

201-14980A

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

**Assessment of Data Availability
and Test Plan**

Prepared for:

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

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Prepared by:

Toxicology/Regulatory Services, Inc.

December 29, 2003

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Fatty Nitrogen Derived Nitriles Category High Production Volume (HPV) Chemicals Challenge Program Assessment of Data Availability and Test Plan

Introduction

The Fatty Nitrogen Derived (FND) Nitriles Category chemicals are closed-system intermediates that fall within the realm of the U.S. EPA HPV Chemicals Challenge Program. This category includes 14 FND Nitriles chemicals that are similar as to their physical/chemical properties, environmental fate, ecotoxicity, and human health-related data. The chemicals in this category have been evaluated according to the EPA “Guidance for Testing Closed System Intermediates for the HPV Challenge Program” (U.S. EPA, 1999a). The potential for exposure to the chemicals is a key component of the determination of data development needs for the chemical category, under the HPV Program.

In the following paragraphs, on behalf of the member companies, the American Chemistry Council (ACC) FND Panel Nitriles Task Group (Task Group) provides information which substantiates the position that the FND Nitriles Category chemicals, produced at manufacturing facilities of member companies, meet the definition of closed-system intermediates in the context of the EPA HPV Chemicals Challenge Program.

By definition, closed-system intermediates have a limited potential for release to the environment. In the Challenge Program there are two types of intermediates that are contained in “closed system”:

- a) Isolated intermediates that are stored in controlled on-site facilities; and
- b) Isolated intermediates with controlled transport, i.e. to a limited number of locations within the same company or second parties, which use the chemical in a controlled way as an intermediate with well-known technology.

The companies represented in the ACC FND Panel Nitriles Task Group are major producers of FND Nitriles Category chemicals in the United States. The FND Nitriles Category chemicals sponsored by the ACC FND Panel Nitriles Task Group member companies are eligible for the closed-system intermediates provisions because they fulfill criterion a or b or both in the above definition, as discussed below

The table below shows that FND Nitriles Category chemicals also meet the definition for limited exposure potential based on the limited number of manufacturing sites handling these chemicals. These sites can be either production sites for FND Nitriles Category chemical intermediates or sites where the FND Nitriles Category chemicals are further derivatized.

Number of US Manufacturing Sites for FND Nitrile Category Chemicals

	Akzo Nobel	Goldschmidt	Crompton
Total Number of Sites	5	1	1
Company Sites:			
▪ In the U.S.	2	1	1
▪ Outside the U.S.	3		
Second Party Sites	0	0	0

FND Nitriles Category chemicals are used as intermediates and their use occurs in closed systems. Little to no exposure to workers is expected because the reaction vessels used to manufacture FND Nitriles Category chemicals are part of multi-purpose, closed-system operations. Generally, the equipment is cleaned only after production campaigns, which occur several times per year. Wastewater generated during routine maintenance of the process equipment (occurring typically twice per year) and storage tanks at the Task Group member company facilities is disposed of subject to requirements set forth in current state and federal environmental regulations. Site wastewater is routed to on-site treatment systems where the trace amounts of chemicals present undergo further dilution and microbial degradation, or wastewater is routed directly to an on-site incinerator where it is used as a fuel in the incinerator. These systems help limit environmental releases.

Monitoring data are not routinely collected to assess for potential exposures to FND Nitriles Category chemicals. However, as the toxicological summary contained in this assessment report demonstrates, all of the chemicals in the FND Nitriles Category have a low order of acute toxicity and are not mutagenic.

Routine chemical analyses are not typically conducted for trace amounts of unreacted FND Nitriles Category chemicals in downstream derivatives, but the economics of chemical production drive complete reaction of the intermediate chemicals. Furthermore, the efficiency of conversion to primary amines, the next derivative in the manufacturing process, is typically greater than 99%. Levels of unreacted FND Nitriles Category chemicals in downstream derivatives are also minimized because the odor associated with even trace amounts of FND Nitriles Category chemicals is regarded as unpleasant and can be problematic in downstream products.

As mentioned previously, FND Nitriles Category chemicals can be manufactured at one site and derivatized at a different site. Transportation typically is made in tank truck and tank car to the other company sites. Transfer from storage tanks to transport vehicles and then to either storage tanks or reaction vessels at other company sites is a controlled and routine operation. Should a line or pump fail during one of these operations, all sites use typical spill containment methods to help minimize any environmental contamination. In the unlikely event of an accidental spill or release during transit between locations, FND Nitriles Category chemicals have been shown to be inherently or readily biodegradable in studies conducted under Organization for Economic Cooperation and Development (OECD) test guidelines.

The limited environmental and human exposure potential during production, limited release potential during transportation, and data showing the chemicals' low order of acute toxicity and lack of mutagenicity substantiate the Task Group's decision to follow the reduced testing plan as described in the "Guidance for Testing Closed System Intermediates for the HPV Challenge Program" (U.S. EPA, 1999a). Testing beyond that for the closed-system intermediates is not warranted.

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

The FND Nitriles Category is comprised of 14 separate chemicals with unique CAS Registry Numbers (RNs). The FND Nitriles Category chemicals are identified in the following table:

Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
112-91-4	9-Octadecanenitrile
629-79-8	Hexadecanenitrile
638-65-3	Octadecanenitrile
2437-25-4	Dodecanenitrile
26351-32-6	Propanenitrile, 3-(9-Octadecenylamino)-, (Z)-
61789-53-5	Nitriles, coco
61790-28-1	Nitriles, tallow
61790-29-2	Nitriles, tallow, hydrogenated
68002-64-2	Nitriles, C16 and C18 unsaturated
68002-65-3	Nitriles, C16-18
68153-02-6	Nitriles, C16-22
68513-04-2	Nitriles, C14-18 and C16-18 unsaturated
68514-67-0	Nitriles, soya
68784-70-3	Propanenitrile, 3-amino-, N-tallow alkyl derivatives

Structural Information for the FND Nitriles Category

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

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

CAS RN	Chemical Name	Molecular Formula	Molecular Weight
2437-25-4	Dodecanenitrile	C ₁₂ H ₂₃ N	181
629-79-8	Hexadecanenitrile	C ₁₆ H ₃₁ N	237
638-65-3	Octadecanenitrile	C ₁₈ H ₃₅ N	265
68002-65-	Nitriles, C16-18	C ₁₇ H ₃₃ N	251 ^a

3			
68153-02-6	Nitriles, C16-22	C ₁₉ H ₃₇ N	279 ^b
112-91-4	9-Octadecenitrile	C ₁₈ H ₃₃ N	263
26351-32-6	Propanenitrile, 3-(9-Octadecenylamino)-, (Z)-	C ₂₁ H ₄₀ N ₂	320

^a Based on average chain length = 17

^b Based on average chain length = 19

Rationale for the FND Nitriles Structure-Based Chemical Category

The members of the FND Nitriles category are large molecules. The structure of these molecules result in surfactant-like properties that have physical/chemical properties, environmental fate, and toxicity similar to an even larger family of surfactants including the FND amines, cationics, and amides (each submitted as a separate category in the HPV Chemical Challenge Program). The following table summarizes the long-chain alkyl substituents found in the FND Nitriles

Category Chemicals:

Table C: Chain Length and Degree of Unsaturation for Long-Chain Substituents in the FND Nitriles Category Chemicals

Identifier	Chain Length(s) or Average	Degree of Unsaturation
Dodecane	12	None
Hexadecane	16	None
Octadecane	18	None
C16-C18	Not specified	None
C16-C22	Not specified	None
C14-C18 and C16-C18-unsaturated	Not specified	Not specified
C16 and C18-unsaturated	Not specified	Not specified
Octadecene	18	1
Octadecenyl	18	1
Coco (coconut)	C6: 0-1%	None
	C8: 5-9%	None
	C10: 5-10%	None
	C12: 44-53%	None
	C14: 13-19%	None
	C16: 8-11%	None
	C18: 1-3%	None
	C16: 0-1%	1
	C18: 5-8%	1
C18: 1-3%	2	
Tallow, hydrogenated ¹	C14: 1-6%	None
	C16: 23-46%	None
	C18: 49-67%	None
Tallow	C14: 1-6%	None

¹ Percentages assume 100% hydrogenation of the unsaturated tallow chains.

Table C: Chain Length and Degree of Unsaturation for Long-Chain Substituents in the FND Nitriles Category Chemicals

Identifier	Chain Length(s) or Average	Degree of Unsaturation
	C16: 20-37%	None
	C18: 14-21%	None
	C16: 3-9%	1
	C18: 35-46%	1
	C18: 4-10%	2
	C18: 0-3%	3
Soya (soy bean)	C16: 7-11%	None
	C18: 2-7%	None
	C20: 0-2%	None
	C18: 20-30%	1
	C18: 43-56%	2
	C18: 8-14%	3

As noted in the table above, the fatty acids used for production of the FND Nitriles Category Chemicals are all similar in composition. Overall, the chain length and degree of unsaturation in the FND chemicals have little impact on fate and effects. These chemicals, by the nature of their surfactant properties, are toxic to aquatic organisms at low concentrations. A careful examination of the chemical structures (Table 1) shows a close relationship among all of the chemicals in the category. The following discussion highlights the structural similarities.

Dodecanenitrile, hexadecanenitrile and octadecanenitrile are fixed chain-length substituted nitriles of 12, 16, and 18 carbons, respectively. The available data shows that, over this range, the FND Nitrile Category chemicals as well as the other FND chemicals (amines, cationics, amides) are not expected to, nor exhibit, significant differences in the HPV/SIDS endpoints. Therefore, for the purposes of this screening program, these chemicals are considered essentially equivalent. The remaining alkane-substituted nitriles and 3-aminopropane nitriles have carbon chain distributions ranging from C14 to C22. Several of these chemicals contain minimally unsaturated alkyl chains. Across the FND chemicals, available data show that the degree of unsaturation of the alkyl chain does not alter the toxicological properties of these chemicals. Overall, tallow and hydrogenated tallow are considered identical. Since the natural oils from coconut and soybean are similar to the tallow oils, varying only in percent of chain lengths and degree of unsaturation, all of the natural oil substituted nitriles are essentially the same. These natural oils are also similar to the defined chain length alkyl substituents. Thus, considering the structural similarities and consistent toxicological properties, there are no significant differences among the chemicals in the category that reasonably can be expected to result in differences in the HPV/SIDS endpoints.

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

Approach to Evaluate the Database for the FND Nitriles Category

Special approaches related to closed-system intermediates: Closed-system intermediates are evaluated differently from other HPV chemicals (U. S. EPA, 1999a). The guidance document specifies that “*exposure considerations can impact the battery of tests performed...*”. Further, EPA provides the following guidance: “*For closed system intermediates a reduced test plan package reflecting the information needed to evaluate the hazards in case of an accident is considered the appropriate level of testing for screening purposes. This is because exposures resulting from chemical accidents are likely to be of relatively short versus chronic duration. The reduced testing consists of the Screening Information Data Set (SIDS) minus the tests for repeated dose toxicity and reproductive toxicity, but including a developmental toxicity test.*”

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

1. The chemical names and CAS RNs of the 14 HPV FND Nitriles Category chemicals supported by the Task Group were provided.
2. As available, published and unpublished reports were obtained from the members of the Task Group and other sources; they were organized and reviewed to identify studies that could fulfill SIDS endpoints.
3. Pertinent publicly available databases² were searched and all identified relevant reports were obtained to establish the full extent and nature of the published literature for the 14 HPV FND Nitriles Category chemicals.
4. Each of the reports obtained was reviewed to determine its adequacy for use in the EPA HPV Chemicals Challenge Program according to EPA criteria and reliability scoring according to Klimisch *et al.* (1997).
5. Robust Summaries were prepared for each report with a Klimisch score of 1 or 2, according to the guidelines proposed by the EPA (U.S. EPA, 1999b) for each study type.
6. Estimates were developed for physical/chemical properties and environmental fate and ecotoxicity endpoints by using appropriate Structure Activity Relationships (SARs).
7. Fugacity modeling (Level 3) was performed to estimate transport and distribution into environmental compartments for the FND Nitriles Category chemicals.

² 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 (International Uniform Chemical Information Database), 1996.

Use of Structure-Activity Relationships for the FND Nitriles Category

Approaches recommended in the EPA document on the use of SARs in the EPA HPV Chemicals Challenge Program were employed in the assessment of the FND Nitriles Category chemicals (U.S. EPA, 1999c). Several models were employed to support the review and assessment of the FND Nitriles Category chemicals. The models included several SARs, 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 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.3.10). 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, 2000). The estimation methods employed by AOPWIN are based on the SAR methods developed by Dr. Roger Atkinson and co-workers (Meylan and Howard, 2000). 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 $1.5^6 \text{ molecules}/\text{cm}^3$ 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 HYDROWIN 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 Nitriles Category chemicals do not have the necessary characteristics.

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. 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 initial 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 a commonly tested fish, the fathead minnow (*Pimephales promelas*), 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 0.99g (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 toxicity based on structural features and physical properties, mainly the K_{ow} (Meylan and Howard, 1998).

Modeling Information Specific for FND Nitriles Category Chemicals

Where possible, the models described above were used for the FND Nitriles Category chemicals. Estimations of physical properties, environmental fate and distribution, and ecotoxicity were not possible for 7 of the 14 HPV chemicals in the FND Nitriles Category because they do not have single definable structures. 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. However, since the FND Nitriles Category chemicals are closed-system intermediates, direct release of these chemicals into the environment is not expected under normal operating conditions. To provide a means of fugacity modeling, all input was assumed to be into surface water, representing the “worst-case” scenario for an accidental release, using the chemical- specific parameters to attain estimates of the chemical distributions between environmental compartments.

Physical/Chemical Properties Reliable Data and SAR Estimates

The available reliable data and SAR estimates for physical/chemical properties of the FND Nitriles Category chemicals are presented in Table 2. Robust Summaries for the reliable studies

and SAR estimates are provided in Appendix A. The Test Plan for Physical/Chemical Properties is outlined in Table 4.

Measured data for melting points for the FND Nitriles Category chemicals ranged from < -22 to 41°C. The modeled values ranged from 25 to 148°C. Measured data for boiling points ranged from 220 to 390°C. The modeled boiling point values ranged from 277 to 418°C.

Consistent with similar, large organic molecules, the measured and EPIWIN estimated vapor pressures were low (even at temperatures as high as 200°C) across the FND Nitriles Category, with all values ≤ 0.002 mm Hg for the measured and modeled data, respectively.

The measured and EPIWIN estimated values for the octanol/water partition coefficient ($\log K_{ow}$) ranged from 4.9 to > 6 and 6.1 to 8.2, respectively.

Measured values and model predictions for water solubility indicated that the FND Nitriles Category chemicals have very limited solubility or are insoluble. Reported data indicated that these chemicals are 'insoluble' or 'practically insoluble' and model estimates ranged from 0.0009 to 1.9 mg/l.

Summary – Physical/Chemical Properties

Overall, the FND Nitriles Category chemicals have relatively low melting points when measured or modeled (generally < 100°C) and moderate boiling points, showing chemical decomposition in one case when measured (9-octadecenenitrile). The FND Nitriles Category chemicals are nonvolatile. The octanol/water partition coefficients are generally greater than 5, which are consistent with the very low water solubility determined both experimentally and by computer modeling.

It should be noted that measurement and prediction of physical/chemical properties for chemicals with surfactant properties such as the FND Nitriles Category chemicals are complicated by their behavior in test systems and the environment, including strong adsorption and absorption properties and surface tension activity. The available measured and modeled data for defining the physical/chemical properties of the FND Nitriles Category chemicals are adequate to meet the SIDS/HPV requirements. No additional studies are proposed for the melting point, boiling point, vapor pressure, partition coefficient and water solubility endpoints for the FND Nitriles Category (see Table 4).

Environmental Fate and Ecotoxicity Reliable Data and SAR Estimates

The available reliable data and SAR estimates for environmental fate and effects of the FND Nitriles Category chemicals are presented in Table 3. Robust Summaries for the reliable studies and model determinations are provided in Appendix A. The Test Plan for Environmental Fate and Ecotoxicity Data is outlined in Table 5.

Photodegradation in air was calculated using the Atkinson method and reported in IUCLID summaries for two chemicals (CAS RNs 638-65-3 and 61790-28-1). These data indicated a rapid degradation ($t_{1/2} < 1.5$ days). Similarly, AOPWIN estimates for eight of the remaining

category chemicals indicated estimated half-lives between approximately 1 and 11 hours. Thus, although the low volatility indicates that the FND Nitriles Category chemicals are unlikely to exist in air, they would be expected to degrade rapidly upon exposure to ambient light.

The HYDROWIN submodel 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. These types of long-chain hydrocarbon derivatives are generally not hydrolysable.

An estimation of the transport and distribution of the FND Nitriles Category chemicals in environmental media (percent in air, water, soil and sediment) following entry into the environment via water is presented in Table 3. Except for dodecanenitrile, the only member of the category with an estimated water solubility > 1 mg/L, the predictions indicated high distribution to the sediment ($\geq 77\%$) with the remainder mostly distributed to water and virtually no distribution to air and soil. For dodecanenitrile, the prediction was for higher distribution to water (~ 67%) with the remainder primarily to sediment.

Measured values for biodegradation varied from relatively slow (15% in 28 days for CAS RN 2437-25-4) to readily biodegradable (> 70% in 28 days for CAS RNs 61789-53-5, 61790-29-2, and 61790-28-1). The lowest reported value for biodegradation was for the lowest molecular weight (shortest chain length) FND nitrile, dodecanenitrile. This result reflects the complexity in evaluating biodegradation of molecules with surfactant-like properties that adsorb and absorb to microbes, organic material, and other surfaces. In addition, two OECD 301B tests were conducted for CAS RN 61789-53-5. In the first, only 25% (10 mg test chemical/L) and 45% (20 mg test chemical /L) degradation was seen at 28 days. In the second, 71% degradation was attained at 28 days and the criteria were met for ready biodegradation. These results exemplify the complexities in determining the environmental fate and effects of these types of chemicals. Overall, it is reasonable to conclude from the available data that biodegradation of these chemicals occurs and the rate is dependent on the bioavailability and adaptation of the microorganisms.

Measured LC₅₀ values for acute toxicity to fish ranged from > 1 to < 100 mg/l, and modeled values all were < 0.1 mg/l. For one of the FND Nitriles Category chemicals (CAS RN 68513-04-2) the ECOSAR model predicted “not toxic at solubility” for fish and did not provide an estimate for aquatic invertebrates or plants. In addition, for CAS RN 26351-32-6, the model predicted “not toxic at solubility” for all three aquatic species. Measured EC₅₀ data for acute toxicity to invertebrates for three chemicals (CAS RNs 61789-53-5, 61790-29-2, and 61790-28-1) ranged from 0.005 to 0.26 mg/l and a single measured value for acute toxicity to aquatic plants was 0.497 mg/l (CAS RN 61790-28-1).

Summary – Environmental Fate and Ecotoxicity

Atmospheric photodegradation was predicted to be rapid although fugacity models and the use of FND Nitriles Category chemicals in closed systems suggest minimal potential for distribution of these chemicals to the air. Fugacity models are of limited value for these closed-system intermediates but indicate that all but one (with substantial distribution to water) of the FND Nitriles Category Chemicals would be expected to distribute to sediment in the unlikely event of

environmental exposure. This conclusion is also supported by the limited water solubility of FND Nitriles Category chemicals. Biodegradation data indicate that the FND Nitriles Category chemicals are degradable and accidental release would not pose a long-term environmental contamination concern. From the available data, the FND Nitriles Category chemicals are more toxic to aquatic invertebrates and plants than to fish. This pattern of toxicity is similar to other FND chemicals (amines, cationics, and amides submitted in separate HPV categories) and the relatively high toxicity is likely related to the surfactant-like properties of these chemicals. The FND Nitriles Category chemicals are closed-system intermediates with potential environmental release generally limited to accidents. Therefore, the available data are considered adequate in the HPV screening program to evaluate the environmental fate and ecotoxicity for the entire category (Table 5).

Human Health-Related Reliable Data

The human health-related effects data for SIDS endpoints of the FND Nitriles Category chemicals are limited due to the use of these products as closed-system intermediates. Robust Summaries for the reliable studies are provided in Appendix A. The Test Plan for Human Health-Related Data is outlined in Table 6.

Acute rat oral toxicity LD₅₀ data were available for five of the 14 FND Nitriles Category chemicals. The LD₅₀ values available were for CAS RNs 2437-25-4, (> 2.0 and ≈ 3.4 g/kg), 112-91-4 (> 5.0 g/kg), 61789-53-5 (>2.0 g/kg), 61790-29-2 (>2.0 g/kg), and 61790-28-1 (>2.0, >5.0, and > 6.0 g/kg). Thus the rat oral LD₅₀ values are all greater than 2 g/kg indicating that these chemicals possess slight to negligible acute toxicity by the oral route.

In vitro genetic toxicity studies (*Salmonella* reverse mutation assay) for two of the FND Nitriles Category chemicals (CAS RNs 2437-25-4 and 61790-28-1) were identified. Both tests indicated an absence of mutagenic activity. The data indicate that the FND Nitriles Category chemicals are unlikely to be mutagenic. No chromosomal aberration data are available for the FND Nitriles Category chemicals.

Repeated dose and reproductive toxicity data are not required under the EPA HPV Chemicals Challenge Program for closed-system intermediates. Absence of these studies for the FND Nitriles Category chemicals is not considered to be a data gap.

No developmental toxicity data were available for the FND Nitriles Category chemicals.

Summary – Human Health Related Data

The High Production Volume Chemical Challenge Program design allows for a reduced testing program for closed-system intermediates defined as follows: “*The reduced testing consists of the Screening Information Data Set (SIDS) minus the tests for repeated dose toxicity and reproductive toxicity, but including a developmental toxicity test.*” Adequate studies are available to indicate a low level of acute toxicity across the category. As expected, bacterial mutagenicity studies for chemicals of this type and molecular weight were negative. However, no chromosomal aberration studies were available and an evaluation of this endpoint is considered necessary to complete the review of potential mutagenicity under the program. There

were no developmental toxicity data available; therefore, a determination for this endpoint is required for the program. As noted in the discussion above for the category justification, all of the chemicals in the category can be considered very similar. That is, the differences in chain length, degree of saturation of the carbon chains, source of the natural oils, or addition of an amino group in the chain would not be expected to have an impact on the toxicity profile. This conclusion is supported by a number of studies in the FND family of chemicals (amines, cationics, and amides submitted as separate categories) that show no differences in the length or degree of saturation of the alkyl substituents and is also supported by the limited toxicity of these long-chain substituted chemicals. Therefore, the shortest chain substituent, dodecanenitrile, is selected as the category representative for testing because it will provide for the highest degree of bioavailability. The OECD 473 and OECD 421 studies are proposed.

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Table 1: Structures of FND Nitriles Category Chemicals

$\text{H}_3\text{C}(\text{CH}_2)_{10}\text{N}$ <p>Dodecanenitrile 2437-25-4</p>	$\text{H}_3\text{C}(\text{CH}_2)_{14}\text{N}$ <p>Hexadecanenitrile 629-79-8</p>
$\text{H}_3\text{C}(\text{CH}_2)_{16}\text{N}$ <p>Octadecanenitrile 638-65-3</p>	$\text{R}-\text{N}$ <p>R = C₁₆ – C₁₈</p> <p>Nitriles, C16-18 68002-65-3</p>
$\text{R}-\text{N}$ <p>R = C₁₆ – C₂₂</p> <p>Nitriles, C16-22 68153-02-6</p>	$\text{R}-\text{N}$ <p>R = C₁₄ – C₁₈ and C₁₆ – C₁₈ unsaturated</p> <p>Nitriles, C14-18 and C16-18-unsatd. 68513-04-2</p>
$\text{R}-\text{N}$ <p>R = C₁₆ and C₁₈ unsaturated</p> <p>Nitriles, C16 and C18 unsatd 68002-64-2</p>	$\text{H}_3\text{C}(\text{CH}_2)_{17}(\text{CH}_2)_{16}\text{N}$ <p>9-Octadecenenitrile 112-91-4</p>
$\text{H}_3\text{C}(\text{CH}_2)_{17}(\text{CH}_2)_{17}\text{N}$ <p>Propanenitrile, 3-(9-Octadecenylamino)-, (Z)- 26351-32-6</p>	$\text{R}-\text{N}$ <p>R = coco</p> <p>Nitriles, coco 61789-53-5</p>

Table 1: Structures of FND Nitriles Category Chemicals

<p style="text-align: center;"> $\begin{array}{c} \text{R} \\ \\ \text{N} \end{array}$ </p> <p style="text-align: center;">R = tallow, hydrogenated</p> <p style="text-align: center;">Nitriles, tallow, hydrogenated 61790-29-2</p>	<p style="text-align: center;"> $\begin{array}{c} \text{R} \\ \\ \text{N} \end{array}$ </p> <p style="text-align: center;">R = tallow</p> <p style="text-align: center;">Nitriles, tallow 61790-28-1</p>
<p style="text-align: center;"> $\begin{array}{c} \text{R} \\ \\ \text{N} \\ \\ \text{H} \end{array}$ </p> <p style="text-align: center;">R = tallow alkyl derivs.</p> <p style="text-align: center;">Propanenitrile, 3-amino-, N-tallow alkyl derivs. 68784-70-3</p>	<p style="text-align: center;"> $\begin{array}{c} \text{R} \\ \\ \text{C} \equiv \text{N} \end{array}$ </p> <p style="text-align: center;">R = soya</p> <p style="text-align: center;">Nitriles, soya 68514-67-0</p>

Table 2: Physical/Chemical Properties Data for FND Nitriles Category Chemicals

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
2437-25-4	25	277	0.006	4.9	1.9
629-79-8	72	334	0.0003	> 6	0.11
638-65-3	41	362	0.00005	> 6	insoluble
68002-65-3	81	346	0.0001	7.2	0.009
68153-02-6	99	369	9 E-6	8.2	0.0009
68513-04-2	57	345	0.00009	6.1	0.10
68002-64-2	87	365	0.00001	7.3	0.007
112-91-4	-1	330 – 335 (decomposes)	0.0004	7.5	insoluble
26351-32-6	148	418	2 E-7	7.5	0.02
61789-53-5	4 < -22	220 – 380	£ 0.00038^a	5.0	practically insoluble
61790-29-2					
61790-28-1	1 – 10 5	290 – 390	0.002^b	5.08	not soluble
68784-70-3					
68514-67-0					

Note: Bold print indicates reliable data for which a Robust Summary is provided in Appendix A.

Regular font indicates data obtained from appropriate models for which Robust Summaries are provided in Appendix A.

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

^a Vapor pressure at 50 °C

^b Vapor pressure at 200 °C

Table 3: Environmental Fate and Ecotoxicity Data for FND Nitriles Category Chemicals

CAS RN	Photodegradation ($\text{cm}^3/\text{molecule}\cdot\text{sec}$ for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Toxicity Fish LC_{50} (mg/l)	Acute Toxicity Invertebrates EC_{50} (mg/l)	Acute Toxicity Aquatic Plants EC_{50} (mg/l)
2437-25-4	$k_{\text{phot}} = 11.6 \text{ E-}12$ $t_{1/2} = 11.1 \text{ hr}$	NC	air: 3.0% water: 66.8% soil: < 1% sediment: 30.2%	15% ThOD in 28 d	> 1 < 10	0.33	0.24
629-79-8	$k_{\text{phot}} = 17 \text{ E-}12$ $t_{1/2} = 7.46 \text{ hr}$	NC	air: < 1% water: 21.9% soil: < 1% sediment: 77.6%		0.031	0.043	0.034
638-65-3	50% after 0.8 d	NC	air: < 1% water: 21.9% soil: < 1% sediment: 77.6%		0.034	0.048	0.038
68002-65-3	$k_{\text{phot}} = 18.6 \text{ E-}12$ $t_{1/2} = 6.89 \text{ hr}$	NC	air: < 1% water: 10.9% soil: < 1% sediment: 89%		0.002	0.004	0.003
68153-02-6	$k_{\text{phot}} = 21.5 \text{ E-}12$ $t_{1/2} = 6.0 \text{ hr}$	NC	air: < 1% water: 10.2% soil: < 1% sediment: 89.8%		0.0003	0.0005	0.00045
68513-04-2	$k_{\text{phot}} = 140 \text{ E-}12$ $t_{1/2} = 0.92 \text{ hr}$	NC	air: < 1% water: 20.2% soil: < 1% sediment: 79.8%		not toxic at solubility	not calculable	not calculable
68002-64-2	$k_{\text{phot}} = 134 \text{ E-}12$ $t_{1/2} = 0.96 \text{ hr}$	NC	air: < 1% water: 10.8% soil: < 1% sediment: 89.2%		0.002	0.003	0.003

Note: Bold print indicates reliable data for which a Robust Summary is provided in Appendix A.

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

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

Table 3: Environmental Fate and Ecotoxicity Data for FND Nitriles Category Chemicals

CAS RN	Photodegradation (cm ³ /molecule-sec for k _{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Toxicity Fish LC ₅₀ (mg/l)	Acute Toxicity Invertebrates EC ₅₀ (mg/l)	Acute Toxicity Aquatic Plants EC ₅₀ (mg/l)
112-91-4	k _{phot} = 77 E-12 t _{1/2} = 1.67 hr	NC	air: < 1% water: 10.6% soil: < 1% sediment: 89.4%		0.0013	0.002	0.0018
26351-32-6	k _{phot} = 91 E-12 t _{1/2} = 1.41 hr	NC	air: < 1% water: 5.0% soil: < 1% sediment: 95.0%		not toxic at solubility	not toxic at solubility	not toxic at solubility
61789-53-5				43% ThCO₂ in 28d 71% ThCO₂ in 28d	3.53	0.033 0.091	
61790-29-2				110% ThOD in 28 d		0.216	
61790-28-1	50% after 1.4 d (C₁₂) 50% after 0.7 d (C₂₀)			69% and 78% in 28 and 42 d, respectively 64% ThCO₂ in 28 d 72% ThCO₂ in 28 d	> 10 < 100	0.005 0.26	0.497
68784-70-3							
68514-67-0					33.2		

Note: Bold print indicates reliable data for which a Robust Summary is provided in Appendix A.

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

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

**Table 4: Proposed Test Plan for American Chemistry Council FND Nitriles Category
Physical/Chemical Properties**

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient (log Kow)	Water Solubility
2437-25-4	M	M	M	A	M
629-79-8	M	M	M	A	M
638-65-3	A	A	M	A	A
68002-65-3	M	M	M	M	M
68153-02-6	M	M	M	M	M
68513-04-2	M	M	M	M	M
68002-64-2	M	M	M	M	M
112-91-4	A	A	M	M	A
26351-32-6	M	M	M	M	M
61789-53-5	A	A	A	A	A
61790-29-2	C	C	C	C	C
61790-28-1	A	A	A	A	A
68784-70-3	C	C	C	C	C
68514-67-0	C	C	C	C	C

Note: A = Endpoint fulfilled by adequate reliable data or model data.

M = Endpoint fulfilled by model data.

C = Endpoint fulfilled by category read-across.

**Table 5: Proposed Test Plan for American Chemistry Council FND Nitriles Category
Environmental Fate and Ecotoxicity**

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
2437-25-4	M	NC	M	A	A	M	M
629-79-8	M	NC	M	C	M	M	M
638-65-3	A	NC	M	C	M	M	M
68002-65-3	M	NC	M	C	M	M	M
68153-02-6	M	NC	M	C	M	M	M
68513-04-2	M	NC	M	C	M	M	NC
68002-64-2	M	NC	M	C	M	M	M
112-91-4	M	NC	M	C	M	M	M
26351-32-6	M	NC	M	C	M	M	NC
61789-53-5	C		C	A	A	A	C
61790-29-2	C		C	A	C	A	C
61790-28-1	A		C	A	A	A	A
68784-70-3	C		C	C	C	C	C
68514-67-0	C		C	C	A	C	C

Note: A = Endpoint fulfilled by adequate reliable data or model data.

M = Endpoint fulfilled by model data.

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

NC = cannot be calculated; no measured data available

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

**Table 6: Proposed Test Plan for American Chemistry Council FND Nitriles Category
Human Health-Related Data**

CAS RN	Acute Oral Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity	Genetic Toxicity In vitro	Toxicity to Reproduction	Developmental Toxicity
2437-25-4	A	C	NR	A/OECD 473	NR	OECD 421
629-79-8	C	C	NR	C	NR	C
638-65-3	C	C	NR	C	NR	C
68002-65-3	C	C	NR	C	NR	C
68153-02-6	C	C	NR	C	NR	C
68513-04-2	C	C	NR	C	NR	C
68002-64-2	C	C	NR	C	NR	C
112-91-4	A	C	NR	C	NR	C
26351-32-6	C	C	NR	C	NR	C
61789-53-5	A	C	NR	C	NR	C
61790-29-2	A	C	NR	C	NR	C
61790-28-1	A	C	NR	A	NR	C
68784-70-3	C	C	NR	C	NR	C
68514-67-0	C	C	NR	C	NR	C

Note: Reliable data for acute toxicity by the oral route of exposure are considered adequate for other routes of exposure.

A = Endpoint fulfilled by adequate reliable data or model data.

OECD = Specified test guideline for proposed study.

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

NR = Not required for closed-system intermediates