolic processes are not well characterized due to limited availability of toxicokinetic data (Hakk and Letcher, 2003). Metabolism of decaBDE also differs among species. In lactating cows, Kierkegaard et al. (2007) suggested that decaBDE debrominates to hepta-, octa-, and nonaBDEs. Octa- and nonaBDEs were found in liver and kidney of rats fed 100 mg/kg-day BDE-209 for 3 months (Wang et al., 2010a). In contrast, in vitro studies of human hepatocytes have shown evidence of low or no metabolism, possibly because of low entry of BDE-209 into cells under the experimental conditions used (Stapleton et al., 2009).

Based on available studies (Huwe and Smith, 2007; Kierkegaard et al., 2007; Hakk and Letcher, 2003; Mörck et al., 2003; Sandholm et al., 2003), the following pathways for debromination of decaBDE can be deduced for mammals:

1. Deiodinase enzymes can debrominate decaBDE to nona-, octa-, and heptaBDEs.

2. Debrominated neutral metabolites can undergo hydroxylation to potentially form phenols or catechols, possibly via an arene oxide, which could involve the action of cytochrome P450 enzymes.

   a. The formed hydroxylated BDEs can compete with thyroxine for binding to a thyroxine transport protein present in blood serum.

   b. The catechols then are methylated, potentially by the action of catechol-O-methyltransferase, to form guaiacols.

   c. The guaiacol metabolites further oxidize to highly reactive quinones, which bind to cellular macromolecules.

   d. The reactive intermediates are subject to rapid conjugation via Phase II metabolic processes, leading to water-soluble metabolites that are excreted via bile and feces, as observed in conventional and cannulated rats.

Two toxicokinetic studies of fetal rats were identified. In a study by Riu et al. (2008), radiolabeled ^{14}C-BDE-209 (99.8% pure, dissolved in peanut oil) was administered orally to pregnant rats on Gestation

Days (GD) GD16–GD19 (2 mg/kg-day). The toxicokinetic results were similar to those noted previously in this section. Approximately 72% of the dose was found in the feces and the digestive tract contents, while 0.1% was excreted in the urine. The remainder of the dose was distributed in various tissues, with 6.5% in the liver and 5.3% in the digestive tract contents. All other tissues contained less than 1% of the administered dose. The fetuses (sum for the whole litter) contained 0.43% of the dose. In a recent study by Cai et al. (2011), BDE-209 and its metabolites were detected in the placenta and milk, and eventually in the fetuses or neonates when BDE-209 (prepared in peanut oil) was administered to pregnant Sprague-Dawley rats from GD7 to PND4. In the same study, detectable amounts of nonaBDEs (BDE-206, 207, 208) and octaBDEs (BDE-196, 197/204, 198/203) were observed in the dosed rats. The predominant debrominated metabolites of BDE-209 detected in fetuses were nonaBDEs (BDE-208, 207, 206). The level of BDE-206 in the fetal or pup bodies was significantly lower on GD21 and PND4 than on GD7. The octaBDEs BDE-196, BDE-198, and BDE-203 were observed in fetuses and pups, but were minor debromination metabolites of BDE-209.

No animal studies have been identified that evaluate decaBDE ADME upon inhalation and dermal exposures.

H.4.2.6.2. Internal Dose and Body Burden

Levels of decaBDE in human tissues have been reported in several occupational studies and in studies of the general public. A study in workers at an electronics dismantling plant in Sweden evaluated levels of five PBDEs in serum samples from plant workers. The mean concentration of BDE-209 in that study was as high as 5 ng/gram lipid (Darnerud et al., 2001). Total PBDE serum levels in hospital cleaners, computer clerks, and electronics dismantlers were 3, 4, and 26 ng/gram lipid, respectively (Darnerud et al., 2001). As discussed in the previous section, decaBDE can accumulate in adipose tissue over time with chronic exposure (Hardy et al., 2009). DecaBDE also might biomagnify in the food web from lower trophic levels to higher trophic levels. DecaBDE can debrominate to lower PBDE congeners in the body, which are more bioaccumulative than decaBDE (Yogui and Sericano, 2009).

As shown in Table H-5, the median level of BDE-209 in the serum reported in one U.S. study was less than 0.96 ng/gram liquid weight. International studies reported median serum levels ranging from 0.77 to 18.5 ng/gram liquid weight. The highest median levels reported were in men aged 40–50 years in Norway and Sweden, and the lowest median levels were from maternal serum in a study in the Faroe Islands (Frederiksen et al., 2009).

BDE-209 has been detected in breast milk in American women at a measured mean concentration of 0.92 ng/gram liquid weight (see Table H-5). A study that evaluated the breast milk of women in the

Pacific Northwest region of Canada and the United States observed a median level of 0.43 ng/gram liquid weight.

Table H-5. Median tissue concentration ranges (in ng/gram liquid weight) for three polybrominated diphenyl ether congeners in humans.

Country	BDE-47	BDE-99	BDE-209
Breast Milk			
United States	7.69–27.8[1]	1.46–5.7	0.92[2]
International	0.03–27.8	0.02–5.36	0.1–2.9
Adipose Tissue			
United States	29.3	10.3	NR
International	0.52–2.3	0.236–1.4	NR
Blood (Serum)			
United States	0.63–46	0.32–13	<0.96
International	0.25–4.55	0.09–1.94	1.1–18.5
Cord Blood			
United States	13.6–25	4.3–7.1	Below detection[3]
International	0.98–3.8	0.07–4.3	2.2
Placenta			
United States	NR	NR	NR
International	0.25–0.77	0.12–0.41	1.0

[1]High level observed in a joint United States/Canada study.
[2]Mean concentration reported.
[3]Detection limits not reported.
NR = Not reported.
Source: Frederiksen et al. (2009).

Worldwide, median detected levels of BDE-209 in breast milk ranged from 0.1 to 2.9 ng/gram liquid weight (Frederiksen et al., 2009). Decline in the use of decaBDE flame retardants containing BDE-209 are expected to result in a decline in breast milk concentrations over time.

Breastfeeding infants, and even infants who are fed infant formula, are likely to be exposed to BDE-209 through consumption of breast milk and formula. Levels of BDE-209, and levels of total PBDEs, are higher in American samples of breast milk than levels found in infant formula. The levels in

both breast milk and formula, however, are far lower than the amount detected in household dust (Frederiksen et al., 2009).

H.4.3. Ecological Exposure and Kinetics Leading to Dose

H.4.3.1. Factors Impacting Ecological Exposure

In biota, potential exposure routes for decaBDE include ingestion, inhalation, or direct contact. The potential for exposure via each route along with subsequent uptake and dose depends on several factors, including properties of the environmental media and physiological and behavioral characteristics of aquatic and terrestrial organisms. These factors can, in turn, influence the bioavailability of decaBDE. As discussed in Section H.3, the physicochemical properties of BDE-209 dictate partitioning into the environment. This partitioning drives the exposure potentials for water-dwelling, sediment-dwelling, and terrestrial organisms. For example, BDE-209 preferentially binds to soils and sediment when released to the environment (Hale et al., 2006) and likely will be present only in limited quantities in surface water or ground water (see Section H.4.1.2.2) (U.S. EPA, 2010a). Sediment-dwelling organisms are therefore key ecological receptors of BDE-209.

H.4.3.2. Absorption, Distribution, Metabolism and Excretion in Ecological Receptors

As discussed in Section H.4.2.6, an understanding of ADME processes can be used to relate exposure concentrations to the concentration, or dose, of material that reaches the tissues of an organism. Elucidation of organism-specific ADME processes can help explain observations of high body burdens that were not predicted based on environmental fate and partitioning alone. ADME processes influence whether and for how long a material is retained in a tissue (i.e., whether the material will bioaccumulate) and how such retention rates might differ among trophic levels (i.e., whether concentrations of the material will biomagnify in a food web).

Bioaccumulation and biomagnification have been shown to influence ecological exposures for decaBDE, as described further in Sections G.4.2.3 and H.4.3.4. Bioaccumulation is the process by which an organism takes a chemical into the body through all exposure routes and dilutes the chemical through excretion, metabolism, and growth, but accumulates a net "body burden" of the chemical (Environment Canada, 2010; U.S. EPA, 2010a). Biomagnification is the process by which a chemical increases in concentration in tissues as it moves up trophic levels in an ecosystem (U.S. EPA, 2010a). Bioaccumulation factors, the ratio of the chemical contaminant in the tissue of the biota (from dietary exposure and uptake directly from media) to chemical contaminant in the medium, and biomagnification

factors (BMFs), the ratio of the chemical concentration in an organism's tissue to the concentration of the same chemical in the tissues of its diet, are used as measures of persistence and potential for impacts as a chemical moves through an ecosystem (U.S. EPA, 2010a). A substance is considered bioaccumulative when it has a high bioaccumulation factor, generally greater than 5,000 (U.S. EPA, Final Rule 40 Code of Federal Regulations 372). Bioaccumulation studies that show body burdens in organisms in remote locations far from a direct, nondietary exposure source (e.g., water, air), such as those in Greenland peregrine falcons or Florida coastal sharks, are indicative of trophic biomagnification through the food web (Environment Canada, 2010). Biomagnification can be modeled using fugacity-based dynamic fate models that consider environmental conditions, ecosystem properties, and food-web dynamics (Lim and Lastoskie, 2011).

Ecological receptors are likely to be exposed to decaBDE through treated products or scraps and debris from products generated during end-of-life stages of the product life cycle (see Section H.2). The materials released during these processes can contain components other than the contaminant of concern (e.g., textile material, glue, composite ingredients). As discussed at the beginning of this section (H.4) and throughout Section H.4.2, studies are lacking on the matrix-bound state of these compounds and how exposure characteristics and dose implications differ for the free and matrix-bound forms. As for the discussion of human exposures in Section H.4.2, exposure considerations for ecological receptors are informed by data on BDE-209 not embedded in a polymer matrix or associated with other product ingredients (e.g., textile fibers, coating ingredients). Field studies have found raw PBDEs in environmental media, which indicates that the compounds can leach from the product matrix (see Appendix E).

H.4.3.3. Exposure Pathways in Aquatic Systems

PBDEs primarily transition to the sediment in aquatic ecosystems (Mikula and Svobodová, 2006); as a result, benthic organisms might take up decaBDE via absorption or ingestion of sediment. Secondary exposure via movement through the food web results in greater body burdens of PBDEs in predatory fish than in herbivorous or omnivorous fish (Mikula and Svobodová, 2006). In fish, uptake of PBDE from the water column via gills is limited by the large molecular size of PBDEs, but dietary uptake efficiencies have been shown to range from 40 to 92% (Mikula and Svobodová, 2006). Due to the tendency for PBDEs to partition into sediment and the inefficiency of uptake via gills, the more likely route of exposure for fish is secondary exposure due to bioaccumulation and biomagnification in the food web.

Toxicokinetics and Body Burden in Aquatic Systems

Limited information is available on the mechanisms of BDE-209 ADME in aquatic organisms; most studies to date have measured concentrations of PBDEs in tissues of aquatic organisms to estimate body burdens. BDE-209 and the lower brominated congeners BDE-206, BDE-207, and BDE-208 were experimentally shown to accumulate in the liver of juvenile lake whitefish (*Coregonus clupeaformis*) as a result of exposure to BDE-209 via the diet (Kuo et al., 2010). Fish exposed to 2 μg/gram diet BDE-209 for 30 days accumulated a mean of 5.80 nmol/gram lipid in the liver, compared to 0.208 nmol/gram lipid for the rest of the body and 0.183 nmol/gram lipid in the liver of control fish. Liver concentrations of BDE-206, BDE-207, and BDE-208 also were higher compared to control, although concentrations were less than 0.01 nmol/gram lipid for each congener (Kuo et al., 2010).

Similarly, juvenile lake trout (*Salvelinus namaycush*) exposed to various PBDE congeners for 56 days accumulated measurable PBDE concentrations, and depuration half-lives ranged from 26 to 346 days (Tomy et al., 2004). When BDE-209 was present in the diet at 3.4 ng/gram dry weight, the uptake rate constant was calculated as 132 grams/day. When the concentration of BDE-209 in the diet was raised to 27.5 ng/gram dry weight, the uptake rate constant was much lower—6.1 grams/day. Study authors determined a half-life for BDE-209 of 26 ± 5 days, and a BMF of 0.3 (Tomy et al., 2004). BMFs of other congeners ranged from 1.6 to 45.9.

Body burdens of PBDEs in aquatic organisms have been studied in top predators such as piscivorous birds of prey and top-level fish and in lower level organisms like insects and crabs (Environment Canada, 2010; U.S. EPA, 2010a; Environment Canada, 2006) (see Section E.2 of Appendix E). Bottom feeders and bivalves often have the lowest PBDE body burdens, eels and higher level fish like sole and flounder have the highest body burdens, and shrimp have mid-range body burdens (U.S. EPA, 2010a). Studies have shown accumulation of BDE-209 (exceeding 100 ng/gram) in top predators, including sharks in coastal Florida and marine mammals such as harbor porpoise and white-beaked dolphin (Environment Canada, 2010). Although BDE-209 likely only accumulates at low levels in lower trophic-level organisms, biomagnification can lead to relatively greater concentrations in higher trophic levels.

Bioaccumulation rates of BDE-209 and other PBDE congeners are affected by significant biotransformation and debromination (Tomy et al., 2004), so determining the level or pattern of PBDE uptake from the environment and accumulation in biota is difficult. Laboratory-based studies that control the exposure rates and measure tissue concentrations allow for calculations of uptake rates, depuration rates, and BMFs. For example, in a study by Kierkegaard et al. (1999), juvenile rainbow trout (*Oncorhynchus mykiss*) were exposed to technical-grade decaBDE via diet for 120 days, and then observed for 71 days postexposure. The level of decaBDE in the diet ranged from 7.5 to 10 mg/kg body

weight per day. Study authors determined that the total uptake in muscle was between 0.02 and 0.13% of the exposure level. Fish tissue concentrations of BDE-209 increased over the course of the exposure period, reaching 38 ng/gram fresh weight in muscle and 870 ng/gram fresh weight in the liver at Day 120. Concentrations declined during the 71-day depuration period to 9.5 ng/gram fresh weight in muscle tissue and 30 ng/gram fresh weight in the liver (Kierkegaard et al., 1999).

Bioavailability and bioaccumulation of BDE-209 are limited by the high molecular weight of BDE-209 and its strong sorption to soils and sediments (Kierkegaard et al., 2004). In general, PBDEs can bioaccumulate and biomagnify in the aquatic food web (Agrell et al., 2004). Their propensity to bioaccumulate and biomagnify depends in large part on their level of bromination. Highly brominated congeners like BDE-209 have a tendency to sink into aquatic sediments and are a minor congener found in aquatic biota. Benthic sediments are a major sink for PBDEs, but BDE-209 does not appear to be readily available to benthic organisms for uptake, although some movement through the food web does occur (Ciparis and Hale, 2005). To what extent BDE-209 can be transformed in the environment to lower brominated congeners like BDE-47 and BDE-99 is uncertain; BDE-47 and BDE-99 have been identified as the congeners frequently found in biota (Watanabe and Sakai, 2003).

Studies analyzing tissue levels and body burdens of PBDEs in organisms having various roles in a specific ecosystem and food web best illustrate biomagnification, as they quantify the body burdens of different organisms and relate these to food web relationships. In a study by Law et al. (2006a), authors illustrated biomagnification of brominated flame retardants (including PBDEs) in Lake Winnipeg, Canada by determining trophic structure, assessing trophic transfer, and quantifying the magnitude of biomagnification. Samples of water, sediment, plankton, mussels, and six fish species were collected over a four-year period and analyzed for whole-body (in invertebrates) or muscle-tissue (in vertebrates) concentrations of contaminants (see Appendix E, Table E-8). As Table H-6 shows, biomagnification of various PBDE congeners in individual species predator-prey relationships ranged from very positive (BDE-209 concentration in emerald shiner was 33 times higher than in zooplankton) to negative (BDE-99 concentration in emerald shiner was 10 times lower than in zooplankton) (Law et al., 2006a). The general trend illustrates, however, that higher level predators generally have higher body burdens of PBDEs than lower level prey. The authors determined a trophic magnification factor (which represents the average predator-prey transfer through a food web, as opposed to a BMF, which represents a transfer for a single predator-prey relationship) of 3.7 for total PBDEs in the system, and congener-specific trophic magnification factors of 5.2 for BDE-47 (tetraBDE), 1.5 for BDE-99 and 3.0 for BDE-100 (pentaBDEs), and 10.4 for BDE-209 (decaBDE) (Law et al., 2006a).

H.4.3.4. Exposure Pathways in Terrestrial Systems

Although PBDEs are detected commonly in terrestrial ecosystems, exposure levels are higher for terrestrial organisms with diets that consist of animals from the aquatic system than for herbivorous organisms or organisms with diets consisting of animals from the terrestrial system (Mikula and Svobodová, 2006). As discussed in Section H.3.2, LRT can result in exposure to terrestrial organisms far from the initial source of release (de Wit et al., 2010; Su et al., 2009; Breivik et al., 2006; Agrell et al., 2004).

Toxicokinetics and Body Burden in Terrestrial Systems

Table H-6. Biomagnification factors of select PBDE congeners in an aquatic ecosystem.

Predator	Prey	BDE-47	BDE-99	BDE-100	BDE-153	BDE-209
System: zooplankton → emerald shiner → walleye, burbot[1]						
Walleye	Emerald shiner	0.3	1.2	0.2	0.3	0.6
Burbot	Emerald shiner	0.7	9.5	1	1.7	2.4
Emerald shiner	Zooplankton	5.2	0.1	2.2	1.2	33
System: zooplankton, mussels → white sucker → walleye[1]						
Walleye	White sucker	0.2	2.1	0.1	0.2	2
White sucker	Zooplankton	6.1	0.1	3.4	2.2	9.9
White sucker	Mussels	3.4	0.1	2.9	1.5	0.2

[1]Trophic levels: mussel → zooplankton, whitefish → goldeye, emerald shiner, white sucker → burbot, walleye.

Note: Biomagnification factor (BMF) is the lipid-corrected BDE concentration in predators / lipid-corrected BDE concentration in prey. BMF >1 indicates concentration in predator higher than in prey; BMF <1 indicates concentration in prey higher than in predator. Gray shading highlights where BMF >1, indicating that biomagnification has occurred as one moves up trophic levels.

Source: Law et al. (2006a).

Table H-6, cont.: Biomagnification factors of select PBDE congeners in an aquatic ecosystem.

Predator	Prey	BDE-47	BDE-99	BDE-100	BDE-153	BDE-209
System: zooplankton, mussels → goldeye → walleye[1]						
Walleye	Goldeye	0.2	0.1	0.1	0.1	0.6
Goldeye	Zooplankton	7.2	6.5	4.9	5.5	34
Goldeye	Mussels	4	4.4	4.2	3.9	0.8
System: zooplankton → whitefish → walleye[1]						
Walleye	White fish	8.9	1.7	3.9	4.6	6.8
White fish	Emerald shiner	0.1	0.7	0.1	0.1	0.1
White fish	Zooplankton	0.2	0.1	0.1	0.1	2.9

[1]Trophic levels: mussel → zooplankton, whitefish → goldeye, emerald shiner, white sucker → burbot, walleye.

Note: Biomagnification factor (BMF) is the lipid-corrected BDE concentration in predators / lipid-corrected BDE concentration in prey. BMF >1 indicates concentration in predator higher than in prey; BMF <1 indicates concentration in prey higher than in predator. Gray shading highlights where BMF >1, indicating that biomagnification has occurred as one moves up trophic levels.

Source: Law et al. (2006a).

Limited information is available on the mechanisms of BDE-209 ADME in terrestrial organisms; most studies to date have measured concentrations of PBDEs in specific tissues of terrestrial organisms to estimate body burdens. Body burdens of PBDEs in terrestrial organisms have been studied in top predators such as piscivorous and carnivorous mammals and birds of prey. DecaBDE studies have shown high accumulation (exceeding 100 ng/gram) in the liver and muscle tissues of top predators, including kestrel and sparrowhawk in China, the United Kingdom, and Sweden; peregrine falcon in the United Kingdom, Sweden, and Greenland; and buzzard and red fox in Belgium (Environment Canada, 2010). An EPA (2010a) review reported total PBDE concentrations in tissues of predatory birds ranged from below detection limits in some tissue types to greater than 12,000 ng/gram weight in some muscle and liver tissues (see Appendix E, Table E-7).

As previously discussed, the high molecular weight and strong sorption of BDE-209 to soils and sediments would suggest that bioavailability and bioaccumulation are limited in terrestrial systems. Body burdens of BDE-209, however, have been identified in some—but not all—terrestrial organisms, suggesting that biomagnification does sometimes occur. The complexity of food web interactions that cross aquatic and terrestrial systems makes it challenging to determine whether the source of BDE-209 in terrestrial food webs stems from contaminated abiotic media in the aquatic environment (e.g., sediments, interstitial waters), the terrestrial environment (e.g., soils, pore water), or a combination of both.

H.4.4. Aggregate Exposures

Assessing aggregate exposures involves characterizing exposures to a single chemical across multiple exposure routes. Due to the range of applications for which decaBDE can be used, release from multiple products and subsequent exposure via multiple routes is anticipated.

BDE-209 and the other PBDEs are ubiquitous in the environment (Daso et al., 2010). The average daily intake of PBDEs from various routes has been evaluated, and inhalation of dust provides the highest contribution to body burden of PBDEs. As discussed in Section H.4.1.2.5, levels of BDE-209 in household dust are orders of magnitude higher than in other matrices, by weight. BDE-209 is also the main PBDE contaminant in household dust (Daso et al., 2010). Data are not available on the relative contribution to household dust of BDE-209 from textile sources.

Measurable levels of BDE-209 are found in various types of food worldwide, including milk, fish, shellfish, eggs, beef, chicken, cheese, butter, and other dairy products. The highest concentrations in food have been reported for cod liver, with fish generally making up the highest dietary source of BDE-209 (Daso et al., 2010; Frederiksen et al., 2009).

As a result of exposure from various sources, BDE-209 has been detected in breast milk, serum samples, umbilical cord blood, and the placenta of humans (Daso et al., 2010; Frederiksen et al., 2009). Ingestion of food, ingestion of dust, inhalation of dust, and dermal contact with soil and dust are the known pathways by which humans are primarily exposed to BDE-209. One review estimates that exposure to BDE-209 from ingestion and dermal contact with soil and dust represents more than 29% of total PBDE exposure from these exposure routes, and that exposure through those routes accounts for 82% of total PBDE exposure from all routes (Lorber, 2008).

H.4.5. Cumulative Exposures

As stated in *The Exposure Factors Handbook* (U.S. EPA, 2011), "Cumulative exposure is defined as the exposure to multiple agents or stressors via multiple routes." For the purpose of this case study, the "multiple agents or stressors" considered to contribute to cumulative exposure include those substances that are produced or released as a result of the product life cycles of decaBDE flame-retardant upholstery textile coatings, facilitate uptake of decaBDE into humans and biota, are taken up as a result of decaBDE exposures, or induce effects in humans or biota through a comparable or synergistic mode of action.

As discussed in Section H.4.4 on aggregate exposure, PBDEs are ubiquitous in the environment due to their widespread use and physicochemical characteristics. The lower brominated congeners can be metabolites of higher congeners such as BDE-209, and subsequent exposure to lower congeners is likely

when BDE-209 is released to the environment. Like BDE-209, many of the lower brominated congeners such as BDE-47 and BDE-99 can bioaccumulate, and the lower brominated congeners generally are more toxic than BDE-209. Exposure to the lower brominated metabolites of BDE-209 is also likely following environmental degradation or aging of composites or textiles containing BDE-209 (Lagalante et al., 2011; Christiansson et al., 2008).

Manufactured textiles treated with decaBDE could include impurities from the synthesis process such as PBDDs and PBDFs (Ren et al., 2011). Breakdown or aging of flame-retardant textiles could contribute trace amounts of these pollutants to the environment. In addition, disposal or incineration of these textiles might generate more impurities.

Synergistic and antagonistic reactions have been observed in composites. Antimony compounds, which are typically used in the formulation of flame retardants containing decaBDE, tend to act synergistically with halogenated flame retardants to produce highly corrosive hydrogen chloride gas or hydrogen bromide gas, for example (Textile Exchange, 2012). These exposures likely would be limited to manufacturing activities. The decomposition or incineration of manufactured textiles, however, might release other gases that could cause synergistic reactions.

H.5. Potential Human Health, Ecological, and Other Impacts

The final step of compiling information into the CEA framework is to link the information described in the previous chapters on the product life cycle; transport, transformation, and fate; and exposure-dose with potential impacts to receptors. The CEA framework includes information relevant to impacts on human health and ecological receptors, similar to what might be investigated in traditional risk assessment processes, as well as other plausible impacts that might be considered in life-cycle-focused assessments (e.g., socioeconomics, climate change, resource depletion).

Section H.5.1 discusses potential impacts of exposure to decaBDE, and related contaminants on human health. This section relies heavily on evidence from experimental studies with laboratory animals, the results of which could be extrapolated to humans using established quantitative toxicity assessment techniques. As discussed in Section H.4, humans could be exposed to decaBDE or related contaminants from flame-retardant upholstery textiles through a variety of pathways, reaching receptors through dermal deposition, oral ingestion, or inhalation of these contaminants. This section discusses potential health impacts from these exposure routes; data are grouped to illustrate the types of impacts (e.g., pulmonary

toxicity, skin irritation, reproductive effects) observed in studies with laboratory animals exposed to decaBDE and sub-grouped by exposure routes for each impact.

Section H.5.2 discusses the potential impacts of environmental media contaminated with decaBDE on ecological health, which encompasses impacts on the organism, population, and ecosystem levels. This section is therefore approached from an ecosystem perspective (aquatic vs. terrestrial), and data on groups of organisms within those ecosystems are summarized. The discussion of impacts to ecological health focuses on identifying and comparing data on exposure levels that might cause significant mortality, delayed growth or development, reproductive defects, or other impacts that could alter community structure and potentially cause ecosystem collapse.

Finally, Section H.5.3 discusses other plausible impacts resulting from the product life cycles of decaBDE in flame-retardant upholstery textiles. The section includes a consideration of the energy input requirements for synthesis of decaBDE, the economic impacts related to the cost of material production, and the potential for disproportionate impacts on populations with lower socioeconomic status.

H.5.1. Human Health Effects

This section discusses the potential human health effects resulting from exposures to decaBDE. As noted in Section H.4, exposure to decaBDE from aggregate sources is likely; no studies were found that investigate impacts to human health that can be attributed directly to exposure to decaBDE or related compounds released during the life cycles of decaBDE flame-retardant upholstery textile coatings. Toxicology studies presented for decaBDE generally were conducted using BDE-209. As discussed in Section H.3 (see Text Box H.3-1), environmental degradation and debromination of decaBDE results in contamination of media with lower PBDE congeners. These lower PBDEs have toxicological relevance, as they are more bioavailable than decaBDE and potentially more toxic; toxicity of PBDEs generally decreases with increased number of bromine atoms (Rahman et al., 2001).

Toxicology studies conducted on animals comprise much of the information discussed in this chapter because studies on humans in the literature are limited. Effects observed in animal studies are typically extrapolated to humans when conducting quantitative toxicity assessments (e.g., when calculating an RfD or RfC; see Section H.4.2.5). Potential health effects associated with all routes of exposure (dermal, inhalation, and oral) are presented in this section because each is plausible for humans (see Section H.4 for additional exposure scenario information).

Dermal and oral exposures to decaBDE in dust seem to be the primary routes of exposure for consumer populations (see Section H.4.2.2). Because of higher levels of decaBDE contamination in dust and on other particles, the oral and dermal routes might also be expected to be prominent for general

public exposures (see Section G.4.1.1). Available data for decaBDE indicate that the inhalation exposure route appears to dominate for workers (see Section H.4.2.1). Although inhalation is a possible route of exposure, especially for workers, many inhalation toxicology studies identified were conducted by administering the test material (decaBDE) via intratracheal instillation and pharyngeal aspiration; these routes of administration require an invasive delivery of chemicals or particles and are not as physiologically relevant for risk assessment purposes, but could provide biological information useful for qualitative, mode-of-action determinations.

Available information on these exposure routes in experimental animal studies is grouped by the main types of health impacts observed in the literature, namely, in vivo and in vitro data on systemic toxicity, pulmonary toxicity, eye irritation, skin irritation, reproductive effects, developmental effects, immune system effects, genotoxicity/mutagenicity, carcinogenicity, and susceptible populations. Toxicology studies were reviewed and determined to be key if the following criteria were met:

- appropriate species and test system were used,
- appropriate dose levels were used,
- route of exposure was appropriate for humans,
- control groups were appropriate, and
- the study was consistent with standard principles and practices.

In some cases, multiple studies investigating the same endpoint were available, and the most robust study or the study that most closely aligned with current guidelines for toxicity testing was chosen as key. In other cases, no studies were available that met all the criteria provided above; available studies were then summarized with deficiencies noted in the text. If the study was considered key, a written summary was included in the appropriate section of this appendix. Key studies and supporting non-key studies are summarized in Table F-3 through Table F-11 in Appendix F. Because a large amount of published data is available for decaBDE, key studies presented in text are primarily those summarized by reviews or agency reports, and only a representative subset of studies are included in Appendix F.

The paragraph that follows (see Table 5-1 in Chapter 5) provides an overview of the findings for human health effects of decaBDE, after which a detailed discussion of the available data is presented.

Most toxicological studies for decaBDE involve the oral route of exposure (see Section H.4.2.2 for discussion on why the oral route appears to be a primary exposure pathway for decaBDE), with thyroid and liver changes observed in rats and mice in subchronic and chronic studies (NTP, 1986; Norris et al., 1975). Several studies (Johansson et al., 2008; Viberg et al., 2008; Viberg et al., 2007; Tseng et al., 2006; Viberg et al., 2003) also reported effects of neonatal exposure, including changes in sperm parameters (Tseng et al., 2006) and changes in locomotor activity or altered expression of proteins in the

central nervous system (Johansson et al., 2008; Viberg et al., 2008; Viberg et al., 2007; Viberg et al., 2003). EPA calculated an RfD of 0.007 mg/kg-day in 2008 (U.S. EPA, 2008b) based on the developmental neurobehavioral effects observed in the Viberg et al. (2003) study (see Section H.5.1.1.1 for details on RfD derivation).

With regard to carcinogenicity, the National Toxicology Program (NTP) stated that there was "some evidence of carcinogenicity" for male and female rats based on significantly increased incidences of neoplastic nodules of the liver, and "equivocal evidence of carcinogenicity" for male mice based on a significantly increased incidence of hepatocellular tumors in only the low-dose group and nonstatistically significant increases in thyroid follicular cell tumors in both dose groups (NTP, 1986). Additionally, the International Agency for Research on Cancer determined that decaBDE is not classifiable as a human carcinogen (Group 3) based on limited evidence in animals (IARC, 1998). In 2008, EPA used the descriptor "suggestive evidence of carcinogenic potential" for decaBDE (U.S. EPA, 2008b) under relevant guidelines (U.S. EPA, 2005b) (see Section 5.1.11).

H.5.1.1. Quantitative Toxicity Assessment

In a quantitative toxicity assessment, appropriate toxicity information is collected and evaluated. These data then are used to derive toxicity values, such as an RfD for oral exposure or RfC for inhalation exposure. Similar to an RfD (as defined in Section H.4.2.5), an RfC is an estimate of a continuous inhalation exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. Both values, an RfC and an RfD, are derived from a benchmark dose lower confidence limit, no-observed-adverse-effect level (NOAEL), a lowest-observed-adverse-effect level (LOAEL), or another suitable point of departure, with uncertainty/variability factors applied to reflect limitations of the data used. Other types of toxicity values also can be derived to provide exposure limit values for other exposure durations (e.g., acute or subchronic), more specific populations (e.g., healthy workers), or specific exposure contexts (e.g., emergency response or occupational exposure; see Section H.4.2.5). The sections that follow discuss the derivation of an RfD for decaBDE; due to limited data, an RfC for decaBDE has not been determined.

H.5.1.1.1. Health Reference Values

As mentioned in Section H.4.2.5, EPA (2008b) calculated an RfD of 0.007 mg/kg-day, based on developmental neurobehavioral effects observed in the Viberg et al. (2003) study (see Section H.5.1.7). The NOAEL of 2.22 mg/kg from this study was used as the point of departure. A total uncertainty factor of 300 was applied to account for interspecies differences (10×), intraspecies differences (10×), and

dosing duration (3×). As mentioned previously, due to the limited toxicity data available, an RfC for decaBDE has not been determined.

H.5.1.2. Systemic Toxicity

H.5.1.2.1. Acute

Acute toxicity studies for all routes of exposure were identified for decaBDE. Results indicate that, for all routes of exposure, decaBDE exhibits low acute toxicity. No mortality occurred after a 1-hour inhalation exposure in rats (5 animals/sex/group) to 200 mg/L BDE-209; no gross pathological changes were observed during the 2-week observation period (CPTC, 1978).

The low acute oral toxicity of decaBDE (Zhou et al., 2001; Kierkegaard et al., 1999; Norris et al., 1973) might be due in part to poor gastrointestinal absorption. No clinical signs of toxicity or death were observed when a single dose (up to 5,000 mg/kg) of BDE-209 was administered to rats via gavage (Great Lakes Chemical Corporation, 1994; IRDC, 1974).

The low acute dermal toxicity of decaBDE is presumed based on lack of treatment-related effects in rabbits following single administrations of 200 or 2000 mg/kg BDE-209 to clipped intact skin for 24 hours (14-day observation period) (Great Lakes Chemical Corporation, 2000b; IRDC, 1974).

H.5.1.2.2. Subchronic

In humans, an increase in primary hyperthyroidism and a significant reduction in calf sensory and fibula motor nerve velocities were observed in workers exposed to decaBDE during manufacturing [(Bahn et al. (1980) as cited in NTP (1986); Bialik (1982), as cited in HSDB (2011)]; whether these effects are due to decaBDE or polybrominated biphenyls is unclear, however, because only polybrominated biphenyls were detected in blood.

Numerous subchronic oral studies were identified for decaBDE, and all studies considered, including those summarized below, are presented in F.1.2 in Appendix F. DecaBDE-related thyroid and liver changes were observed in male rats when administered a lower purity (77.4%) form of decaBDE (Norris et al., 1975; Norris et al., 1973). Effects included thyroid hyperplasia, increased liver weight, and hepatic centrilobular cytoplasmic enlargement and vacuolation (Norris et al., 1975; Norris et al., 1973).

H.5.1.2.3. Chronic

Numerous chronic oral studies were identified for decaBDE, and all studies considered, including those summarized below, are presented in Section F.1.2 in Appendix F. In a chronic study conducted by NTP (1986), a dose-dependent increase in thyroid follicular cell hyperplasia was observed in male mice

fed BDE-209 (purity 94–97%) in the diet for 103 weeks (NTP, 1986); these effects were not observed in female mice or female and male rats that were similarly exposed to BDE-209. Centrilobular hypertrophy (consisting of enlarged hepatocytes with frothy vacuolated cytoplasm) also was observed in male mice, but not in female mice or in male and female rats (NTP, 1986). Incidences of thrombosis and degeneration of the liver were increased in male rats at the LOAEL (2,240 mg/kg-day), but not at 1,120 mg/kg-day (NOAEL); these hepatic effects were not observed in female rats or in mice of either sex. The NTP (1986) studies were considered for the basis of the EPA (2008b) quantitative cancer assessment (see Section H.5.1.11). Observed changes in liver weight and hepatocytomegaly might have been due to enzyme induction, as supported by recent studies conducted by Van der Ven et al. (2008) and Bruchajzer et al. (2010) (see Table F-7 in Appendix F).

H.5.1.3. Pulmonary Toxicity

When BDE-209 was administered to rats via a single intratracheal injection of 20 mg BDE-209 dust (purity 77.4%) suspended in rat serum (Dow Chemical Co, 1990b), minimal histopathological changes (scattered focal aggregates of alveolar macrophages) occurred, consistent with retention of large dust particles that would not normally reach the lungs during inhalation. Rats exposed to 2,000 or 48,000 mg/m^3 BDE-209 for 1 hour exhibited dyspnea at both dose levels (Great Lakes Chemical Corporation, 1994; IRDC, 1974); all animals survived until study termination and were normal at the end of the 14-day observation period (see Table F-5 in Appendix F).

H.5.1.4. Eye Irritation

All in vivo eye irritation studies considered are presented in Section F.1.2 (Table F-3). Key studies are summarized below.

DecaBDE does not appear to be an eye irritant. Ocular exposure to dry solid decaBDE caused transient conjunctival irritation in washed and unwashed rabbit eyes when 100 mg of decaBDE was administered via instillation to the conjunctival sac (NRC, 2000; IRDC, 1974) [Effects in some rabbits included very slight conjunctival redness and chemosis and slight or moderate discharge (Great Lakes Chemical Corporation, 1994)]. Investigators concluded that the effects were not serious enough to be considered primary eye irritation (Norris et al., 1975; IRDC, 1974). Pharmakon (1994) similarly reported that decaBDE (Saytex 102) did not cause primary eye irritation when instilled once (100 mg/eye) into the eyes of rabbits. Rats exposed to 2,000 or 48,000 mg/m^3 BDE-209 dust in the ambient air for 1 hour, however, exhibited ocular porphyrin discharge at both dose levels, and eye squint at the high

concentration (IRDC, 1974); all animals survived until study termination and were normal at the end of the 14-day observation period.

H.5.1.5. Skin Irritation

The material characteristics and study details associated with the in vivo dermal studies considered for decaBDE and MWCNTs are presented in Section F.1.2. in Appendix F

DecaBDE does not appear to be a skin irritant based on observations from a human skin irritation study (Dow Chemical Co, 1990a; Norris et al., 1975; Norris et al., 1973), a skin irritation study in rabbits (Norris et al., 1975; IRDC, 1974; Norris et al., 1973), and an acne-genesis study in rabbits (Pharmakon Research International, 1994). Dermal studies were conducted with BDE-209.

H.5.1.6. Reproductive Effects

In general, studies found that decaBDE was not a reproductive toxicant at doses up to and exceeding 1,000 mg/kg-day (Tseng et al., 2008; Hardy et al., 2002; Dow Chemical Co, 1990c; NTP, 1986). Van der Ven et al. (2008) reported significant, decaBDE dose-related changes in epididymis and seminal vesicle weight for male rats and decreased activity of CYP17, a key enzyme in the androgen synthesis pathway, for female rats administered 1.9–60 mg/kg by oral gavage. No corresponding histopathological changes, sperm counts, or morphology of epididymal sperm, however, were observed. Based on these results, the authors concluded that BDE-209 might represent a hazard to reproductive health.

H.5.1.7. Developmental Effects

Several studies reported no developmental effects for decaBDE at doses up to and exceeding 1,000 mg/kg-day (Hardy et al., 2009; Tseng et al., 2008; Hardy et al., 2002; Dow Chemical Co, 1990c). A significant increase in CYP450 activity in adult male CD-1 mouse offspring was noted in the study conducted by Tseng et al. (2008) at doses of 1,500 mg/kg-day; this dose level, however, exceeds the current dose limit (e.g., 1,000 mg/kg-day) recommended by international toxicity testing guidance documents (OECD, 2007; U.S. EPA, 1998). Another study found significant increases in numbers of rat litters with subcutaneous edema and delayed ossification of skull bones at 1,000 mg/kg-day (Norris et al., 1975); dams for this study were administered BDE-209 (77.4% containing 21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide) via gavage at dose levels of 0, 10; 100; or 1,000 mg/kg-day. Consequently, the NOAEL and LOAEL for fetal effects in this study were 100 and 1,000 mg/kg-day, respectively; the NOAEL for maternal effects was 1,000 mg/kg-day.

In contrast, several studies did observe adverse effects when neonatal mice or rats were exposed orally to decaBDE at lower doses (Johansson et al., 2008; Viberg et al., 2008; Viberg et al., 2007; Tseng et al., 2006; Viberg et al., 2003). Effects of neonatal exposure included changes in sperm parameters (Tseng et al., 2006) and changes in spontaneous behavior or altered expression of proteins in the central nervous system (Johansson et al., 2008; Viberg et al., 2008; Viberg et al., 2007; Viberg et al., 2003). Rice et al. (2007) orally exposed male and female mouse pups to decaBDE at doses of 0, 6, or 20 mg/kg-day from postnatal days PND2 through PND15. Treatment-related effects occurred only in the high-dose group and included a reduction in palpebral reflex on PND14, a reduction in forelimb grip in males on PND16, a change in the slope of the linear trend for serum T_4 in males on PND21, and a change in the linear slope of motor activity on PND70. Of the available studies, Viberg et al. (2003) was selected for the derivation of the RfD (see Section H.5.1.1.1).

H.5.1.8. Immune System Effects

No immunology studies were identified for decaBDE.

H.5.1.9. In Vitro Data

In vitro data can be used to make judgments on the toxic potential of stressors, but the relevance of in vitro data to predicting toxicological responses of "real-world" exposures is not always clear.

No in vitro data were identified for decaBDE.

H.5.1.10. Genotoxicity/Mutagenicity

DecaBDE does not appear to be genotoxic and generally did not induce (1) gene mutations in bacteria (*Salmonella typhimurium*) in Ames assays (Chemical Manufacturers Association, 1998; GSRI, 1990; Huntingdon Life Sciences, 1990; NTP, 1986; Haworth et al., 1983; Litton Bionetics, 1976), (2) gene mutations in mouse L5178Y lymphoma cells, (3) chromosomal aberrations in mouse bone marrow cells, or (4) sister-chromatid exchanges or cell transformation in Chinese hamster ovary cells (Myhr et al., 1990; McGregor et al., 1988). These findings are consistent with those reported by EPA (U.S. EPA, 2008b). Because decaBDE has consistently failed to produce genotoxic or mutagenic responses, the aforementioned studies are not summarized in Appendix F.

H.5.1.11. Carcinogenicity

Carcinogenicity studies considered for decaBDE are presented in Table F-10 of Appendix F. The target organs for decaBDE carcinogenicity appear to be the liver and thyroid; decaBDE was not, however, included on the most recent U.S. NTP list of carcinogens.[30]

Information on the carcinogenicity of decaBDE is available from three chronic feeding studies in rodents (Kociba et al., 1994; NTP, 1986; Kociba et al., 1975). In the NTP study (1986), a treatment-related increase in liver neoplastic nodules was observed in low- and high-dose male rats (7/50 and 15/49, respectively, compared to 1/50 in controls) and high-dose female rats (9/50 compared to 1/50 and 3/49 in control and low-dose groups, respectively). F344/N rats were fed BDE-209 (94–98% pure) at dietary concentrations of 0, 25,000, or 50,000 ppm for 103 weeks (equivalent to 0, 1,120, and 2,240 mg/kg-day in male rats; 0, 1,200, and 2,550 mg/kg-day in female rats). The increase in liver neoplastic nodules was not accompanied by an increase in hepatocellular carcinomas in rats. Hepatocellular adenomas or carcinomas (combined), however, were observed in low- and high-dose male mice (8/50 controls, 22/50 low-dose mice, 18/50 high-dose mice). Male mice also exhibited a marginal increase in thyroid gland follicular cell adenomas or carcinomas (combined) at the low and high doses (0/50 controls, 4/50 low-dose mice, 3/50 high-dose mice). The possible significance of this finding was strengthened by increased incidences of follicular cell hyperplasia in the male mice (2/50 controls, 10/50 low-dose mice, 19/50 high-dose mice), but was weakened by increased mortality in control animals. Based on these results, the NTP (1986) study concluded that there was "some evidence of carcinogenicity" for male rats in the low-dose group and both male and female rats in the high-dose group based on significantly increased incidences of neoplastic nodules of the liver, and "equivocal evidence of carcinogenicity" for male mice based on a significantly increased incidence of hepatocellular tumors in only the low-dose group and nonstatistically significant increases of thyroid follicular cell tumors in both dose groups. Although the International Agency for Research on Cancer (1998) reports that decaBDE is not classifiable as a human carcinogen (Group 3) based on limited evidence in animals, EPA, under the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005b), determined that the descriptor "suggestive evidence of carcinogenic potential" is appropriate for decaBDE (U.S. EPA, 2008b) based on the data from NTP (1986) demonstrating evidence of carcinogenicity in more than one species, sex, and site.

[30]The U.S. NTP 12th Report on Carcinogens (released June 2011) is available at http://ntp.niehs.nih.gov/?objectid=03C9AF75-E1BF-FF40-DBA9EC0928DF8B15

H.5.1.12. Susceptible Populations

Sacks et al. (2011) defined susceptibility as "individual- and population-level characteristics that increase the risk of health effects in a population, including, but not limited to, genetic background, birth outcomes (e.g., low birth weight, birth defects), race, sex, life stage, lifestyle (e.g., smoking status, nutrition), preexisting disease, socioeconomic status (e.g., educational attainment, reduced access to health care), and characteristics that may modify exposure … (e.g., time spent outdoors)." In this section, populations susceptible to decaBDE impacts based on characteristics such as age, genetic background, and disease are considered. Characteristics that could modify exposure and increase susceptibility were discussed previously in Section H.4.2.4; for a discussion on impacts related to socioeconomic status, see Section H.5.3.

Results regarding developmental neurotoxicity studies are conflicting. Whether young children comprise a sensitive (i.e., more susceptible) population is therefore unclear. A few animal studies have indicated that BDE-209 might cause developmental neurotoxicity, affecting motor and cognitive domains; however, in discussing susceptible populations for decaBDE, EPA noted that differences in the effects of decaBDE on neurodevelopment are unclear and whether other targets (thyroid and liver) are more sensitive in children is unknown (U.S. EPA, 2008b). Disposition studies using pregnant rats indicate that fetuses are less exposed to decaBDE than mothers. Fetuses (whole litter) contained only 0.43% of the dose in a study by Riu et al. (2008). In a study by Inoue et al. (2006), higher brominated congeners like decaBDE transferred from blood to milk to a lesser degree than did lower brominated congeners. In a study by Fukata et al. (2005), BDE-209 was not detected in umbilical cord tissue, but was found at 23 ng/gram lipid weight in umbilical cord serum and 10 ng/gram lipid weight in maternal serum. Exposure to decaBDE in infants, however, appears to be greater than in adults. Additional information regarding populations that are susceptible to greater levels of exposure can be found in Section H.4. No sources indicating that specific genetic polymorphisms increase susceptibility were identified.

H.5.2. Ecological Effects

This section presents a summary of data on the potential ecological impacts of environmental contamination with decaBDE. Specific information from the studies reviewed for this case study can be found in Section F.2 in Appendix F. Considerations for ecological impact include the absolute and relative toxicity of the decaBDE and other factors such as bioaccumulation and biomagnification potential (see Section G.4.2.1). For aquatic ecosystems, much information was available for decaBDE primarily because decaBDE has been studied extensively in aquatic vertebrates. Conversely, little information was

identified on the potential effects of decaBDE in terrestrial ecosystems. The terrestrial ecosystem studies focus on agriculturally relevant plants and soil microbes. In both aquatic and terrestrial ecosystems, studies are predominantly laboratory-based experiments on single species. Few studies address how exposure and uptake of PBDEs relate to ecological health and effects in the field (Vonderheide et al., 2008). Some field studies show correlations between PBDE exposure, reproductive behavior, and immunosuppression, but ecological consequences and potential population-level impacts of environmental PBDE contamination in general, and decaBDE in particular, remain uncertain (Vonderheide et al., 2008). As mentioned in Section G.4.2.1, ecological receptors can be exposed to decaBDE attached to textile fibers, embedded in polymers, or sorbed to other particles, all of which are more likely to occur in the environment than exposure to the pristine compound. Studies examining exposure to larger textile scraps, polymer particles, and other heterogeneous compounds containing decaBDE, however, are lacking. The results of laboratory studies using pristine compounds must therefore be considered, recognizing that results might not translate directly into real-world exposure scenarios.

As discussed in Section H.3 (see Text Box H.3-1), environmental degradation and debromination of decaBDE result in contamination of media with lower PBDE congeners, which are generally more bioavailable and more toxic than decaBDE. Also as stated previously in Section H.3, debromination of decaBDE is expected to contribute significantly to the environmental presence of BDE-47, a tetraBDE, and BDE-100 and BDE-99, which are both pentaBDEs, among other congeners (Gandhi et al., 2011; Ross et al., 2009). In this section, information is presented on the acute toxicity of decaBDE and other PBDEs, as appropriate. Considerations for negative ecological impacts from continual long-term exposures in an ecosystem are also discussed.

H.5.2.1. Aquatic Receptors

DecaBDE has been shown not to be acutely toxic to species of fish or marine algae studied to date (Hardy, 2002a). Few studies were identified regarding the acute or chronic toxicity of decaBDE to marine or freshwater algae and benthic invertebrates (see Section H.5.2.1.1). No information was identified regarding toxic effects on aquatic plants or water-dwelling invertebrates (see Section H.5.2.1.1); some information was identified on toxicity to aquatic vertebrates (see Section H.5.2.1.2).

DecaBDE is not expected to be chronically toxic to aquatic organisms at environmentally relevant concentrations due to its physicochemical properties, specifically high molecular weight and low water solubility (Hardy, 2002a) (see Section H.1). These properties suggest that decaBDE accumulation directly from water into biota is unlikely; a more likely route of exposure is dietary (Gandhi et al., 2011).

But as noted previously, the factors affecting bioavailability of decaBDE are not well understood. Comparatively, however, lower PBDEs such as pentaBDEs are known to have high potential for bioaccumulation (U.S. EPA, 2010a). Because these congeners are transformation products of decaBDE, their chronic toxicity is considered.

H.5.2.1.1. Algae, Aquatic Plants, and Aquatic Invertebrates

The paragraphs that follow describe literature identified for the effects of decaBDE on algae, aquatic plants, and aquatic invertebrates. Table F-12, Table F-14, and Table F-15 in Appendix F summarize details of the studies identified and reviewed for this section.

No studies were identified that investigated the effects of decaBDE on algae or on aquatic plants. A single study on water-dwelling aquatic invertebrates was identified involving freshwater bivalve zebra mussels (*Dreissena polymorpha*) exposed to technical-grade decaBDE at sublethal levels of 0.1, 2, or 10 µg/L. This study showed DNA damage that increased as levels of decaBDE exposure increased, indicating potential for genotoxicity (Riva et al., 2007). A review by Hardy (2002a) stated that decaBDE was nontoxic to marine algae and sediment oligochaetes, but no details on the derivation of these conclusions were provided. The review also investigates toxicity of octaBDE and pentaBDE, concluding that octaBDE is neither acutely toxic nor chronically toxic to a species of water flea, and pentaBDE is not acutely toxic to algae, up to the limit of their water solubility (Hardy, 2002a). Details on endpoints observed were not provided.

Environment Canada (2006) reviewed ecotoxicity studies for multiple PBDE mixtures. They report high (>5,000 mg/kg) no-observed-effect levels and median (>50 mg/kg) effective concentration values for chronic survival and reproduction effects for a freshwater oligochaete (*Lumbriculus variegatus*) exposed to sediments that contained a mixture of 55% pentaBDE and 36% tetraBDE as well as a mixture containing 97% decaBDE. For water fleas (*Daphnia magna*), Environment Canada (2006) reported toxicity values in the low µg/L range for survival, growth, and reproduction following chronic exposure to a commercial pentaBDE mixture [(Drottar and Krueger (1998) as cited in Environment Canada (2006)]. Some water fleas are therefore more sensitive to PBDEs than oligochaete worms, but as mentioned in Section H.3.3, decaBDE is not likely to remain in the water column; instead, it partitions to sediment, where benthic invertebrates are expected to be exposed.

H.5.2.1.2. Aquatic Vertebrates

Table 5-3 in Chapter 5 describes key toxicity values identified for the effects of decaBDE and MWCNTs on aquatic vertebrates. Table F-13, Table F-16, and Table F-17 in Appendix F summarize details of the studies identified and reviewed for this section.

A review by Hardy (2002a) reports on acute toxicity of decaBDE, octaBDE, and pentaBDE, stating that all three congeners have a fish 48-hr median lethal concentration of greater than 500 mg/L, indicating that the congeners are not acutely toxic to fish up to the limit of their water solubility. No effects on egg mortality were observed in rainbow trout (*Oncorhynchus mykiss*) at doses up to 12 µg pentaBDE per egg, and no effects on reproduction or spawning success were observed in three-spined stickleback (*Gasterosteus aculeatus*) exposed to pentaBDE (Hardy, 2002a).

Tests conducted on frogs often measure low-dose, chronic thyroid disruption, because metamorphic development from tadpole to frog is controlled by thyroid hormones (Qin et al., 2010). African clawed frog (*Xenopus laevis*) tadpoles (Table 5-3 in Chapter 5) exposed to decaBDE in their water at sublethal doses ranging from 1 to 1,000 ng/L experienced histopathological alterations in thyroid gland cell shapes and decreases in thyroid hormone expression in tail tissue during metamorphosis at all tested doses. Additionally, researchers observed a concentration-dependent trend of delay in time to metamorphosis with a statistically significant delay at 1,000 ng/L (Qin et al., 2010).

Endocrine effects also have been studied in Chinese rare minnow (*Gobiocypris rarus*) and lake trout (*Salvelinus namaycush*) chronically exposed to decaBDE via water and diet, respectively (Li et al.; Tomy et al., 2004). Expression of thyroid hormone-related genes was variably affected in both studies; indicating the potential for chronic endocrine disruption but not elucidating a mechanism for those effects or a clear effect level. Chronic toxicity of decaBDE in fish is complicated by biotic debromination of decaBDE, which can result in bioaccumulation of octa-, hepta-, hexa-, and pentaBDE congeners (Gandhi et al., 2011; Stapleton et al., 2004) (as discussed in Section H.4.2.6.1). Most informative, therefore, are studies of multiple PBDEs or PBDE mixtures. In one such study, induction of vitellogenin production was observed in hepatocyte cell cultures of rainbow trout (*Oncorhynchus mykiss*) exposed to PBDE mixtures (Nakari and Pessala, 2005).This estrogenic response raises concerns for population dynamic impacts due to endocrine disruption (Mikula and Svobodová, 2006).

H.5.2.2. Terrestrial Receptors

A limited amount of information was found regarding toxicity of decaBDE to soil microbes, plants, and terrestrial invertebrates (see Sections H.5.2.2.1 and H.5.2.2.2). No information was identified regarding toxicity to terrestrial vertebrates (see Section H.5.2.2.3); nevertheless, some assumptions can be made for mammals based on toxicity studies intended for human health purposes presented in Section H.5.1. Many studies of decaBDE in terrestrial ecosystems have focused on bioaccumulation and biomagnification; important considerations for potential ecological hazard (see Section H.4.3.4). These studies, however, did not investigate occurrence of toxic effects.

H.5.2.2.1. Soil Microbes and Terrestrial Invertebrates

Changes in soil microbial activity result in changes to nutrient cycling; therefore, studying the impact of contaminants on soil microbes can provide insight on how those contaminants might affect ecosystem function (Chung et al., 2011). Similarly, effects on terrestrial invertebrates, such as worms, can influence health and fertility of a soil ecosystem (Xie et al., 2011). Table F-18 and Table F-19 in Appendix F summarize details of the studies identified and reviewed for this section.

Two studies were identified that investigated the toxicity of decaBDE to soil microbes. Although Sverdrup et al. (2006) showed no effects on nitrifying ability of bacteria following exposure to decaBDE at levels up to 2,274 mg/kg in soil, Liu et al. (2011a) found that microbial cytotoxicity significantly increased at doses 10-fold lower (100 mg/kg), and community structure was altered following long-term exposure to decaBDE. The rate of community diversity increase over time was significantly slower from Day 90 through the last day of the study (Day 180) when soil contained 1–100 mg/kg decaBDE. After six months, the total bacterial count in the soil containing 100 mg/kg decaBDE was approximately half that of the control plot. Treatment soil microcosms were dominated by *Pseudomonas*, *Bacillus*, and uncultured bacteria types, and had significantly reduced cell counts for *alpha, beta, and gamma* type proteobacteria and the Cytophaga-Flavobacterium-Bacteroides group (Liu et al., 2011a).

Studies of oligochaete worms [*Enchytraeus crypticus* (a soil worm) and *Eisenia fetida* (earthworms)] showed that survival, reproductive behavior, and number of offspring are not affected by long-term exposure to decaBDE in soil in the grams/kg range [Sverdrup et al. (2006); ACC (2001) as cited in Environment Canada (2006)]. Earthworms, however, experienced a sublethal, dose-dependent increase in hydroxyl radical generation and subsequent oxidative stress after 1 week of exposure to 0.1–10 mg/kg decaBDE (Xie et al., 2011). Oxidative stress in earthworms is considered a biomarker indicative of potential for greater impacts of soil contaminants within terrestrial ecosystems (Xie et al., 2011).

H.5.2.2.2. Terrestrial Plants

Table F-18 and Table F-20 in Appendix F summarize details of the studies identified and reviewed for this section.

Few studies were identified that investigated effects of PBDEs on plants; those reviewed found no adverse effects at environmentally relevant concentrations. No effects on seedling emergence were observed in red clover *(Trifolium pretense*) exposed to decaBDE or corn *(Zea mays)* exposed to a PBDE mixture (55% pentaBDE and 36% tetraBDE) at levels in the grams/kg range (Sverdrup et al., 2006; Great Lakes Chemical Corporation, 2000a). In corn, mean shoot height was unaffected at concentrations up to 125 mg/kg, but was significantly reduced at 250 mg/kg and above [Great Lakes Chemical Corporation

(2000a) as cited in Environment Canada (2006)]. As discussed in Section H.3.4, soils are a major sink for PBDEs in terrestrial systems, and uptake by plants is possible. Recent measured concentrations in soil have been in the ng/gram (0.001 mg/kg) range (see Table E-5 in Appendix E).

H.5.2.2.3. Terrestrial Vertebrates

No studies were identified that specifically investigated the effects of decaBDE on terrestrial vertebrates outside the laboratory setting. Results from extensive testing performed in mammals for toxicological relevance to humans are reported in Section H.5.1.

Chronic effects of PBDEs at environmentally relevant exposure concentrations are a possibility in terrestrial vertebrates, primarily due to assumed ecological impacts associated with high biomagnification rates, as discussed previously in Section G.4.2.1.

H.5.3. Other Impacts

As stated in Section H.1, the CEA framework considers not only human and ecological health impacts, but also aesthetic, environmental, social, legal, ethical, and economic impacts. Such impacts might be associated with impacts on specific socioeconomic sectors (e.g., disparate impacts on environmental justice communities), the environment as a whole (e.g., climate change, depletion of natural resources, energy demand), or the built environment (e.g., damage to building facades).

Apart from the impacts discussed in Sections H.5.1 and H.5.2, the only other impacts considered in this case study are those for which a plausible premise can be developed to support assumptions that a discernible impact might occur as a result of the life cycles of decaBDE flame-retardant upholstery textile coatings. Empirical data have revealed a correlation between decaBDE body burdens and socioeconomic status, indicating that effects having environmental justice implications are plausible for decaBDE.

H.5.3.1. Environmental Justice

Environmental justice is defined by EPA as the "fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies."[31] The goal of environmental justice is to give all people "…the same degree of protection from environmental and

[31]U.S. EPA Compliance and Enforcement. Environmental Justice. http://www.epa.gov/environmentaljustice/

health hazards and equal access to the decision-making process…"[32] As a result, environmental justice impacts include those in which a particular group or geographic area experiences a disproportionate share of the impacts associated with an environmental contaminant.

Releases of decaBDE throughout the life cycle of a flame-retardant upholstery coating product could disproportionately impact certain communities. In a review by Zota et al. (2010), findings from several recent studies suggest that racial and ethnic minorities and populations having lower socioeconomic status (i.e., low income, low educational attainment) experience disproportionate exposures to PBDEs. For example, Rose et al. (2010) observed that body burdens of BDE-209, among other congeners, were significantly higher in children aged 2–5 years born to mothers of lower educational attainment compared to those born to mothers achieving a college degree or higher.

The causal pathway connecting low socioeconomic status to elevated PBDE exposure is not well understood, but Zota et al. (2010) hypothesized that furniture quality and the characteristics of the living spaces (e.g., size, ventilation, age), which populations of lower socioeconomic status might occupy, contribute to elevated exposure to PBDEs. Indeed, Rose et al. (2010) demonstrated that higher maternal education attainment is correlated with larger living spaces, and in turn, children living in larger homes had lower body burdens of BDE-209. Similarly, Stapleton et al. (2012) found that variation in PBDE serum concentrations in children could be explained by handwipe levels, house dust levels, father's education, breast feeding duration, age, and gender (different factors associated with different PBDE congeners).

H.5.3.2. Energy Demand and Natural Resource Depletion

No information was identified that examined impacts on energy demand and natural resource depletion associated with the production of decaBDE flame-retardant textile coatings.

H.5.3.3. Climate Change

No information was identified that examined climate change impacts due to decaBDE flame-retardant textile coatings.

[32]ibid

H.5.3.4. Economics

No information was identified that calculated the cost of manufacturing decaBDE or decaBDE flame-retardant textiles.

Appendix H References

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Appendix I. External Review Draft Comments and Agency Responses

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Appendix I. External Review Draft Comments and Agency Responses

I.1. Background

The External Review Draft of this case study (U.S. EPA, 2012a) served as the starting point for identifying and prioritizing research gaps that, if pursued, could inform future assessments and subsequent risk management decisions for multiwalled carbon nanotubes (MWCNTs) in flame-retardant upholstery textiles or similar materials and applications. As discussed in more detail in Chapter 1, the draft was the basis for the collective judgment step of the comprehensive environmental assessment (CEA) process (see Figure 1-2), in which experts read the case study document, participated in an online data prioritization exercise, and (for a subset of experts) attended a workshop. The collective judgment step resulted in the identification of elements and risk relevant factors of the CEA framework as priority areas for future assessment or research due to data gaps and importance to risk management. These areas are hereafter referred to as "Priority Research Areas." Some of these areas are most relevant to individuals who plan research. These areas are those that the experts rated as important to consider in risk assessments but in which they were not confident the available data could support risk management decisions. Other priority areas are more relevant to individuals who develop assessments or are responsible for risk management efforts (e.g., researching which type of risk management plan would be most suitable given current information); those areas are the ones experts rated as important to consider in risk assessments and in which they had greater confidence that available data might support risk management decisions (see Section 1.1.3). Notably, in applying the CEA approach to MWCNTs, the majority of priority areas that emerged are most pertinent to research planning rather than developing assessments. Throughout the revision process for the case study, efforts were made to streamline the document so that it would clearly reflect each priority that emerged from the CEA collective judgment step, input from public comments, and the opinions of expert stakeholders involved in prioritizing the research gaps.

This appendix documents how the External Review Draft of the case study was revised to: (1) respond to public comments and input from experts participating in the collective judgment step of the CEA process (Figure 1-2), and (2) reflect the priorities identified through the CEA collective judgment step.

I.1.1. Appendix Development Process

As part of the collective judgment step of the CEA process (Figure 1-2) described in Section 1.1.3, 23 experts provided written responses to the following charge questions:

1. Do you know of additional, specific studies on MWCNTs that should be included in the case study to help identify data gaps that are important to support future assessment and risk management efforts for MWCNTs in flame-retardant textile coatings?

1. Is the science accurately conveyed throughout the document? If not, please list any areas that need improvement and provide specific comments in the text to highlight areas that should be refined.

2. Does the comparison of decaBDE and MWCNTs in the case study document help to identify research gaps to support future assessments and risk management decisions for MWCNTs? If not, please briefly explain.

3. Do you have any specific comments on how this document could be improved?

One of the 23 experts also provided a PDF copy of the case study with free-form comments (i.e., not specific to a charge question) linked to specific regions of text. In addition, four members of the public provided input during the public comment period announced in a July 2, 2012 *Federal Register* Notice.[33] Finally, an interagency commenter provided input on the draft document during the public comment period. Affiliations of the experts are provided in Table I-1; affiliations of the interagency and public commenters are provided in Table I-2.

All charge question responses, public comments, and expert free-form comments received on the External Review Draft were tracked with the aid of an Excel-based comment tracking sheet. Longer responses and public comments were broken down into distinct, individual thoughts and assigned unique comment numbers. Each unique comment was assigned to the most relevant portion of the detailed CEA framework (Figure 1-3), which was also used for the online collective judgment prioritization exercises of the CEA process.[34]

Comments then were assigned "themes" based on recurring topics so that similar comments related to the same CEA framework area could be grouped and comments with similar concepts that crossed multiple CEA framework areas also could be grouped. Themes were determined progressively and the list of themes was reconsidered and revised as more comments were considered, to develop a limited number of themes that created broad categories. Multiple themes were often, but not always,

[33] http://www.gpo.gov/fdsys/pkg/FR-2012-07-02/html/2012-16137.htm

[34] Note that the CEA framework does not include the introductory and background topics from Chapter 1 of the case study, such as flame-retardant regulations or the choice of nanomaterial and application. Comments that referred to topics outside of the framework areas were assigned to a numbered section of the actual case study as opposed a CEA framework area. Specific chapter assignments were also used in place of CEA framework area in cases of highly specific comments that referred to a specific line of text within the case study.

applied to a single comment to either increase the degree of specificity of the theme (e.g., a general comment stating that the comparison between decaBDE and MWCNTs was not useful compared to a comment that specified *why* the comparison was not useful) or to account for multiple unrelated themes in the same comment (e.g., a comment noting that information on release rates and exposure are data gaps and noted the need for better analytical techniques). The themes provided a flexible and inclusive method for grouping similar comments.

Table I-1. Expert affiliations and area of expertise.

Expertise Area	Sector Affiliation
Ecological Effects	Academic Institutions and Centers
Exposure & Dose	Government
Ecological Effects	Government
Human Health Effects	Government
Policy	Nongovernmental Organization
Material Characterization	Academic Institutions and Centers
Exposure and Dose	Government
Exposure and Dose	Academic Institutions and Centers
Material Characterization	Government
Human Health Effects	Independent Consulting
Policy	Academic Institutions and Centers
Material Characterization	Government
Human Health Effects	Independent Consulting
Environmental Fate and Transport	Academic Institutions and Centers
Manufacturing	Industry
Ecological Effects	Academic Institutions and Centers
Policy	Government
Exposure and Dose	Industry
Environmental Fate and Transport	Government
Ecological Effects	Independent Consulting
Exposure and Dose	Academic Institutions and Centers
Risk Assessment	Industry
Risk Assessment	Government

Note: Order of expertise area and affiliation is not associated with author identification numbers in Table I-11 and Table I-12, to preserve anonymity of experts.

Table I-2. Public Commentators affiliations and area of expertise.

Commentator ID	Expertise Area	Sector Affiliation
IA1	Not Identified	Government
P1	Not Identified	Industry
P2	Not Identified	Industry
P3	Not Identified	Government
P4	Not Identified	Nongovernmental Organization

Finally, Agency responses were drafted for each comment using consistent language where possible to connect comments from multiple commenters that expressed the same basic ideas and themes. Responses were focused on applying one of the five main categories of action taken, as described in detail in Chapter 1 and summarized in Table I-3. In some cases, more than one response category was appropriate for the same comment or group of comments. This is particularly true for comments that applied to broader themes or CEA framework areas. The "Agency Response" includes references to multiple categories (e.g., addition of Information Highlight Boxes as well as in-text edits) as necessary to describe the complete actions that were taken in response to each comment or group of comments.

I.1.2. Appendix Organization

This appendix contains three types of comment tables:

1. Table I-4, Table I-5, Table I-6, Table I-7, Table I-8, and Table I-9: Response tables for comments that were addressed in the body of the document based on the first four response types described in Table I-2 (this includes some cases where the comment was acknowledged but no major action was taken because the related CEA area was not identified as important by the collective judgment process), organized by relevant chapters of the case study document;
2. Table I-11: Response table for comments that were not specifically addressed through revisions or edits to the main body of the case study because the comment did not suggest that any action needed to be taken; and
3. Table I-12, Table I-13, and Table I-14: Look-up tables for the comment IDs listed in the response tables, organized by the way in which the comment was submitted (i.e., expert charge question responses, expert free-form comments, and public comments). Original commenter text excerpts are provided, along with the commenter and comment ID numbers, and the theme or themes applied to each comment. Note that while commenter ID numbers are provided in Table I-2 above for public commentators, they are not included in Table I-1, to preserve anonymity of expert input.

As noted previously, comments were grouped according to similar themes, so several unique comments are presented as relevant to a single Agency response, as indicated by the ID numbers in the far right column of the response tables. The comments have been collectively summarized to provide readers with a relatively quick overview of the common theme among the comments and to illustrate how the group of comments relate to the action taken by the Agency. As noted above, the original individual comments and assigned themes are provided in the final tables of this appendix (Table I-12, Table I-13, and Table I-14).

Table I-3. Agency response categories.

Response Category	Purpose	Actions Taken	Notes
1	Emphasize outcomes of collective judgment step to support MWCNT research planning in this application of CEA	Added Priority Research Area Highlight Boxes	Text boxes were embedded into the case study to indicate the outcomes of the collective judgment process, outlined in red for priority areas and outlined in gray for unprioritized areas.
		Moved unprioritized sections to Appendix	For areas of the detailed CEA framework that experts determined were of lesser importance to consider in a future risk assessment of MWCNTs, all text was moved to Appendix G to help focus the revised document on the most important information.
		Added final Priority Focus Section 6.3	A final section of the case study was added that discusses the "Priority" areas in detail. The section includes further details on workshop participants' rationale for designating the area a priority, and notes additional relevant literature not previously included in the case study, but identified by commenters, workshop participants, or targeted literature searches, which might inform future research in the priority area
2	Update discussion of Priority Research Areas to reflect current state of the science and full range of topics	Added "Information Highlight Text Boxes"	Text boxes were embedded in the case study to draw attention to scientific concepts related to priority areas that commenters felt were under-represented or incompletely represented in the External Review Draft. Boxes, outlined in blue, highlighted literature not previously included in the case study that was provided by the commenters and workshop participants, or identified through a targeted literature search.
		Added new figures and tables	New figures and tables were added to draw attention to scientific concepts previously under-represented or incompletely characterized in the case study (due to, for example, insufficient data at the time the case study was written). These new figures and tables are clearly described as new in the caption and where possible have been outlined in blue.

Table I-3, cont.:. Agency response categories

Response Category	Purpose	Actions Taken	Notes
3	Improve accuracy	Text edits to pre-existing text	Some specific revisions were made to text that appeared in the External Review Draft version of the draft case study in order to clarify and improve the accuracy of statements.
4	Streamline document to support MWCNT research planning in this application of CEA	Moved decaBDE discussions to appendix	Detailed information on decaBDE that originally appeared in the main body of the document was moved to Appendix H.
		Added "DecaBDE Comparison Boxes" to main text	A series of DecaBDE Comparison Text Boxes was added to the body of the document (outlined in green) to illustrate how information from decaBDE could be used to inform MWCNT research planning in priority areas; these boxes refer the reader to Appendix H for more detailed information.
5	No action necessary	No action	Many comments provided informative feedback that the Agency appreciates, but did not require any edits or changes to the body of the case study document. This was either due to the fact that the comment pertained to an area of the CEA framework that was not identified as a priority area by workshop participants or did not suggest specific action to be taken.

I.2. Responses to Comments

I.2.1. Addressed Comments

Table I-4. Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
General	Five comments generally noted the utility of highlighting or emphasizing Priority Research Areas and data gaps in the case study.	A series of text boxes was added throughout the document to highlight Priority Areas (i.e., red outlined text boxes) for research, along with those areas distributed elsewhere in the Importance / Confidence Matrix during the collective judgment step of the CEA process (see Section 1.1.3). In addition, a final section (Section 6.3) was added that discusses the outcomes of the collective judgment prioritization process in more detail. Future applications of the CEA approach will strive to include more figures and tables as appropriate to summarize and highlight research priorities or data gaps.	1, 2	39, 61, 103, 120, 140
General	Thirteen comments did not find the comparison with decaBDE useful overall (for example, due to differences in physicochemical properties or because it added length to the document)	In revising the document, effort was made to clarify the purpose of comparing MWCNT and decaBDE. The primary purpose of providing decaBDE information, to inform research gap identification for MWCNT, was carried out in the collective judgment step with the external review draft of the case study; as such, decaBDE information is now primarily in Appendix H. In addition, efforts were made to succinctly highlight how understanding decaBDE data might inform research planning for MWCNT priority topics by adding "DecaBDE Comparison Text Boxes."	4	27, 28, 29, 34, 61, 62, 68, 90, 98, 99, 112, 113, 203
General	One comment found the comparison with decaBDE to be useful, but suggested that segregating the information, rather than alternating back and forth, would improve the document.	Discussion of decaBDE was moved to Appendix H to provide continuity in the presentation of information on decaBDE and MWCNT; efforts were made to succinctly highlight how understanding decaBDE data might inform research planning for MWCNT priority topics by adding "DecaBDE Comparison Text Boxes."	4	73

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
General	One comment expressed concern that rather than highlighting research needs and data gaps for MWCNT, comparison with decaBDE could make MWCNT appear to be relatively "good" or "safe."	The document was reviewed to check for any biased statements related to the use of decaBDE or MWCNTs. No instances of bias were found; however, the purpose of including the comparison in the document was clarified in response to this and other comments on the utility of comparing decaBDE and MWCNT in research planning efforts (see Section 1.1.4). Further, detailed discussion regarding decaBDE was moved to Appendix H to provide greater focus on MWCNTs.	2, 3, 4	34
General	Eight comments recommended that the CEA case study put greater emphasis on in vitro assessment of toxicity for nanomaterials rather than traditional in vivo assessments, which would align well with the Agency's Nanomaterial Research Strategy, Strategic Plan for Evaluating the Toxicity of Chemicals, and NexGen.	As noted in Chapter 1, the case study was developed without a particular regulatory or policy objective in mind and is not intended to establish or evaluate specific testing protocols; however, discussion was added to Chapter 1 to clarify the purpose of the case study and its relationship to other research frameworks, including the Nanomaterial Research Strategy, EPA's Strategic Plan for Evaluating the Toxicity of Chemicals, and OECD (2012) that were developed to inform decision-making for nanomaterials to provide greater context for the Agency's direction for future risk assessment efforts. Further, because "Impacts: Human (Cancer, Non Cancer, and reproductive/developmental)" was identified as a Priority Research Area by workshop participants, information regarding NexGen and integrated testing strategy (ITS) was included in Additional Information Highlight Box 15, which describes the trend toward developing innovative biologically/toxicologically relevant in vitro models.	2, 3	254, 256, 257, 258, 292, 293, 294, 297, 298, 299
General	One comment suggested focusing the case study more on recently published data than on review papers published prior to 2010.	In writing and revising the document, efforts were made to include current, accurate, and validated information.	3	160

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
General	Two comments noted the use of non-peer reviewed sources to inform the case study and expressed concern that this publication would offer validity to "gray" literature. Another questioned the use of a specific reference that only represented a report abstract.	As nanomaterials are new, emerging compounds, research in the field is rapid and ever-progressing. The literature chosen for inclusion in this case study was intended to thoroughly illustrate the state of the science and depth of research in the field at the time the case study was written. Inclusion of literature in the case study should not be interpreted as validation of that literature, or establishment of particular piece of literature as key and substantial in the field. Information in the CEA framework (i.e., the case study document) is intended to be iteratively updated through the CEA process; key concepts presented in this case study are subject to scientific challenges as the emerging field of nanotechnology progresses. The Agency acknowledges the fact that the accuracy of all scientific publications is ultimately determined through the process of repetition, or lack thereof, by other researchers in the field and that the concepts presented in this case study are subject to scientific re-evaluation as the emerging field of nanotechnology progresses. A statement was added to Section 1.1.2 regarding the date of the last literature review and associated search terms, as well as clarifying the use of unpublished literature to supplement peer-reviewed literature when appropriate.	3	12, 13, 165
General	Two comments noted the need for not only presenting the most important information, but also discussing conflicting evidence to present a more balanced discussion.	Generally, Information Highlight Text Boxes and Priority Research Area Highlight Boxes have been added to the document to help highlight data gaps and, where applicable, to clearly present conflicting evidence (e.g., no effect versus effect findings). As these comments were general, no specific actions were taken to address these comments.	1, 2	125, 22
General	One comment noted the need for incorporating value of information analysis into the CEA.	The Agency appreciates the feedback. Value of Information (VOI) was incorporated into the workshop breakout group exercises for the areas identified as research priorities. Future applications of the CEA approach will attempt to incorporate greater VOI analysis during earlier steps in the process.	3	79
Chapter 1/ Chapter 6	One comment questioned whether the case study could be used to accomplish more than its intended purpose of identifying and prioritizing research gaps.	The purpose of the draft case study document and its relationship to any future regulatory decisions for MWCNT was clarified in Chapter 1 (see Section 1.3) and expanded upon in Chapter 6 (see Section 6.3).	3	35

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Chapter 1/ Chapter 6	One comment suggested an OECD (2012) publication regarding important issues in the risk assessment of nanomaterials. Another suggested this reference to describe a predictive toxicological paradigm for the assessment of nanomaterials.	The purpose of the draft case study document and its relationship to any future regulatory decisions for MWCNT was clarified in Chapter 1 (see Section 1.3) and expanded upon in Chapter 6 (see Section 6.3). In particular, the OECD (2012) publication was used to highlight research needs and data gaps in the assessment of nanomaterials in Section 6.3.	3	154, 146
Product life cycle: Raw Materials, Synthesis AND Chapter 1/ Chapter 4	Four comments noted the need for more information regarding material synthesis (e.g., functionalization, handling). One of these comments additionally noted the need to focus on chemistry and functionalization specific to use in flame retardants.	"Product Life Cycle: Material Synthesis, Material Processing, and Product Manufacturing" was identified by workshop participants as a Priority Research Area; therefore, additional information was incorporated into the relevant Priority Research Area Highlight Box and Section 6.3.1.1. Additionally, Figure 2-1 and Additional Information Highlight Box 6 were added to clarify the distinction(s) between as-manufactured versus modified MWCNTs by incorporation into products or transformation in the environment. This topic is also discussed in Chapter 4. Additionally, Table I-13 was added to Chapter 1 regarding functionalization and chemistry of MWCNT specific to use in flame retardants.	1, 2, 3	6, 213, 214, 216
Product life cycle: Product manufacturing; AND Exposure Route: Human Occupational, Human Consumer	Eleven references were provided along with a comment that these studies indicate MWCNT alone will not be useful as a flame retardant unless they are combined with other chemicals/materials to achieve flame-retardant performance.	The suggested literature was incorporated into the relevant Additional Information Highlight Box 3 to reflect that MWCNT are likely to be used in combination with other chemicals/materials to achieve flame-retardant performance needs. Additionally, Priority Research Area Highlight Boxes and Sections 6.3.1.3, 6.3.3.1, and 6.3.3.2 were included since "Product Life Cycle: Product Manufacturing", "Exposure Route: Occupational", and "Exposure Route: Consumer" were identified by workshop participants as Priority Research Areas.	1, 2	40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Product Life Cycle: Use, Release Rate AND Exposure Route: Human	One comment suggested identifying data gaps clearly and prioritizing accordingly using the specific example of release of CNT from different media.	Additional Information Highlight Box 4 was added to Section 2.2.4.2 to highlight release of MWCNT from different product matrices, and Additional Information Highlight Box 12 was added to Section 4.2.2 to highlight the exposure routes that seem most likely or most dominant of all the potential routes. Additionally, because "Product Life Cycle: Use: Release Rate" and "Exposure Route: Human" were identified by workshop participants as Priority Research Areas, this comment was considered and addressed through the addition of Priority Research Area Highlight Boxes and Sections 6.3.1.4 and 6.3.3.	1, 2	114
Product life cycle: Material Synthesis and Processing AND Exposure route: Human: Occupational	Three comments noted the lack of information regarding material synthesis and potential for human occupational exposure. The comments provided details and references (or names of individuals to contact) for more information regarding the current scale, outlook, manufacturing processes, and potential exposure in MWCNT industry.	Suggested literature was reviewed and incorporated to enhance the discussion of materials synthesis (by adding Table 2-2 to summarize estimated growth in the industry, quantities produced, etc., and adding Additional Information Highlight Box 2 in Chapter 1 regarding the fact that currently MWCNTs are not widely used in flame-retardant textiles). This was also addressed by the addition of a Priority Research Area Highlight Boxes and Sections 6.3.1.1 and 6.3.3.1 given that "Product Life Cycle: Material Synthesis" and "Exposure Route: Human: Occupational" were identified as Priority Research Areas in the workshop. The suggested individuals were contacted; one responded. Their input was incorporated as a footnote in Section G.2.1.1.	1, 2, 3	54, 214, 216
Product Life Cycle: Product manufacturing AND Exposure Route: Human: Occupational	Two comments suggested literature on potential release and exposure in occupational environments that was already incorporated into the case study.	Although the provided references were already included in the case study, this comment was considered and addressed by adding greater emphasis to potential release and exposure during product manufacturing in a new discussion in Section 6.3. In addition, Priority Research Area Highlight Boxes and Sections 6.3.1.3 and 6.3.1.1 were added for "Life Cycle: Product manufacturing" and "Exposure: Human: Occupational" as they were identified by workshop participants as Priority Research Areas.	1, 3	144, 224

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Dose: Human: Absorption AND Impacts: Human: Cancer, Non-Cancer	Three comments noted additional references pertaining to the mode of action of MWCNTs in the lungs, sub-pleural deposition and pleural translocation in the lung, as well as structural similarities to other particles of concern (i.e., asbestos), and potential similarities to other particles of toxicological concern. References were also provided.	Additional Information Highlight Box 13 was added to discuss the comparison of MWCNTs and asbestos. Additionally, the text was revised regarding the toxicological concern from inhalation of MWCNTs. Finally, because "Dose: Human: Absorption" and "Impacts: Human Cancer and Non-cancer" was identified by workshop participants as a Priority Research Area, Priority Research Area Highlight Boxes were added and the topics are now discussed in Sections 6.3.3.3 and 6.3.4.1.	1, 2, 3	64, 122, 135
Chapter 4/ Chapter 6	One comment questioned whether information from two sources regarding decaBDE use in cars/aircraft was accurate.	The cited literature was reviewed and accuracy of the statement was verified. Additional sources corroborating the statement were added.	3	229
Chapter 4/ Chapter 6	One comment questioned whether information in reports regarding MWCNT flame-retardant action was accurately conveyed in that the flame-retardant effects of MWCNT alone are not sufficient for regulatory standards.	Information regarding the use of MWCNTs in combination with other chemicals/materials was included in Additional Information Highlight Box 3. Additionally, uncertainty of MWCNT use in flame retardants due to small scale (mostly R&D) and flame-retardant selection has been added in Additional Information Highlight Box 2.	2, 3	244

Table I-4, cont.: Relevant to the general case study or multiple sections of the case study.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Section 4.2.5/ Section 5.1.7	Several additional references were provided to improve the discussion of decaBDE in the case study.	Information on decaBDE is now primarily in Appendix H; however, the provided references were reviewed and incorporated into the text as appropriate.	3	2, 23
Multiple DecaBDE Sections	Two comments recommended additional information and sources relevant to decaBDE, including physicochemical properties and toxicokinetics, suggesting some sources in the case study were outdated (a specific example was water solubility). Another noted that additional information might be available regarding resource demands of decaBDE synthesis.	Basic information regarding decaBDE was reviewed for accuracy and edited as needed. The document currently defines the water solubility of decaBDE as <0.1 µg/L in Table 1-8; no changes to this table were made as a result of this comment. A targeted literature search was performed but no new information on energy and resource demands of raw material extraction for synthesis of decaBDE was found so no changes were made. "Product Life Cycle: Material Synthesis" was identified by workshop participants as a Priority Research Area for MWCNTs but decaBDE was not the focus of this document.	3	1, 24, 82

Table I-5. Relevant to Chapter 1 (including Preface and Executive Summary).

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Preface	One comment suggested that the characterization of the amount of literature available on uptake of MWCNTs in aquatic organisms was incorrect.	The statement was revised and clarified.	3	162
Executive Summary/ Chapter 1	One comment suggested there may be more recently published literature relevant to MWCNTs.	Text in the Executive Summary and in Section 1.1.2 was revised to clarify that the original literature search was conducted in November 2011. A second, limited literature search was conducted in May 2012 with the goal of capturing literature published since November 2011. Additional targeted literature searches were performed in November 2012 to address data gaps in priority areas identified by workshop participants. The case study; however, is not intended to be a comprehensive literature review. New literature was added only if it enhanced discussions on key priority areas or data gap sections identified in the collective judgment step of the CEA process. For example, although an article published in 2012 corroborating details from two previously published studies already included in the case study might not add to efforts to plan research for MWCNTs, literature showing a new or conflicting finding would inform research planning that supports future decision-making.	3	129
Chapter 1	Twenty four comments noted that MWCNT in fire retardant might not be the primary application available to consumers, and questioned whether a larger scale application might have been a more appropriate selection. One comment questioned using a single manufacturer of MWCNT fire-retardant product as evidence of the application's feasibility.	Efforts will be made to include greater consideration of the current market share of a particular application in future applications of the CEA approach. In addition, greater detail related to information considered in the selection process, which was originally in Appendix A, is now also included in Chapter 1. New text describing the selection rationale is also included in Chapter 1. Additional details regarding the use of flame-retardant MWCNT products were provided through personal communication with Nanocyl, publicly available Nanocyl promotional materials, and several other publications, as indicated in the text. Finally, additional citations were included that suggest more manufacturers will enter the market soon.	3	8, 30, 75, 53, 192, 193, 195, 199, 202, 204, 205, 206, 207, 209, 211, 227, 230, 234, 238, 239, 240, 242, 243, 248, 250, 251, 252, 253

Table I-5, cont.: Relevant to Chapter 1 (including Preface and Executive Summary).

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Chapter 1	Two comments noted that use of MWCNTs in fire retardant will be determined by their ability to pass specific fire-retardant regulatory tests, which will in turn dictate the feasibility of a large-scale application.	Additional Information Highlight Box 2 has been added to Section 1.3.2 to clarify that the use of MWCNTs in flame-retardant textiles is at an exploratory stage. Although research and development efforts have shown the material's capability as a flame retardant, many considerations will determine whether MWCNT use in flame-retardant textiles will grow. Additional Information Highlight Box 1 was added to clarify the factors influencing selection of fire-retardant materials. In addition, Table 1-3 lists some regulatory standards for flame-retardant textiles, including California Technical Bulletins 116, 117, and 133. Table 1-11 and Table 1-12 provide details on the comparative flame-retardant performance of decaBDE and MWCNTs. Additionally, Table 1-13 has been added to clarify the physicochemical properties of MWCNTs that are related to flame-retardant performance.	2	210, 211
Section 1.2.2	Two comments suggested highlighting the factors influencing selection of fire retardant and the uncertainty involved in MWCNT success in this application compared to other applications. One of these also suggested that alternative applications of MWCNTs will be more prominent in the future than the selected application.	Additional Information Highlight Box 1 was added to clarify the factors influencing manufacturers' selection of fire-retardant materials. Another Information Highlight Box was added to describe the uncertainty surrounding which applications MWCNTs will be used in (Additional Information Highlight Box 2). In addition, greater detail related to information considered in the selection process, which was formerly in Appendix A, is now also included in Chapter 1. New text describing the selection rationale is also included in Chapter 1.	2, 3	56, 59

Table I-5, cont.: Relevant to Chapter 1 (including Preface and Executive Summary).

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Chapter 1	Two comments suggested a more detailed discussion on the distinction between different chemistries, surface functionalizations, and classes of MWCNTs rather than more general discussion would improve the document. Another comment requested that the term "functionalization" be defined.	A goal of the case study is to provide information on an emerging nanomaterial—MWCNTs—illustrated through that material's use in a specific application—flame-retardant textiles. Given the relative dearth of information on specific formulations of MWCNTs used in flame-retardant coatings, or other applications, information on a variety of MWCNT formulations is included in the case study to provide a greater scope of details on the nanomaterial in general. Additional Information Highlight Box 7 and Figure 3-1 have been added to highlight variations in MWCNT formulations and functionalization, and how these variations affect the product life-cycle. Table 1-13 was added describing the chemistry/functionalization described in literature specific to use as a fire retardant. Existing Text Box 1-1, Text Box 4-2, Text Box 5-1, and Table 2-4 contain generalized information regarding functionalization and how physicochemical properties of MWCNTs affect release, environmental fate, exposure, and toxicity. Functionalization is defined in Section 2.2.3.1.	2, 3	7, 9, 11
Chapter 1	One comment noted that chirality might not be a consideration for MWCNTs. A reference was provided.	The Agency appreciates the suggestion but the source used for information on chirality, Gustavsson et al. (2011) mentions specifically the variation for MWCNTs. The literature provided by the commenter is for double-walled carbon nanotubes and was therefore not included in the case study.	5	163

Table I-6. Relevant to Chapter 2.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Product Life Cycle: Raw Materials; Product Life Cycle: Material Synthesis	Two comments suggested additional literature might be available to fill in data gaps pertaining to MWCNT feedstocks and replace the surrogate SWCNT information currently in the case study.	"Product Life Cycle: Material Synthesis" was identified by workshop participants as a Priority Research Area. A Priority Research Area Highlight Box and Section 6.3.1.1 were added; a targeted literature search was performed to inform the sections. Data for SWCNTs were used to describe feedstock stages of the product life-cycle because no data on MWCNT feedstock were identified at the time. Because "Product Life Cycle: Raw Materials" was not identified as a priority research gap, no additional focus was given to improving this portion of the case study with new information. Healy (2008), however, was deemphasized to focus on just presenting the more recent information regarding SWCNT feedstocks by Zhang et al. (2011b).	1, 2, 3	83, 214
Section 2.1.1	Two comments questioned the logic regarding synthesis yields of CNTs.	The reported values were verified in the literature.	5	84, 85
Chapter 2	Three comments identified additional information that might be available from NIOSH and Albermale regarding material synthesis, processing, and potential release of decaBDE.	The purpose of including comparative information for decaBDE was to better inform the collective judgment process by helping highlight data gaps and research needs for MWCNTs; as noted in Section 1.1.2, detailed information on decaBDE has been moved to Appendix H and replaced with succinct comparison highlight text boxes to focus the Peer Review Draft on only the most important and relevant information for the Priority Research Areas for MWCNTs as identified by the workshop experts. As such, no additional information was incorporated to enhance the discussion of decaBDE in the case study.	3	212, 217, 218
Chapter 2	One comment noted that not all laboratories, particularly small R&D facilities or older facilities, have the same engineering controls.	This text was revised and clarified. Additionally, "Product Life Cycle: Material Synthesis" and "Exposure: Human: Occupational" were identified as Priority Research Areas and this comment was considered and addressed through the addition of Priority Research Area Highlight Boxes and Sections 6.3.1.1 and 6.3.3.1.	1, 3	216

Table I-6, cont.: Relevant to Chapter 2.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Section 2.5.4	Three comments noted a data gap regarding the impact of MWCNTs on wastewater treatment plants, particularly in terms of suggested evidence of antimicrobial activity. Two of these also suggested literature.	Additional consideration of the impact of MWCNT contamination on functionality of wastewater treatment plants has been added in Additional Information Highlight Box 5. Readers are referred to Section G.5.1.1.and Appendix Table F-18 for details on the toxicity of MWCNTs to microbes. This comment was also considered in developing text for Section 6.3.2.2 given that "Env TT&F: Waste Water" was identified by workshop participants as a Priority Research Area.	1	18, 19, 72
Chapter 2	One comment noted a step during Feedstock Extraction (cleaning between reactor runs) that might have been overlooked in discussion of release rates during this process.	Text was revised to clarify this point.	3	215
Product Life Cycle: Disposal/ Recycling	One comment noted the possibility of MWCNT being both bound or free during end-of-life stages.	"Product Life Cycle: Disposal/Recycling" was identified by workshop participants as a Priority Research Area, and this comment was considered and addressed through the addition of a Priority Research Area Highlight Box and Section 6.3.1.5. Additionally, Figure 2-1 has been updated to illustrate the potential for MWCNTs to become "free" during end-of-life stages of the life-cycle process.	1, 3	81

Table I-7. Relevant to Chapter 3.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Env. TT&F (Analytical Techniques)	Two comments provided references pertaining to analytical techniques for MWCNT in environmental media and impacts of release.	Analytical techniques were discussed by workshop participants as related to several research priorities within environmental transport, transformation, and fate. As such, the suggested literature was incorporated into the related sections of Section 6.3.2 or in Additional Information Highlight Box 10, which was added to describe the weaknesses of current analytical techniques as relevant.	1, 2	128, 139
Env TT&F	One comment noted a data gap regarding environmental decomposition and transformation of MWCNTs	Several aspects of environmental transport, transformation, and fate were identified by workshop participants as Priority Research Areas. Priority Research Area Highlight Boxes and Section 6.3.2 have been included. The current lack of data noted by this comment is highlighted in the discussion of these priority areas in Section 6.3.2.	1	201
Chapter 1 or 3	Eight comments discussed MWCNT release, transformation, and fate in the environment in terms of potential variation in polymer chemistry; references were also provided.	Additional Information Highlight Box 6 and Additional Information Highlight Box 7 were added to Chapter 3 to address these issues; the provided literature was included where relevant. In addition, release and processes that influence release in various media were identified by workshop participants as a Priority Research Area and thus discussed in Section 6.3.2.	2	127, 219, 220, 221, 222, 225, 226, 228
Env TF&T: Soil	Three comments noted an instance where the authors of a reference appeared to be speculating rather than stating definitive evidence.	The statements were revised and clarified.	3	168, 169, 170

Table I-7, cont.: Relevant to Chapter 3.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Env TT&F	One comment discussed the influence of environmental parameters on the aggregation process and toxicity of MWCNT. Two references were provided.	As noted by workshop participants, uncertainty exists concerning how properties of the environmental media influence MWCNT fate and transport, and conversely, how MWCNT properties influence fate, transport, and toxicity. New figures have been added to the main text of the document (Figure 2-1 and Figure 3-1) showing variations in MWCNTs formulations and functionalization throughout the lifecycle, and how various environmental properties can affect MWCNT transport and fate. Additionally, readers are reminded of existing tables in Appendix D that summarize studies on behavior of MWCNTs in various environmental media; several of these studies identify environmental conditions that influence MWCNT behavior. Text Box 1-1, Text Box 4-2, Text Box 5-1, and Table 2-4 contain generalized information regarding how physicochemical properties of MWCNTs affect release, environmental fate, exposure, and toxicity.	2, 3	21, 65, 66
Env TT&F: Soil/Sediment: Bioavailability	One comment suggested literature pertaining to soil/sediment bioavailability of MWCNT	"Env TT&F: Sediment: bioavailability" was identified by workshop participants as a Priority Research Area. A Priority Research Area Highlight Box and Section 6.3.2.3 were added on this topic. The suggested literature was reviewed and incorporated into Section 6.3.4.3.	1	161
Env TT&F: Air (Analytical Techniques)	One comment suggested literature relevant to analytical techniques for urban air.	The suggested reference was included in Additional Information Highlight Box 10, which discusses analytical techniques for detecting MWCNTs in urban air.	2	92
Env TT&F	One comment noted the use of lipophilicity and hydrophobicity was not always clear and that the sources used might be outdated.	The distinction between hydrophobicity and lipophilicity was identified as an important research topic by workshop participants. Text was clarified as necessary throughout the document.	3	164
Chapter 3	One comment suggested that discussion of different mechanisms of soil transport, for example colloid-facilitated transport, physical straining, and site blocking, be included in the case study.	Additional Information Highlight Box 8, which discusses transport mechanisms, was added to the document.	2	22
Note: Env TT&F = Environmental Transport, Transformation, and Fate				

Table I-8. Relevant to Chapter 4.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Exposure Route: Human: Occupational	One comment noted occupational exposure is a data gap for MWCNTs; another suggested a reference relevant to this topic.	"Exposure: Human: Occupational" was identified by workshop participants as a Priority Research Area. A Priority Research Area Highlight Box and Section 6.3.3.1 were added for MWCNT occupational exposure, and the suggested literature was incorporated.	1	38, 152
Exposure Route: Human-Consumer	One comment noted a reference to elucidate potential consumer exposure to MWCNTs.	"Exposure: Human: Consumer" was identified by workshop participants as a Priority Research Area, as denoted by a Priority Research Area Highlight Box on this topic. The suggested literature was incorporated into Section 6.3.3.2.	1	197
Exposure Route: Human	One commenter asked if there was additional supporting evidence for the findings of Aschberger et al. (2010).	The statement attributed to Aschberger et al. (2010) was corroborated by an additional source that is now included in the case study document.	3	223
Section 4.2.1	One comment noted that the discussion of dermal absorption might not reflect the most recent and accurate science; further, the comment indicated that discussion can be drawn from information available in previous case studies.	Information on dermal absorption was reviewed for accuracy. In addition, because this area was identified as a priority research gap, discussion on dermal absorption of nanomaterials from past case studies on Nano-Ag and Nano-TiO_2 was included in Additional Information Highlight Box 11 along with information (as available) from a targeted literature search to present the most accurate and current information on dermal absorption.	1, 2, 3	110
Dose (Kinetics)	One comment noted challenges related to understanding toxicokinetics of nanomaterials due to limitations in traditional analytical techniques. Another suggested a reference regarding interspecies scaling of pharmacokinetics.	"Dose (Kinetics): Human" was identified by workshop participants as a Priority Research Area; as such, information regarding limitations in standard "mass concentration" metrics and analytical techniques was added to Additional Information Highlight Box 9 to support research planning that involves extrapolating kinetic and toxicity results from laboratory animals to humans.	1, 2	260, 262

Table I-8, cont.: Relevant to Chapter 4.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Section 4.3 Dose (Kinetics): Aquatic Biota—Absorption AND Env TT&F: Biota: Bioaccumulation	Four comments noted that more recent literature suggests that MWCNTs do not appear to be absorbed across the gut lining or into other tissues, and therefore are not expected to act in a similar manner to bioaccumulative substances. References were also provided.	The provided literature has been added to Additional Information Highlight Box G1 in Appendix G to further discuss uptake and absorption in aquatic food webs.	2	174, 175, 177, 172
Dose: Human: Absorption	Three comments suggested literature to enhance the discussion about absorption of MWCNTs in humans.	The suggested literature was incorporated into Section 6.3.3.3. In addition, "Dose: Human: Absorption" was included in a Priority Research Area Highlight Box as it was identified by workshop participants as a Priority Research Area.	1	63, 64, 153
Chapter 4	One comment recommended the ATSDR (2004) toxicological profile for PBDEs as a reference.	The ATSDR document was included in several instances; however one of the aims of this version of the case study was to reduce the focus on decaBDE and instead shift focus toward highlighting only those aspects of decaBDE that could be particularly useful to risk assessment of MWCNTs. Therefore, rather than including an exhaustive review of the potential exposure scenarios and relevant information for decaBDE by delving further into the ATSDR Toxicological Profile for PBDEs, emphasis was placed on condensing decaBDE information.	3	157
Dose (Kinetics): Terrestrial Biota: Absorption	One comment noted that a reference describing lipophilicity/accumulation potential in roots was speculative rather than definitive, and two references were provided regarding the absorption and impacts of MWCNTs on terrestrial biota.	The text was reviewed and removed as appropriate. Although the Agency appreciates the additional literature, it was not incorporated into the body of the document because the area of "Impacts: Terrestrial Biota" was not identified by workshop participants as a Priority Research Area.	3	150, 151, 176

Table I-8, cont.: Relevant to Chapter 4.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Section 4.3	Two comments noted potential errors in transcription from primary sources.	The statements were revised and clarified.	3	173, 177
Text Box 4-1	One comment noted that there are currently no mass-spectrometry techniques for MWCNTs, and the methodology described in the case study measures only metal concentrations still associated with MWCNTs.	The statement was revised and clarified.	3	171
Dose: Aquatic Biota: Absorption	One comment noted that the discussion of potential absorption of carbon materials in the gut was not clear and further suggested additional literature where absorption across the gut tract was not observed.	The statement was revised and clarified to accurately convey the science. The provided literature has been added to the discussion in Appendix G. Because uptake vs. absorption is a key issue that impacts toxicity, Additional Information Highlight Box G1 also was included in Appendix G.	3	172

Table I-9. Relevant to Chapter 5.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Chapter 5	One comment suggested an alternative definition of "fibers" with additional references.	A general discussion of aspect ratios for CNTs and comparisons to asbestos has been added in Additional Information Highlight Box 13; this box includes one of the references suggested by the commenter. The second reference pertained to carbon nanofibers and was therefore not included. The discussion regarding the 3:1 aspect ratio for fibers as defined by the World Health Organization was not revised, however, because it represents the current measuring classification.	2	111
Chapter 5	One comment provided a reference to replace SWCNT surrogate data regarding acute oral toxicity of MWCNTs.	The document was updated to reflect the provided literature. Data on SWCNTs was included only when data on MWCNTs was extremely limited and when the SWCNT data is highly relevant; SWCNT is clearly identified as such.	3	117
Section 5.1.5	One comment suggested additional literature to support the discussion related to dermal sensitization of MWCNTs.	The discussion in Section 5.1.5 was revised to better reflect the scientific results of the suggested literature. In addition, Pauluhn et al. (2010) was reviewed and included in the discussion. Table 5-1 already indicated that skin sensitization is negative, so no additional revisions were made.	3	121
Section 5.1.6	One comment suggested an additional reference on reproductive toxicity that had originally been omitted due to the less relevant route of exposure.	Text was revised to clarify that no key studies were identified for reproductive effects related to MWCNT exposure. Although the use of a less relevant exposure route (i.e., intravenous injection) in the study by Bai et al. (2010) precluded its use as a key study, the area of "Impacts: Human: Reproductive/ Developmental" was identified as a Priority Research Area, and thus this study has been noted in Section 6.3.4.2.	3	115
Human Impacts: Non-cancer	Four comments reiterated the influence of physicochemical properties on toxicokinetics and toxicity. One comment suggested carboxylated CNTs are more likely to degrade and therefore are less likely to induce profibrogenic effects, as colloid-facilitated transport is an important factor.	"Impacts: Human" was identified by workshop participants as a Priority Research Area. Additional information was incorporated into Section 6.3.4. Additionally, Text Box 5-1 describes influences of physicochemical properties on MWCNT toxicity. The Agency reviewed the suggested literature and determined that making conclusions regarding whether dispersion state/carboxylated MWCNTs influence fibrosis based on this study is difficult, as metal concentration varied with degree of carboxylation. Therefore, it was not added to the document.	1, 2	261, 263, 264, 265, 10

Table I-9, cont.: Relevant to Chapter 5.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Impacts: Human	Seventeen comments noted significant advancements in complex in vitro models that have resulted in reproducible effects and showing good concordance with in vivo data. Comments suggested such approaches would prove useful for MWCNT assessment in the future.	"Impacts: Human" was identified by workshop participants as a Priority Research Area. Additional Information Highlight Box 15 was added to highlight the trend toward developing innovative biologically/toxicologically relevant in vitro models.	2	275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291
Section 5.2.2.1	Two comments recommended references pertaining to accumulation in terrestrial biota.	The suggested literature was reviewed and incorporated as deemed relevant into Additional Information Highlight Box G2 in Appendix G, which discusses toxicity to terrestrial invertebrates.	2	182, 183
Impacts: Human	One comment noted the results found in intratracheal instillation studies in mice corroborated those reported via inhalation.	Four studies on intratracheal instillation are currently included in Section 5.1.3 along with a comment that these studies show similar endpoints as the inhalation studies. In addition, seven alternative exposure route pulmonary studies are included in Appendix Table F-6. Additionally, Additional Information Highlight Box 14 was added, which discusses inhalation study designs for MWCNTs.	2	37
Impacts: Human	Ten comments questioned the applicability of traditional in vivo toxicological (particularly inhalation) models for MWCNTs; several references were provided noting potential weaknesses/confounding factors.	"Impacts: Human" was identified by workshop participants as a Priority Research Area. References and discussion regarding the complexity/confounding nature of MWCNTs in traditional in vivo models were included in Additional Information Highlight Box 14. Additionally, Additional Information Highlight Box 15 was added regarding the trend toward the development of innovative toxicologically/biologically relevant in vitro models.	1, 2, 3	259, 266, 267, 268, 269, 270, 271, 272, 273, 274

Table I-9, cont.: Relevant to Chapter 5.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Impacts: Human: Non-Cancer	One comment noted respiratory sensitization as an example of where conflicting data exists, but the consensus of most evidence should be highlighted.	Throughout the document, information highlight text boxes have been added to the document to help highlight data gaps and present a balanced representation of evidence of a finding, or lack thereof. Specific to this comment, "Impacts: Human: Non-cancer" was identified by workshop participants as a Priority Research Area, which corresponds with the identification in this comment of respiratory sensitization as an example of an area with conflicting data. Non-cancer respiratory effects, including inflammatory changes and immune responses characteristic of respiratory sensitization, are discussed in Section 5.1.3 and Additional Information Highlight Box 13 further discusses available evidence on health impacts from MWCNT inhalation exposures.	3	125
Impacts: Aquatic Biota Table 5-2, Table 5-4, Table 5-5	Seven comments suggested additional literature regarding the impacts of MWCNTs to benthic invertebrates, soil/sediment organisms, or other aquatic biota.	Impacts: Aquatic Biota" was identified by workshop participants as a Priority Research Area. The topic was thus highlighted in a Priority Research Area Highlight Box and discussed in Section 6.3.4.3. Additional Information Highlight Box 17 was added regarding toxicity to benthic and aquatic invertebrates in Section 5.2.1.1, incorporating provided literature where applicable. Additionally, Table 5-2 was updated to include the rest of the suggested literature (literature was split up into each of these action elements to avoid redundancy). Specific to comment 178, Shen et al. (2012) was not included in the added text because the primary focus involved the bioaccumulation of polycyclic aromatic hydrocarbons.	1, 2, 3	126, 138, 178, 180, 181, 182, 183
Section 5.2.1	One comment identified an improperly cited statement.	The text was revised.	3	179

Table I-10. Relevant to Chapter 6 and appendices.

Related to CEA Framework Area	Comment Theme	Response	Response Category	Related to Global Comment ID
Chapter 6	One comment suggested the usefulness of highlighting the information leading to voluntary phase-out of decaBDE.	Text was revised in Section 1.1.4 to further emphasis the type of information considered in decisions surrounding the voluntary phase-out of decaBDE.	3	74
Impacts: Human: Cancer, Non-cancer	Three comments identified additional literature pertaining to SWCNT that might be useful as surrogate or supportive data for MWCNTs. One comment stated that major studies were presented already, and that the additional SWCNT studies would not be relevant.	Studies on SWCNTs were not the focus of this case study. Some information on SWCNTs, however, is provided in the various appendix tables when information on MWCNTs did not exist, especially if this area was considered a Priority Research Area.	3	96, 116, 118, 119
Appendix J	One commenter felt summary tables and figures contained too much information to be useful as summary or highlight text.	Efforts to clearly convey information in summary tables and figures is part of ongoing work to refine the CEA approach. See Appendix J for an example of current pilot-stage efforts to use knowledge maps to more clearly convey information in tables and text.	3	149

Table I-11. Comments that required no action.

Related to CEA Framework Area	Comment Theme	Agency Response	Related to Comment ID
General	One comment recommended that inferences be more clearly stated as such.	The Agency appreciates the feedback; however, effort was made in the original draft to distinguish inferences (i.e., "could occur") from documented information (i.e., "has been shown to occur"). This decision was made explicitly to avoid implying that any inferences were supported by documented scientific data; rather, such inferences were drawn from literature that, in the absence of concrete evidence specific to MWCNTs, suggested the likelihood of certain statements occurring. As such, no action was taken in response to this comment.	109
General	One commenter stated that the science was general comprehensive but some areas could be improved. They did not indicate which areas.	In revising the document, efforts were made to improve key areas identified as Priority Research Areas; however, no specific revisions have been made in regards to this comment.	120
General	14 commenters stated that the science was accurately conveyed in the case study document.	The Agency appreciates the feedback.	26, 52, 67, 147, 32, 58, 77, 97, 101, 105, 130, 134, 155, 189
General	20 commenters stated that the comparison of MWCNT to decaBDE was useful. Commenters defended this position with a variety of reasons, such as the comparison helped to identify research gaps, helped the reader understand the process of regulating a chemical and identifying knowledge gaps, or illustrating the manufacturing process and exposure scenarios for flame-retardant upholstery.	The Agency appreciates the feedback.	33, 55, 60, 123, 124, 141, 184, 196, 235, 69, 78, 86, 94, 102, 106, 131, 136, 148, 156, 190.

Table I-11, cont.: Comments that required no action.

Related to CEA Framework Area	Comment Theme	Agency Response	Related to Comment ID
Chapter 1	One commenter stated that the science was accurately portrayed however the Chapter on characterization was not complete.	No specific revisions were identified to address this comment; however, efforts were made throughout the document to present complete information.	89
Product Life Cycle: Release Rate / Impacts	One commenter stated that the science was accurately portrayed however some issues of terminology could be clarified.	No specific revisions were identified to address this comment; however, efforts were made throughout the document to use consistent terminology, particularly in relation to specific types of MWCNT emissions and toxicological effects, when such information was available.	93
Env TT&F:Soil	Two comments suggested additional literature pertaining to Env.TT&F in wastewater and soil that were already included in the case study.	Zhang et al. (2011a) was already included in Section 3.3.1 (transport, transformation, and fate n surface water and sediment). Holbrook et al. (2010) was already included in Appendix Table D-2, which summarizes studies relevant to MWCNT fate and transport in aqueous media, including sediment. The two studies were not added to Section 3.4 because Env TT&F: Soil was not identified by workshop participants as a Priority Research Area.	166, 167
Env TT&F:Soil: bioavailability	One commenter called out a section of the preface which they felt was not fully representative of the body of science. A second commenter asked for more detail about surface chemistry of MWCNTs in the preface.	No revisions were made to the preface because the preface is not intended to include this level of detail.	161, 200
Env TT&F: Soil / Impacts: Other	Two commenters provided literature already included in the case study or specific to SWCNTs.	The Agency appreciates the suggestion. However, the literature was not incorporated into the Case Study because the references are not specific to MWCNT and the behavior of metal oxide nanomaterials is not considered appropriate to predict the effects of MWCNT.	71, 144

Table I-11, cont.: Comments that required no action.

Related to CEA Framework Area	Comment Theme	Agency Response	Related to Comment ID
Env TT&F (Aqueous media)	One comment provided a reference pertaining to MWCNT in aqueous media.	The suggested reference was previously included in the case study in Section 3.3.1.	143
None	16 comments were received that did not require agency action.	The Agency appreciates the feedback.	3, 4, 20, 194, 198, 208, 231, 232, 236, 237, 241, 245, 249, 255, 296
None	12 commenters stated that there were no additional literature they were aware of that should be included in the case study.	The Agency appreciates the feedback.	25, 31, 57, 76, 80, 88, 100, 104, 108, 133, 159, 188
None	10 commenters stated that they did not have any comments on improving the document, or that their comments for improvements were incorporated into the other charge question responses.	The Agency appreciates the feedback.	5, 95, 187, 70, 87, 107, 132, 142, 158, 191

I.3. Full Comment Excerpts

Table I-12. Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
25	E1	1	I think this report was thorough and included all available literature on MWCNTs.	No additional literature
26	E1	2	I believe that the science was presented in an objective and clear manner.	Science accurate
27	E1	3	Further, I believe this comparison made things confusing, since it is impossible to compare the fate and transport and effects of two types of compounds that are completely different in their chemistry and physical properties. So what has been found for flame retardants in relation to their movement in the environment, half-life, uptake by biota, and ultimately effects, is rather meaningless when applied to MWCNTs.	Comparison NOT useful; decaBDE was bad comparison choice; fundamentally different compounds don't overlap
28	E1	3	No, this comparison was not useful. I am not sure why this was done, but have the impression that it was used to “beef” up the document since so little information exists on MWCNTs.	Comparison NOT useful; added length
29	E1	4	Remove the flame retardant vs. MWCNTs comparison. As already mentioned, this comparison doesn’t help when trying to elucidate research gaps as related to MWCNTs.	Comparison NOT useful; highlighted data gaps
30	E1	4	Also, the use of MWCNTs as flame retardants has not been materialized, so why solely focus on this particular application?	Choice of nanomaterial and application; application not currently in use
31	E2	1	At this point in time, I must admit that I cannot think of any studies that might help and I find the Draft Case Study Document to be very comprehensive	No additional literature
32	E2	2	To the best of my knowledge the science is accurately conveyed	Science accurate
33	E2	3	I do think that the comparison makes sense that it is good to have facts and data on decaBDE to measure information up against.	Comparison WAS useful; highlighted data gaps
34	E2	3	My only concern is that decaBDE is a problematic substance and bans and limitations have been put on its use and hence comparing MWCNTs with such a problematic substance would inevitably make MWCNTs look good	Comparison NOT useful; decaBDE was bad comparison choice

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
35	E2	4	Somehow I feel that the purpose of "identifying and prioritizing research" is too modest a scope for all the work that has been put into drafting this comprehensive report. Identification of the most appropriate manner in which to regulate MWCNTs, it would be in line with effort put into this.	CEA framework/ methodology; purpose of CEA
36	E3	1	See response to question # 2. In general, the draft document cites most of the relevant published literature on MWCNT that would permit the identification of research gaps.	No additional literature
37	E3	2	The review of the health data on MWCNT described in Chapter 5 and summarized in Table 5-1, doesn't completely capture all the relevant evidence regarding adverse pulmonary effects from exposure to MWCNT. Studies with mice and rats exposed to MWCNT by pharyngeal aspiration and by intratracheal administration support findings of pulmonary irritation, granulomas, alveolar septal thickening, and pulmonary fibrosis that were consistent with effects observed in inhalation studies.	Highlight data gap; additional considerations for section
38	E3	3	In the absence of occupational exposure information on decaBDE and MWCNT it's not possible to determine the potential extent of exposure or exposure characteristics (e.g., physical and chemical state of MWCNT, other contaminants). The absence of such data makes it's difficult to assess the potential hazard risk.	Highlight data gap
39	E3	4	See comment to # 3 regarding focus of document. It would have been informative if the authors of the document would have listed at the end of each Chapter their perspective as to research data gaps.	Highlight data gap; suggestion for improvement
40	E4	1	"Synergistic effect of carbon nanotubes and decabromodiphenyl oxide/Sb2O3 in improving the flame retardancy of polystyrene" Lu, H.; Wilkie, C. A. Polym. Degrad. Stab. 2010, 95, 564-571.	Choice of nanomaterial and application; alternative products/ formulations
41	E4	1	"Role of Surface Interactions in the Synergizing Polymer/Clay Flame Retardant Properties" Pack, S.; Kashiwagi, T.; Cao, C.; Korach, C. S.; Lewin, M.; Rafailovich, M. H. Macromolecules 2010, 43, 5338-5351.	Choice of nanomaterial and application; alternative products/ formulations
42	E4	1	"Segregation of Carbon Nanotubes/Organoclays Rendering Polymer Blends Self-Extinguishing" Pack, S.; Kashiwagi, T.; Stemp, D.; Koo, J.; Si, M.; Sokolov, J. C.; Rafailovich, M. H. Macromolecules 2009, 42, 6698-6709.	Choice of nanomaterial and application; alternative products/ formulations

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
43	E4	1	"Nanoclay and carbon nanotubes as potential synergists of an organophosphorus flame retardant in poly(methyl methacrylate)" Isitman, Nihat Ali; Kaynak, Cevdet Polym. Degrad. Stab. 2010, 95, 1523 – 1532	Choice of nanomaterial and application; alternative products/ formulations
44	E4	1	"Layered silicate polymer nanocomposites: new approach or illusion for fire retardancy? Investigations of the potentials and the tasks using a model system" Bartholmai, M.; Schartel, B. Polymers for Advanced Technologies 2004, 15, 355-364.	General information on flame retardancy of nanocomposites
45	E4	1	"Filler blend of carbon nanotubes and organoclays with improved char as a new flame retardant system for polymers and cable applications" Beyer, G. Fire Mater. 2005, 29, 61-69.	Choice of nanomaterial and application; alternative products/ formulations
46	E4	1	"Flame retardancy of nanocomposites based on organoclays and carbon nanotubes with aluminum trihydrate" Beyer, G. Polym. Adv. Technol. 2006, 17, 218-225.	Choice of nanomaterial and application; alternative products/ formulations
47	E4	1	"Fire behaviour of polyamide 6/multiwall carbon nanotube nanocomposites" Schartel, B.; Potschke, P.; Knoll, U.; Abdel-Goad, M. European Polymer Journal 2005, 41, 1061-1070.	General information on flame retardancy of nanocomposites
48	E4	1	"Some comments on the main fire retardancy mechanisms in polymer nanocomposites" Schartel, B.; Bartholmai, M.; Knoll, U. Polym. Adv. Technol. 2006, 17, 772-777.	General information on flame retardancy of nanocomposites
49	E4	1	"Flame retarded polymer layered silicate nanocomposites: a review of commercial and open literature systems" Morgan, A. B. Polym. Adv. Technol. 2006, 17, 206-217.	General information on flame retardancy of nanocomposites
50	E4	1	"Flammability reduction of flexible polyurethane foams via carbon nanofiber network formation" Zammarano, M.; Kramer, R. H.; Harris, R.; Ohlemiller, T. J.; Shields, J. R.; Rahatekar, S. S.; Lacerda, S.; Gilman, J. W. Polym. Adv. Technol. 2008, 19, 588-595.	General information on flame retardancy of nanocomposites
51	E4	1	While the papers by Schartel above do not always look at nanotubes, they help make it clear why nanotubes alone are not enough to obtain a passing flammability result in most regulatory tests. Therefore, nanotubes alone will not be useful as a flame-retardant product unless they are combined with other flame retardants, which is a very different product than that outlined in this draft document.	Choice of nanomaterial and application; alternative products/ formulations; application not currently in use

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
52	E4	2	In regards to the science being accurately conveyed in the document, the answer is yes and no. Yes in that the MWCNT chemistry and known toxicity and its complexity is accurately captured, …	Science accurate
53	E4	2	In regards to the science being accurately conveyed in the document, the answer is yes and no … but no in that the application for MWCNT which would drive its use is very wrong. The driving factors for flame-retardant solution use (why an industry would use the technology) are completely missing, and therefore the choice of MWCNT in textile back-coatings is unfortunately incorrect. MWCNT will be used in greater quantities in other applications, not in the one selected in this draft case study.	Choice of nanomaterial and application ;application not currently in use
54	E3	3	Most, if not all, of MWCNT use in the United States is in research laboratories or small scale pilot manufacturing processes [Schubauer-Berigan et al. 2011: Engineered carbonaceous nanomaterials manufacturers in the United States: workforce size, characteristics, and feasibility of epidemiologic studies. J Occup Environ Med 53 (Suppl 6):S62-S67]. The draft document could have just focused on the toxicology data (e.g., in vitro, in vivo) with MWCNT (and other CNTs) which would have provided an equally sufficient amount of information to permit a determination of research needed to support future assessments and risk management decisions.	Choice of nanomaterial and application; application not currently in use
55	E4	3	For the comparison of MWCNT to decaBDE, the document does and does not identify the research gaps. It correctly represents the research gaps in regards to nanotube toxicity, exposure and release….	Comparison WAS useful; impacts; exposure
56	E4	4	For specific comments on how to improve the document, the document needs to explain better why certain flame retardants are chosen for an application and why CNT will not be used, but something else may be – or better yet, what applications are more likely to have a high percentage of using MWCNT in their application, and what the risk factors are associated with that application. MWCNT are far more likely to be used in polymer composites than in textiles for furniture, and that is a completely different exposure model, especially if most of the composites enter into aerospace use.	Choice of nanomaterial and application ;suggestion for improvement
57	E5	1	No, I am unaware of any other studies.	No additional literature
58	E5	2	Yes, the science is conveyed accurately throughout the document.	Science accurate
59	E4	3	For the comparison of MWCNT to decaBDE, the document does and does not identify the research gaps … does not correctly show what applications that MWCNT will be used in, nor does it show the uncertainty around which applications MWCNT will be used in that would drive studies like this.	Comparison NOT useful; choice of nanomaterial and application; application not currently in use

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
60	E5	3	Yes and no, yes because it is very nice to have the comparison because it is much easier to see the data gaps for MWCNT when compared to a well-studied material.	Comparison WAS useful; highlighted data gaps
61	E5	4	The document was very thorough and well written, however, for volunteers to read, comprehend, and analyze all the data gaps it was quite time consuming, especially with tight timelines. Certain sections of the document were a little verbose and could be shortened. … Perhaps some of the data in text could be put into a tabular form to reduce the length of the document but allow the reader to visually see where the data gaps are.	Added length
62	E5	4	As mentioned in the previous response, the document did a wonderful job pointing out the data gaps for MWCNTs but it seemed that the document focused more on decaBDE due to the excess of information available for the chemical. The decaBDE data could be distilled down a bit to shorten the document.	Comparison NOT useful; highlighted data gaps; decaBDE focus
63	E6	1	"Evaluation of the interactions between multiwalled carbon nanotubes and CACO-2 cells," by Clark, KA et al. DOI 10.1080/15287394.2011.589105 (relevant to Chapter 4 and/or 5)	Additional considerations for section
64	E6	1	"Cell permeability, migration, and reactive oxygen species induced by multiwalled carbon nanotubes in human microvascular endothelial cells," by Pacurari, M et al. DOI 10.1080/15287394.2012.625549 (relevant to Chapter 4 and 5)	Additional considerations for section
65	E6	1	"Impact of Porous Media Grain Size on the Transport of Multi-walled Carbon Nanotubes," by Mattison, NJ et al, DOI 10.1021/es2017076 (relevant to Chapters 2 and 3)	Additional considerations for section
66	E6	1	"Sorption of Peat Humic Acids to Multi-Walled Carbon Nanotubes," by Wang, XL et al. DOI 10.1021/es202258q (relevant to Chapter 3)	Additional considerations for section
67	E6	2	I was impressed by the thoroughness and accuracy of the science presented in the document.	Science accurate
68	E5	3	Yes and no … No, because I felt like the information about decaBDE started to overtake the document because there are not significant amounts of information available for MWCNTs for all the scenarios covered in the case study.	Comparison NOT useful; decaBDE focus
69	E6	3	I was initially skeptical about the ability of decaBDE to help identify the research gaps in MWCNTs due to the unique properties of nanomaterials; however, I grew to think it was an excellent model for comparison as went through the process.	Comparison WAS useful; fundamentally different compounds don't overlap

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
70	E6	4	I don't have any specific comments on improving the document.	--
71	E7	1	I am not aware of additional studies specifically on MWCNT, but rather two papers that demonstrate the potential issues that future research needs to address: 2. Soybean susceptibility to manufactured nanomaterials with evidence for food quality and soil fertility interruption John H. Priester, Yuan Ge, Randall E. Mielke, Allison M. Horst, Shelly Cole Moritz, Katherine Espinosa, Jeff Gelb, Sharon L. Walker, Roger M. Nisbet, Youn-Joo An, Joshua P. Schimel, Reid G. Palmer, Jose A. Hernandez-Viezcas, Lijuan Zhao, Jorge L. Gardea-Torresdey, and Patricia A. Holden. PNAS Plus: Soybean susceptibility to manufactured nanomaterials with evidence for food quality and soil fertility interruption. PNAS, August 20, 2012 DOI: 10.1073/pnas.1205431109 + Abstract Based on previously published hydroponic plant, planktonic bacterial, and soil microbial community research, manufactured nanomaterial (MNM) environmental buildup could profoundly alter soil-based food crop quality and yield. However, thus far, no single study has at once examined the full implications, as no studies have involved growing plants to full maturity in MNM-contaminated field soil. We have done so for soybean, a major global commodity crop, using farm soil amended with two high-production metal oxide MNMs (nano-CeO2 and -ZnO). The results provide a clear, but unfortunate, view of what could arise over the long term: (i) for nano-ZnO, component metal was taken up and distributed throughout edible plant tissues; (ii) for nano-CeO2, plant growth and yield diminished, but also (iii) nitrogen fixation—a major ecosystem service of leguminous crops—was shut down at high nano-CeO2 concentration. Juxtaposed against widespread land application of wastewater treatment biosolids to food crops, these findings forewarn of agriculturally associated human and environmental risks from the accelerating use of MNMs.	Recent literature published; additional considerations for section

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
72	E7	1	I am not aware of additional studies specifically on MWCNT, but rather two papers that demonstrate the potential issues that future research needs to address 1) The use of CNT as treatment technologies for contaminants in wastewater treatment applications. While CNT's may be effective in removing the contaminants, without further study, the CNTs (or MWCNT) could potentially damage the waste water treatment capability or as noted in the second paper, become part of the sewage sludge that is then applied to agricultural crops. Even with relatively non-toxic materials such as nano ZnO, some crop damage was demonstrated. Carbon nanotubes – the promising adsorbent in Wastewater treatment 2007 J. Phys.: Conf. Ser. 61 698 (http://iopscience.iop.org/1742-6596/61/1/140) Y. H. Li,1* Y. M. Zhao,1 W. B. Hu,1 I. Ahmad,1 Y. Q. Zhu,1 X. J. Peng,2 Z. K. Luan2 Abstract. Carbon materials are a class of significant and widely used engineering adsorbent. As a new member of the carbon family, carbon nanotubes have exhibited great potentials in applications as composite reinforcements, field emitters for flat panel display, sensors, energy storage and energy conversion devices, and catalysts support phases, because of their extraordinary mechanical, electrical, thermal and structural properties. In particular, the large specific surface areas, as well as the high chemical and thermal stabilities, make carbon nanotubes an attractive adsorbent in wastewater treatment. The adsorption properties of the carbon nanotubes to a series of toxic agents, such as lead, cadmium and 1,2-dichlorobenzene have been studied and the results show that carbon nanotubes are excellent and effective adsorbent for eliminating these harmful media in water. The effects of the morphologies and the surface status on the carbon nanotube adsorption capacities are also discussed.	Recent literature published; additional considerations for section
73	E7	2	The document seems to be very well done, thorough, and comprehensive. The organization of the document—alternating between decaBDE and MWCNT is discordant and a challenge to read when trying to identify the issues for MWCNT-polymers as flame retardants. These two materials are not related, except to provide a function. Having the information for decaBDE available is valuable to understand what the high-level issues are and what to be concerned about for the MWCNT-polymers, but segregating the information would have made reading and referencing the document easier.	Comparison WAS useful; fundamentally different compounds don't overlap

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
74	E7	3	See response to Q2. The information presented about decaBDE was interesting, but it would have been helpful if the information was highlighted that led to the voluntary agreement to stop using decaBDE. This would have highlighted what the issues were for deca and to make sure they were avoided for MWCNT-polymer flame retardants.	Comparison NOT useful; suggestion for improvement
75	E7	4	Not the document per se, but rather the choice of the material for this CEA evaluation. The information about MWCNT-polymer flame retardants is so uncertain and so little known about what the characteristics are of the MWCNT-polymers that may be used as flame retardants that the exercise has not elucidated unique approaches, but rather what should be done for any new material that will have wide distribution and application. Thus, so much of the priority research is recommended in the Confidence Matrix in the "Red" box—important and not confident. A study of MWCNT alone may be more productive and provide a better research agenda.	Choice of nanomaterial and application
76	E8	1	no	No additional literature
77	E8	2	yes	Science accurate
78	E8	3	Yes, and the comparative assessment is helpful.	Comparison WAS useful
79	E8	4	Link (at least conceptually) to Value of Information analysis.	Highlight data gap; suggestion for improvement
80	E9	1	No, I don't.	No additional literature
81	E9	2	In Fig2-1 at End of Life MWCNT Release Form is only considered as Matrix Bound, but if they might be Free at every other life cycle stage, including In Use, they may also become Free at End of Life.	--
82	E9	2	In the first paragraph of 2.1.1 it is declared that "No data were found on the energy and resource demands of raw material extraction for synthesis of decaBDE." It seems that this information should be obtainable.	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
83	E9	2	In the 2nd paragraph of 2.1.1., LCA inputs from SWCNT are used, but it occurs to me that just as a very specific application of MWCNTs is selected to focus on for the CEA, so should the data inputs such as energy used in LCA and cost be kept consistent with the material in question. The low yield/ high cost of SWCNTs is not relevant. Focus on the synthesis method used for the current commercial source of MWCNTs for flame-retardant upholstery coatings or similar methods that may be used for that purpose.	--
84	E9	2	In the 2nd paragraph of 2.1.1. yields of CNT synthesis reactions are listed as ranging from 1% to 17,900%. How is a yield of >100% physically possible?	--
85	E9	2	I find the claim in the 2nd paragraph of 2.1.1 that "… synthesis of MWCNTs requires larger amounts of precursor material than SWCNTs" to be dubious. The fact that MWCNTs are much cheaper to produce than SWCNTs would not support the claim that they are lower yield.	--
86	E9	3	Yes. With the same application and similar concerns regarding types of risks, the decaBDE is a valuable existing case study to inform evaluation of MWCNT.	Comparison WAS useful
87	E9	4	no comment	--
88	E10	1	I don't know of any additional studies that would be appropriate.	No additional literature
89	E10	2	I thought that the science was accurately portrayed. Although, the Chapter on characterization was not complete.	Science accurate
90	E10	3	The materials are quite different in mode of action and potential concerns from an environmental standpoint. Possibly, comparison of MWCNT to existing treatments would be quite useful to understand the requirements of the application. However, I didn't find the detailed comparison of the two materials illuminating because of the quite different properties. From a practical standpoint, the additional information on decaBDE created a very thick document. (I like to work from paper and it was hard to carry around.)	Comparison NOT useful; added length; fundamentally different compounds don't overlap
91	E10	4	A technical summary would have been useful.	Suggestion for improvement

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
92	E11	1	There are several new ES&T articles on CNT analysis – here is one Doudrick et al. (DOI: 10.1021/es300804f)	Detection/measurement analytics; additional considerations for section
93	E11	2	yes. The question is really around terminology. A major issue is emission rates and toxicity. I understand the life-cycle perspective, but I think it is really important to get at these emission rates and toxicity.	Science accurate; purpose of CEA
94	E11	3	yes	Comparison WAS useful
95	E11	4	The framework is fine for pre-workshop. There are rapidly developing sciences around this issue which should be included as references.	Recent literature published; purpose of CEA; suggestion for improvement
96	E12	1	No, I believe the major studies were presented. There are some studies of SWCNT, but they have such different properties that I don't think they would be useful.	No additional literature
97	E12	2	Yes, the information on MWCNT is done well.	Science accurate
98	E12	3	No, it is more of a distraction than anything. If the intent were to consider synergistic interactions, that might have been helpful. However, that was not the case. There is virtually nothing in the discussion of decaBDE that transfers to MWCNT. The only thing that the inclusion did was confuse the issues. Had all of the extraneous material been eliminated, the document would have been much smaller and mostly would have exposed the huge gaps in what is known about MWCNTs	Comparison NOT useful; highlighted data gaps; fundamentally different compounds don't overlap
99	E12	4	See above – eliminate all of the decaBDE discussion.	Comparison NOT useful; decaBDE focus
100	E13	1	No.	No additional literature
101	E13	2	Yes.	Science accurate
102	E13	3	Yes.	Comparison WAS useful

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
103	E13	4	The document is long and detailed. It will be best to have a short pare that summarizing the main conclusion part at the beginning or the end of the document.	Added length; suggestion for improvement
104	E14	1	I don't know of any additional studies.	No additional literature
105	E14	2	Yes.	Science accurate
106	E14	3	Yes.	Comparison WAS useful
107	E14	4	No.	--
108	E15	1	a) No. I am not aware of any published or unpublished data.	No additional literature
109	E15	2	I find the document heavily weighted toward supposition, e.g., exposure "could" occur; MWCNT "could" be released. This language leaves the reader believing that such phenomena have already been documented. This is incorrect. Examples: Page 72, lines14, 19, 20, 27 are examples of "…could occur …" It would be more appropriate to indicate that while potential exposures have been identified, none have been supported by actual data.	Suggestion for improvement
110	E15	2	There are occasional instances where outdated references have been cited when more recent information speaks otherwise. For example, page 120, line 16 refers to a paper by Maynard (2004) that speaks about the potential dermal exposure to CNTs. Numerous studies on the sunscreen nanomaterials, TiO2 and ZnO, have shown that while dermal exposure might occur, dermal penetration is unlikely. Therefore, dermal uptake should be updated to reflect the more recent information.	--
111	E15	2	Page 135, line 4 cites the WHO definition of a fiber, referring to the aspect ratio of 3:1. However, data for small particles such as CNTs suggests that the aspect ratio of 20:1 is more appropriate (DeLorme et al, 2012; Schinwald et al, 2012).	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
112	E15	3	a) Not really. The comparison of a molecule to a particle does not help – each has its own properties that drive the exposure assessment and risk management procedures. The physical properties dictate exposure and risk management. For example, exposure to a semi-volatile molecule is different than exposure to a particle that can agglomerate and grow in size when it is suspended in air. It would be better to focus solely on MWCNTs and the properties that dictate toxicity, exposure, etc.	Comparison NOT useful; decaBDE was bad comparison choice; fundamentally different compounds don't overlap
113	E15	4	Remove the comparison to decaBDE. This substance can be introduced as a justification for the industry to look at other substances that may provide flame retardation, but it does not provide a framework for the assessment of MWCNTs.	Comparison NOT useful
114	E15	4	b) Describing potential exposure scenarios is important, but should be followed by either identification of data gaps and research ideas, or prioritizing those scenarios using the available information. For example, can information about release of CNTs from other media be used to give a likelihood of release of CNTs from textiles? Using release of other substances is inappropriate.	Highlight data gap; suggestion for improvement
115	E16	1	Reproductive Toxicity The majority of additional studies that should be included are listed in the next section. However in terms of the reproductive effects where the report states there are no studies, the authors could report on the study by Bai et al. (2010). They found that intravenous injection of functionalized MWCNT resulted in accumulation in the testes, oxidative stress and decreased the thickness of the seminiferous epithelium in the testis at day 15 without effecting the quality or quantity of sperm production. By 60 days the damage was repaired and the treatment did not affect the pregnancy rate and delivery success of female mice that mated with the treated male mice when compared with controls.	Additional considerations for section

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
116	E16	1	Genotoxicity/ Carcinogenicity Within the sections on genotoxicity and carcinogenicity, the report also could consider the work of by Sargent at al. (2011) where the authors looked at mitotic spindle aberrations in an epithelial cell line at concentrations anticipated in exposed workers, specifically at doses equivalent to 20 weeks of exposure at the Permissible Exposure Limit for particulates not otherwise regulated (Sargent et al. 2011). The study showed significant disruption of the mitotic spindle at occupationally relevant doses and concluded that the increased proliferation in carbon nanotube-exposed cells indicates a greater potential to pass the genetic damage to daughter cells. Based on these findings and the knowledge that disruption of the centrosome is common in many solid tumors such as lung cancer and that aneuploidy is an early event in the progression of many cancers (suggesting a role in both tumorigenesis and tumor progression), the authors suggested that caution should be used in the handling and processing of carbon nanotubes (Sargent et al. 2011).	Human carcinogenicity mechanisms for SWCNTs
117	E16	1	Oral Toxicity The report states there “no data was identified on the acute toxicity of MWCNT following oral or dermal exposure” however within the derivation of an OEL for Baytubes, Pauluhn (2010) reported that based on the OECD TG 423 (Acute Oral Toxicity – Acute Toxic Class Method) that the MWCNTs’ tested (Baytubes) were not acutely toxic with an LD_{50}-oral of>5000 mg/kg bw.	Additional considerations for section
118	E16	1	In a later study, the authors looked at these effects in relation to other particles and found that at equal dose, diesel exhaust particles generated larger levels of 8-oxodG in rat liver than carbon black did and exposure to fullerenes C60 and SWCNT were the least potent (Møller et al 2012). Based on these interesting findings, the authors noted that the extent of translocation from the gut is largely unresolved but should be investigated further.	Additional considerations for section
119	E16	1	As well as the Kolosnjaj-Tabi et al 2010 study using SWCNT mentioned in the decaBDE MWCNT report, Folkmann et al (2009) investigated oxidative DNA damage in outlying tissues, specifically the liver and the lung after intragastric administration of SWCNT at a low dose of 0.064 or 0.64 mg/kg body weight. They noted that oral exposure to low doses of SWCNT was associated with elevated levels of markers of oxidative DNA damage, specifically 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) in the liver and lung.	Additional considerations for section

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
120	E16	2	Overall the science is portrayed comprehensively however there are a few incidences which could have been improved.	Science accurate
121	E16	2	One area where the scientific interpretation could be improved is in relation to sensitization as there are actually 2 reports in the literature examining dermal sensitization, both of which appear negative (Pauluhn et al 2010, Ema et al 2011) and this should be reflected in Table 5.1.	--
122	E16	2	In terms of the mechanisms by which MWCNT may reach and persist in the pleura, this is dealt with very sparsely. At very least the authors should have reported the findings of Ryman-Rasmussen et al 2009 Mercer et al 2010, showing sub-pleural deposition in the case of the former but most crucially pleural translocation was demonstrated in the case of the latter after lung instillation. The argument surrounding this has also been laid out by Donaldson et al (2010) with evidence of the basis of pleural retention from Murphy et al. (2011 and 2012) and most recently by Schinwald et al (2012). This whole section could do with more consideration.	--
123	E16	3	I have found the comparison with decaBDE very useful not least as it reminds us all that standard chemicals also suffer from the same problem of insufficient information and that it is not just new nano-materials. Therefore it is good as it helps us understand that it is not realistic to want 100% clarity across every area of a risk assessment as almost no substance has this and instead we must focus on what gaps must be filled and which would be nice to fill but are not a priority.	Comparison WAS useful; highlighted data gaps
124	E16	3	In addition, I found the information regarding the release of decaBDE from textiles and its concentration in dusts found in office buildings particularly in drawing conclusions about CNT release.	Comparison WAS useful
125	E16	4	An issue with documents as all-encompassing as this is that it is certainly impossible to include everything so often the focus is on the most important studies and results. However I would like to have seen more depth and discussion around the hazard data within the reports and summery evaluations. For instance, there is always conflicting data within science but it is sometimes helpful to summarize on balance what the majority of studies shows (specifically giving negative and positive data equal footing). An example of this is in terms of respiratory sensitization where I would suggest most studies point toward exacerbatory effects of MWCNT when given in conjunction with OVA rather than direct sensitization – note this is relatively common amongst particles including diesel soot.	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
126	E17	1	Edgington AJ, Roberts AP, Taylor LM, Alloy MM, Reppert J, Rao, AM, Mao J, Klaine SJ. 2010. The Influence of natural Organic Matter on the Toxicity of Multiwalled Carbon Nanotubes. Environ. Toxicol. Chem. 29(11): 2511-2518.	Additional considerations for section
127	E17	1	Nowack B, Ranville JF, Diamond S, Gallego-Urrea J, Metcalfe C; Rose J, Horne N, Koelmans AA, Klaine SJ. 2012. Nanoparticle Release, Aging and Transformation in the Environment. Environmental Toxicology and Chemistry 31(1): 50-59.	MWCNT physical/ chemical properties
128	E17	1	von der Kammer F, Ferguson PL, Holden PA, Masion A, Rogers K, Klaine SJ, Koelmans AA, Horne N, Unrine JM. 2012. Analysis of Nanomaterials in Complex Matrices (Environment and Biota): General Considerations and Conceptual Case Studies. Environmental Toxicology and Chemistry 31(1): 32-49.	Detection/measurement analytics
129	E17	1	A quick Web of Science lit review for the past year reveals a few more.	Recent literature published
130	E17	2	Yes	Science accurate
131	E17	3	Yes	Comparison WAS useful
132	E17	4	From an ecotox and environmental fate perspective this is a very good presentation. As this is my first experience with this process, I found the integration of the lifecycle assessment information and concepts very helpful in my comprehension of how this differs from a traditional risk assessment.	Praise for case study
133	E18	1	No.	No additional literature
134	E18	2	Overall I believe the science is accurately conveyed throughout the document.	Science accurate
135	E18	2	However, in my opinion some of the studies are underplayed in their demonstration of toxicological concern. I would suggest a greater emphasis on toxicological concern for studies showing MWCNT could induce mesothelioma and behave in a similar manner to asbestos. These inhalation studies are strong indicators of potential toxicological concern. The document merely states that the inhalation route of exposure for MWCNT “might be of toxicological concern.” (see Section 5-7, line 8 and 9).	--
136	E18	3	Yes.	Comparison WAS useful

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
137	E18	4	No.	--
138	E19	1	Below are two recent studies investigating the impact of MWCNT releases within the environment that may be of interest for determining effects and proper characterization techniques for MWCNT then they enter complex media. 1- Mwangi, J. N., Wang, N., Ingersoll, C. G., Hardesty, D. K., Brunson, E. L., Li, H. and Deng, B. (2012), Toxicity of carbon nanotubes to freshwater aquatic invertebrates. Environmental Toxicology and Chemistry, 31: 1823–1830.	Recent literature published
139	E19	1	Below are two recent studies investigating the impact of MWCNT releases within the environment that may be of interest for determining effects and proper characterization techniques for MWCNT then they enter complex media. 2- Nowack, B., Ranville, J. F., Diamond, S., Gallego-Urrea, J. A., Metcalfe, C., Rose, J., Horne, N., Koelmans, A. A. and Klaine, S. J. (2012), Potential scenarios for nanomaterial release and subsequent alteration in the environment. Environmental Toxicology and Chemistry, 31: 50–59.	Recent literature published
140	E19	2	The science and information is accurately communicated in the document. The use of tables and flow charts is helpful and illustrative. In future documents; it may also be beneficial to include more representative graphs and photographs from the literature to effectively portray the results generated.	Science accurate; suggestion for improvement
141	E19	3	The comparison of decaBDE and MWCNT is helpful in assisting reviewers with understanding the process typically utilized for regulating a more traditional chemical by helping to identify knowledge gaps in the process. Also, the ability to compare some of the pitfalls and phasing out of decaBDE allows researchers to make more informed decisions about how MWCNT can be objectively investigated and incorporated into the flame retardants.	Comparison WAS useful; highlighted data gaps
142	E19	4	The document is well organized.	--
143	E20	1	Natural Organic Matter Stabilizes Carbon Nanotubes in the Aqueous Phase Hoon Hyung, John D. Fortner, Joseph B. Hughes, and Jae-Hong Kim	--
144	E20	1	A Review of Carbon Nanotube Toxicity and Assessmentof Potential Occupational and Environmental Health Risks Chiu-wing Lam, John T. James, Richard McCluskey, Sivaram Arepalli, Robert L. Hunter	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
145	E20	1	Utilization of selected area electron diffraction patterns for characterization of air submicron particulate matter collected by a thermophoretic precipitator. John J Bang, Elizabeth A Trillo, Lawrence E Murr	--
146	E20	1	A Predictive Toxicological Paradigm for the Safety Assessment of Nanomaterials. Huan Meng, Tian Xia, Saji George, and Andre E. Nel	--
147	E20	2	To my knowledge, the document conveys scientific aspect of our limited knowledge and related issues about MWNT in fairly reasonable way.	Science accurate
148	E20	3	It is believed that the comparison helps reviewers understand the underlying issues in MWCNT applications and identify research gaps for exposure assessment and risk management decisions	Comparison WAS useful; highlighted data gaps
149	E20	4	In some tables and figures, the authors seemed to include too much information that can make reviewers miss the main point for each table/figure. This could be a subjective opinion.	--
150	E21	1	1) Larue, C.A, Pinault, M.B, Czarny, B. C, Georgin, D.D, Jaillard, D.E, Bendiab, N.F, Mayne-L'Hermite, M.B, Taran, F.D, Dive, V.C, Carrière, M, Quantitative evaluation of multi-walled carbon nanotube uptake in wheat and rapeseed, (2012) Journal of Hazardous Materials, 227-228, pp. 155-163.	--
151	E21	1	2) Wang, X., Han, H., Liu, X., Gu, X., Chen, K., Lu, D. Multi-walled carbon nanotubes can enhance root elongation of wheat (*Triticum aestivum*) plants, (2012) Journal of Nanoparticle Research, 14 (6), art. no. 841,	--
152	E21	1	3) Evaluation of exposure risk in the weaving process of MWCNT-coated yarn with real-timeparticle concentration measurements and characterization of dust particles (2012) Industrial Health, 50 (2), pp. 147-155	--
153	E21	1	4) Clark, K.A., O'Driscoll, C., Cooke, C.A., Smith, B.A., Wepasnick, K., Fairbrother, D.H., Lees, P.S.J., Bressler, J.P., Evaluation of the interactions between multiwalled carbon nanotubes and caco-2 cells (2012) Journal of Toxicology and Environmental Health - Part A: Current Issues, 75 (1), pp. 25-35.	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
154	E21	1	5) I found the OECD recent document (March 2012 on Nano Risk Assessment useful: Important Issues on Risk Assessment of Manufactured Nanomaterials Series on the Safety of Manufactured Nanomaterials, No. 33, at http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2012)8&doclanguage=en	--
155	E21	2	Yes it is well done.	Science accurate
156	E21	3	Yes.	Comparison WAS useful
157	E21	3	Another good reference for decaBDE is the ASTDR Toxicological Profile for Polybrominated Biphenyls and Polybrominated Diphenyl Ethers at: http://www.atsdr.cdc.gov/toxprofiles/tp68.pdf It is from 2004 but it shows that there is substantial exposure data in addition to what is mentioned in the case study document.	DecaBDE data needs improvement
158	E21	4	no	--
159	E22	1	I answer this question more fully in combination with number 2 where I identify places where I don't think the science is accurately conveyed in this case through the omission of relevant references. Specific references that I describe in response to question 2 are the following	--
160	E22	2	One overall comment is for the authors of this report to focus more on data that has been published rather than speculations from review papers published prior to much reason being conducted (i.e., before 2008). The science is at a stage when prior expectations need to be evaluated based on currently available evidence rather than rely upon early speculations. Many of the early speculations have been proven to be wrong and are now outdated.	Recent literature published; suggestion for improvement
161	E22	2	Page xxi, lines 1-2 – Some published papers indicate that MWCNTS function similarly to hard carbons decreasing MWCNT availability to organisms in soils and sediments (i.e., Petersen, E. J. et al. Environ. Sci. Technol. 2009, 43 (11), 4181-4187.; Shen, et al. Environ. Toxicol. Chem. 2012, 31 (1), 202-209.).	Highlight data gap; additional considerations for section
162	E22	2	Page xxii, lines 19-20 – Actually, numerous studies, probably >20, have been conducted on the effects and uptake of MWCNTs to aquatic organisms.	Highlight data gap; suggestion for improvement

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
163	E22	2	Table 1-9 – Chirality only is relevant for SWCNTs and the inner tube of DWCNTs (Yang, S. W.; Parks, A. N.; Saba, S. A.; Ferguson, P. L.; Liu, J., Photoluminescence from Inner Walls in Double-Walled Carbon Nanotubes: Some Do, Some Do Not. Nano Letters 2011, 11, (10), 4405-4410.).	Recent literature published; additional considerations for section
164	E22	2	Table 3-2 – It is unclear why the authors mean by "potential lipophilicity" and how this would differ from "hydrophobic"; hydrophobic sorbents would typically adsorb lipids in addition to organic contaminants. Those sources are all extremely old, so this is probably just speculation from before many experimental measurements were taken. I suggest deleting this section of the table.	Suggestion for improvement
165	E22	2	Page 3-8, lines 31-33 – This reference is highly questionable since it only refers to an abstract.	Suggestion for improvement
166	E22	2	Page 3-12, line 29 – The Holbrook et al. 2010 reference is also highly relevant here.	Additional considerations for section; suggestion for improvement
167	E22	2	Page 3-14 – The Zhang et al. 2011 reference is also relevant in this section since it discusses sorption of MWCNTs onto peat, a soil component.	Additional considerations for section; suggestion for improvement
168	E22	2	Page 3-14, line 17 – The review papers cited here about MWCNT adsorption onto soil surfaces were published before sorption studies had been conducted. These articles are reviews that probably just contained speculation along these lines, so this sentence could be deleted.	Suggestion for improvement
169	E22	2	Page 3-14, line 28-29 – Again, those authors did not know how those properties would affect nanoparticle sorption, but they probably speculated. The wording should be changed to reflect this or else this sentence just deleted.	Additional considerations for section; suggestion for improvement
170	E22	2	Page 3-15, lines 1-2 – This sentence is just speculation and could be deleted.	Suggestion for improvement
171	E22	2	Text box 4-1 – There are not mass spectrometry techniques for characterizing MWCNTs, nor is that provided in Appendix B other than ICP-MS which only measures metal concentrations still associated with the MWCNTs.	--

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
172	E22	2	Page 4-48, line 5 – It is unclear what the authors mean to indicate by stating that absorption of carbon materials can occur in the gut. In the study cited, the authors showed light microscope pictures of carbon nanotubes in the gut tract, not absorption across the gut tract. Another study by Edgington et al. (Edgington, A. J. et al. Environ. Toxicol. Chem. 2010, 29 (11), 2511-2518.) did not find MWCNT absorption across the gut tract.	Recent literature published; additional considerations for section
173	E22	2	Page 4-49, line 6 – These values were BSAF values, not BAF values. This sentence should be edited accordingly.	Suggestion for improvement
174	E22	2	Page 49, lines 18-20 – This sentence is entirely speculation. In studies of CNT uptake by a wide range of organisms (excluding plants), absorption into tissues is consistently minimal (see Table 2 of Petersen et al. 2011, ES&T pages 9837-9856).	Recent literature published; highlighted data gaps
175	E22	2	Page 4-49, line 21-27 – What these statements do not include is the lack of CNT absorption across gut linings in a wide variety of organisms. Also, changing the octanol-water partitioning behaviors of MWCNTs did not change their uptake, so MWCNTs' apparent lipophilicity and hydrophobicity do not appear to impact bioaccumulation (Petersen et al., 2010, Environ. Toxicol. Chem., pages 1106-1112). Thus, the expectation in lines 24-25 goes against the data trend for MWCNT absorption in a range of studies (see previous comment for the relevant citation). A critical step not mentioned is that the compound has to be absorbed across the microvilli which did not appear to occur for MWCNTs in any study.	MWCNT physical/ chemical properties; suggestion for improvement
176	E22	2	Page 4-50, lines 9-10 – This paper was published before data was collected on this topic and thus this speculation can be deleted. Moreover, being lipophilic is insufficient for expectations of accumulation in root lipids because transport into the cells and roots would need to occur first.	Suggestion for improvement
177	E22	2	Page 4-51, lines 10-13 – The study cited (Petersen 2010) actually shows that MWCNTs probably do not behave similar to other bioaccumulative substances because changing the octanol-water distribution behavior did not change BAF values. The purpose of that study was to investigate whether MWCNTs behaved similar to bioaccumulative substances such as hydrophobic organic chemicals and the findings suggested that they did not apparently as a result of a lack of absorption across the gut tract and into the organism. The Helland 2007 review is an outdated paper from 2007 that just speculates about this topic.	MWCNT physical/ chemical properties

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
178	E22	2	Page 5-22 lines 22-23 – Actually, there are numerous studies on benthic invertebrates (i.e., Kennedy 2008 cited on page R-12 and Shen et al. 2012 and Kennedy et al. 2009 cited in response to question 1). A list of studies on CNT toxicity to soil and sediment organisms is available as Table 3 in Petersen et al. 2011 ES&T pages 9837-9856.	Recent literature published
179	E22	2	Page 5-22, lines 27-28 – The study cited has nothing to do with bioaccumulation in aquatic systems. Numerous papers have been conducted on exactly this topic and some of these studies were described in the previous Chapter.	Suggestion for improvement
180	E22	2	Table 5 -2 – This table missing numerous important citations for MWCNTs as described in previous comments.	--
181	E22	2	Page 5-23, lines 18-20 – The authors are missing a ton of studies on the effects of MWCNTs to aquatic organisms. Some have been described above and many others are cited in Chapter 4 of this document and in the review paper by Petersen et al. 2011 ES&T pages 9837-9856. There are probably >20 references overall on this topic.	Highlight data gap; suggestion for improvement
182	E22	2	Table 5-4 and discussion on page 5-29 – This table is missing the important reference for Scott-Fordsmand et al. (2008 Ecotox. Environ. Saf. 616-619.). Many papers testing accumulation of MWCNTs also have information about weight change, lipid content change and acute toxicity even though those endpoints were not the purpose of the study (Petersen et al. Environ. Sci. Technol. 2011, 45 (8), 3718–3724.; Petersen, E. J. et al. Environ. Sci. Technol. 2008, 42 (8), 3090-3095.; and Petersen et al. Environ. Sci. Technol. 2009, 43 (11), 4181-4187).	Recent literature published
183	E22	2	Page 5-31, lines 3-5 – There have actually been papers showing positive effects from MWCNT exposure such as Khodavorosky et al. 2009, 2011, so it is unnecessary to start the discussion about nanoparticles in general or describe nano-Al2O3 plant findings.	Recent literature published; suggestion for improvement
184	E22	3	Having the decaBDE as a comparison was helpful in some ways and a hindrance in others. The ways that this comparison were helpful is that it gave me an idea of the amount of information available for a compound that has been studied for a much longer time period than MWCNTs. Otherwise, it would have just been comparing the research available for MWCNTs against our perception of what a good amount of data would have been for the risk assessment.	Comparison WAS useful

Table I-12, cont.: Comments received in response to the expert charge questions.

Comment ID	Author ID	Charge Question	Comment Text Excerpt	Themes
185	E22	3	However, this comparison was limiting in that it was unclear how big of a deal the data gaps that still do exist for decaBDE actually were for risk assessors. I would have been curious, and perhaps this is not information that could have been shared, about how limited risk assessors felt about the current state of information and their ability to make a judgment about decaBDE.	Comparison NOT useful; suggestion for improvement
186	E22	3	Another limitation of including this comparison is that I had to more carefully skim through the document when I was doing the hazard ranking to focus solely on the MWCNT data. I read through the decaBDE information the first time I read the document but mostly skipped it subsequent times when doing the prioritization exercise.	Comparison NOT useful; added length
187	E22	4	Most of my comments were addressed in response to the other questions. I think it is a good document overall, but there are definitely places where it could be improved. The huge controversy in the news about whether BDE actually effectively worked in the ways it was described to in this document as a result of the Chicago Tribune series on flame retardants (http://media.apps.chicagotribune.com/flames/index.html) made me wonder the fire research on BDEs and the ways they supposedly worked was accurate.	--
188	E23	1	No	No additional literature
189	E23	2	Yes	Science accurate
190	E23	3	Yes, the comparison of decaBDE and MWCNT in the case study document is useful in identifying research gaps.	Comparison WAS useful
191	E23	4	No	--

Table I-13. Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
192	E4-F	Preface, pg xiii lines 12-13	But is this application really relevant?? MWCNT will not be used in textile coatings alone since they are unable to pass the tests by themselves. If they cannot pass the regulatory test, they will never be used in the application. I do not think this is a good application to study MWCNT release into the environment as MWCNT are more likely to be used in electronics and aerospace rather than commodity consumer goods.	Choice of nanomaterial and application; choice constricted science of MWCNTs
193	E4-F	Preface, pg xvi lines 21-22	One unknown - can MWCNT really be mixed with binding agents, applied to textiles, AND pass the necessary regulatory tests? If they cannot, then they won't be used and this study may be misled by focusing on textiles when potential exposure could be in other applications not looked at by this CEA.	Choice of nanomaterial and application; choice constricted science of MWCNTs
194	E4-F	Preface, pg xvi lines 31-33	Agreed - composition of MWCNT mixture can be a major factor to consider when studying these materials. Purity of the MWCNT particle, the other components of the raw material (amorphous carbon, catalysts, etc.) will likely all have an effect on toxicity and human exposure issues.	--
195	E4-F	Preface, pg vvii lines 3-4	Do any commercial products exist? I think the answer is no, and possibly for good reason (MWCNT alone does not work)	Choice of nanomaterial and application
196	E4-F	Preface, pg vvii lines 7-8	Agree - manufacturing equipment won't be different for treating fabrics, and so any way of applying decaBDE will be used to apply MWCNT.	Comparison WAS useful
197	E4-F	Preface, pg xviii lines 8-9	Need to look at Nyden paper from Interflam 2010 - MWCNT in ash from cone calorimeter fires can be shaken lose and made airborne.	Additional references
198	E4-F	Preface, pg xix lines 5-8	Seems that environmental chemistry of MWCNT is an unknown that needs to be researched, regardless of its use in textile back-coatings or not	Highlight data gap
199	E4-F	Preface, pg xix lines 25-26	This is because MWCNT use is way too new in most cases - its use in consumer goods is limited. Need to gather information on what MWCNT is actually used in today to determine realistic environmental exposure routes.	Choice of nanomaterial and application; choice constricted science of MWCNTs
200	E4-F	preface, pg xx lines 12-13	But with which type of MWCNT? What surface chemistry for these materials?	MWCNT physical/ chemical properties

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
201	E4-F	preface, pg xxi lines 12-13	Seems that environmental decomposition/transformation of MWCNT is unknown and should be studied. Do MWCNT degrade into something else that is bioactive? Or are they environmentally stable (persistent)?	Highlight data gap
202	E4-F	Chapter 1, pg 1-2 lines 3-7	Are any of these really commercially viable? Perhaps at the time of the start of this study to proactively look for systems of concern this made sense, but I think this original premise needs to be revisited. Are these really the PRIME applications of MWCNT in the future where emissions could are from, or are there applications missed in this original assessment more likely to be the ones that should be looked at?	Choice of nanomaterial and application; choice constricted science of MWCNTs
203	E4-F	Chapter 1, pg 1-2 lines 23-26	Yes and no. Yes for other MWCNT coatings on other objects (paints for example) but no for polymer applications where the MWCNT is well embedded in the final part (polymer composites, injection molded plastic parts) - unless said parts are deliberately abraded/reground, in which case textile abrasion data may be relevant to MWCNT in composite and injection molded applications.	Choice of nanomaterial and application; alternative products/ formulations
204	E4-F	Chapter 1, pg 1-6 lines 21-22	Given this point, really important then that some application survey research be done to make sure that the key uses of MWCNT are truly captured rather than assuming the textile application will be the key one.	Choice of nanomaterial and application; choice constricted science of MWCNTs
205	E4-F	Chapter 1, pg 1-7 lines 1	Agree - you can't look at everything, but if you end up looking at an application that can NEVER occur, are you really spending your time wisely? I think looking at MWCNT coming off of aerospace composites that are ground/sanded/drilled is a far better use of time and volumes there will likely be higher than in the textile application, where it is not yet even proven that MWCNT will even work.	Choice of nanomaterial and application; choice constricted science of MWCNTs
206	E4-F	Chapter 1, pg 1-8 lines 11-13	Not necessarily. You're assuming that they will work as flame retardants in all applications, something that has yet to be proven. Yes, they do show flame-retardant effects, but not enough to pass required regulatory tests. If they don't pass the regulatory fire tests, they will never be used - ever.	Choice of nanomaterial and application
207	E4-F	Chapter 1, pg 1-11 lines 6-17	Very true, but if something doesn't work, then the performance criteria ensures that this particular flame retardant is NEVER used in this specific application.	Choice of nanomaterial and application

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
208	E4-F	Chapter 1, pg 1-15 Table 1-5	MWCNT can also be melt compounded into plastic, but not a lot of data out there saying that this nanocomposite can actually be spun into fiber for lowered flammability textile strands/fibers.	Choice of nanomaterial and application
209	E4-F	Chapter 1, pg 1-21 lines 3-4	This is the key issue. It is unknown if MWCNT will EVER be used in this application to provide fire safety to textiles or furniture. Therefore - it this really a proper focus of study? Sure - look at MWCNT emissions for use in products, but I am not convinced that MWCNT will ever be used to provide fire protection of fabrics.	Choice of nanomaterial and application; choice constricted science of MWCNTs
210	E4-F	Chapter 1, pg 1-23 lines 1-2	Flawed premise here. Just because it shows these flammability effects does not mean it can be used in future textiles. Nanocomposites alone rarely pass regulatory tests by themselves, and if MWCNT does not pass the regulatory tests, then it will never be used. Therefore need to conduct research on IF MWCNT can actually be used in this application or not.	Choice of nanomaterial and application; alternative products/ formulations
211	E4-F	Chapter 1, pg 1-24 Table 1-12	Note that the data does not say if it passed a particular test or not. It needs to be validated that MWCNT CAN actually bring FR performance in a PU foam application. If it cannot, it will never be used and its potential environmental exposure routes change completely.	Choice of nanomaterial and application; alternative products/ formulations
212	E4-F	Chapter 2, pg 2-1 figure 2	This is incorrect for decaBDE in regards to handling/packaging, equipment cleaning, and accidents - where there are known releases of decaBDE. See Albemarle for details - they have known data showing releases will occur from this part of the process.	DecaBDE data needs improvement; Additional references
213	E4-F	Chapter 2, pg 2-4 lines 11-12	You probably won't easily get this information from the MWCNT manufacturers, but, it's clear you need this data. How MWCNT and SWCNT are made can be very different - different metal catalysts, different impurities, and different CNT length, all of which are important to your study.	Highlights research need

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
214	E4-F	Chapter 2, pg 2-4 lines 22-23	There are much better references out there. Please talk with some US based CNT synthesis researchers for details. JM Tour - Rice University, K Lafdi - University of Dayton - either one of these two professors can quickly bring you up to speed with more accurate information.	Additional references
215	E4-F	Chapter 2, pg 2-5 lines 2-3	Well … maybe. It depends on if the reactors for making the CNTs need to be cleaned out between runs. If they do need to be cleaned out, there could be CNT or decaBDE release at this point. More likely that CNT release would occur if the reactor is not fully cleaned out before synthesis.	Product life cycle
216	E4-F	Chapter 2, pg 2-6 lines 22-23	Don't make this assumption. Some R&D labs have no clue how to safely handle nanoparticles, and releases are quite common if hoods and engineering controls are limited, as they often are in older research buildings at established universities.	Product life cycle
217	E4-F	Chapter 2, pg 2-7 lines 6-7	There is a report from work done at the University of Dayton Research Institute in cooperation with NIOSH. Let me see about getting you the data - or connecting you to the NIOSH researchers who generated the data back in 2008.	Additional references
218	E4-F	Chapter 2, pg 2-14 Table 2-5	Again, information incorrect here from Handling/packaging, equipment cleaning, accidental releases. See Albemarle for details.	Additional references
219	E4-F	Chapter 3, pg 3-1 lines16-18	For MWCNT-polymer complex, there are two types to consider - those bound through intermolecular entanglement, and those where the MWCNT is covalently bound to the polymer. They will behave quite differently in the final environment and will likely also have different emission schemes into the environment. DecaBDE can only have intermolecular entanglement (van der Waals forces) and therefore can escape/migrate from polymers easier than MWCNT.	MWCNT chemistry and nature of bond with polymer/product
220	E4-F	Chapter 3, pg 3-6 lines 1-2	All of this will depend upon how the MWCNT interacts with the polymer. If it is covalently bound to the polymer, it may not ever be in single or bundle form. If just mixed into the polymer matrix, then yes, it will likely migrate into the environment via the same pathways as decaBDE.	MWCNT bond with polymer not adequately described for implications in release/exposure; MWCNT chemistry and nature of bond with polymer/product

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
221	E4-F	Chapter 3, pg 3-8 lines 11-12	Assuming MWCNT actually end up in this application (which I think I've made clear I severely doubt), then the length of the tubes and how they interact with the polymer is a whole area of study that is very situation and MWCNT specific. Something that is chemically bound to the polymer may not come out at all as the textile back-coating degrades unless the polymer is biodegraded away upon ingestion/environmental exposure. And that final form of the MWCNT when the polymer is finally worn/decomposed/digested away may be very different than the starting form of the MWCNT. So if you're really going to look at this, I think you need to actually do a couch mockup and put it through the paces and properly measure what happens as a function of MWCNT purity, length, and surface chemistry as I am quite confident the results will be very different for each different type of MWCNT.	MWCNT chemistry and nature of bond with polymer/product
222	E4-F	Chapter 3, pg 3-10 lines 24-25	Don't make this assumption - see my comments above about the surface chemistry of the MWCNT. If they are designed to chemically react with the textile back-coating, their final solubility when they escape into the environment may be very different than what is shown here.	--
223	E4-F	Chapter 4, pg 4-10 lines 17-18	Very interesting … I did not know this. Have these results been verified?	--
224	E4-F	Chapter 4, pg 4-13 lines 1-2	May still be able to use the NIOSH report here (Methner 2010). Not relevant for textile back-coating, but still useful to see where nanotube release and exposure could realistically occur in a manufacturing environment.	Additional references
225	E4-F	Chapter 4, pg 4-25 lines 22-23	A lot here will depend upon what chemistry and process is used to get the MWCNT into the final product. If the CNT are chemically bound to polymer while being applied, primary exposure may be to CNT + Polymer particulates, not CNT directly. If CNT is not chemically bound to polymer, then using the decaBDE models is appropriate.	MWCNT physical/ chemical properties; Nature of bond with polymer/product

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
226	E4-F	Chapter 4, pg 4-26 lines 1-2	Again, see comments on the chemistry of the MWCNT and its interaction with the polymer, as this will dictate how they may be emitted during post-product use handling (grinding, incineration, conversion to scrap, etc.) Very likely the textiles would be treated the same way as textiles are handled today at the end of their lifetime, but how the MWCNT interacts with the polymer (covalent vs. van der Waals) will dictate potential exposure as a function of recycle/end-of-use operation.	MWCNT physical/ chemical properties; Nature of bond with polymer/product
227	E4-F	Chapter 4, pg 4-26 lines 14-15	This indicates that validation of MWCNT exposure route via particular application needs to be studied as a high priority item. Going back to specific MWCNT chemistry, how that MWCNT will affect potential release just as much as end-use application, and so I think first some time is needed to ensure what applications are really likely to use MWCNTs so that one finds the right applications to be concerned about, and doesn't miss any that may not be obvious at first glance.	Choice of nanomaterial and application; Highlighted data gaps; research applications of particular concern and widespread use/ choice constricted science of MWCNTs
228	E4-F	Chapter 4, pg 4-26 lines 20-21	I'm not sure about this assumption. If the MWCNT is covalently bound to the polymer, then it cannot be released in particle form. Rather, it would be released in a polymer+MWCNT agglomerate which likely has its own unique exposure issues. MWCNT that is not covalently bound to the polymer may indeed come out of the polymer and then agglomerate, but there are not studies out that that show what MWCNTs will do if they have no adjacent MWCNTs to agglomerate with. Will they prefer to agglomerate with household dust, or will they agglomerate with soils/minerals preferentially? Completely unknown and it should be looked at.	MWCNT physical/ chemical properties; Highlighted data gaps; Nature of bond with polymer/product
229	E4-F	Chapter 4, pg 4-30 lines 10-11	Deca is not used in automotive seat cushions, or really in any part of the car. So I'm not sure the data in the two reports here is accurate. Deca is used in aircraft though, but not in the seat cushions or fabrics. Rather it is used in other parts of the aircraft - mostly non-structural facia and other plastic parts. So exposure from airplanes and cars will be different - as it will be with MWCNTs. Just because Deca is used in an application does not mean that MWCNT will be used as a replacement technology. MWCNT will only be used IF it yields a pass of the specific material flammability regulation.	DecaBDE data needs improvement

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
230	E4-F	Chapter 4, pg 4-30 lines 28-29	Again, I don't think this is correct since Deca is not used in cars today. Given the very easy flammability test for automobiles, MWCNT will not be used to provide fire protection because there are far cheaper solutions out there.	DecaBDE data needs improvement
231	E4-F	Chapter 4, pg 4-30 lines 31-32	This however, I do agree with. I think studying what exactly has built up in aircraft over the years would be a study worth looking into.	--
232	E4-F	Chapter 4, pg 4-32 lines12-13	So this would be worthwhile to determine.	Highlight data gap
233	E4-F	Chapter 4, pg 4-32 lines 22-23	MWCNT stability to environmental conditions would also be a worthwhile study to investigate - not just for environmental resins, but for product durability as well. This would make a great “dual use” study.	Highlight data gap
234	E4-F	Chapter 4, pg 4-34 line 1	I think once you figure out what MWCNT will actually be used in, then this question starts to get answered and you'll quickly figure out through demographic studies who is most likely to be a part of a high-exposure population. If MWCNTs get mostly used in higher-end performance applications (example - used a lot today in high end golf clubs) then you may find that the highly exposed population is actually the affluent, and not lower income or children.	Choice of nanomaterial and application; choice constricted science of MWCNTs
235	E4-F	Chapter 4, pg 4-43 (section 4.3 heading)	Regardless of application - once MWCNT gets into the environment then all of this is relevant and I think is well established science. Perhaps there are some unknowns specific to MWCNTs, but in general, I would say that using decaBDE as the model, or any pollutant for that matter, is a very reasonable and well thought out place to start. My comment here applies to section 4.4 and 4.5 as well.	Comparison WAS useful
236	E4-F	Chapter 5, pg 5-1 lines 12-13	Assuming of course that MWCNT gets used in upholstery textiles. Again, I doubt they will, but if they actually do, then yes, this is correct.	Choice of nanomaterial and application; choice constricted science of MWCNTs

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
237	E4-F	Chapter 5, pg 5-2 (section 5.1 heading)	I somehow doubt you'll ever be able to definitively get data on this for MWCNT or any other material since human testing is banned. You may be able to gather this information from post-mortem studies, but otherwise I don't think this area should be studied due to the practical issues of being unable to exposure humans to these chemicals or MWCNT deliberately. However, funded research into mimics of human health effects with artificially grown tissue or perhaps really strong modeling software would be worthwhile to pursue. This would be good dual-use research in that it would benefit both environmental and pharmaceutical/medicine fields.	Highlight data gap
238	E4-F	Chapter 5, pg 5-20 section heading 5.1.12	See my comments above regarding application driving who will likely be a high exposure population. Until you know the actual applications that MWCNT will likely be used in, you really cannot extrapolate Deca data to MWCNT population exposure. If indeed MWCNT gets out of multiple future household projects and ends up in household dust then maybe you can make the correlation. Otherwise I think you have to wait until you get the application identified, which again supports that research into the most likely applications of MWCNT technology is a high priority research item that needs to be answered.	Choice of nanomaterial and application; choice constricted science of MWCNTs
239	E4-F	Chapter 5, pg 5-21 section heading 5.2	Agree that MWCNT reaction with environment is unknown and should be studied. I cannot comment on the priority though - that would have to be determined based upon the known applications and likely release of MWCNT to the environment. While there are lots of unknowns here, I think they are low priority to assess until you address what MWCNT will be used in, and in what form, so you can see the vectors of release to the environment/population.	Choice of nanomaterial and application; choice constricted science of MWCNTs
240	E4-F	Chapter 5, pg 5-34 lines 3-4	See my comment about the affluent likely to be the group most likely to be exposed to MWCNT first. I don't know if that is really an issue of environmental justice or not, but I suspect that the rich will be initially exposed to MWCNT at higher levels than anyone else initially.	Choice of nanomaterial and application; choice constricted science of MWCNTs
241	E4-F	Chapter 5, pg 5-34 lines 24-25	Very interesting observation. A good life cycle analysis of MWCNT synthesis as a function of the different manufacturing routes would be useful to research and develop. Likely a good dual-use research project that could be supported by industry so that they reduce their production costs.	Highlight data gap

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
242	E4-F	Chapter 5, pg 5-38 line 21 (MWCTN section)	These current costs are why MWCNT will not be used in textiles anytime soon. Prices have greatly dropped in recent years (please contact NanoCyl in Belgium to get an idea of how much - we're talking hundreds of dollars per kilogram these days) and NanoCyl calculates prices dropping even further, but not likely to be at the levels to be a cost effective flame retardant for consumer goods, especially since MWCNT alone has been unable, to date, to pass any regulatory fire tests. If it cannot pass the test, it will never be used. More likely, MWCNT will be used in other goods requiring improved electrical, thermal, and mechanical properties (structural composites, electronics) and so economic impacts could be quite different in these areas - with positive effects in generating light weight composites that yield fuel savings over metal on aircraft today. All of this is why I think a really good LCA for MWCNT use, manufacture, and total impacts is needed.	Choice of nanomaterial and application; choice constricted science of MWCNTs; other applications should have been considered
243	E4-F	Chapter 6, pg 6-2 lines 3-4	If in the end, effort is spent really focusing on MWCNT as if it was going to be used in flame-retardant textiles, then I think this entire program will be wasted effort with maybe a few gems of good information that come out of it. I strongly recommend spending some time up front making sure the applications for MWCNT are correct (what will they REALLY be used in with a high probability of occurring) and then other aspects of this study come into play. I do feel MWCNT release into the environment should be looked at in a proactive manner, but it needs to be done with an application that makes sense so that the research effort is focused and targeted and yields information that practically addresses potential MWCNT release and exposure.	Choice of nanomaterial and application; choice constricted science of MWCNTs
244	E4-F	Chapter 6, pg 6-2 lines 23-28	These papers DO NOT suggest this. The results of the papers have unfortunately been misinterpreted. MWCNT does have flame-retardant effects, but not enough of a flame-retardant effect to be used in this application.	Choice of nanomaterial and application

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
245	E4-F	Chapter 6, pg 6-5 lines11-12	Assuming of course enough members of the group know how to accurately assess the niche information about material flammability and what drives the selection of a particular chemical or nanoparticle into an application. I would not assume that this information is adequately covered by the community in the CEA since flame retardant research is a niche field of applied engineering. Hopefully there are other material fire scientists in this process. If I'm the only one, then I am concerned that my one vote/voice in the CEA process will be missed and again, this effort will be spent on something which may yield some good information, but fails to address in a proactive manner potential MWCNT releases and how they will affect our society and environment.	CEA framework/ methodology; Choice of nanomaterial and application
246	E4-F	Appendix A, pg A-1 lines 13-14	Why not electronics? Sporting goods?	Choice of nanomaterial and application; alternative products/ formulations
247	E4-F	Appendix A, pg A-1 line 17	Aerospace composites - very likely	Choice of nanomaterial and application; alternative products/ formulations
248	E4-F	Appendix A, pg A-2 line 15	There is more than you think - again, talk with NanoCyl in Belgium. They are mostly used in polymers requiring enhanced electrical, thermal, and mechanical properties that can justify the significant increase in cost - so higher end applications, not general consumer goods.	Choice of nanomaterial and application; alternative products/ formulations; Additional references
249	E4-F	Appendix A, pg A-2 lines 17-18	Agree on this - and this is DEFINITELY worth looking into.	Highlight data gap
250	E4-F	Appendix A, pg A-5 Figure A-1 “medium list”	I would argue is that this is where you went wrong in your selection study. Given all the deca release from E-waste, MWCNT release from electronics seems the next most logical step for study as it is in high use, and consumer electronics are being disposed of at an ever increasing rate.	Choice of nanomaterial and application; alternative products/ formulations

Table I-13, cont.: Free-form comments received from experts.

Comment ID	Author ID	Context (of External Review Draft)	Comment Text Excerpt	Themes
251	E4-F	Appendix A, pg A-6 Table A-1 (SWCNT comparison)	This is far more likely to go into commercial production with in the next decade when compared to MWCNTs for textiles.	Choice of nanomaterial and application; alternative products/ formulations
252	E4-F	Appendix A, pg A-7 Table A-2 (on the market)	This is incorrect. I know NanoCyl claimed it, but no one is actually buying it and using it, so this assumption is incorrect. I strongly disagree that you can make this statement with high confidence given what drives material selection in the flame retardant field.	Choice of nanomaterial and application
253	E4-F	Appendix A, pg A-8 lines 15-16	Now that I see this … I see where the problem really lies. The compromise hybrid solution does not reflect reality since it misses the realistic drivers which determine what flame retardants will be used in a specific application. I would propose you go back and look at SWCNTs in textiles or MWCNTs in flame-retardant composites (only when the MWCNTs are combined with other flame retardants though) and pick one, rather than pursuing this hybrid.	Choice of nanomaterial and application; choice constricted science of MWCNTs

Table I-14. Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
1	P1	"… there is significant information on decaBDE which is not included … example … cited water solubility of 20-30 μg/L as reported in the 1994 WHO IPCS document … was based on the 1970's published work of Norris et al., and reflects that of the then commercial product which was approximately 77% decabromodiphenyl ether … That … does not reflect the commercial product (>=97% decabromodiphenyl ether) that has been in use for about 20 years. The water solubility of decaBDE is considerably lower than 20-30 μg/L. The measured water solubility, determined in a guideline/GLP-compliant study in 1997, of the >=97% decaBDE product is <0.1 μg/L."	DecaBDE data needs improvement; p-chem properties
2	P1	"I would like to make you aware of critical papers on decaBDE … I will provide these papers in separate emails due to size."	DecaBDE data needs improvement; impacts
3	P2	"I wish to express appreciation for the EPA's methodical efforts on the three case studies. It provides a point of constancy across a broad and widely dispersed community."	Praise for Case Study; nanomaterial series
4	P2	"Comparison allows reader to consider incremental risk … The range of issues considered in a CEA leads the reader to assume that every question must be resolved. The comparison brings perspective and some surprise on how public knowledge for a registered substance may still have many gaps worthy of further examination."	Praise for Case Study; comparison element
5	P2	"The Agency continues to grapple with using the CEA to formulate and prioritize research goals. With the three case studies, this is illustrated by the changing format for the external review: from a large, diverse meeting for TiO2 to a much smaller one for Ag and, now, to a two day mix of public and closed meetings, the latter incorporating an RTI-led methodology."	CEA framework/ methodology; purpose of CEA
6	P2	"With the MWCNT case study, the flame-retardant formulation imposes constraints on MWCNT chemistry, where the crux is surface functionalization. While decaBDE is comparable to other brominated substances when preparing a flame-retardant formulation, MWCNT chemistry is not as robust and should not be generalized to be any MWCNT (PEI functionalized, pristine, carboxylated, and so on). … By being drawn to a specific application, flame retardants in textiles, the reader expects the CEA to focus consideration on the relevant MWCNT chemistry, which is not clear in the draft. For this case study, two categories of MWCNTs are involved; one manufactured and one surface modified."	Choice of nanomaterial and application; choice constricted science of MWCNTs
7	P2	"The tension between description (draft case study) and evaluation (identifying meaningful, constructive research goals) occurs at the point of selecting a specific application when examining a class of materials. Does one focus on the particulars of the example, as I have done, or does one use the particulars as an introduction to the generalized chemistry, as the three case studies do?"	CEA framework/ methodology; purpose of CEA

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
8	P2	"This specific application is not well established commercially, which means that there are few who can speak from their "own knowledge of multiwalled carbon nanotubes (MWCNT) and flame-retardant materials" (page 6-1). The external group is being asked to craft a context while addressing an encyclopedic listing of facts and literature citations."	Choice of nanomaterial and application; choice constricted science of MWCNTs
9	P2	"the textile case involves two forms of MWCNT, the commercial one and the modification found in the fire retardant formulation. … MWCNT kinds (classes, groupings, sub-categories) are not visible in the draft, which is written to generalize MWCNT chemistry in order to encompass the many stages of a CEA."	Choice of nanomaterial and application; choice constricted science of MWCNTs
10	P2	"Recent studies have demonstrated that carboxylated CNTs are less likely to induce profibrogenic effects (Reference for MWCNTs: Wang et al., 2011, ACS Nano 5(12):9772-9787) and are more likely to degrade (Reference for SWCNTs: Liu et al., 2010, Carbon 48:1961-1969). … These references are not in the draft and would bolster the discussion surrounding Jain's article (page 5-3). As with Magic Nano and aerosol spray exposure, colloid facilitated transport is a significant factor."	MWCNT physical/ chemical properties
11	P2	"Also, a discussion on the meaning of functionalizing would be appropriate."	Material Processing; define terminology
12	P2	"… the difficult theme of scientific relevance. I note that the earlier case studies cited presentations to society meetings and unpublished papers. The current draft is more circumspect."	CEA framework/ methodology; references/ literature
13	P2	"Yet, an EPA-sponsored document inherently provides an imprimatur or implies a relevancy to any articles cited. Unfortunately, there have been several mis-steps in the literature, especially for carbonaceous materials, e.g., fullerenes (Henry et. al, Env. Health Perspectives, 2007, 115(7):1059-1065) and carbon nanotubes (Jakubek et al, Biomaterials 2009, 30:6351–6357). And, it may take a considerable time for such mis-steps to be undone, e.g., ~3 years for dispersing fullerenes in THF. This means that the CEA methodology, in taking a broad view of product chemistry at all points along the product life cycle and in attempting scientific currency, encourages the citing of ephemeral literature, meaning articles that are within the time scale of the literature's self-correcting dynamics. Insubstantial questions result placing the review panel in an awkward position."	CEA framework/ methodology; references/ literature
14	P2	"Obviously, the colleagues at the October meetings face challenges. Supplementing the life cycle approach with concepts from the NNI's EHS plan or the principles from the recent NRC report on EHS are options, but utilizing the Agency's approach to SNURs and SNUNs is perhaps more pertinent. "	CEA framework/ methodology; other frameworks

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
15	P2	"As a possible contribution to this dialog, examining the MWCNT case history using SNUR (material submitted for a PMN) and SNUN (extension of a SNUR to new applications/use patterns) perspectives, leads to questions on MWCNT categories and their relationship to properties. A: Categorization of MWCNTs: 1. Are categories of MWCNTs recognizable, as argued above? 2. Do the many papers, including past mis-steps, point to MWCNT groupings (sufficient equivalency for risk assessment purposes)? 3. Can biological outcomes be combined with physicochemical characterization in defining an MWCNT sub-category? 4. Is there sufficient equivalency among the carboxylated MWCNT studies to identify it as an MWCNT group that requires a separate PMN (SNUR) and a separate CEA? 5. Does the flame retardant specific case require a modified MWCNT that nevertheless remains part of the unmodified MWCNT group? B: Categorization of Properties: 1. Can MWCNT properties be divided into intrinsic and context dependent categories? 2. Are biological responses from in vitro or in vivo testing better described as dependent outcomes than as independent properties? 3. Do MWCNTs display the chemical-particle duality of nanoscale-Ag? 4. Is biopersistence a context-dependent property of the use pattern such that durability in non-lung fluids can dominate risk assessment for some MWCNT modifications? 5. What are the CEA instances of characterization (defined stages in the life cycle that should be common to all MWCNT materials, e.g., "as manufactured") that are useful for comparisons and informatics? 6. Can the relevance of the case study's cited literature be informed by these considerations?"	CEA framework/ methodology; questions to consider for risk assessment
16	P2	"In summary, it may be that an MWCNT- CEA is not well suited for setting research priorities when being constrained to a linear raw material-to landfill sequence, while also incorporating the recent scientific literature. The virus life cycle, for example, starts with a virus entering the cell, follows virus replication and cell exit, but does not normally include dispersal in the environment. Using SNUR/SNUN administrative concepts, or perhaps those of other templates, in combination with the CEA would provide a useful perspective and focus when setting priorities."	CEA framework/ methodology; other frameworks
17	P2	References	References

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
18	P3	"The EPA's "Nanomaterial Case Study: Comparison of Multiwalled Carbon Nanotube and Decabromodiphenyl Ether Flame-Retardant Coatings Applied to Upholstery Textiles (DRAFT)" does not adequately address the potential impacts to wastewater treatment plants (WWTPs) from the introduction of multiwalled carbon nanotubes (MWCNTs)."	Other impacts; Additional considerations for section
19	P3	"The study identifies the potential release of MWCNTs to WWTPs during the manufacturing, storage and distribution, use, and reuse/ recycling/ end-of-life stages (2-29). The study's executive summary states that laboratory-based studies of MWCNTs established acute antimicrobial activity at low exposure concentrations (xxii). Many WWTPs use biological treatment extensively in their processes. MWCNTs behavior and interaction with WWTP microbiology may be influenced by: size, morphology, surface area, chemical composition; surface chemistry and reactivity; solubility and dispersion; and conductive, magnetic, and optical properties (1-19). It is essentially unknown how MWCNTs will behave in WWTPs or what their potential impacts on biological treatment processes may be. It is strongly recommended that evaluation of potential impacts to WWTPs be incorporated into the EPA's comprehensive environmental assessment (CEA) framework during the impact assessment stage whenever the potential for the introduction of a contaminant to a WWTP during its life cycle is identified."	Other impacts; Additional considerations for section
23	P1	"…please see the following web address for decaBDE's EU risk assessment completed in 2002: http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/decabromodiphenyletherreport013.pdf . That document discusses decaBDE's use in textiles, and has an up to date (as of 2002) discussion of decaBDE's toxicology. "	DecaBDE data needs improvement; impacts
24	P1	"For information on decaBDE's potential for absorption and metabolism, please see Hardy et al. 2009 (Critical Reviews in Toxicology) and the Biesemeier et al papers I sent last week. After 20 years studying decaBDE, my opinion is that publications over the last decade claiming substantial absorption or metabolism of decaBDE are incorrect and are due to faulty methodology."	DecaBDE data needs improvement; toxicokinetics
254	P4	Companies manufacturing MWCNTs should be required to assess potential risks using an integrated testing scheme that relies on best current practices in the field while actively reducing reliance on animal-based testing methods.	CEA framework/ methodology; Future of risk assessment
255	P4	We recognize EPA's recent efforts to encourage manufacturers to test nanomaterials using nanomaterial-specific, high-throughput, analytical and in vitro methods rather than relying on animal-based methods that have not proven reliable for this purpose.	In vitro methods

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
256	P4	We note that EPA's recent Nanomaterial Testing Strategy outlines a preference for using analytical methods for in-depth characterization followed by assessment of toxicity using in vitro methods. Within the Strategy, animal tests are considered to be a final tier of toxicity testing and are to be considered on a case-by-case basis. We encourage EPA to maintain this position as data needs for multi-walled carbon nanotubes continue to be assessed, rather than resort to the de facto prescription of unproven animal-based testing.	In vitro methods; Future of risk assessment
257	P4	Consistent with EPA's 2009 Strategic Plan for Evaluating the Toxicity of Chemicals recommendations contained in the National Academy of Science's Toxicity Testing in the 21st Century: A Vision and a Strategy should be followed for any testing of nanomaterials. This report states, "[T]oxicity testing is approaching a scientific pivot point…It is poised to take advantage of the revolutions in biology and biotechnology. Advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology could transform toxicity testing from a system based on whole-animal testing to one founded primarily on in vitro methods…" The field of nanotechnology is in a position to take full advantage of these new approaches, and we expect that EPA will be involved with continued development and validation of new, primarily non-animal methods for assessment of nanomaterials.	Future of risk assessment
258	P4	We request that EPA make clear to registrants that the test methods required will be decided on a case-by-case basis with preference given to in vitro nanomaterial-specific methods.	In vitro methods
259	P4	In addition to the problems with extrapolating information from animal studies to humans for conventional chemicals, nanomaterials possess unique physical and toxicological properties that render animal testing even more problematic. Well known confounding issues include: variations in responses to chemicals in different species and strains of animals, variations in target organs and tissue effects in different species and strains, as well as different toxic thresholds between species including humans	Highlight data gap; Analytical techniques
260	P4	Additionally, because mass concentration is not sufficient for comparison of nanomaterials of the same chemical composition and because number concentration is affected by the subjective exclusion parameters as well as by the analytical parameters used, toxicokinetics is then even more problematic for nanomaterials. Further, most laboratories are not even capable of making the measurements required for nanomaterial-related toxicokinetics, thereby making these studies even more suspect.	Toxicokinetics; Analytical techniques

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
261	P4	As EPA notes, many factors influence the toxicity profile of MWCNTs. Critical factors include variations in aggregation/agglomeration, bundling, fiber length, fiber width, surface functionalization, surface coating, heavy metal contaminants, and wall number. Each factor listed (as well as others yet to be identified or studied) is capable of completely changing the toxicity profile and the manner in which the MWCNT is absorbed and distributed in the body.	p-chem properties
262	P4	Paxton, JW. The allometric approach for interspecies scaling of pharmacokinetics and toxicity of anti-cancer drugs. Clin. Exp. Pharmacol. Physiol. 1995; 22: 851-854.	Toxicokinetics
263	P4	Wako, K., et al. Effects of preparation methods for multi-wall carbon nanotube (MWCNT) suspensions on MWCNT induced rat pulmonary toxicity. J Toxicol Sci. 2010 Aug; 35(4):437-46.	Analytical techniques
264	P4	Liu, D et al. Different cellular response mechanisms contribute to the length-dependent cytotoxicity of multi-walled carbon nanotubes. Nanoscale Res Lett. 2012 Jul 2;7(1):361.	Impacts; In vitro methods
265	P4	Coccini, T. et al., Toxicology. Effects of water-soluble functionalized multi-walled carbon nanotubes examined by different cytotoxicity methods in human astrocyte D384 and lung A549 cells. Toxicology. 2010 Feb 28;269(1):41-53.	Impacts; In vitro methods
266	P4	EPA also notes that many studies result in data that may be in conflict with existing data. This conundrum is due in part to the extreme heterogeneity of MWCNTs and also because animal-based studies have repeatedly failed to give reproducible results. Because of the infinite number of toxicity profiles from the unending number of modifications that can be made on each type of MWCNT, it is impossible to conduct conclusive in vivo studies for any class of nanomaterials, and MWCNTs are not an exception.	In vitro methods; Highlight data gap
267	P4	While EPA describes inhalation toxicity as one of the main exposure scenarios of concern, it should be noted that inhalation toxicity testing using animals results in a myriad of practical and scientific problems. Inhalation toxicity testing using rats has proven to be expensive and technically challenging with respect to delivering an appropriate dose of nanomaterials.	Highlight data gap; Analytical techniques
268	P4	More importantly, biological relevance is unlikely with rat-based tests. Issues relating to breathing mode, physiology, relative sizes of nerve bulbs and the different rate of particle clearance of rats compared to humans all point to important anatomical and physiological differences that preclude clear data extrapolation between species.	Toxicokinetics; Analytical techniques
269	P4	Warheit, D. Nanoparticles Health Impacts? Nanomaterials Today. 2004;7: 32-35.	Impacts

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
270	P4	Nikula, KJ, et al. Influence of exposure concentration or dose on the distribution of particulate material in rat and human lungs. Environmental Health Perspectives. 2001; 109(4): 311-318.	Analytical techniques
271	P4	Intratracheal instillation and laryngeal aspiration are the least costly in vivo methods and therefore are the most commonly used methods for assaying the pulmonary toxicity of nanomaterials. However, scientific concerns related to these methods are expressed by the European Commission (EC): "[t]his mode of exposure is not physiological…the lung surface receives particles contained in a liquid, which is likely to affect the defense systems of the lung." Thus the EC clarifies that often, the reaction is to the liquid bolus highly concentrated with nanomaterials and the response often has little to do with the actual toxicity of a given nanoparticle. The dose, dose rate, and dispersive abilities of this method are often criticized as lacking relevance.	Highlight data gap
272	P4	Scientific Committee on Emerging and Newly-Identified Health Risks. Opinion on the Appropriateness of the Risk Assessment Methodology in Accordance with the Technical Guidance Documents for New and Existing Substances for Assessing the Risks of Nanomaterials. 2007.	Impacts; Future of risk assessment
273	P4	Osier, M and Oberdorster, G. Intratracheal inhalation vs Intratracheal Instillation: Differences in Particle Effects. Fundamental and Applied Toxicology. 1997; 40, 220-227.	Analytical techniques
274	P4	Laryngeal aspiration has problems similar to those described for intratracheal instillation, including both a high dose and high dose rate. The EC also notes that laryngeal aspiration also results in "unusually high doses to the bronchioles and the induction of alveolar inflammation." The EC goes further to specify that, "neither [intratracheal instillation or laryngeal aspiration] can be used to determine NOEL.	Analytical techniques; Future of risk assessment; Highlight data gap
275	P4	Because of the problems associated with these (and other) in vivo tests, there is a concerted effort to begin using human cell-based co-cultures to assay potential toxicity for this exposure route. In vitro models using human cell co-cultures have proven to be informative and will help to move inhalation toxicity testing from studies on rats toward methods that are relevant to humans.	In vitro methods; Future of risk assessment
276	P4	Gasser, M. et al., Pulmonary surfactant coating of multi-walled carbon nanotubes (MWCNTs) influences their oxidative and pro-inflammatory potential in vitro. Part Fibre Toxicol. 2012 May 24;9(1):17.	In vitro methods; Highlight data gap
277	P4	Geys J, Nemery B, Hoet PH. Optimisation of culture conditions to develop an in vitro pulmonary permeability model. Toxicol In Vitro. 2007; 21(7): 1215-9.	In vitro methods; Analytical techniques

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
278	P4	Bur M, Rothen-Rutishauser B, Huwer H, Lehr CM. A novel cell compatible impingement system to study in vitro drug absorption from dry powder aerosol formulations. Eur J Pharm Biopharm. 2008 Aug 17.	In vitro methods; Highlight data gap
279	P4	Human -relevant in vitro methods: VitroCell has published on a variety of experiment types, including in vitro repeat exposure, in vitro exposure using 3D organotypic exposure to cigarette smoke (as an alternative to rat inhalation), exposure to complex mixtures and sequential exposure to pollutants, as well as reports on prevalidation studies on the toxic effects of inhalable substances.	In vitro methods; Highlight data gap
280	P4	http://www.vitrocell.com/index.php?Nav_Nummer=8&	In vitro methods; Highlight data gap
281	P4	Human -relevant in vitro methods: Companies such as MatTek have tested nanomaterials in concert with corporations such as Proctor and Gamble and have achieved in vitro-in vivo data concordance using the MatTek EpiAirway three-dimensional tissue constructs.	In vitro methods; Highlight data gap
282	P4	http://www.mattek.com/pages/nanoparticles/	In vitro methods; Highlight data gap
283	P4	In vitro models using cell cultures and co-cultures have proven to be informative.	In vitro methods
284	P4	Geys J, Nemery B, Hoet PH. Optimisation of culture conditions to develop an in vitro pulmonary permeability model. Toxicol In Vitro. 2007; 21(7): 1215-9.	In vitro methods; Highlight data gap
285	P4	Bur M, Rothen-Rutishauser B, Huwer H, Lehr CM. A novel cell compatible impingement system to study in vitro drug absorption from dry powder aerosol formulations. Eur J Pharm Biopharm. 2008 Aug 17.	In vitro methods; Highlight data gap
286	P4	Rothen- Rutishauser et al. developed a triple co-culture comprised of epithelial cells, macrophages, and dendritic cells which the author states, “simulates the most important barrier functions of the epithelial airway.” Measurement of cellular responses to MWCNTs, including reactive oxygen species, release of tumor necrosis factor, and apoptosis illustrate the effectiveness of pre-coating MWCNTs to decrease toxicity. This model system has been compared to in vivo results with good data concordance.	In vitro methods; Highlight data gap

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
287	P4	Gasser, M. et al., Pulmonary surfactant coating of multi-walled carbon nanotubes (MWCNTs) influences their oxidative and pro-inflammatory potential in vitro. Part Fibre Toxicol. 2012 May 24;9(1):17.	In vitro methods; Highlight data gap
288	P4	Alfaro-Moreno et al. found that bicultures and tricultures of human lung cells released granulocyte colony-stimulating factor (G-CSF), macrophage inflammatory protein (MIP)- 1beta, interleukin (IL)-1beta, IL-6, tumor necrosis factor alpha, and MIP-1alpha. The authors go on to state that these effects are consistent with those systemic effects described for particulate matter and correspond to inflammation, endothelial dysfunction, and bone marrow cell mobilization.	In vitro methods; Highlight data gap
289	P4	Alfaro-Moreno, E. et al. Co-cultures of multiple cell types mimic pulmonary cell communication in response to urban PM10. Eur Respir J. 2008; 32:1184-1194.	In vitro methods
290	P4	Cavallo, et al. made use of A549 (human lung epithelial) cells to study the mode of toxicity caused by MWCNTs. Early cytotoxic and genotoxic effects were observed (including membrane damage, surface morphological changes, and direct DNA damage). These data contribute to understanding the mechanism by which MWCNTs may induce toxic effects.	In vitro methods; Highlight data gap
291	P4	Cavallo, D. et al., J Appl Toxicol. Jan 23. Multi-walled carbon nanotubes induce cytotoxicity and genotoxicity in human lung epithelial cells. J Appl Toxicol. 2012 Jun;32(6):454-64.	In vitro methods
292	P4	Because nanomaterials differ from traditional chemicals and have proven difficult to test using some of the outdated animal-based methods used for traditional chemicals, it is critical to completely and accurately characterize nanomaterials, as is described by EPA's Nanomaterial Testing Strategy, and to then apply in vitro and in silico methods within an integrated testing strategy (ITS). ITS take into account existing data to design a rational, chemical-specific testing strategy to satisfy regulatory needs without relying primarily on animal testing.	Future of risk assessment
293	P4	We suggest that MWCNTs (as well as other nanomaterials) be tested using NexGen Respiratory Toxicity Model developed by EPA's Office of Research and Development. This model system takes advantage of both an air-liquid-interface in vitro cell-based construct coupled with omics-based mechanistic pathway and biomarker identification.	Future of risk assessment; in vitro methods
294	P4	http://nas-sites.org/emergingscience/files/2012/06/Devlin.pdf	Future of risk assessment

Table I-14, cont.: Comments received in response to the public comment period.

Comment ID	Author ID	Comment Text Excerpt	Themes
295	P4	In the event that additional toxicity data is requested, we urge EPA to require manufacturers to use high-throughput methods that have been specifically designed for MWCNTs in order to reduce reliance on animal-based testing, as described above.	Future of risk assessment; in vitro methods
296	P4	We look forward to seeing progress made toward the replacement of animal-based testing methods and encourages EPA to continue working toward this goal.	Future of risk assessment; In vitro methods
297	P4	Environmental Protection Agency, "Nanomaterial Research Strategy," 2009.	Future of risk assessment
298	P4	Environmental Protection Agency. 2009. The U.S. Environmental Protection Agency's Strategic Plan for Evaluating the Toxicity of Chemicals. Office of the Science Advisor, Science Policy Council, U.S. EPA (http://www.epa.gov/osa/spc/toxicitytesting/docs/toxtest_strategy_032309.pdf	Future of risk assessment
299	P4	National Research Council, "Toxicity Testing in the Twenty-First Century: A Vision and a Strategy," report of the Committee on Toxicity and Assessment of Environmental Agents, June 2007.	Future of risk assessment

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Appendix J. Knowledge Map Pilot: Environmental Transport, Transformation and Fate

Appendix J. Knowledge Map Pilot: Environmental Transport, Transformation and Fate

Appendix J presents work from a pilot project to continue refining the CEA approach. The main objective of this work is to develop methods for visually and concisely representing information in the CEA Framework. Specifically, Chapter 3, "Environmental Transport, Transformation and Fate" in the External Review Draft of this case study document (Chapter 3, Section G.3, and Section H.3 in the current Peer Review Draft) was selected to develop a proof of concept for a particular method to visually convey information. Here, this method is briefly described followed by the products to date from this pilot.

J.1. Knowledge Maps

Knowledge maps are used in a variety of fields (e.g., organization management, journalism) to visually represent concepts and how they relate to one another (Novak and Cañas, 2008; Kim et al., 2003). Given their wide applicability and utility in representing complex concepts, knowledge maps were selected for this pilot to visually convey information in the CEA framework. A knowledge map is composed of a network of nodes (usually presented as common shapes) connected by edges (depicted as lines or arrows). Nodes usually represent concepts, whereas edges show relationships between the concepts.

J.2. Transport, Transformation and Fate Knowledge Maps: Overview

The knowledge maps developed in this pilot are three conceptually linked portions of one map displaying environmental transport, transformation, and fate for either decabromodiphenyl ether (decaBDE) or multiwalled carbon nanotubes (MWCNT). Showing all of the information related to environmental transport, transformation, and fate on one map would result in a great amount of detail in a small amount of space, and thus for readability the information pertinent to each process is displayed in three distinct maps. The Physicochemical Properties Map (PPM) focuses on the material itself, providing

a sense of the basic properties of the material, which might in turn influence how the material partitions in the environment after release from a product life cycle stage (e.g., product manufacturing, use, disposal/recycling). The Transport Map (TpM) portrays how the material might subsequently move between environmental zones (i.e., aquatic, atmospheric, terrestrial) based on available information. In addition, it provides a sense of which zone(s) are sinks for the material, and thus would likely have higher concentrations of the material than others would. Once the material makes it to a zone, the Transformation Map (TfM) depicts how the material might be transformed due to the combination of material and environmental properties within a given zone.

Note that because the maps are conceptually a single unit, symbols mean the same thing across all the maps. For example, black edges with a solid arrowhead always represent movement whenever they appear in any of the maps. Similarly, the environmental zones look the same in all three maps.

Each type of map (i.e., PPM, TpM, TfM) is described in greater detail below, along with a brief comparison of the decaBDE and MWCNT maps in each category.

J.3. Physicochemical Properties Maps

The PPM[35] shows the properties of a material likely to influence its behavior in the environment, the corresponding effects on environmental behavior, and finally how resulting behaviors influence movement to environmental zones.

The PPM has three banks of nodes. In the top bank, material properties are represented in rectangular nodes. The nodes are color-coded based on information in Table 3-2 and Table H-3; nodes are dark red if the value is high and light red if the value is low[36], whereas light green means that the property can vary according to the specific sample of the material (e.g., MWCNT with one type of surface coating versus another) and light purple indicates a property which may or may not occur based on environmental conditions.

The middle bank of nodes contains effects in ovals. Like the properties, they are color coded so that high effects are dark yellow, while low effects are light yellow. Where variability exists, such that the effect can be high or low, a dark yellow and a light yellow circle have been placed in a box that represents that effect. A white oval with a dashed border indicates an effect that is predicted to occur based on

[35] Note: These maps are based primarily on Table 3-1 (for MWCNT) and Table H-3 (for decaBDE), and although details from other parts of Chapter 3, Section G3, and Section H.3 are included where relevant, the PPMs represent a translation of information in tabular form to figures in this pilot work.

[36]Note: Scaling the shading of red to present values more specific than “low” or “high” was determined to be too confusing for this representation.

material properties but has not yet been observed. The effect nodes are connected to the property nodes via green edges with diamond arrowheads; these edges indicate a simple causal relation, i.e., that a particular property leads to a particular effect. Green edges that connect to boxed effect nodes indicate that the given property might lead to a high or low effect, given varying circumstances.

The lower bank of nodes contains the environmental zones, which are more fully described in the transport map. Black edges connect effect nodes to zone nodes to indicate that the effect facilitates transport to that zone. Levels of transport are differentiated, with high transport represented by thick, solid lines and low transport presented with thin, dashed lines.

Overall, the map can be read as a three-part sentence that follows the edges from property to effect, to zone. For example, "the low water solubility of decaBDE leads to high sorption to organic matter, which causes a high level of transport to the soil."

The decaBDE and MWCNT PPMs are consistent with each other in their use of symbols; however, there are notable differences between the two maps. For example, the PPM for MWCNT includes more types of nodes (e.g., light green property nodes and boxed effect nodes) because MWCNT properties can vary based on size, shape, surfactant, and other conditions. In addition, while all property nodes in decaBDE are separated by whitespace, property nodes that are two poles of the same property (like "Size: single" and "Size: cluster") are placed next to each other on the MWCNT map, again due to the variability associated with the material.

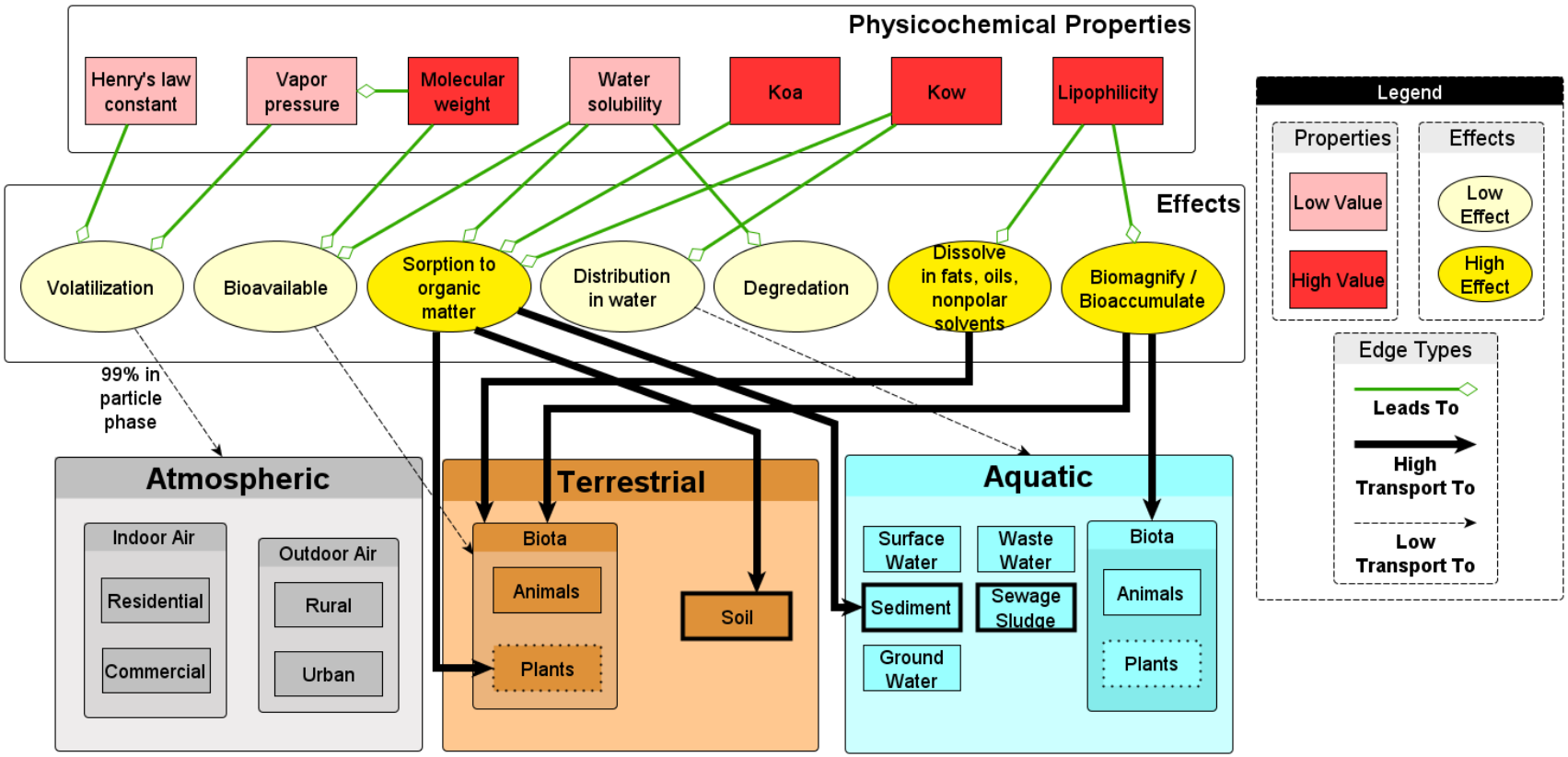

Figure J-1. Physicochemical properties map: Decabromodiphenyl ether.

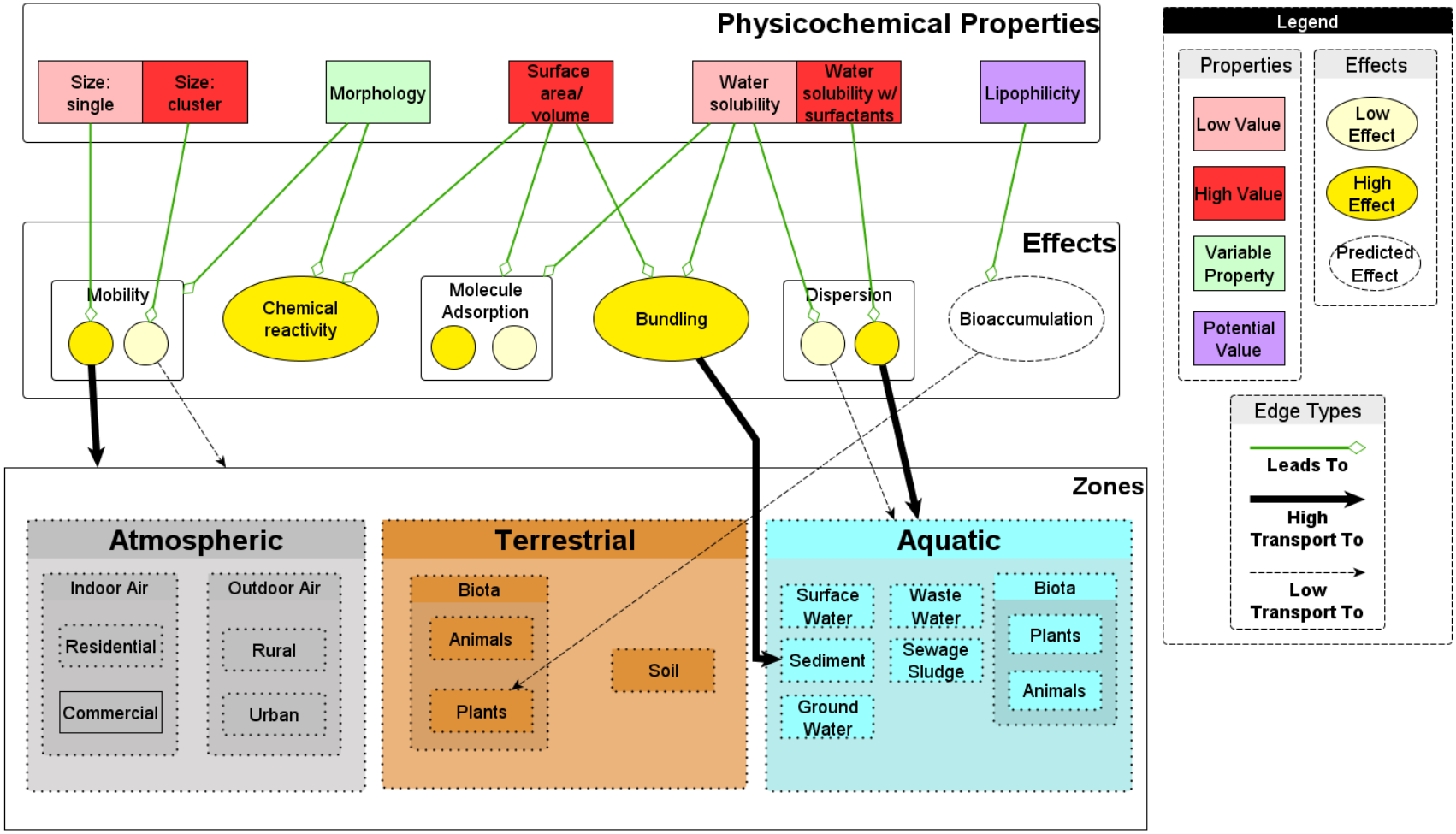

Figure J-2. Physicochemical properties map: Multiwalled carbon nanotubes.

J.4. Transport Map

The TpM begins with the release of a material in a product life cycle stage (see PPM). From there the map shows how the material might travel between or within spatial zones, the environmental properties that affect material transport, and some processes that describe the movement.

The TpM has only one bank of nodes, containing the environmental zones. There are three main zones: atmospheric (grey), terrestrial (brown), and aquatic (blue). Within each of these zones there are more specific sub zones (e.g., waste water, surface water, sediment within the aquatic zone). Zones that are sinks for the material, based on information available in Chapter 3, Section G.3, and Section H.3 of the document, have a thick black border. When no data were found on the concentration of the material in that zone, the border is dotted.

Transport is represented by solid or dotted black lines leading from one zone to another. The bold solid lines represent movement described as "most likely to occur," based on information available in Chapter 3, Section G.3, and Section H.3. Dotted lines thus represent data inferred from other materials or likely due to chemical properties, but for which explicit measurements have not been taken (e.g., MWCNT leeching from soil to groundwater). For instance, in the decaBDE TpM a dotted line is used to depict decaBDE transport from surface water to sediment is most likely to occur based on low water solubility and other material properties (see Figure J-3).

For many of the transport processes, the text in Chapter 3, Section G.3, and Section H.3 used a term to describe the process (such as deposition, leaching, or runoff), and those terms are listed as a label on the appropriate edge. Any environmental properties of the spatial zones that were cited in the chapter as affecting material transport are represented by numbers to highlight the influence these factors might have on the extent, rate, or direction of transport.

Overall, the maps can be read as a sentence that follows the edges from release to a spatial zone and then to another spatial zone. For example, "decaBDE is released to the atmospheric zone, where is can be transported through deposition to waste water, with the extent of deposition influenced by the amount of total organic carbon (TOC) in the air, precipitation, wind, and temperature."

When comparing the decaBDE and MWCNT TpMs, it is clear that the spatial zones and environmental properties are the same; however, as expected, there are differences in the specific types of transport that occur and the environmental properties that influence them. More notably, there are no known sinks for MWCNT, whereas there are three for decaBDE (soil, sediment, and sewage sludge). For MWCNT there is also much less data on concentrations in the zones and therefore many more dotted lines than in the decaBDE map.

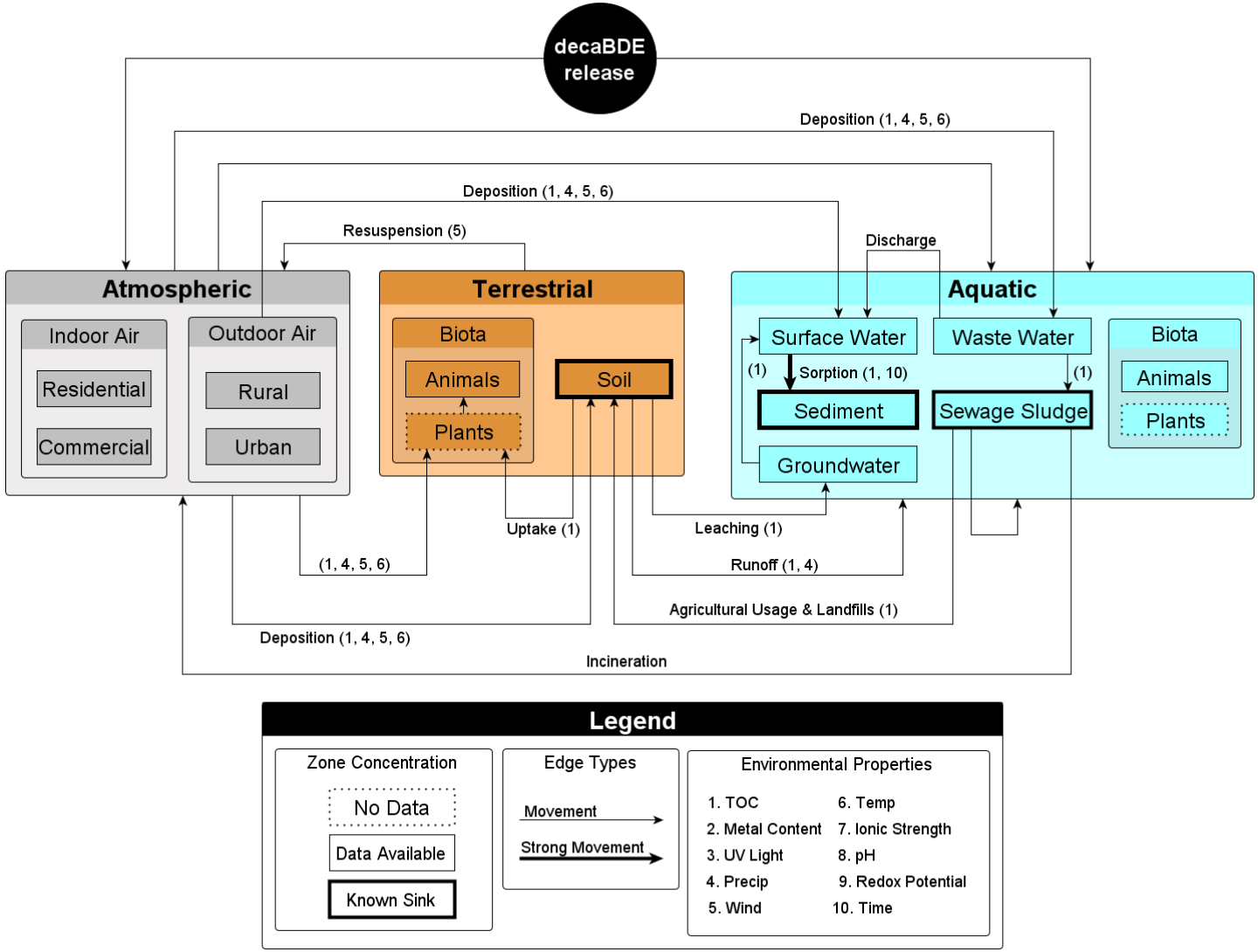

Figure J-3. Transport map: Decabromodiphenyl ether.

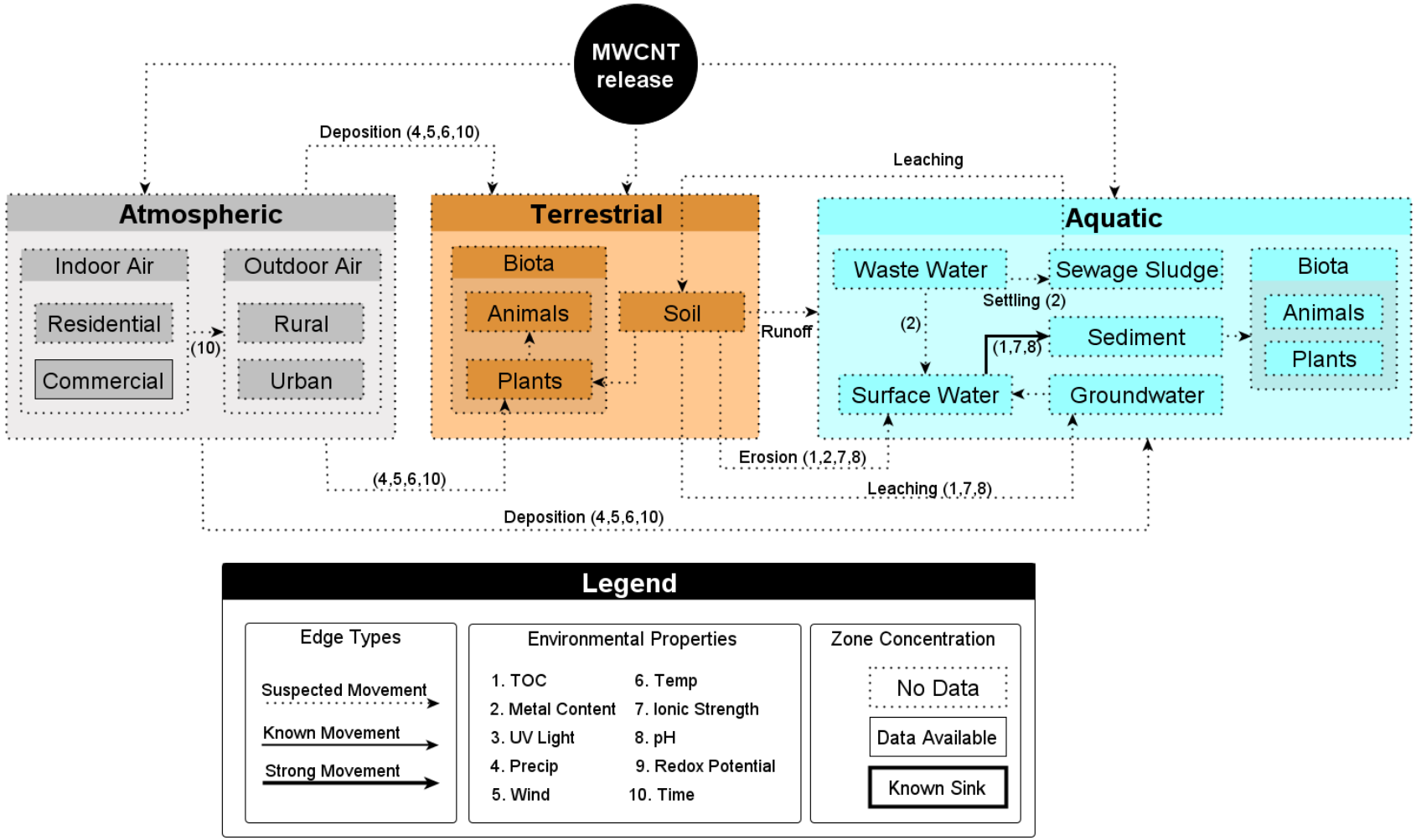

Figure J-4. Transport map: Multiwalled carbon nanotubes.

J.5. Transformation Map

Each TfM begins with the material entering spatial zones, either from release in a product life cycle stage (see PPM), or movement between spatial zones (see TpM). From there the map shows transformations that occur within those zones, the environmental properties that affect the transformation, and the resulting compounds.

There are three banks of nodes in the TfMs. The top bank represents the spatial zones (carried over from the previous two maps and including known sinks). The second bank of nodes represents the transformations that are associated with the spatial zones. Transformations are grouped into three main categories: chemical, biological, and physical, which are represented by yellow (photo, thermal and geochemical degredation), red (sorption), or green (biological degredation) parallelograms, respectively. Many of the spatial sub-zones are associated with specific transformations; these instances are denoted by a red edge linking the sub-zone with the particular transformation (e.g., plants within "terrestrial biota" are associated with biological degradation in the decaBDE map). An edge to the main "Transformations" box implies an association with all of the transformations within that box (e.g., Soil within "terrestrial" is associated with biological, photo, and geochemical degradation in the decaBDE map). When the text in Chapter 3, Section G.3, and Section H.3 cites reason to infer data that has not been explicitly measured or proven, it is represented by a dashed line throughout the map.

As in the TpM, available information from the text on the environmental properties that might influence transformation is represented by numbers next to the relevant edge connecting the zone and the transformation.

The third bank of nodes is nested inside of the transformations and represents the compounds that result from the transformation that occurred. A black line with an open circle is used as the edge connecting each transformation to the resulting compound. The resulting compounds are then represented by solid black shapes, such as a triangle to represent polybrominated/-chlorinated dibenzofurans in the decaBDE map.

The spatial zones, general transformation types, and environmental properties are the same in the legend of both the decaBDE and MWCNT TfMs; however, there are differences between the maps for each material in the specific transformations that occur and the environmental properties that influence them. Notably, there are fewer types of transformation products associated with MWCNTs compared with decaBDE, although this may be due to a lack of data. Similar to the transport map, there are more dashed edges in the MWCNT map than the decaBDE map, representing greater uncertainty in the particular type of transformations that might occur for MWCNT. Overall, the maps can be read as a three-

part sentence that follows the edges from spatial zone to transformation to resulting compound. For example, "decaBDE can be transported to surface water in the aquatic zone, which is associated with photodegradation, the extent of which is influenced by quantity of UV light and results in polybrominated/-chlorinated dibenzo furans."

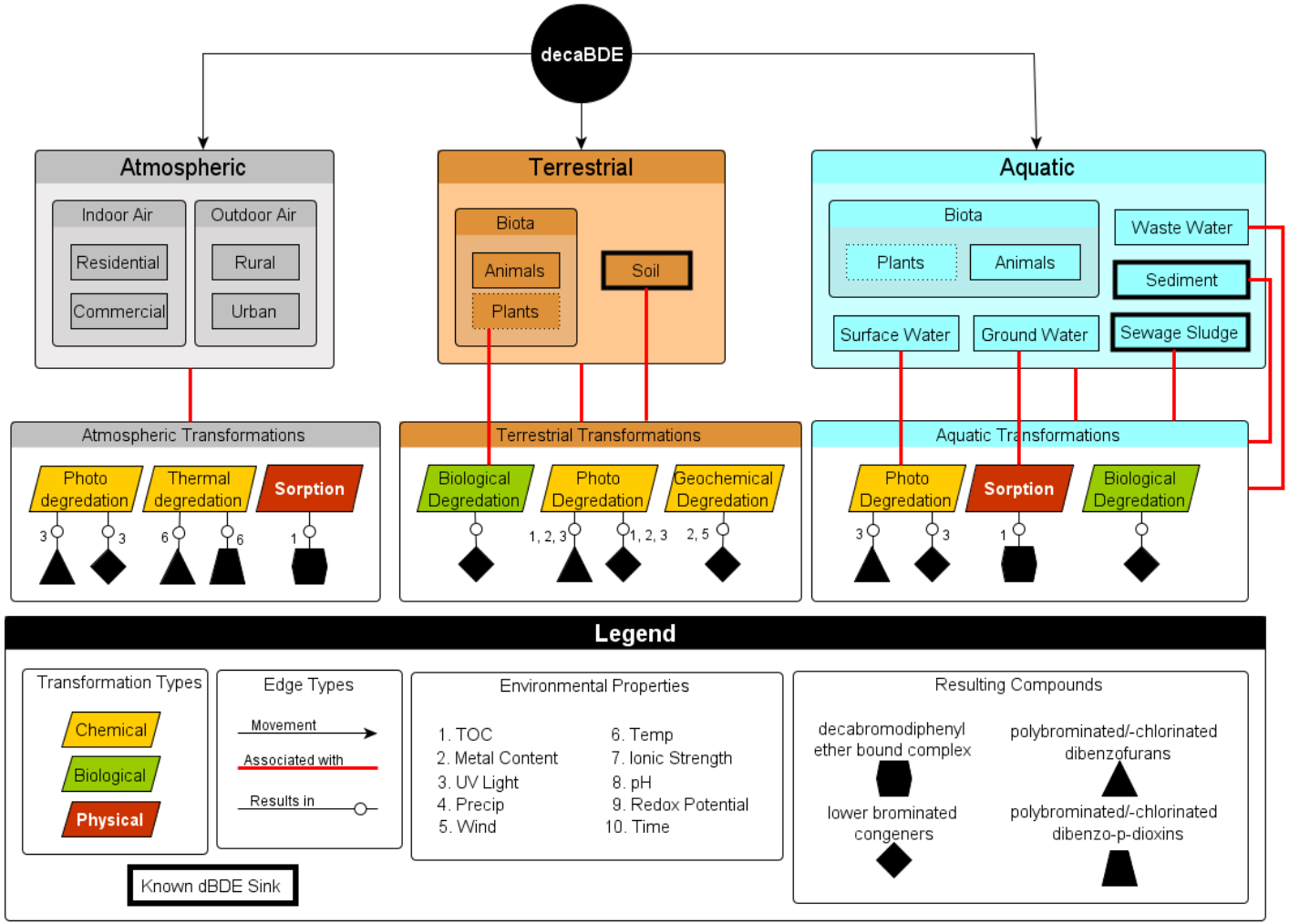

Figure J-5. Transformation map: Decabromodiphenyl ether.

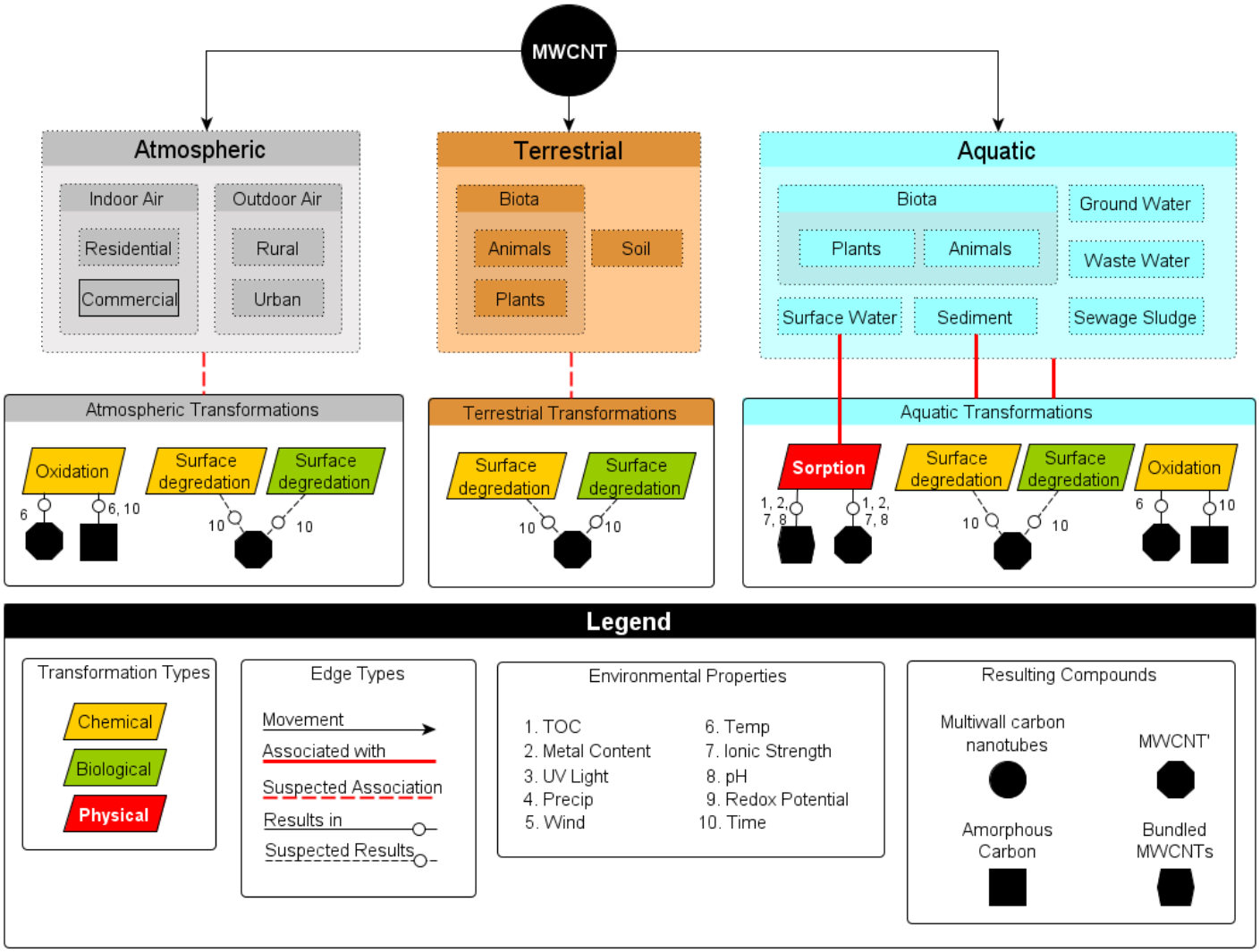

Figure J-6. Transformation map: Multiwalled carbon nanotubes.

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