

AR201-13407A

**Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV)
Chemicals Challenge**

Test Plan

Prepared for:

**American Chemistry Council
Fatty Nitrogen Derivatives Panel
Cationics Task Group**

Prepared by:

Toxicology/Regulatory Services, Inc.

December 13, 2001

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Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge Test Plan

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Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge Test Plan

This document provides the Test Plan for the Fatty Nitrogen Derived Cationics Category.

Definition of Fatty Nitrogen Derived (FND) Cationics Structure-Based Chemical Category

The FND Cationics Category is comprised of 13 separate quaternary ammonium compounds (quats) with unique Chemical Abstracts Service Registry Numbers (CAS RNs; see Text Table A). The chemicals in the FND Cationics Category consist of the following:

Five mono-alkyl chain quats (CAS RNs 112-00-5, 112-02-7, 8030-78-2, 112-03-8 and 68607-29-4); seven di-alkyl chain quats (CAS RNs 61789-77-3, 68391-05-9, 68002-59-5, 68783-78-8, 68002-58-4, 61789-80-8 and 61789-81-9); and one tri-alkyl chain quat (CAS RN 67784-77-4).

In addition, three non-HPV chemicals, which are structurally closely-related to the FND Cationics Category, were identified to provide supplemental data for the category. These supporting chemicals consist of a tri-alkyl chain quat (tricetylmethyl ammonium chloride, i.e. TMAC; CAS RN 52467-63-7), a di-alkyl chain quat (didecyldimethylammonium chloride; i.e. DDAC; CAS RN 7173-51-5) and a benzyl mono-alkyl chain quat (Alkyl (C12-16) dimethylbenzylammonium chloride; i.e. ADBAC; CAS RN 68424-85-1), with similar toxicologic properties to DDAC. Although full reports for DDAC and ADBAC could not be obtained by the FND Cationics HPV Task Group, and therefore, Robust Summaries could not be prepared, official government reviews (U. S. EPA Data Evaluation Reviews) of the toxicity, environmental fate and ecotoxicity studies for these chemicals were available and are considered reliable to support fulfilling HPV endpoints for the FND Cationics Category (U. S. EPA Data Evaluation Reports; Environment Canada, 1998 and Ministry of Environment, Lands, and Parks, 1992; see Appendix B).

U. S. EPA clustered quaternary ammonium compounds into four groups for the purpose of toxicology testing needed for reregistration under FIFRA (U. S. EPA, 1988). Although the FND Cationics Category chemicals are not part of this FIFRA reregistration, based on their structures, they all fit into Group I of the EPA clustering scheme. EPA designated DDAC as the representative member of Group I, meaning that data developed for this chemical would be representative for the other quats in the Group. ADBAC was designated by EPA as representative of a second group, Group II, of quaternary ammonium compounds, those with a benzyl substituent. For the purpose of determining environmental toxicity, DDAC and ADBAC remained the representative members of their respective groups (U. S. EPA, 1993). It was determined during the testing for reregistration under FIFRA that, despite their structural diversity, the quats included in EPA Groups I and II all had similar toxicological, environmental fate and ecotoxicological profiles. The FND Cationics Category chemicals appropriately fit into the EPA scheme for Group I, and the inclusion of data for DDAC in support of the category is appropriate. Although the FND Cationics Category chemicals do not include benzene

substituted quaternary amines, the similar toxicological profile for ADBAC and DDAC warrant the inclusion of ADBAC as a second supporting chemical for the category.

The FND Cationics Category chemicals and supporting non-HPV chemicals are identified in the following table:

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
112-00-5	Ammonium, dodecyltrimethyl-, chloride
112-02-7	Ammonium, hexadecyltrimethyl-, chloride
8030-78-2	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides
112-03-8	Trimethyloctadecylammonium chloride
7173-51-5 <i>non-HPV</i>	<i>Didecyltrimethylammonium chloride (DDAC)</i>
61789-77-3	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides
68002-59-5	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides
68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates
61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride
61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates
52467-63-7 <i>non-HPV</i>	<i>1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride (Tricetylmethyl ammonium chloride, TMAC)</i>
67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides
68607-29-4	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride
68424-85-1 <i>non-HPV</i>	<i>Alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC)</i>

Evaluation of Matrix Data Patterns – Reliable Data and QSAR Predictions

Physical/Chemical Properties

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Melting Point, Boiling Point and Vapor Pressure: Melting point and boiling point data as predictors of environmental or toxicological behavior for chemicals such as the FND Cationics Category chemicals are of minimal value. The QSAR estimates for melting point and boiling point appear to provide values higher than would be expected. A measured boiling point for TMAC was considered to be confounded by impurities. Overall, the measured and modeled values are adequate for defining melting and boiling points for the FND Cationics Category chemicals.

As expected for molecules of this size, model predictions for the chemicals with definable structures indicate they are nonvolatile. A measured vapor pressure value suggesting TMAC is volatile was considered to be confounded by impurities. Overall, the available information is adequate to meet HPV requirements.

Additional Data: No additional data are proposed for the melting point, boiling point and vapor pressure endpoints (see Table 1).

Octanol/Water Partition Coefficient (K_{ow}) and Water Solubility: Predicted or measured K_{ow} values are of limited practical use for cationic substances to estimate their physical properties or behavior in the environment. An inherent property of cationic surfactants is that they accumulate at the interface between two phases. Thus, the accurate measurement of the K_{ow} for any surfactant is difficult. Even if such measurements were made accurately, the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior because cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters.

The water solubility for the FND Cationics Category appears to be influenced by substituent groups, chain lengths and molecular weight. However, due to the physical/chemical properties of these surfactants described above, water solubility values for the FND Cationics Category chemicals are of limited value in predicting their environmental fate and toxicity. Thus, the available modeled and measured data for the FND Cationics Category chemicals and additional chemicals are considered adequate to meet the requirements of the HPV program.

Additional Data: No additional data are proposed for the partition coefficient or water solubility endpoints (see Table 1).

Environmental Fate and Ecotoxicity

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Photodegradation, Water Stability and Transport and Distribution: Due to the extremely low volatility of the FND Cationics Category chemicals, atmospheric photodegradation estimates are of no practical value. However, photodegradation was predicted for three of the FND Cationics Category chemicals and the three non-HPV chemicals. These predictions indicate that these chemicals would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 2.8 to 5.9 hours). In addition, a measurement for CAS RN 61789-80-8 adsorbed to silica indicated some evidence of photodegradation.

The water stability of these chemicals could not be modeled since the structures of the FND Cationics Category chemicals did not meet the requirements of the model's database. Due to the surfactant properties of the FND Cationics Category chemicals, water stability estimates are of little practical value. The measured data available from a hydrolysis test with DDAC indicate that the test substance was stable in water for 30 days at pHs of 5, 7 and 9. Similar results would be expected for the FND Cationics Category chemicals.

The fugacity model (Level III) predictions for transport and distribution are consistent with the model dependency on K_{ow} and water solubility. Thus, for the chemicals with lower K_{ow} estimates and higher water solubility estimates, the model predicts high distribution into water. Conversely, for chemicals with higher K_{ow} and lower water solubility predictions, the model predicts high distribution to sediment.

Additional Data: Due to the extremely low volatility of the FND Cationics Category chemicals, atmospheric photodegradation estimates are of no practical value and no testing is proposed. In addition, due to the surfactant properties of the FND Cationics Category chemicals, water stability estimates are of little practical value and no testing is proposed. For purposes of the HPV program, model predictions available for chemicals with definable structures are adequate to describe distribution and transport for the FND Cationics Category chemicals and no additional data development is proposed (see Table 2).

Biodegradability: There are adequate measured data across the FND Cationics Category to allow the conclusion that these chemicals are biodegradable although tests are frequently confounded by adsorption phenomena. For the non-HPV chemical, ADBAC, the most recent review by Environment Canada (1998; Appendix B) concludes, "It is not persistent in the water column; movement to the solid phase and microbial degradation are expected to be the main routes of dissipation." This conclusion is consistent with the information available for the FND Cationics Category chemicals as well.

Additional Data: No additional data development is proposed for the biodegradation endpoint (see Table 2).

Aquatic Toxicity: The reliable data for acute toxicity to aquatic organisms indicate that the FND Cationics Category chemicals, like surfactants in general, may adversely affect some species (LC₅₀ and EC₅₀ values as low as 0.07 mg/l). Chronic toxicity to fish and invertebrate species varied considerably, with NOECs ranging from 4.15 µg/l to 12.7 mg/l. The numerous studies of aquatic toxicity, many of which were conducted in natural waters with and without added effluents, indicate that the source and composition of the test water dramatically affects the toxicity of the test substance. These results are consistent with the known behavior of these materials in the environment. Cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. Thus the extreme variability of the measured values is predictable. Further, as would be anticipated, the modeling programs were inconsistent in their accuracy for aquatic toxicity endpoints with some values similar to measured or expected and others divergent. Overall, there are substantial aquatic toxicity experimental data for the FND Cationics Category chemicals and these data are similar to a number of published values for similar quaternary ammonium compounds (Boethling and Lynch, 1992).

The values for toxicity to aquatic plants for two of the chemicals (CAS RNs 68783-78-8 and 61789-80-8) in the FND Cationics Category are consistent with 1) published data for similar quaternary ammonium compounds (Boethling and Lynch, 1992), 2) the value for the structurally-related non-HPV chemical, DDAC (Ministry of Environment, Lands, and Parks, 1992), and 3) the acute effects on other aquatic organisms. Toxicity to aquatic plants could not be modeled using ECOSAR for the chemicals in the FND Cationics Category. Values for toxicity to aquatic plants for the non-HPV chemical, TMAC, were similar to other reported values.

Additional Data: Based on the close similarity of FND Cationics Category aquatic toxicity data (measured and modeled) to those known for other quaternary ammonium compounds as well as the confounding potential of adsorption to environmental substances, additional acute toxicity testing of aquatic animals and plants will not provide new data of consequence to better understand the aquatic toxicity of cationic surfactants. Therefore, no additional data development is proposed (see Table 2).

Human Health-Related Data

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Acute Toxicity: Acute oral toxicity studies were available for nine of the FND Cationics Category chemicals, as well as for the two non-HPV chemicals, DDAC and ADBAC. These studies indicate a range of acute oral toxicity from approximately 200 to > 2000 mg/kg. An oral LD₅₀ of > 16.3 g/kg was found for the high molecular weight, non-HPV chemical, TMAC.

Repeated Dose and Reproductive Toxicity: The available data for four FND Cationics Category chemicals support the assessment of repeated dose toxicity; two of these studies meet the SIDS/HPV requirements for reproductive screening. For purposes of the HPV program, the repeat dose study for the non-HPV chemical, TMAC, as well as the extensive repeat dose and reproductive testing of the two non-HPV chemicals, DDAC and ADBAC, adequately support the evaluation of the FND Cationics Category chemicals.

Genetic Toxicity *in vitro*: Mutagenicity data with some limitations (several of the existing studies do not meet current testing guidelines for the number of strains to be tested) are available for the HPV chemicals. The available data indicate that the FND Cationics Category chemicals are unlikely to be mutagenic. The conclusion of a lack of mutagenicity and clastogenicity for FND Cationics Category chemicals is supported robustly by the full complement of studies available for the three non-HPV chemicals, including a negative *in vivo* mouse micronucleus assay for ADBAC (see Appendix B) and a negative *in vivo* chromosomal aberration assay for TMAC (see Appendix A).

Developmental Toxicity: The data available from tests for developmental toxicity for five FND Cationic Category chemicals and the two non-HPV chemicals, DDAC and ADBAC, indicate that these chemicals are neither embryo/fetal toxicants nor teratogens. For purposes of the HPV program, the available studies adequately support the evaluation of the FND Cationics Category chemicals.

Additional Data: For HPV program purposes, the available data are sufficient for the evaluation of the FND Cationics Category chemicals. Therefore, no additional data development is proposed for the acute toxicity, repeated dose and reproductive toxicity, genetic toxicity *in vitro* or developmental toxicity endpoints (see Table 3).

References

Boethling, R. S. and D. G. Lynch. 1992. Quaternary Ammonium Surfactants. *Handbook of Environ. Chem.* 3: 145-177.

Environment Canada. 1998. Water Quality Guideline for the Protection of Freshwater Aquatic Life for Didecyl Dimethyl Ammonium Chloride (DDAC). Guidelines and Standards Division, Science Policy and Environment Quality Branch, Environment Canada, Hull, Quebec, December 1998.

Ministry of Environment, Lands, and Parks. 1992. “A Review of the Environmental Impact and Toxic Effects of DDAC.” Victoria, British Columbia.

U. S. EPA. 1988. PR Notice 88 – 2. Notice to Producers, Formulators, Distributors and Registrants: Clustering of Quaternary Ammonium compounds

U. S. EPA. 1993. Memorandum: OPPTS’ Structure Activity Clustering of OPP’s Quaternary Ammonium Compounds for Environmental Toxicity.

**Table 1. Proposed Test Plan for American Chemistry Council FND Cationics Category
 Physical/Chemical Properties**

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient (log K _{ow})	Water Solubility
112-00-5	A	A	A	A	A
112-02-7	A	A	A	A	A
8030-78-2	C	C	C	C	C
112-03-8	A	A	A	A	A
<i>7173-51-5 non-HPV</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>
61789-77-3	C	C	C	C	C
68391-05-9	C	C	C	C	C
68002-59-5	C	C	C	C	C
68783-78-8	C	C	C	C	C
68002-58-4	C	C	C	C	C
61789-80-8	A	C	C	C	A
61789-81-9	C	C	C	C	C
<i>52467-63-7 non-HPV</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>
67784-77-4	C	C	C	C	C
68607-29-4	C	C	C	C	C
<i>68424-85-1 non-HPV</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>

Note: Shaded areas represent adequate reliable data, adequate model data.
 CAS RN and data in italics are for additional chemicals [non-HPV].
 A = Adequate reliable data or model data exist.
 C = Endpoint fulfilled by category read-across from existing data.

Table 2. Proposed Test Plan for American Chemistry Council FND Cationics Category Environmental Fate and Ecotoxicity^a

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
112-00-5	A	C	A	A	A	A	C
112-02-7	A	C	A	A	A	A	C
8030-78-2	C	C	C	A	C	A	C
112-03-8	A	C	A	A	A	A	C
<i>7173-51-5 non-HPV</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>
61789-77-3	C	C	C	A	C	C	C
68391-05-9	C	C	C	C	C	C	C
68002-59-5	C	C	C	C	C	C	C
68783-78-8	C	C	C	C	A	A	A
68002-58-4	C	C	C	C	C	C	C
61789-80-8	A	C	C	A	A	A	A
61789-81-9	C	C	C	C	C	C	C
<i>52467-63-7 non-HPV</i>	<i>A</i>	<i>C</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>
67784-77-4	C	C	C	C	C	C	C
68607-29-4	C	C	C	A	C	C	C
<i>68424-85-1 non-HPV</i>	<i>A</i>	<i>C</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>C</i>

Note: Shaded areas represent adequate reliable data or adequate model data

CAS RN and data in italics are for additional chemicals [non-HPV].

A = Adequate reliable data or model data exist.

C = Endpoint fulfilled by category read-across from existing or proposed test data.

^a In addition to the SIDS/HPV endpoints for aquatic toxicity, chronic toxicity studies exist, are discussed in the Assessment of Data Availability, and are included in the Robust Summaries in Appendix A.

**Table 3. Proposed Test Plan for American Chemistry Council FND Cationics Category
 Human Health-Related Data**

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity NOEL	Genetic Toxicity <i>In vitro</i>	Toxicity to Reproduction	Developmental Toxicity
112-00-5	A	C	C	C	A	C	A
112-02-7	A	C	A	A	A	C	A
8030-78-2	A	C	A	C	A	C	C
112-03-8	A	C	C	C	A	C	A
<i>7173-51-5 non-HPV</i>	<i>A</i>	<i>C</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>
61789-77-3	A	C	C	C	A	C	C
68391-05-9	A	C	C	A	C	C	C
68002-59-5	C	C	C	C	C	C	C
68783-78-8	A	C	C	C	A	C	A
68002-58-4	C	C	C	C	C	C	C
61789-80-8	A	A	C	A	C	A	C
61789-81-9	C	C	C	A	C	A	A
<i>52467-63-7 non-HPV</i>	<i>A</i>	<i>C</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>C</i>	<i>C</i>
67784-77-4	C	C	C	C	C	C	C
68607-29-4	A	C	C	C	C	C	C
<i>68424-85-1 non-HPV</i>	<i>C</i>	<i>C</i>	<i>C</i>	<i>A</i>	<i>A</i>	<i>A</i>	<i>A</i>

Note: Shaded areas represent adequate reliable data.

CAS RN and data in italics are for additional chemicals [non-HPV].

Reliable data for acute toxicity by any of the three routes of exposure are considered adequate under the EPA HPV Challenge Program.

A = Adequate reliable data exist.

C = Endpoint fulfilled by category read-across from existing or proposed test data.

**Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV)
Chemicals Challenge**

Assessment of Data Availability

Prepared for:

**American Chemistry Council
Fatty Nitrogen Derivatives Panel
Cationics Task Group**

Prepared by:

Toxicology/Regulatory Services, Inc.

December 13, 2001

Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge Assessment of Data Availability

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Appendix B

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Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge Assessment of Data Availability

Introduction

Surfactants have a long history of safe use and have been studied extensively for environmental fate and effects and human health effects. The Fatty Nitrogen Derived (FND) Cationics Category chemicals are similar to the surfactants class in general as to physical/chemical properties, environmental fate and toxicity. Some typical applications of FND Cationics Category chemicals are: fabric softeners, multifunctional liquid laundry detergents, antistatic sprays, germicides, deodorizers, emulsifiers, hair-care preparations, and industrial lubricants and corrosion inhibitors (Boethling and Lynch, 1992).

Of the three non-HPV chemicals included in the FND Cationics Category, DDAC and ADBAC are FIFRA registered antimicrobial chemicals with germicidal, fungicidal and algicidal activity. They are used extensively as bactericides, fungicides, sanitizers, deodorants and disinfectants in the restaurant, dairy, food, laundry and medical industries (Ministry of Environment, Lands, and Parks, 1992). The third non-HPV chemical included in the FND Cationics Category, TMAC, is a trialkyl quat of similar use as the HPV chemicals.

The low order of toxicity indicates that the use of FND Cationics Category chemicals does not pose a significant hazard to human health.

Definition of Fatty Nitrogen Derived (FND) Cationics Structure-Based Chemical Category

The FND Cationics Category is comprised of 13 separate quaternary ammonium compounds (quats) with unique Chemical Abstracts Service Registry Numbers (CAS RNs; see Text Table A). The chemicals in the FND Cationics Category consist of the following:

Five mono-alkyl chain quats (CAS RNs 112-00-5, 112-02-7, 8030-78-2, 112-03-8 and 68607-29-4); seven di-alkyl chain quats (CAS RNs 61789-77-3, 68391-05-9, 68002-59-5, 68783-78-8, 68002-58-4, 61789-80-8 and 61789-81-9); and one tri-alkyl chain quat (CAS RN 67784-77-4).

In addition, three non-HPV chemicals, which are structurally closely-related to the FND Cationics Category, were identified to provide supplemental data for the category. These supporting chemicals consist of a tri-alkyl chain quat (tricetylmethyl ammonium chloride, i.e. TMAC; CAS RN 52467-63-7), a di-alkyl chain quat (didecyldimethylammonium chloride, i.e. DDAC; CAS RN 7173-51-5) and a benzyl mono-alkyl chain quat (Alkyl (C12-16) dimethylbenzylammonium chloride; i.e. ADBAC; CAS RN 68424-85-1), with similar toxicologic properties to DDAC. Although full reports for DDAC and ADBAC could not be obtained by the FND Cationics HPV Task Group, and therefore, Robust Summaries could not be prepared, official government reviews (U. S. EPA Data Evaluation Records for ADBAC and summaries for DDAC) of the toxicity, environmental fate and ecotoxicity studies for these chemicals were available and are considered reliable to support fulfilling HPV endpoints for the

FND Cationics Category (U. S. EPA Data Evaluation Report [DERs]; Environment Canada 1998; and Ministry of Environment, Lands, and Parks, 1992; see Appendix B).

U. S. EPA clustered quaternary ammonium compounds into four groups for the purpose of toxicology testing needed for reregistration under FIFRA (U. S. EPA, 1988). Although the FND Cationics Category chemicals are not part of this FIFRA reregistration, based on their structures, they all fit into Group I of the EPA clustering scheme. EPA designated DDAC as the representative member of Group I, meaning that data developed for this chemical would be representative for the other quats in the Group. ADBAC was designated by EPA as representative of a second group, Group II, of quaternary ammonium compounds, those with a benzyl substituent. For the purpose of determining environmental toxicity, DDAC and ADBAC remained the representative members of their respective groups (U.S. EPA, 1993). It was determined during the testing for reregistration under FIFRA that, despite their structural diversity, the quats included in EPA Groups I and II all had similar toxicological, environmental fate and ecotoxicological profiles. The FND Cationics Category chemicals appropriately fit into the EPA scheme for Group 1, and the inclusion of data for DDAC in support of the category is appropriate. Although the FND Cationics Category chemicals do not include benzene substituted quaternary amines, the similar toxicological profile for ADBAC and DDAC warrant the inclusion of ADBAC as a second supporting chemical for the category.

The FND Cationics Category chemicals and supporting non-HPV chemicals are identified in the following table:

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112-02-7	Ammonium, hexadecyltrimethyl-, chloride
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112-03-8	Trimethyloctadecylammonium chloride
7173-51-5 non-HPV	<i>Didecyldimethylammonium chloride (DDAC)</i>
61789-77-3	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides
68002-59-5	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides
68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates
61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride
61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates
52467-63-7 non-HPV	<i>1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride (Tricetylmethyl ammonium chloride, TMAC)</i>
67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides
68607-29-4	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride
68424-85-1 non-HPV	<i>Alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC)</i>

Structural Information for the FND Cationics Category and Supplemental Chemicals

The following table presents the molecular formula and molecular weight data for the chemicals with defined structures or structures for which average chain lengths can be determined. The structures for these and the remaining chemicals in the FND Cationics Category and non-HPV chemicals are provided in Table 1.

Text Table B: Molecular Formula and Molecular Weight of Chemicals with Defined Structures

CAS RN	Name	Molecular Formula	Molecular Weight
112-00-5	Ammonium, dodecyltrimethyl-, chloride	C ₁₅ H ₃₄ NCl	263
112-02-7	Ammonium, hexadecyltrimethyl-, chloride	C ₁₉ H ₄₂ NCl	319
112-03-8	Trimethyloctadecylammonium chloride	C ₂₁ H ₄₆ NCl	347
<i>7173-51-5</i>	<i>Didecylmethylammonium chloride</i>	<i>C₂₂H₄₈NCl</i>	<i>361</i>
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides	C ₃₂ H ₇₄ NCl ^a	507
68002-59-5	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides	C ₃₄ H ₇₈ NCl ^b	535
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates	C ₃₃ H ₇₇ NSO ₄ ^a	583
<i>52467-63-7</i>	<i>Tricetylmethyl ammonium chloride</i>	<i>C₄₉H₁₀₂NCl</i>	<i>739</i>
<i>68424-85-1</i>	<i>Alkyl (C12-16) dimethylbenzylammonium chloride</i>	<i>C₂₃H₄₅NCl^c</i>	<i>370</i>

Entries in italics are non-HPV chemicals

^a Based on average chain length = 15

^b Based on average chain length = 16

^c Based on average chain length = 14

Rationale for the FND Cationics Structure-Based Chemical Category

The FND Cationics Category surfactants are included as a single HPV chemical category based on the following generalities:

- Structural and functional similarities of cationic surfactants;
- Similar measured and modeled physical properties such as melting point, boiling point, vapor pressure, partition coefficient (log K_{ow}) and water solubility;
- Similar biodegradability;
- Aquatic toxicity observed at low concentrations, as observed with surfactants in general;
- Moderate to negligible mammalian toxicity;

- Similar uses and disposition patterns in the environment; and
- Chemicals of the Category fitting into a “clustering” group established by EPA during the reregistration of quaternary ammonium compounds used as antimicrobials under FIFRA.

Available Data to Fulfill HPV Screening Information Data Set (SIDS) Endpoints

Approach to Evaluate the Database for the FND Cationics Category

The following approach was used to obtain and analyze data relevant to the assessment of the FND Cationics Category.

1. The chemical names and CAS RNs of the 13 HPV FND Cationics Category chemicals supported by the American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group (Task Group) were provided.
2. The names of three non-HPV chemicals and their CAS registry numbers, structurally and functionally similar to the members of the proposed FND Cationics Category, were added.
3. Available published and unpublished reports were obtained from the members of Task Group and other chemical industry companies; they were organized and reviewed to identify studies that could fulfill SIDS endpoints.
4. Pertinent databases¹ were searched and all relevant reports were obtained to establish the full extent and nature of the published literature for the 13 FND Cationics Category and three non-HPV supplemental chemicals.
5. Each of the reports obtained was reviewed (except government reports for DDAC and ADBAC, which were considered to be reliable *a priori*) to determine adequacy according to EPA criteria and reliability according to Klimisch *et al.* (1997).
6. Robust summaries were prepared for each report with Klimisch scores of 1 or 2, according to the guidelines proposed by the EPA (U. S. EPA, 1999a) for each study type.
7. Estimates for physical/chemical properties, environmental fate and ecotoxicity values were developed by using appropriate Quantitative Structure Activity Relationships (QSARs).
8. Fugacity modeling was performed to estimate transport and distribution into environmental compartments for the HPV and non-HPV chemicals.

¹ Databases include ChemIDplus HSDB (Hazardous Substances Data Bank), IRIS (Integrated Risk Information System), CCRIS (Chemical Carcinogenesis Research Information System), GENE-TOX, EMIC (Environmental Mutagen Information Center), DART/ETIC (Developmental and Reproductive Toxicology and Environmental Teratology Information Center), MEDLINE, TOXLINE, RTECS (Registry of Toxic Effects of Chemical Substances), TSCATS (Toxic Substances Control Act Test Submissions), IUCLID, 1996 (International Uniform Chemical Information Database)

Use of Structure Activity Relationships for the FND Cationics Category

Approaches recommended in the EPA document on the use of structure activity relationship (SAR) in the HPV Chemicals Challenge Program were employed in the assessment of the FND Cationics Category (U. S. EPA, 1999b). Several models were employed to support the review and assessment of the FND Cationics Category chemicals. The models included several based on structure-activity relationships (SAR), as well as Mackay-type fugacity-based modeling. The SAR models for physical properties were used to estimate boiling point, melting point, aqueous solubility, octanol-water partition coefficient and vapor pressure. Other SAR models were used to estimate hydroxyl radical mediated atmospheric photo-oxidation and biodegradation potential. SAR models also were used to obtain conservative estimates of acute toxicity to aquatic organisms.

Common Features of the Models

All of the models (except the Mackay-type models) require the input of a molecular structure to perform the calculations. The structure must be entered into the model in the form of a SMILES (Simplified Molecular Input Line Entry System) notation or string. SMILES is a chemical notation system used to represent a molecular structure by a linear string of symbols. The SMILES string allows the program to identify the presence or absence of structural features used by the submodels to determine the specific endpoint. The models contain files of structures and SMILES strings for approximately 100,000 compounds, accessible via CAS RNs. SMILES strings cannot be developed for mixtures or chemicals without a single, definable structure.

Estimation of Physical/Chemical Properties

The SAR models for estimating physical properties and abiotic degradation were obtained from Syracuse Research Corporation 2000 (Estimation Programs Interface for Windows, Version 3.05 or EPIWIN v.3.05). The models were used to calculate melting point, boiling point, vapor pressure (submodel MPBPVP), octanol-water partition coefficient (K_{ow}) (submodel KOWWIN) and aqueous solubility (submodel WSKOWWIN). The calculation procedures are described in the program guidance and are adapted from standard procedures based on analysis of key structural features (Meylan and Howard, 1999a, b and c).

Estimation of Environmental Fate Properties

Atmospheric photo-oxidation potential was estimated using the submodel AOPWIN (Meylan and Howard, 2000a). The estimation methods employed by AOPWIN are based on the SAR methods developed by Dr. Roger Atkinson and co-workers (Meylan and Howard, 2000a). The SAR methods rely on structural features of the subject chemical. The model calculates a second-order rate constant with units of $\text{cm}^3/\text{molecules}\cdot\text{sec}$. Photodegradation based on atmospheric photo-oxidation is in turn based on the rate of reaction ($\text{cm}^3/\text{molecules}\cdot\text{sec}$) with hydroxyl radicals ($\text{HO}\bullet$), assuming first-order kinetics and an $\text{HO}\bullet$ concentration of $1.5 \text{ E} + 6 \text{ molecules}/\text{cm}^3$ and 12 hours of daylight. Pseudo first-order half-lives ($t_{1/2}$) were then calculated as follows: $t_{1/2} = 0.693/[(k_{\text{phot}} \times \text{HO}\bullet) \times (12\text{-hr}/24\text{-hr})]$.

The database that supports the modeling of water stability provides only for neutral organic compounds that have structures that can be hydrolyzed. Therefore, no model estimates for

hydrolytic stability are available since the FND Cationics Category chemicals do not have the necessary characteristics.

Biodegradation potential was estimated using the submodel BIOWIN (Meylan and Howard, 2000b). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental micro-organisms. Estimates are based on fragment constants that were developed using multiple linear and nonlinear regression analyses (Meylan and Howard, 2000b). BIOWIN uses the probabilities to estimate a potential pseudo first-order half-life for aerobic biodegradation of the subject chemical in surface water, soil and sediment.

Estimation of Environmental Distribution

The Level 3 Mackay-type, fugacity-based models were obtained from the Trent University's Modeling Center. The specific model used was the generic Equilibrium Concentration model (EQC) Level 3, version 1.01. These models are described in Mackay *et al.* (1996a and b). Fugacity-based modeling is based on the "escaping" tendencies of chemicals from one phase to another. For instance, a Henry's Law constant calculated from aqueous solubility and vapor pressure is used to describe the "escape" of a chemical from water to air or vice versa, as equilibrium between the phases is attained. The key physical properties required as input parameters into the model are melting point, vapor pressure, K_{ow} and aqueous solubility. The model also requires estimates of first-order half-lives in the air, water, soil and sediment. An additional key input parameter is loading of the chemical into the environment.

Estimation of Acute Aquatic Toxicity

Models developed by the U. S. Environmental Protection Agency (EPA) were employed to make estimates of acute toxicity to aquatic organisms, specifically to the fathead minnow (*Pimephales promelas*), a commonly tested fish; a water column dwelling invertebrate (*Daphnia magna*); and a commonly tested green alga, *Selenastrum capricornutum*. The models are incorporated in a modeling package called ECOSAR, version 0.99f (U. S. EPA, 2000). ECOSAR may be obtained from the EPA website for the Office of Pollution Prevention and Toxics, Risk Assessment Division. The models calculate inherent toxicity based on structural features and physical properties, mainly the K_{ow} (Meylan and Howard, 1998).

Modeling Information Specific to the FND Cationics Category

When CAS RNs were included in the files of structures, the models described above were used for the FND Cationics Category chemicals and the three non-HPV chemicals. Estimations of physical properties, environmental fate and distribution, and ecotoxicity were not possible for 10 of the 13 HPV chemicals in the FND Cationics Category because they do not have single definable structures and/or were not available in the files of structures of the models. Model predictions were available for the three non-HPV chemicals. As noted above, the ECOSAR models are heavily dependent on calculation of the octanol/water partition coefficient, K_{ow} . Therefore, it is important to note that, for cationic substances, K_{ow} estimation is of limited value in estimating their physical properties or behavior in the environment. An inherent property of cationic surfactants is that they accumulate at the interface between two phases. Thus, the accurate measurement of the K_{ow} for any surfactant is difficult. Even if such measurements were made accurately, the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting

environmental behavior. Cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. The model did not provide estimates of stability in water for this class of chemicals because the model cannot calculate this parameter for chemicals that do not meet the criteria of neutral organic compounds with structures that can be hydrolyzed. Since the FND Cationics Category chemicals are considered to be released into wastewater treatment systems (Boethling and Lynch, 1992) for treatment prior to release into surface water, release to soil and air were considered to be minor avenues of entry for FND Cationics Category chemicals into the environment. Therefore, for fugacity modeling, all input was assumed to be into surface water using the chemical specific parameters to attain estimates of the chemical distributions between environmental compartments. The ECOSAR model has not been developed to provide an estimate of toxicity to aquatic plants for the cationic surfactants.

Availability of Reliable Data for the FND Cationics Category

Robust summaries for SIDS/HPV endpoint studies and other supporting studies with reliable data (according to Klimisch criteria) for the HPV chemicals and tricetylmethyl ammonium chloride (TMAC; non-HPV chemical) are provided in Appendix A and are summarized in Tables 2 through 4. Data for the non-HPV chemicals, DDAC and ADBAC, obtained from U. S. EPA Data Evaluation Reports, Environment Canada (1998) and Ministry of Environment, Lands, and Parks (1992), are included in Appendix B and are summarized in Tables 2 through 4.

Reliable data were available for one HPV chemical (CAS RN 61789-80-8) for melting point and water solubility to meet the physical/chemical properties SIDS/HPV endpoints. Reliable, measured melting point, boiling point, vapor pressure, octanol/water partition coefficient, and water solubility values were available for the non-HPV chemical, TMAC. In addition, Environment Canada (1998) includes partition coefficient and water solubility information for the non-HPV chemical, DDAC.

Reliable data were available for environmental fate and ecotoxicity endpoints as shown in the following table:

Text Table C: Number of Available Reliable Environmental Fate and Ecotoxicity Studies

CAS RN	Photodegradation	Biodegradation	Acute Tox. to Fish	Acute Tox. to Invertebrates	Acute Tox. to Aquatic Plants	Chronic Tox. to Aquatic Species
112-00-5		2	1	2		7
112-02-7		3	1			1
8030-78-2		4		1		1
112-03-8		1	1			
7173-51-5 <i>non-HPV</i>		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	
61789-77-3		2				
68391-05-9						
68002-59-5						
68783-78-8			2	6 ^b	2 ^b	3
68002-58-4						
61789-80-8	1	2	4 ^b	1 ^b	1 ^b	
61789-81-9						
52467-63-7 <i>non-HPV</i>		2	1	1	1	2 ^c
67784-77-4						
68607-29-4		1				
68424-85-1 <i>non-HPV</i>			<i>a</i>	<i>a</i>		<i>a</i>

Note: Empty block denotes data were not found or that relevant data were found but judged inadequate.

^a Data for the non-HPV chemicals DDAC and ADBAC are taken from Ministry of Environment, Lands, and Parks, 1992 and/or Environment Canada, 1998 (DDAC), or U. S. EPA DERs (ADBAC) and are included in Appendix B.

^b More than one value for different species may be summarized in one Robust Summary (Appendix A).

^c Includes a bacterial toxicity study

Reliable data were available for human health-related toxicity endpoints as shown in the following table:

Text Table D: Number of Available Reliable Human Health-Related Studies

CAS RN	Acute Oral Tox.	Acute Inhalation Tox.	Acute Dermal Tox.	Repeated Dose Tox.	Genetic Tox.	Toxicity to Reproduction	Developmental Tox.
112-00-5	2				4		1
112-02-7	1		1	1	3		1
8030-78-2	1		2		2		
112-03-8	1				1		1
7173-51-5 <i>non-HPV</i>	<i>a</i>		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
61789-77-3	1				1		
68391-05-9	1			1			
68002-59-5							
68783-78-8	1				1		1
68002-58-4							
61789-80-8	2	1		2		1 ^b	
61789-81-9				1		1 ^b	1
52467-63-7 <i>non-HPV</i>	1		1	1	2		
67784-77-4							
68607-29-4	1						
68424-85-1 <i>non-HPV</i>				<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>

Note: Empty block denotes data were not found or that relevant data were found but judged inadequate.

^a Data for the non-HPV chemicals DDAC and ADBAC are taken from Ministry of Environment, Lands, and Parks, 1992 and/or Environment Canada, 1998 (DDAC), or U. S. EPA DERs (ADBAC) and are included in Appendix B.

^b Repeated dose toxicity study meets the SIDS requirement for a reproductive screen (i.e. histological evaluation of reproductive organs).

Physical/Chemical Properties QSAR Estimates and Correlation to Reliable Data

The available reliable data and QSAR estimates for physical/chemical properties of the FND Cationics Category chemicals are presented in Table 2. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

As described above, the physical/chemical property estimation program, EPIWIN 1.c. 3.05, was used to derive estimates. The EPIWIN estimates must be interpreted with a great deal of professional judgment.

The QSAR estimates are based on structure and, therefore, can be made only for substances for which a structure can be defined. Thus, a complete set of model data was generated for three of the 13 HPV chemicals with discrete structures (CAS RNs 112-00-5, 112-02-7 and 112-03-8). In addition, model predictions for physical/chemical properties were generated for the three non-

HPV chemicals, DDAC, TMAC and ADBAC. The compositional variability of the chemicals without definable structures also makes the experimental measurement of physical/chemical properties of these chemicals of minimal practical value for prediction of their environmental behavior or toxicological properties. Therefore, the chemicals in the FND Cationics Category without defined structures are best supported by the other chemicals in the category for which the properties can be measured and/or modeled.

The available data for physical/chemical properties are summarized below:

EPIWIN predicted melting points ranged from 182 to 350 °C. The available measured value, for CAS RN 61789-80-8 was 50 to 60 °C, but this chemical could not be modeled to allow comparison of measured to modeled data. For the non-HPV chemical, TMAC, the measured value of 46.0 to 53.5 °C compared poorly with the model estimate of 350°C. Estimates made for boiling points ranged from 454 to 848 °C. The modeled value for TMAC, 848 °C, compared poorly with the measured value of 121.5 °C. However, the low boiling point measurement was thought to be the result of impurities; the “true boiling point” was estimated from the experimental work and theoretical properties of the chemical to be > 2000 °C .

As expected, based on extensive practical experience with these and similar large organic molecules, the EPIWIN estimated vapor pressures were extremely low for the three FND Cationics Category chemicals, and the non-HPV chemicals, DDAC and ADBAC (i.e. nine to 11 orders of magnitude lower than water). A high vapor pressure was reported for the non-HPV chemical, TMAC (1.8 mm Hg). However, this value was considered erroneous and likely due to solvent impurities in the sample. The FND Cationics Category chemicals are essentially nonvolatile, as is generally the case for molecules of this size and complexity.

The EPIWIN estimated values for the octanol/water partition coefficient ($\log K_{ow}$) ranged from 1.22 to 17.9. The value of 4.66 for the non-HPV chemical, DDAC, is compared with the stated $\log K_{ow}$ of zero (Appendix B; Ministry of Environment, Lands, and Parks, 1992). The value of 17.9 for the non-HPV chemical, TMAC, suggests that the model cannot adequately calculate values for molecules of such high molecular weight. Attempts to measure the partition coefficient for TMAC did not produce a definitive value with the specified result being > 5.9.

Model predictions for water solubility ranged from insoluble for the non-HPV chemical, TMAC, to slightly soluble (1795 mg/l for CAS RN 112-00-5). The measured value for water solubility of the HPV chemical, CAS RN 61789-80-8, indicated very low solubility of < 0.001 mg/l. The modeled value (0.55 mg/l) for the non-HPV chemical, DDAC, is compared with the published information that the chemical has a water solubility of 700 mg/l (Appendix B; Environment Canada, 1998); this difference in modeled and measured values is consistent with the difference in $\log K_{ow}$ noted above. Measurement of water solubility for the non-HPV chemical, TMAC, indicated that the chemical forms a colloidal dispersion in water and the solubility was < 10 mg/l.

Summary - Physical/Chemical Properties

For melting points, model estimates were approximately 3 to 9 times higher than the available measured values. Boiling points were estimated to be high and it is probable that these chemicals would degrade before boiling. Vapor pressures were estimated to be very low (except

for the non-HPV chemical, TMAC, where contaminants were thought to confound the measurement), as expected, and the FND Cationics Category chemicals were considered to be essentially nonvolatile. Water solubility estimates varied from insoluble to slightly soluble, with higher solubility predictions tending to occur for lower molecular weight chemicals. Log K_{ow} values less than 5 were predicted for all of the chemicals that could be modeled, except for the non-HPV chemical, TMAC. As noted previously, measurement and prediction of physical/chemical properties for surfactants are complicated by their behavior in test systems and the environment, and the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior. Although predictions vary, the overall data and knowledge of the chemicals support the conclusion that the FND Cationics Category chemicals have closely related structures and behave similarly from the perspective of physical/chemical properties.

Environmental Fate and Ecotoxicity QSAR Estimates and Correlation to Reliable Data

The available reliable data and QSAR estimates for the environmental fate and effects of the FND Cationics Category chemicals are presented in Table 3. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Models for atmospheric photodegradation were used according to EPA guidelines. However, the fugacity models predict virtually no occurrence of the FND Cationics Category chemicals in air. Nonetheless, modeling of the HPV and non-HPV substances indicates that these chemicals would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 2.8 to 5.9 hours). In addition, a measurement for CAS RN 61789-80-8 adsorbed to silica indicated some evidence of photodegradation.

The HYDROWIN model did not provide estimates of stability in water for this class of chemicals because the model cannot calculate this parameter for chemicals that do not meet the criteria of neutral organic compounds with structures that can be hydrolyzed.

An estimation of the transport and distribution of the FND Cationics Category chemicals in environmental media (percent in air, water, soil and sediment) following entry into the environment via water is presented in Table 3. For the HPV and non-HPV chemicals, the model predicts distribution to the water and/or sediment correlated with the predicted water solubility (see above). For chemicals with higher predicted water solubility (CAS RNs 112-00-5 and 112-02-7), the distribution predictions were > 98% to water. For chemicals with lower predicted water solubility (CAS RN 112-03-8, DDAC, ADBAC, and TMAC), the predictions for water distribution ranged from approximately 5% to 90%, with the remainder primarily in sediment. Some of these estimates may be inaccurate based on the differences in modeled and measured water solubility described above.

For biodegradation, measured data exist for seven of the 13 FND Cationics Category chemicals. In a number of cases, data were available for a two-day, non-standard measurement which indicated very rapid degradation. These tests, measuring disappearance of test substance, are considered of limited value since the high “degradation” is not confirmed in standard tests and presumably the test substance was adsorbed. Other assays indicated degrees of biodegradation

varying from none detected to values that would be considered inherently degradable. For the non-HPV chemical, ADBAC, the most recent review by Environment Canada (1998; Appendix B) concludes, “It is not persistent in the water column; movement to the solid phase and microbial degradation are expected to be the main routes of dissipation.” The biodegradation for the non-HPV chemical, TMAC, indicated that no degradation was observed, which was thought most likely to be due to adsorption. In a SCAS test with TMAC, 100% removal was observed in 10 days either via degradation or adsorption. Model predictions for biodegradation were made for the three HPV chemicals in the category with definable structures, as well as for the three non-HPV chemicals. For the two cases for which modeled data could be compared to measured values for HPV chemicals, the model predictions were relatively accurate (e.g. predictions of $t_{1/2}$ values of 15 days for both chemicals with measured degradation rates of approximately 35% in 10 days and of approximately 50% in 28 days). Adsorption phenomena were considered significant confounders in the non-HPV chemical degradation measurements, and thus measured and modeled data could not be compared.

More than 30 studies evaluating the acute and chronic toxicity of the FND Cationics HPV chemicals to aquatic organisms were available. Reliable data for aquatic toxicity of the non-HPV chemicals was also available. In addition, ECOSAR estimates for acute fish and daphnid toxicity were made for the three HPV chemicals with defined structures. The model could not estimate toxicity to algae for these chemicals. Measured acute fish toxicity data were available for five of the 13 FND Cationics Category chemicals and the three non-HPV chemicals. In three of six cases for HPV and non-HPV chemicals, model predictions could be compared to measured values; the model prediction was accurate for CAS RN 112-00-5 (9.77 mg/l for the model and 6.0 mg/l measured), DDAC (2.3 mg/l for the model and a range of approximately 0.3 to 2.8 mg/l measured) and ADBAC (1.78 mg/l for the model and measured values of approximately 0.5 mg/l). The model under-predicted the toxicity for CAS RN 112-02-7 (2.24 mg/l for the model and 0.07 mg/l measured), CAS RN 112-03-8 and TMAC (not toxic at solubility predicted by the model for each chemical, compared to measured values of 0.07 mg/l and approximately 15.1 mg/l, respectively). Measured EC_{50} values for acute toxicity to invertebrates were available for four HPV and the three non-HPV chemicals (values ranging from 0.006 to > 50 mg/l). For CAS RN 68783-78-8, studies for daphnia, Ceriodaphnia, Eastern oyster, mysid shrimp, Pink shrimp and Blue crabs were included in the dataset. Modeled values for acute toxicity to aquatic invertebrates were made for the three FND Cationics Category chemicals and two of the three non-HPV chemicals (TMAC and ADBAC; the model did not provide a value for DDAC). The predicted values were similar to those for fish and none were accurate, with ADBAC modeled value of 1.78 mg/l compared to approximately 0.05 mg/l measured and CAS RN 112-03-8 and TMAC predicted to have no toxicity at solubility with measured values of approximately 0.07 and approximately 15.1 mg/l, respectively. Two FND Cationics Category chemicals (CAS RNs 68783-78-8 (2 studies) and 61789-80-8) had measured EC_{50} values for toxicity to aquatic plants ranging from 0.21 to ≤ 10 and 0.026 to 1.8 mg/l, respectively. A study with TMAC indicated E_bC_{50} (growth; 0-96-hour) of 0.113 mg/l and E_rC_{50} (growth rate; 0-96-hour) of 0.177 mg/l. The Ministry of Environment, Lands, and Parks, (1992; Appendix B) states that the non-HPV chemical, DDAC, is toxic to aquatic plants at approximately 3.5 mg/l.

In addition to the SIDS/HPV endpoints for acute toxicity to aquatic species, chronic toxicity studies with aquatic organisms have been conducted for several FND Cationics Category

chemicals. These include studies with fish, Ceriodaphnia, clams, and rotifers for CAS RN 112-00-5 (NOECs and LC₅₀ values ranging from approximately 0.05 to >1.25 mg/l), a rotifer study for CAS RN 112-02-7 (LC₅₀ value of 0.067 mg/l), a daphnid study for CAS RN 8030-78-2 (NOEC = 6.8 – 99.1 µg/l, and a fish and Ceriodaphnia study for CAS RN 68783-78-8 (NOECs of 12.7 and 0.7 – 0.82 mg/l, respectively). In addition, a toxicity study to bacteria (EC₅₀ = 371 mg/l) and chronic toxicity to aquatic invertebrates (NOECs of 0.04, 0.04, and 0.08 mg/l for toxicity, reproduction, and time to first brood, respectively) were available for TMAC. A chronic toxicity to aquatic invertebrates and a fish early life stage assay were also available for ADBAC, with NOECs of 0.00415 and 0.0322 mg/l, respectively.

Summary – Environmental Fate and Ecotoxicity

As anticipated in the EPA guidance for HPV chemicals, only model estimates were available for atmospheric photodegradation and fugacity. The other exclusively modeled value, stability in water, could not be calculated for this category of chemicals. Atmospheric photodegradation was predicted to be rapid, although fugacity models suggested very minimal distribution of these chemicals to the air. Some evidence of photodegradation of one of the FND Cationic Category chemicals was observed when the chemical was bound to silica. Predicted distribution of the chemicals in the environment was to water and/or sediment compartments based on the assumption that release of the chemicals to the environment is exclusively via water. For chemicals with higher predicted water solubility (lower K_{ow}), the water compartment was favored. Measured biodegradation rates were variable and frequently confounded by adsorption. Overall, the FND Cationic Category chemicals are biodegradable, which is consistent with the conclusion of Environment Canada for the non-HPV chemical, DDAC. Measured aquatic toxicity values indicated acute LC₅₀ and EC₅₀ values generally less than approximately 25 mg/l for fish, daphnid and algae (a single study indicated an LC₅₀ > 24 mg/l for fish). Other species may be less sensitive to the toxicity of these surfactants with acute LC₅₀ values of 36 and > 50 mg/l recorded for shrimp and crabs, respectively. Chronic toxicity to aquatic organisms varied considerably, with NOECs ranging from 4.15 µg/l to 12.7 mg/l. These studies of aquatic toxicity, many of which were conducted in natural waters with and without added effluents, indicate that the source and composition of the test water dramatically affects the toxicity of the test substance. As noted previously, cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. Thus the extreme variability of the measured values is predictable. Further, as would be anticipated, the modeling programs were inconsistent in their accuracy for aquatic toxicity endpoints with some values similar to measured or expected and others divergent. Overall, the available data support the conclusion that, because of their closely-related structures, FND Cationics Category chemicals possess similar environmental fate and ecotoxicity across the category.

Human Health-Related Reliable Data

The human health effects data for SIDS endpoints of the 13 FND Cationics Category chemicals and three related supplemental chemicals are presented in Table 4. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in

Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Rat acute oral toxicity LD₅₀ data were available for nine of the 13 FND Cationics Category chemicals and two of the non-HPV chemicals, TMAC and DDAC. For the FND Cationics Category chemicals, rat oral LD₅₀s range from approximately 200 to > 2000 mg/kg indicating that the chemicals possess moderate to slight acute toxicity by the oral route. Stated LD₅₀ values for DDAC ranged from approximately 60 to 400 mg/kg and a value > 16,300 mg/kg was determined for TMAC. Rabbit acute dermal toxicity studies for two FND Cationics Category chemicals (CAS RN 112-02-7 and 8030-78-2) failed to confirm an LD₅₀ but suggest that the value is slightly less than 4000 mg/kg indicating these chemicals have minimal acute toxicity in rabbits via skin application. Percutaneous LD₅₀s for DDAC ranged from > 228 to > 3480 mg/kg, and a percutaneous LD₅₀ > 2000 mg/kg was determined for TMAC. In addition, an acute inhalation study for the FND Cationics Category chemical, CAS RN 61789-80-8, indicted this chemical caused no toxicity at > 180 mg/l following a 1-hour exposure. Additional information (included as Additional Remarks in Robust Summaries Appendix A) indicated very little skin penetration (≈ 0.5% of the dose) of CAS RN 68391-05-9 following a single application of radiolabeled chemical.

A repeated dose toxicity study was available for four of the FND Cationics Category chemicals (CAS RNs 112-02-7, 68391-05-9, 61789-80-8 and 61789-81-9). Repeated dermal dose studies in rabbits for CAS RNs 112-02-7 (28-day) and 68391-05-9 (13-weeks) were conducted using a single dose of 10 mg/kg/day since this was the highest dose that could be applied based on irritation. No effects except for mild irritation were observed. For CAS RN 61789-80-8, a 90-day toxicity study in dogs was reported with a NOAEL > 100 mg/kg/day, the highest dose tested. There were no effects related to toxicity of the test substance in this study. Skin irritation but no other toxic effects were observed following 13 weeks of dermal dosing in rabbits with 10 or 140 mg/kg/day. Additional information (included as Additional Remarks in Robust Summaries Appendix A) indicated that following 90 days of dosing 2800 ppm of this chemical in the diet of rats, approximately 16% of the consumed dose was found in the excreta of males and 6% in excreta of females. In a rat subchronic study of 13 or 22 weeks duration, no NOAEL was established for CAS RN 61789-81-9. The LOAEL was reported to be 170 mg/kg/day. The treatment-associated changes observed were principally in the mesenteric and pulmonary lymph nodes, adrenal glands and liver. A number of subchronic and chronic toxicity studies were available for the three non-HPV chemicals (DDAC, TMAC and ADBAC). At high doses (approximately 500 mg/kg/day and greater) DDAC and ADBAC are lethal to rats due to localized effects in the gastrointestinal tract. At doses below those that result in severe, direct effects on the g.i. tract, these studies indicate no organ-specific toxicity, with effects in 90-day and chronic toxicity studies limited to body weight changes and other general responses. NOAELs for the studies with DDAC ranged from 10 mg/kg/day in a chronic dog study to > 100 mg/kg/day in 90-day rat studies. The NOAELs for studies with ADBAC were > 20 mg/kg/day for a dermal 90-day study in rats (dose levels limited by irritant properties of the test substance) and approximately 40 mg/kg/day for an oral 90-day study in rats. The NOAEL for ADBAC was approximately 80 mg/kg/day for chronic toxicity studies in rats and mice. A subchronic study with TMAC reported a NOAEL of 40 mg/kg/day with histiocytic hyperplasia of the mesenteric lymph nodes being the only finding of significance at 200 and 1000 mg/kg/day.

In vitro genetic toxicity studies (*Salmonella* reverse mutation assay) for five of the FND Cationics Category chemicals were identified. CAS RN 112-00-5 was negative in a standard assay. Three tests for two of the chemicals (CAS RNs 112-02-7 and 112-03-8) indicated no mutagenic activity, but only two tester strains were evaluated. Inconsistent results were observed for CAS RN 8030-78-2 with one test indicating no mutagenic activity and a second showing a minimal, three-fold, increase in back mutations in one of the cell lines tested. A test with CAS RN 61789-77-3 was negative in the four tester strains used. CAS RN 112-00-5 was also negative in the *in vitro* mouse lymphoma and UDS assays as well as in an *in vivo* cytogenetics assay. A nonstandard *in vitro* test examining morphological transformations for CAS RN 112-02-7 was also negative and an *in vivo* mouse micronucleus assay for CAS RN 68783-78-8 was negative. Results from a series of *in vitro* tests were available for the two non-HPV chemicals, DDAC and ADBAC. There were no mutagenic effects, no effect on DNA synthesis, and no chromosomal aberrations observed. In addition, a *Salmonella* reverse mutation assay and an *in vivo* mammalian bone marrow cytogenetics assay were negative for the non-HPV chemical, TMAC. Overall, the available data indicate the chemicals in the FND Cationics Category are unlikely to be mutagenic, as would be expected based on the structures, molecular weights, and knowledge of related chemicals.

For the FND Cationics Category chemicals, evaluation of potential reproductive effects is satisfied by the histological evaluation of reproductive organs in the repeat dose toxicity study in dogs for CAS RN 61789-80-8 and in rats for CAS RN 61789-81-9. No effects on the gonads or other reproductive organs were observed at any dose level in these studies. Thus the NOAELs for reproductive screening were > 100 mg/kg/day for CAS RN 61789-80-8 and > 750 mg/kg/day for CAS RN 61789-81-9. Two-generation reproduction studies in rats were available for the two non-HPV chemicals, DDAC and ADBAC. The NOAEL for DDAC was approximately 56 mg/kg/day for adult and offspring toxicity, with no reproductive effects found. For ADBAC, the NOAELs for toxicity were > 146 mg/kg/day for parents and 73 mg/kg/day for offspring, with no reproductive effects noted.

Developmental toxicity studies were available for five FND Cationics Category chemicals (CAS RNs 112-00-5, 112-02-7, 112-03-8, 68783-78-8 and 61789-81-9) and the two non-HPV chemicals, DDAC and ADBAC. For CAS RN 112-00-5, the oral NOAEL for maternal and developmental toxicity was 24 mg/kg/day with no embryo/fetal toxicity or teratogenicity observed. For CAS RNs 112-02-7, the percutaneous NOAEL for maternal and developmental toxicity in rabbits was > 10 mg/kg/day and for CAS RN 112-03-8, the percutaneous NOAELs for maternal and developmental toxicity in rats were > 12.5 mg/kg/day. No embryo/fetal toxicity or teratogenicity was observed in either study. Studies for CAS RNs 68783-78-8 and 61789-81-9 with two dose levels (100 and 500 mg/kg/day) via gavage and a single dietary concentration (to yield a target dose of 500 mg/kg/day) were available. The NOAEL for maternal toxicity for CAS RN 68783-78-8 was > 500 mg/kg/day via gavage but no NOAEL was established via diet, with minimal body weight and feed consumption changes noted. The developmental NOAEL for this chemical was > 500 mg/kg/day by either exposure route. For CAS RN 61789-81-9, the maternal and developmental NOAELs were greater than the highest dose by either route of exposure (500 or 475 mg/kg/day via gavage or diet, respectively). Results for two developmental toxicity studies were available for the non-HPV chemical, DDAC. The NOAELs for rabbits were 1.0 and 3.0 mg/kg/day for maternal and developmental toxicity, respectively.

Corresponding values for rats were 1.0 and 20.0 mg/kg/day. No teratogenic effects were observed for either species. For the non-HPV chemical, ADBAC, the oral maternal and developmental NOAELs were 10 and > 100 mg/kg/day, respectively for rats, and 3 and > 9 mg/kg/day for rabbits with no embryo/fetal toxicity or teratogenicity observed.

Summary – Human Health-Related Data

Adequate acute oral LD₅₀ studies were available throughout the category. They indicate minimal to moderate acute toxicity of the chemical class with LD₅₀ values ranging from approximately 60 to > 16,000 mg/kg. Repeat dose toxicity studies supported the conclusion that the chemicals in the FND Cationics Category have minimal toxicity potential below acutely toxic doses. Available *in vitro* and *in vivo* assays indicated the FND Cationics Category chemicals and supplemental chemicals are unlikely to have mutagenic activity. A reproductive screening evaluation from two repeat dose toxicity studies, two reproductive toxicity studies and results from available developmental toxicity studies, indicated that the FND Cationics Category chemicals are unlikely to cause reproductive effects and are not developmental toxicants. The available data support the conclusion that, because of their closely-related structures and similar physical/chemical properties, the FND Cationics Category chemicals possess similar human health-related effects across the category.

References

Boethling, R. S. and D. G. Lynch. 1992. Quaternary Ammonium Surfactants. *Handbook of Environ. Chem.* 3: 145 - 177.

Environment Canada. 1998. Water Quality Guideline for the Protection of Freshwater Aquatic Life for Didecyl Dimethyl Ammonium Chloride (DDAC). Guidelines and Standards Division, Science Policy and Environment Quality Branch, Environment Canada, Hull, Quebec, December 1998.

Ministry of Environment, Lands, and Parks. 1992. "A Review of the Environmental Impact and Toxic Effects of DDAC." Victoria, British Columbia.

Klimisch, H. J., M. Andreae and U. Tillmann. 1997. A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Reg. Toxicol. Pharmacol.* 25:1 - 5.

Mackay, D., A. Di Guardo, S. Paterson, G. Kicsi and C. E. Cowan. 1996a. Assessing the Fate of New and Existing Chemicals: A Five-stage Process. *Environ. Toxicol. Chem.* 15(9): 1618 - 1626.

Mackay, D., A. Di Guardo, S. Paterson and C. E. Cowan. 1996b. Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. *Environ. Toxicol. Chem.* 15(9): 1627 - 1637.

Meylan, W. and P. H. Howard. 1998. User's Guide for the ECOSAR Class Program, Version 0.99d. Syracuse Research Corporation, North Syracuse, NY.

Meylan, W. and P. H. Howard. 1999a. User's Guide for MPBPVP, Version 1.4. Syracuse Research Corporation, North Syracuse, NY.

Meylan, W. and P. H. Howard. 1999b. User's Guide for KOWWIN, Version 1.6. Syracuse Research Corporation, North Syracuse, NY.

Meylan, W. and P. H. Howard. 1999c. User's Guide for WSKOWWIN, Version 1.3. Syracuse Research Corporation, North Syracuse, NY.

Meylan, W. and P. H. Howard. 2000a. User's Guide for AOPWIN, Version 1.9. Syracuse Research Corporation, North Syracuse, NY.

Meylan, W. and P. H. Howard. 2000b. User's Guide for BIOWIN, Version 4.0. Syracuse Research Corporation, North Syracuse, NY.

Syracuse Research Corporation. 2000. Users Guide for Estimation Programs Interface for Windows, Version 3. Syracuse Research Corporation, North Syracuse, NY.

U. S. EPA. Data Evaluation Records (Tabs 1-20): See Appendix B.

U. S. EPA. 1988. PR Notice 88 – 2. Notice to Producers, Formulators, Distributors and Registrants: Clustering of Quaternary Ammonium Compounds. U. S. Environmental Protection Agency, Washington, DC.

U. S. EPA. 1993. Memorandum: OPPT's Structure Activity Clustering of OPP's Quaternary Ammonium Compounds for Environmental Toxicity. U. S. Environmental Protection Agency, Washington, DC.

U. S. EPA. 1999a. Draft Guidance on Developing Robust Summaries.
<http://www.epa.gov/chemrtk/robsumgd.htm>.

U. S. EPA. 1999b. The Use of Structure-activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. <http://www.epa.gov/chemrtk/sarfin11.htm>.

U. S. EPA. 2000. ECOSAR Program, Risk Assessment Division (7403). U. S. Environmental Protection Agency, Washington, DC.

Table 1. Structures of FND Cationics Category Chemicals

$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_{12}\text{H}_{25}-\text{N}^+-\text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>Ammonium, dodecyltrimethyl-, chloride 112-00-5</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_{16}\text{H}_{33}-\text{N}^+-\text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>Ammonium, hexadecyltrimethyl-, chloride 112-02-7</p>
$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R}-\text{N}^+-\text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = tallow alkyl</p> <p>Quaternary ammonium compounds, trimethyltallow alkyl, chlorides 8030-78-2</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_{18}\text{H}_{37}-\text{N}^+-\text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>Trimethyloctadecylammonium chloride 112-03-8</p>
$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_{10}\text{H}_{21}-\text{N}^+-\text{C}_{10}\text{H}_{21} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p><i>non-HPV</i> <i>Didecyltrimethylammonium chloride (DDAC)</i> 7173-51-5</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R}-\text{N}^+-\text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = coco alkyl</p> <p>Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides 61789-77-3</p>
$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R}-\text{N}^+-\text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = C₁₂ – C₁₈ alkyl</p> <p>Quaternary ammonium compounds, di-C₁₂₋₁₈-alkyldimethyl, chlorides 68391-05-9</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R}-\text{N}^+-\text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = C₁₄ – C₁₈ alkyl</p> <p>Quaternary ammonium compounds, di-C₁₄₋₁₈-alkyldimethyl, chlorides 68002-59-5</p>

Table 1. Structures of FND Cationics Category Chemicals (continued)

$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R} - \text{N}^+ - \text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = tallow alkyl</p> <p>Quaternary ammonium compounds, dimethylditallow alkyl, chlorides 68783-78-8</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R} - \text{N}^+ - \text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{CH}_3\text{SC}_4^-$ <p>R = C₁₄ – C₁₈ alkyl</p> <p>Quaternary ammonium compounds, di-C₁₄₋₁₈-alkyldimethyl, Me sulfates 68002-58-4</p>
$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R} - \text{N}^+ - \text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{Cl}^-$ <p>R = hydrogenated tallow alkyl</p> <p>Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride 61789-80-8</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R} - \text{N}^+ - \text{R} \\ \\ \text{CH}_3 \end{array} \right] \text{CH}_3\text{SC}_4^-$ <p>R = hydrogenated tallow alkyl</p> <p>Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates 61789-81-9</p>
$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{C}_{16}\text{H}_{33} - \text{N}^+ - \text{C}_{16}\text{H}_{33} \\ \\ \text{C}_{16}\text{H}_{33} \end{array} \right] \text{Cl}^-$ <p><i>non-HPV</i> <i>1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride</i> <i>(Tricetylmethylammonium chloride, TMAC)</i> 52467-63-7</p>	$\left[\begin{array}{c} \text{CH}_3 \\ \\ \text{R} - \text{N}^+ - \text{R} \\ \\ \text{R}' \end{array} \right] \text{Cl}^-$ <p>R = hydroxyethyl R' = tallow alkyl</p> <p>Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides 67784-77-4</p>

Table 1. Structures of FND Cationics Category Chemicals (continued)

<div style="text-align: center;"> <p>R = tallow alkyl</p> <p>Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride 68607-29-4</p> </div>	<div style="text-align: center;"> <p>R = C₁₂ – C₁₆ alkyl</p> <p><i>non-HPV</i> <i>Alkyl (C₁₂₋₁₆) dimethylbenzylammonium chloride</i> <i>(ADBAC) 68424-85-1</i></p> </div>
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Table 2. Physical/Chemical Properties Data for FND Cationics Category Chemicals (continued)

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
112-00-5	182	454	9.3 E-9	1.22	1795
112-02-7	213	500	2.8 E-10	3.23	16.3
8030-78-2					
112-03-8	223	523	5.4 E-11	4.17	1.76
<i>7173-51-5 non-HPV</i>	<i>229</i>	<i>535</i>	<i>2.3 E-11</i>	<i>4.66</i> 0	<i>0.55</i> 700
61789-77-3					
68391-05-9					
68002-59-5					
68783-78-8					
68002-58-4					
61789-80-8	50 - 60				< 0.001
61789-81-9					
<i>52467-63-7 non-HPV</i>	<i>350</i> 46.0 – 53.5	<i>848</i> 121.5^a	<i>3 E-21</i> 1.8^b	<i>17.9</i> > 5.9^c	<i>Insoluble</i> < 10 mg/l forms a colloidal dispersion
67784-77-4					
68607-29-4					
<i>68424-85-1 non-HPV</i>	<i>241</i>	<i>561</i>	<i>3.5 E-12</i>	<i>3.91</i>	<i>2.2</i>

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.

Regular font indicates data obtained from appropriate models as described in the text.

CAS RN and data in italics are for supplemental chemicals [non-HPV].

Empty block denotes data either are not available or are available and judged inadequate.

^a The “true boiling point” was calculated to be > 2000 °C; the measured value was considered to be affected by impurities.

^b Calculated value at 25 °C using the measured boiling point; the value is considered inaccurate based on the structure of the chemical, and the high vapor pressure is considered likely to be associated with solvent impurities.

^c Estimated according to Guideline OECD 107 (see Robust Summary).

Table 3. Environmental Fate and Ecotoxicity Data for FND Cationics Category Chemicals

CAS RN	Photodegradation (cm ³ /molecule-sec for k _{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish LC ₅₀ (mg/l)	Acute Tox. to Invertebrates EC ₅₀ (mg/l)	Toxicity to Aquatic Plants EC ₅₀ (mg/l)	Chronic Toxicity to Aquatic Species (mg/l) ^a
112-00-5	k _{phot} = 28.5 E-12 t _{1/2} = 4.5 hr	NC	air: < 1% water: 99.8% soil: < 1% sediment: < 1%	t _{1/2} water = 15 d t _{1/2} soil = 15 d t _{1/2} sediment = 60 d 35% by 10 d 98% by 2 d	9.77 6.0	3.24 0.39 0.345	NBD	NOEC Fish = 0.5 to > 1.25 LC ₅₀ CD = 0.31 LC ₅₀ CD = 0.30 – 0.45 NOEC CD = 0.05 – 0.25 NOEC CD (Surv.) = 0.25 NOEC Clam ≈ 0.046 (8 wk) EC ₅₀ Rotifer = 0.23 (48 h)
112-02-7	k _{phot} = 34 E-12 t _{1/2} = 3.9 hr	NC	air: < 1% water: 98.5% soil: < 1% sediment: < 1.5%	t _{1/2} water = 15 d t _{1/2} soil = 15 d t _{1/2} sediment = 60 d 82% by 2 d 65% BOD/ThOD by 28 d (75% by 42 d) 48% BOD/ThOD by 28 d (60% by 56 d)	2.24 0.07	1.59	NBD	EC ₅₀ Rotifer = 0.067 (48 h)
8030-78-2				95% by 2 d 48% BOD/ThOD by 28 d (51% by 35 d) 53% BOD/ThOD by 28 d (79% by 56 d) 40% BOD/COD by 28 d (61% by 42 d)		0.0126 – 0.0989		NOEC Daphnia = 0.0068 – 0.0991 (21 d)
112-03-8	k _{phot} = 37 E-12 t _{1/2} = 3.5 hr	NC	air: < 1% water: 83.3% soil: < 1% sediment: 16.7%	t _{1/2} water = 37.5 d t _{1/2} soil = 37.5 d t _{1/2} sediment = 150 d 98% by 2 d	Not toxic at solubility 0.07	Not toxic at solubility	NBD	
7173-51-5 <i>non-HPV</i>	k _{phot} = 46.3 E-12 t _{1/2} = 5.5 hr	NC Stable (pHs 5, 7, 9 for 30 d)	air: < 1% water: 78.9% soil: < 1% sediment: 21.1% Immobile in soil	t _{1/2} water = 15 d t _{1/2} soil = 15 d t _{1/2} sediment = 60 d Degradable	2.3 0.3 – 2.4 (48 hr) 0.27 – 2.8 (96 hr)	0.09 (daphnia) 0.07 (mysid)	≈ 3.5	

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.

Regular font indicates data obtained from appropriate models as described in the text.

CAS RN and data in italics are for supplemental chemicals [non-HPV].

Empty block denotes data either are not available or are available and judged inadequate.

NC = Not calculable for FND Cationic Category chemicals with the HYDROWIN submodel.

NBD = ECOSAR model has not been developed to predict algal toxicity for cationic surfactants.

^a Values are for 7-day studies unless indicated otherwise; CD = Ceriodaphnia; Surv. = Survival (value for reproduction also available – see Robust Summary);

Table 3. Environmental Fate and Ecotoxicity Data for FND Cationics Category Chemicals (continued)

CAS RN	Photodegradation (cm ³ /molecule-sec for k _{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish LC ₅₀ (mg/l)	Acute Tox. to Invertebrates EC ₅₀ (mg/l) ^a	Toxicity to Aquatic Plants EC ₅₀ (mg/l)	Chronic Tox. to Aquatic Species (mg/l) ^b
61789-77-3				0% BOD/ThOD by 28 d (56% by 214 d) 80.3% by 2 d				
68391-05-9								
68002-59-5								
68783-78-8					0.62 to > 24.0 24	CD = 0.54 – 1.23 DM = 0.19 – 1.06 Oyster = 2.0 MS = 0.22 (96 h) Shrimp = 36 Crab > 50	1.12 0.21 to ≤ 10^c	NOEC Fish = 12.7 LC₅₀ CD = 0.70 LC₅₀ CD = 0.82
68002-58-4								
61789-80-8	Evidence of photodegradation when absorbed to silica			35% BOD by 20 d 4.8% ThOD by 26 d 79% by 2 d	1.33 4.22 3.4 0.29 – 14	0.065 – 3.6	0.026 – 1.8	
61789-81-9								
52467-63-7 non-HPV	<i>k_{phot} = 92.4 E-12</i> <i>t_{1/2} = 2.8 hr</i>	<i>NC</i>	<i>air: < 0.1%</i> <i>water: 4.8%</i> <i>soil: < 0.1%</i> <i>sediment: 95.2%</i>	<i>t_{1/2} water = 37.5 d</i> <i>t_{1/2} soil = 37.5 d</i> <i>t_{1/2} sediment = 150 d</i> No degradation observed 100% removal in 12 days - adsorption likely	<i>Not toxic at solubility</i> ≈ 15.1	<i>Not toxic at solubility</i> 0.11	<i>NBD</i> E_bC₅₀ (0-96-hour) = 0.113; E_rC₅₀ (0-96-hour) = 0.177	NOEC DM (Toxicity) = 0.04; NOEC (Repro.) = 0.04; NOEC (Time to First Brood) = 0.08 Toxicity to Bacteria; EC₅₀ = 371
67784-77-4								
68607-29-4				12% BOD/ThOD by 182 d				
68424-85-1 non-HPV	<i>k_{phot} = 4.36 E-11</i> <i>t_{1/2} = 5.9 hr</i>	<i>NC</i>	<i>air: < 0.1%</i> <i>water: 4.7%</i> <i>soil: 94.7%</i> <i>sediment: 0.5%</i>	<i>t_{1/2} water = 37.5 d</i> <i>t_{1/2} soil = 37.5 d</i> <i>t_{1/2} sediment = 150 d</i>	<i>1.78</i> 0.515 0.923 <i>0.28</i> 0.86	<i>1.78</i> 0.0058 0.055 0.092	<i>NBD</i>	Fish early life stage: NOEC = 0.0322; NOEC DM = 0.00415

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.

Regular font indicates data obtained from appropriate models as described in the text.
 CAS RN and data in italics are for supplemental chemicals [non-HPV].

Empty block denotes data either are not available or are available and judged inadequate.
 NC = Not calculable for FND Cationics Category chemicals with the HYDROWIN submodel.

NBD = ECOSAR model has not been developed to predict algal toxicity for cationic surfactants.

^a All values are for 48-hours unless specified; CD = Ceriodaphnia; DM = Daphnia magna; MS = Mysid shrimp

^b Values are for 7-day studies unless indicated otherwise; CD = Ceriodaphnia; DM = Daphnia magna; Repro. = Reproduction

^c Values are algaestatic concentrations for several species

Table 4. Human Health-Related Data for FND Cationics Category Chemicals

CAS RN	Acute Oral Toxicity LD ₅₀ (mg/kg)	Acute Inhalation Toxicity LC ₅₀ (mg/l)	Acute Dermal Toxicity LD ₅₀ (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
112-00-5	490 560				Negative (Ames) Negative (mouse lymphoma) Negative (UDS in vitro) Negative (<i>In vivo</i> cytogenetic)		Maternal = 24 Developmental = 24 ^a
112-02-7	400 < LD₅₀ < 600		≈ 4300^b	10^c	Negative (Ames) ^d Negative (Ames) ^d Did not produce morphological transformations		Maternal > 10 Developmental > 10 ^c
8030-78-2	1260		< 4000^f < 4700		Negative (Ames) Positive (Ames) ^g		
112-03-8	633 (M) 536 (F)				Negative (Ames)^d		Maternal > 12.5 ^h Developmental > 12.5

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.

Regular font indicates data obtained from appropriate models as described in the text.

Empty block denotes data either are not available or are available and judged inadequate.

M = male

F = female

^a Oral study in rabbits.

^b 50% mortality at the only dose tested.

^c 28-Day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed at the 10 mg/kg/day dose.

^d Only two tester strains used in *Salmonella* reverse mutation assay.

^e Dermal application in rabbits; skin irritation at all doses in dams; no embryo/fetal toxicity or teratogenicity observed.

^f More than 50% mortality at the only dose tested.

^g Three-fold increase in back mutations in a single cell line (TA 1538).

^h Dermal application in rats (no embryo/fetal toxicity or teratogenicity observed).

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD ₅₀ (mg/kg)	Acute Inhalation Toxicity LC ₅₀ (mg/l)	Acute Dermal Toxicity LD ₅₀ (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
<i>7173-51-5 non-HPV</i>	59.5 - 399		> 228 - 3480	<i>> 12ⁱ 107^j 61^j 10^k 32^l 76^m</i>	<i>Not mutagenic No chromosomal aberrations No effect on DNA synthesis</i>	<i>Parental and offspring ≈ 56 No reproductive effects</i>	<i>Rabbit maternal = 1.0 Developmental = 3.0 Rat maternal = 1.0 Developmental = 20.0</i>
61789-77-3	960				Negative (Ames)ⁿ		
68391-05-9	4700			100^o			
68002-59-5							

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B. CAS RN and data in italics are for supplemental chemicals [non-HPV]. Regular font indicates data obtained from appropriate models as described in the text. Empty block denotes data either are not available or are available and judged inadequate.

ⁱ 13-week dermal toxicity study in rats.

^j 90-day feeding toxicity study in rats.

^k 52-week oral toxicity study in dogs.

^l Chronic toxicity study in rats.

^m Chronic toxicity study in mice.

ⁿ TA 98, TA 100, TA 1535 and TA 1537 were tested.

^o 28/91-day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed in the treated animals at 100 mg/kg/day.

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD ₅₀ (mg/kg)	Acute Inhalation Toxicity LC ₅₀ (mg/l)	Acute Dermal Toxicity LD ₅₀ (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
68783-78-8	> 2150				Negative (<i>In vivo</i> mouse micronucleus)		Maternal > 500 via gavage Developmental > 500 via gavage or diet^p
68002-58-4							
61789-80-8	> 500 > 576^q > 432^q	> 180 (1 hr)		> 100^r 140^s		> 100^t	
61789-81-9				LOAEL ≈ 170^u		> 750^v	Maternal > 500 via gavage; > 475 via diet Developmental > 500 via gavage; > 475 via diet^p

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.

Regular font indicates data obtained from appropriate models as described in the text.

Empty block denotes data either are not available or are available and judged inadequate.

^p Developmental toxicity study conducted in rats at two gavage doses (100 or 500 mg/kg/day) or a single dietary concentration to provide a target dose of 500 mg/kg/day).

^q Toxicity study conducted with mice (LD₅₀ > 576) and dogs (LD₅₀ > 432).

^r 90-day oral toxicity feeding study in dogs.

^s 91-day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed at both the 10 and 140 mg/kg/day doses.

^t Evaluation of reproductive organs from the 90-day oral feeding study in dogs adequate for SIDS reproductive screening (included in Robust Summary for 90-day study).

^u 13-Week feeding toxicity study in rats extended to 22 weeks for satellite group; NOAEL was not established at either time point.

^v Evaluation of reproductive organs from the 13/22-week oral feeding study in rats adequate for SIDS reproductive screening (included in Robust Summary for 13/22-week study).

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD ₅₀ (mg/kg)	Acute Inhalation Toxicity LC ₅₀ (mg/l)	Acute Dermal Toxicity LD ₅₀ (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
<i>52467-63-7 non-HPV</i>	> 16,300		> 2000	40	<i>Negative (Ames) Negative (In vivo cytogenetic)</i>		
67784-77-4							
68607-29-4	205						
<i>68424-85-1 non-HPV</i>				> 20^w ≈ 40^g ≈ 80^x ≈ 83^y	<i>Not mutagenic No chromosomal aberrations No effect on DNA synthesis</i>	Parental > 146 Offspring = 73 Reproduction > 146	Maternal = 10 Developmental > 100^z Maternal = 3 Developmental > 9^{aa}

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
 CAS RN and data in italics are for supplemental chemicals [non-HPV].
 Regular font indicates data obtained from appropriate models as described in the text.
 Empty block denotes data either are not available or are available and judged inadequate.

^g 90-day feeding toxicity study in rats.

^w 90-day dermal toxicity study in rats.

^x Combined chronic toxicity/oncogenicity study in rats (NOAEL is for toxicity; no evidence of carcinogenicity).

^y Combined chronic toxicity/oncogenicity study in mice (NOAEL is for toxicity; no evidence of carcinogenicity).

^z Developmental toxicity study in rats via gavage.

^{aa} Developmental toxicity study in rabbits via gavage.