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

**Assessment of Data Availability
and Test Plan**

Prepared for:

**The American Chemistry Council's
Fatty Nitrogen Derivatives Panel's
Nitriles Task Group**

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Prepared by:

Toxicology/Regulatory Services, Inc.

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

Introduction

The Fatty Nitrogen Derived (FND) Ether Nitriles Category chemicals are closed-system intermediates that fall within the realm of the U.S. EPA HPV Chemicals Challenge Program. This category includes three FND Ether 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 activities for the chemical category under the HPV Program.

In the following paragraphs, on behalf of its member companies, the American Chemistry Council’s (ACC) FND Panel Nitriles Task Group (Task Group) provides information which substantiates the position that the FND Ether Nitriles Category chemicals, produced at manufacturing facilities of a member company, 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 company represented in the ACC FND Panel Nitriles Task Group is a major producer of FND Ether Nitriles Category chemicals in the United States. The FND Ether Nitriles Category chemicals sponsored by the ACC FND Panel Nitriles Task Group member company are eligible for reduced testing as closed-system intermediates because they fulfill criterion a or b or both in the above definition, as discussed below.

FND Ether Nitriles Category chemicals are used as intermediates and their use occurs in closed systems. Little or no exposure to workers is expected because the reaction vessels used to manufacture FND Ether 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 ACC FND Panel Nitriles 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 Ether Nitriles Category chemicals. However, as the toxicological summary contained in this assessment report demonstrates, all of the chemicals in the FND Ether 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 Ether Nitriles Category chemicals in downstream derivatives, but the economics of chemical production drive complete chemical reaction of the intermediate chemicals. Furthermore, the efficiency of conversion to primary ether amines, the next derivative in the manufacturing process, is typically greater than 99%. Levels of unreacted FND Ether Nitriles Category chemicals in downstream derivatives are also minimized because the odor associated with even trace amounts of FND Ether Nitriles Category chemicals is regarded as unpleasant and can be problematic in downstream products.

FND Ether Nitriles Category chemicals are not frequently transported. When necessary, transportation typically is made in tank trucks and tank cars 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, typical spill containment methods are used to help minimize any environmental contamination. In the unlikely event of an accidental spill or release during transit between locations, FND Ether Nitrile 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 recommended for the closed-system intermediates is not warranted.

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

The FND Ether Nitriles Category is comprised of three chemicals with unique Chemical Abstracts Service Registry Numbers (CASRN). In addition, seven FND Nitriles (sponsored in the HPV Chemical Challenge Program, in a separate category) are included as supporting the FND Ether Nitriles Category. The FND Ether Nitriles Category HPV and supporting chemicals are identified in the following table:

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
68784-39-4	Propanenitrile, 3-(C8-10-alkyloxy) derivatives
64354-92-3	Propanenitrile, 3-(isodecyloxy)
68239-19-0	Propanenitrile, 3-(tridecyloxy)
2437-25-4	Dodecanenitrile
638-65-3	Octadecanenitrile
112-91-4	9-Octadecenitrile
61789-53-5	Nitriles, coco
61790-29-2	Nitriles, tallow, hydrogenated
61790-28-1	Nitriles, tallow
68514-67-0	Nitriles, soya

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

Structural Information for the FND Ether Nitriles Category

The following table presents the molecular formula and molecular weight data for the FND Ether Nitriles Category and supporting 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.

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

CAS RN	Chemical Name	Molecular Formula	Molecular Weight
68784-39-4	Propanenitrile, 3-(C8-10-alkyloxy) derivatives	C ₉ H ₂₃ NO	161 ^a
64354-92-3	Propanenitrile, 3-(isodecyloxy)	C ₁₃ H ₁₈ NO	204
68239-19-0	Propanenitrile, 3-(tridecyloxy)	C ₁₆ H ₃₁ NO	254
2437-25-4	Dodecanenitrile	C ₁₂ H ₂₃ N	181
638-65-3	Octadecanenitrile	C ₁₈ H ₃₅ N	265
112-91-4	9-Octadecenitrile	C ₁₈ H ₃₃ N	263

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

^a Based on average chain length = 9

Rationale for the FND Ether Nitriles Structure-Based Chemical Category

The members of the FND Ether Nitriles category are large molecules used as closed-system intermediates. 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 nitriles, 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 Ether Nitriles Category and supporting chemicals:

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

Identifier	Chain Length(s) or Average	Degree of Unsaturation
C8-C10	9	None
Isodecyl	10	None
Dodecane	12	None
Tridecyl	13	None
Octadecane	18	None
9-Octadecene	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
	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

¹ Percentages assume 100% hydrogenation of the unsaturated tallow chains. JVM – if they are 100% hydrogenated aren't they no longer unsaturated.

As noted in the table above, the hydrocarbons used for production of the FND Ether Nitriles Category Chemicals are all similar in composition. Overall, the chain length and degree of unsaturation in the FND chemicals has shown 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 the three FND Ether Nitriles chemicals and the supporting chemicals in the category. The following discussion highlights these structural similarities.

The three Propanenitrile derivatives comprising the FND Ether Nitriles Category are essentially the same in relationship to fate and effects. The hydrocarbon chains range only from C8 to C13. This difference in chain length, as with other FND chemicals, does not impart measurable differences in biodegradation, aquatic toxicity, or toxicity to mammalian systems. Therefore, these chemicals are considered here as being equivalent for purposes of the HPV screening program.

For the supporting chemicals, dodecanenitrile and octadecanenitrile are fixed chain length substituted nitriles of 12 and 18 carbons, respectively. Over this range, the supporting chemicals as well as other FND chemicals (amines, cationics, amides) are not expected to, nor do they show, significant differences in the HPV/SIDS endpoints. Therefore, for the purposes of this screening program, these chemicals are considered equivalent. The remaining alkane-substituted nitriles have carbon chain distributions ranging from C8 to C18. Several of these chemicals contain minimally unsaturated alkyl chains. Across the FND chemicals, the degree of unsaturation of the alkyl chain does not appear to 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, there are no significant differences among the chemicals in the category that reasonably can be expected to result in differences in the HPV/Screening Information Data Sets (SIDS) endpoints.

The similarity among toxicity profiles of the FND Ether Nitriles chemicals and the supporting and other FND (amines, cationics, amides) chemicals, as well as the very limited exposure to these chemicals, allows the use of the supporting chemicals for read-across of the data for the HPV endpoints.

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

Approach to Evaluate the Database for the FND Ether Nitriles Category

Special approaches related to closed-system intermediates: Closed-system intermediates are evaluated differently from other HPV chemicals in the EPA HPV Chemicals Challenge Program and OECD SIDS programs (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 Ether Nitriles Category chemicals.

1. The chemical names and CAS RNs of the three HPV FND Ether Nitriles Category chemicals sponsored by the ACC FND Panel Nitriles Task Group and the seven supporting chemicals 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 three HPV FND Ether Nitriles Category and supporting 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 as well as environmental fate and ecotoxicity endpoints by using appropriate Structure Activity Relationships (SAR).
7. Fugacity modeling (Level 3 Mackay) was performed to estimate transport and distribution into environmental compartments for the FND Ether Nitriles Category and supporting chemicals.

Use of Structure Activity Relationships for the FND Ether Nitriles Category

Approaches recommended in the EPA document on the use of Structure Activity Relationships (SAR) in the EPA HPV Chemicals Challenge Program were employed in the assessment of the FND Ether Nitriles Category chemicals (U.S. EPA, 1999c). Several models were employed to support the review and assessment of the FND Ether Nitriles Category chemicals. The models included several 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 estimates of acute toxicity to aquatic organisms.

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), and IUCLID (International Uniform Chemical Information Database), 1996.

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 EPIWIN v.3.11 (Syracuse Research Corporation, 2000). 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, 1999 a, b, 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 $1.5 \text{ E} + 6$ $\text{molecules}/\text{cm}^3$ 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 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 Ether 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 Modeling Center. These models are described in Mackay *et al.* (1996a,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 Ether Nitriles Category Chemicals

Where possible, the models described above were used for the FND Ether Nitriles Category and supporting chemicals. Estimations of physical properties, environmental fate and distribution, and ecotoxicity were not possible for two of the 10 HPV and supporting chemicals in the FND Ether 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. Since the FND Ether Nitriles Category chemicals are closed-system intermediates, there is no expected direct release of these chemicals into the environment. 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 Ether Nitriles Category and supporting 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 of the FND Ether Nitriles Category chemicals ranged from < -22 to 41°C . The modeled values ranged from 25 to 86°C . Measured data for boiling points ranged from 220 to 390°C . The modeled boiling point values ranged from 277 to 347°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 Ether Nitriles Category, with all values ≤ 0.006 mm Hg for the measured and modeled data.

The measured and EPIWIN estimated values for the octanol/water partition coefficient ($\log K_{ow}$) ranged from 4.9 to > 6 and 3.9 to 7.5 , respectively.

Measured values and model predictions for water solubility indicated that the FND Ether Nitriles Category chemicals have very limited solubility or are insoluble. Reported data indicated these chemicals are ‘insoluble’ or ‘practically insoluble’ and model estimates ranged from 0.26 to 9.2 mg/L.

Summary – Physical/Chemical Properties

Overall, the FND Ether Nitriles Category chemicals have relatively low melting points when measured or modeled (generally < 100°C) and moderate boiling points. The FND Ether Nitriles Category chemicals are nonvolatile. The octanol/water partition coefficients are generally greater than 5, which is 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 Ether 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 Ether 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 or water solubility endpoints for the FND Ether 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 Ether Nitriles Category and supporting 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 ($t_{1/2}$ < 1.4 days). Similarly, AOPWIN estimates for four HPV and supporting chemicals indicated estimated half-lives between approximately 2 to 11 hours. Thus, although the low volatility indicates that the FND Ether 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 Ether 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. Modeling could be performed for two of the three HPV chemicals and three supporting chemicals. Predicted distributions were primarily to water and sediment (ranging from 10.6 to 89.4% for each compartment). Predictions for air and soil compartments were < 1% except for one supporting chemical, CAS RN 2437-25-4, with 3% predicted in air.

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 biodegradability. 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. This conclusion is supported by a substantial database for other FND chemicals (amines, cationics, amides) submitted as separate categories in the HPV Chemical Challenge Program.

Measured LC₅₀ values for acute toxicity to fish ranged from > 1 to < 100 mg/L, and modeled values all were < 3 mg/L. 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). Model values for toxicity to daphnia and algae ranged from 0.002 to 2.9 mg/L and 0.0018 to 2.1 mg/L, respectively.

Summary – Environmental Fate and Ecotoxicity

Atmospheric photodegradation was predicted to be rapid although fugacity models and the use of FND Ether 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 distribution to water and sediment compartments would be expected in the event of an accidental release. Biodegradation data for the supporting chemicals as well as other FND chemicals (amines, cationics, and amides submitted in separate HPV categories) indicate that the FND Ether Nitriles Category chemicals are degradable and accidental release would not pose a long-term environmental contamination concern. From the model data, the FND Ether Nitriles Category chemicals should be considered toxic to aquatic species. 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 Ether Nitriles Category chemicals are closed-system intermediates with potential environmental release generally limited to accidents. Overall, the HPV chemicals should be considered toxic and further refinement of LC₅₀ and EC₅₀ values, as appropriate to the HPV Challenge Program, will not further the understanding of the environmental effects of the FND Ether Nitriles chemicals. 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 Ether Nitriles Category and supporting 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 supporting 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) were identified for two of the supporting chemicals (CAS RNs 2437-25-4 and 61790-28-1). Both tests indicated an absence of mutagenic activity. The data indicate that the FND Ether Nitriles Category chemicals are unlikely to be mutagenic. A chromosomal aberration study is proposed for CAS RN 2437-25-4 in the FND Nitriles Category. These data are considered adequate to support the FND Ether Nitriles Category in conjunction with the much larger database for other FND chemicals that are all negative in gene mutation assays.

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

An OECD 421 study is proposed for CAS RN 2437-25-4 in the FND Nitriles Category. These data are considered adequate to support the FND Ether Nitriles Category in conjunction with the much larger database for other FND chemicals that are all negative in developmental toxicity studies.

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.*” In evaluating potential further testing of the FND Ether Nitriles Category chemicals, it is useful to review the available data for the related FND Cationic, FND Amides, and FND Amines Category chemicals. Acute oral toxicity studies (approximately 80 studies for 40 chemicals in the three categories) provide LD₅₀ values from approximately 400 to 10,000 mg/kg with no apparent organ specific toxicity. Similarly, repeated dose toxicity studies (approximately 35 studies for 15 chemicals) provide NOAELs between 10 and 100 mg/kg/day for rats and slightly lower for dogs. More than 60 genetic toxicity studies (*in vitro* bacterial and mammalian cells as well as *in vivo* studies) indicated only one equivocally positive *Salmonella* Reverse Mutation assay and one positive chromosomal aberration assay that was ultimately shown to be unreliable, among more than 30 chemicals tested. For reproductive evaluations, 14 studies evaluated reproductive endpoints and/or reproductive organs for 11 chemicals and 15 studies evaluated developmental toxicity for 13 chemicals indicating no reproductive or developmental effects for the FND group as a whole.

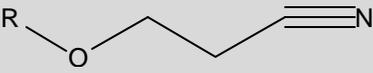
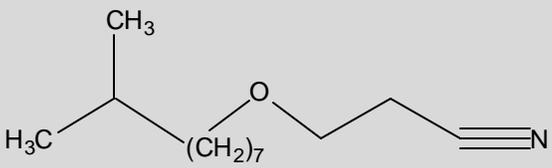
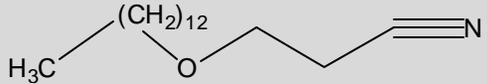
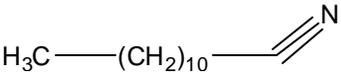
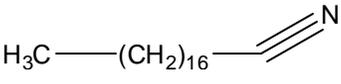
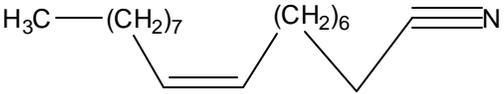
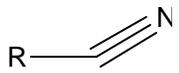
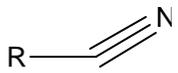
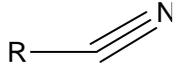
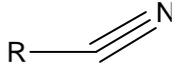
These comparisons clearly provide a strong weight of evidence that the FND Ether Nitriles Category chemicals will not pose significant toxicity to humans. For the FND Ether Nitriles Category, adequate studies for the supporting chemicals are available to indicate a low level of acute toxicity for these types of chemicals. As expected, bacterial mutagenicity studies for chemicals of this type and molecular weight were negative. The proposed chromosomal

aberration and reproductive/developmental screening studies for the supporting chemical, CAS RN 2437-25-4, will adequately support the three FND Ether Nitriles chemicals. Therefore, the available (or proposed) data are considered adequate for the HPV Chemical Challenge Program.

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Table 1: Structures of FND Ether Nitriles Category Chemicals

 <p style="text-align: center;">R = C8-C10</p> <p style="text-align: center;">Propanenitrile, 3-(C8-10-alkoxy) derivatives 68784-39-4</p>	 <p style="text-align: center;">Propanenitrile, 3-(isodecyloxy) 64354-92-3</p>
 <p style="text-align: center;">Propanenitrile, 3-(tridecyloxy) 68239-19-0</p>	 <p style="text-align: center;">Dodecanenitrile 2437-25-4</p>
 <p style="text-align: center;">Octadecanenitrile 638-65-3</p>	 <p style="text-align: center;">9-Octadecenitrile 112-91-4</p>
 <p style="text-align: center;">R = coco</p> <p style="text-align: center;">Nitriles, coco 61789-53-5</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;">R = tallow</p> <p style="text-align: center;">Nitriles, tallow 61790-28-1</p>	 <p style="text-align: center;">R = soya</p> <p style="text-align: center;">Nitriles, soya 68514-67-0</p>

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

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

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
68784-39-4					
64354-92-3	48	299	0.0012	3.9	9.2
68239-19-0	86	347	0.00004	5.5	0.26
2437-25-4	25	277	0.006	4.9	1.9
638-65-3	41	362	0.00005	> 6	insoluble
112-91-4	-1	330 – 335 (decomposes)	0.0004	7.5	insoluble
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	insoluble
68514-67-0					

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

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 are not available.

^a Vapor pressure at 50 °C.

^b Vapor pressure at 200 °C.

Table 3: Environmental Fate and Ecotoxicity Data for FND Ether 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)
68784-39-4		NC					
64354-92-3	$k_{\text{phot}} = 22 \text{ E-}12$ $t_{1/2} = 5.80 \text{ hr}$	NC	air: < 1% water: 89.4% soil: < 1% sediment: 10.6%		2.4	2.9	2.1
68239-19-0	$k_{\text{phot}} = 26 \text{ E-}12$ $t_{1/2} = 4.87 \text{ hr}$	NC	air: < 1% water: 40.6% soil: < 1% sediment: 59.4%		0.10	0.14	0.11
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 and < 10	0.33	0.24
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

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.
 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 are not available.
 NC = Not calculable for FND Ether Nitriles Category chemicals with the HYDROWIN submodel.

Table 3: Environmental Fate and Ecotoxicity Data for FND Ether 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
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 and < 100	0.005 0.26	0.497
68514-67-0					33.2		

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.
 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 are not available.
 NC = Not calculable for FND Ether Nitriles Category chemicals with the HYDROWIN submodel.

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

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient (log Kow)	Water Solubility
68784-39-4	R	R	R	R	R
64354-92-3	A	A	A	A	A
68239-19-0	A	A	A	A	A
2437-25-4	A	A	A	A	A
638-65-3	A	A	A	A	A
112-91-4	A	A	A	A	A
61789-53-5	A	A	A	A	A
61790-29-2	R	R	R	R	R
61790-28-1	A	A	A	A	A
68514-67-0	R	R	R	R	R

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

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

R = Endpoint fulfilled by category read-across.

**Table 5: Proposed Test Plan for American Chemistry Council FND Ether 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
68784-39-4	R	NC	R	R	R	R	R
64354-92-3	A	NC	A	R	A	A	A
68239-19-0	A	NC	A	R	A	A	A
2437-25-4	A	NC	A	A	A	A	A
638-65-3	A	NC	A	R	A	A	A
112-91-4	A	NC	A	R	A	A	A
61789-53-5	R		R	A	A	A	R
61790-29-2	R		R	A	R	A	R
61790-28-1	A		R	A	A	A	A
68514-67-0	R		R	R	A	R	R

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.

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

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

R = Endpoint fulfilled by category read-across.

* Testing is proposed in the FND Nitriles Test Plan.

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

CAS RN	Acute Oral Toxicity	Repeated Dose Toxicity	Genetic Toxicity In vitro	Toxicity to Reproduction	Developmental Toxicity
68784-39-4	R	NR	R	NR	R
64354-92-3	R	NR	R	NR	R
68239-19-0	R	NR	R	NR	R
2437-25-4	A	NR	A*	NR	A*
638-65-3	R	NR	R	NR	R
112-91-4	A	NR	R	NR	R
61789-53-5	A	NR	R	NR	R
61790-29-2	A	NR	R	NR	R
61790-28-1	A	NR	A	NR	R
68514-67-0	R	NR	R	NR	R

Note: Shaded cells indicate the three FND Ether Nitriles sponsored chemicals.
 A = Endpoint fulfilled by adequate reliable data or model data.
 R = Endpoint fulfilled by category read-across.
 NR = Not required for closed-system intermediates.
 * Testing is proposed in the FND Nitriles Test Plan.