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**Fatty Nitrogen Derived Amides Categories
High Production Volume (HPV)
Chemicals Challenge**

**Assessment of Data Availability
and Test Plan**

Prepared for:

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

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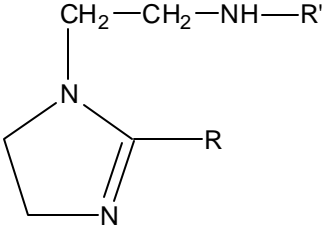
Introduction

The Fatty Nitrogen Derived (FND) Amides chemicals have been organized in three Categories (Category I – FND Amides; Category II – FND Imidazoline Derivatives; Category III – FND Amphoterics) plus two individual chemicals for the HPV Chemicals Challenge Program. The FND Amides are mixtures of long-chain alkyl substituted amides or amide producing chemicals. The commercial products are generally produced based on performance characteristics and/or cost considerations and generally the alkyl chain components are reacted from natural products such as coconut, soya, tallow and pine oils. Therefore, the products are most often complex mixtures. The FND Imidazoline Derivatives (Category II) as commercially sold may not be amides but form amides in a reversible reaction with water. The Imidazoline is produced to provide stability (e.g. in colder environments). Some typical applications of FND Amides are: masonry cement additives; curing agents for epoxy resins; slip and antiblocking additives for polymers; dispersants for printing and dyeing; mold release agents; corrosion inhibitors in oil well applications; liquid hand and body soaps; hand dish detergent; other household, industrial and institutional cleaners; degreasers, dispersants and emulsifiers for personal care applications; high foaming, cleaning and viscosity modification for personal care applications. For consideration of environmental fate and toxicity, the chemicals in the Categories have surfactant properties (e.g. comprised of hydrophobic and hydrophilic ends, form micelles, alter/reduce surface tension, form oil/water emulsions). Therefore, the FND Amides chemicals are members of a much larger family of FND chemicals (amines, cationics, nitriles and amides) and an even larger family of surfactants that have similar fate and effects. Within the framework of the HPV program, this larger database can be used as a basis for comparison and allows for an approach that focuses on confirmation of the known fate and effects of the FND chemicals.

Definition of Fatty Nitrogen Derived (FND) Amides Structure-Based Chemical Categories

The HPV FND Amides are comprised of 29 chemicals with unique Chemical Abstracts Service Registry Numbers (CAS RN; see Text Table B). They are grouped into three Categories (Category I – FND Amides; Category II – FND Imidazoline Derivatives; Category III – FND Amphoterics) and two individual chemicals. For ease in discussion, Category I (FND Amides) has been grouped into three Subcategories. The Categories and Subcategories are defined as follows:

Text Table A: General Description of Chemicals in the FND Amides Categories

	Category/ Subcategory Name	Alkyl Substituents	Primary Functionality	Generic Structure
CATEGORY I	FND Amides			
Subcategory 1	Fatty Acid Amides	C18 – C22	Unsubstituted functional nitrogen	$\text{R}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$
Subcategory 2	Fatty Alkanol- amides	R = C12 – C18 R' = H or Ethanol	Hydroxy functional nitrogen	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{N}-\text{CH}_2-\text{CH}_2-\text{OH} \\ \\ \text{R}' \end{array}$
Subcategory 3	Fatty Acid Reaction Products with Amines	R = C17 – C18 R' = H, R, or Acetates	Alkyl functional nitrogen	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-[\text{NH}-\text{CH}_2-\text{CH}_2]_x-\text{NH}-\text{R}'$
CATEGORY II	FND Imidazoline Derivatives	R = C17 – C18 (tall oil) R' = ethanol, ethanamine, or C18	Amide formed following hydrolysis	
CATEGORY III	FND Amphoteric (N-carboxymethyl substituted)	C16/Coco	Quaternary nitrogen/ zwitter ion	$\begin{array}{c} \text{CH}_3 \\ \\ \text{R}-\text{N}^+-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^- \\ \\ \text{CH}_3 \end{array}$

In addition, six supporting chemicals that are not part of the US HPV Chemical Challenge Program, but are structurally related to the FND Amides Chemicals, are included to provide supporting data for the Categories. These six chemicals are termed “supporting chemicals” throughout this document.

The chemicals in the FND Amides Categories and supporting chemicals are described in the following table. The supporting chemicals are shaded and italicized for ease of identification.

Text Table B: CAS Registry Numbers and Chemical Names

CATEGORY I: FND Amides	
Subcategory 1: Fatty Acid Amides	
Stearamide	124-26-5
Oleamide	301-02-0
Erucamide	112-84-5
<i>Amides, tallow, hydrogenated</i>	<i>61790-31-6</i>
Subcategory 2: Fatty Alkanolamides	
Dodecanamide, N-(2-hydroxyethyl)-	142-78-9
Dodecanamide, N,N-bis(2-hydroxyethyl)-	120-40-1
Amides, coco, N,N-bis(hydroxyethyl)	68603-42-9
Oleamide, N,N-bis(2-hydroxyethyl)-	93-83-4
Amides, tall-oil fatty, N,N-bis(hydroxyethyl)	68155-20-4
Amides, soya, N,N-bis(hydroxyethyl)	68425-47-8
Amides, coco, N-(hydroxyethyl)	68140-00-1
Coconut oil, reaction products with diethanolamine	8051-30-7
Fatty acids, coco, compounds with diethanolamine	61790-63-4
<i>Amides, C12-18, N,N-bis(hydroxyethyl)</i>	<i>68155-06-6</i>
Subcategory 3: Fatty Acid Reaction Products with Amines	
Octadecanamide, N,N'-ethylenebis	110-30-5
Fatty acids, tall-oil, reaction with diethylenetriamine	61790-69-0
Fatty acids, tall-oil, reaction products with tetraethylenepentamine	68953-36-6
Fatty acids, tall-oil, reaction with polyethylenepolyamines	68910-93-0
Fatty acids, tall-oil, reaction with polyethylenepolyamines acetates (essentially acetates of CAS RN 68910-93-0)	64754-93-4
Fatty acids, tall-oil, low boiling, reaction products with 1-piperazineethanamine	71820-35-4
Amides, coco, N-[3-(dimethylamino)propyl]	68140-01-2
<i>Fatty acids, tall-oil, reaction products with polyalkylenepolyamines, dodecylbenzenesulfonates</i>	<i>68910-87-2</i>
CATEGORY II: FND Imidazoline Derivatives	
Imidazolium cmpds., 2-(C17&C-17-unsat. Alkyl)-1[2-(C18 & C18-unsat. amido) ethyl]-4,5-dihydro-1-methyl, Me sulfates	72749-55-4
1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives	61791-39-7
1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall oil alkyl derivatives	68442-97-7
Amides, C14-18, N-[2-(C13-17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]	72623-72-4
1,2-Ethanediamine, N-(2-aminoethyl)-N'-{2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl} ethyl	65817-50-7
<i>Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl) Me sulfate</i>	<i>68122-86-1</i>
CATEGORY III: FND Amphoterics (N-carboxymethyl substituted)	
1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, chlorides, sodium salts	61789-39-7
1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, inner salt (betaine)	61789-40-0
1-Hexadecanaminium, N-(carboxymethyl)-N,N-dimethyl-, inner salt	693-33-4
<i>1-Propanaminium, N-(carboxymethyl)-N,N-dimethyl-3-[(1-oxododecyl)amino]-, inner salt</i>	<i>4292-10-8</i>
<i>Amides, coco, N-[3-(dimethylamino)propyl], alkylation products with chloroacetic acid, sodium salt</i>	<i>70851-07-9</i>
INDIVIDUAL CHEMICALS	
Naphthenic acids, reaction products with diethylenetriamine	68131-13-5
Fatty acids, tall oil, compounds with triethanolamine	68132-46-7

Structural Information for the Chemicals in the FND Amides Categories, Single Chemicals and Supporting Chemicals

The following tables present the molecular formula and molecular weight data for the chemicals with defined structures or average molecular weight data for chemicals without defined structures. In the tables, average chain length or estimated chain length is used where appropriate; where no formula is provided, the molecular weight is an approximation that can be used to define the chemical. For mixtures of undetermined proportion, no molecular weight can be determined (ND in the tables below). Structures are provided in Table 1a-d.

Text Table C: Molecular Formula and Molecular Weight of the Category I FND Amides Chemicals

CAS RN	Name	Molecular Formula	Molecular Weight
Subcategory 1: Fatty Acid Amides			
124-26-5	Stearamide	C ₁₈ H ₃₇ NO	283
301-02-0	Oleamide	C ₁₈ H ₃₅ NO	281
112-84-5	Erucamide	C ₂₂ H ₄₃ NO	337
61790-31-6	<i>Amides, tallow, hydrogenated</i>		277
Subcategory 2: Fatty Alkanolamides			
142-78-9	Dodecanamide, N-(2-hydroxyethyl)-	C ₁₄ H ₂₉ NO ₂	243
120-40-1	Dodecanamide, N,N-bis(2-hydroxyethyl)-	C ₁₆ H ₃₃ NO ₃	287
68603-42-9	Amides, coco, N,N-bis(hydroxyethyl)		302
93-83-4	Oleamide, N,N-bis(2-hydroxyethyl)-	C ₂₂ H ₄₈ NO ₃	375
68155-20-4	Amides, tall-oil fatty, N,N-bis(hydroxyethyl)		361
68425-47-8	Amides, soya, N,N-bis(hydroxyethyl)		366
68140-00-1	Amides, coco, N-(hydroxyethyl)		258
8051-30-7	Coconut oil, reaction products with diethanolamine		ND
61790-63-4	Fatty acids, coco, compounds with diethanolamine		ND
68155-06-6	<i>Amides, C12-18, N,N-bis(hydroxyethyl)</i>		273
Subcategory 3: Fatty Acid Reaction Products with Amines			
110-30-5	Octadecanamide, N,N'-ethylenebis	C ₃₈ H ₇₆ N ₂ O ₂	593
61790-69-0	Fatty acids, tall-oil, reaction with diethylenetriamine		397/636
68953-36-6	Fatty acids, tall-oil, reaction products with tetraethylenepentamine		440/679
68910-93-0	Fatty acids, tall-oil, reaction with polyethylenepolyamines		ND
64754-93-4	Fatty acids, tall-oil, reaction with polyethylenepolyamines acetates (essentially acetates of CAS RN 68910-93-0)		ND
71820-35-4	Fatty acids, tall-oil, low boiling, rx products with 1-piperzineethanamine		ND
68140-01-2	Amides, coco, N-[3-(dimethylamino)propyl]		315
68910-87-2	<i>Fatty acids, tall-oil, reaction products with polyalkylenepolyamines, dodecylbenzenesulfonates</i>		ND

ND = Cannot be determined.

Text Table D: Molecular Formula and Molecular Weight of the Category II FND Amides Chemicals

CAS RN	Name	Molecular Formula	Molecular Weight
72749-55-4	Imidazolium compounds, 2-(C17&C-17-unsat. Alkyl)-1[2-(C18 & C18-unsat. amido) ethyl]-4,5-dihydro-1-methyl, Me sulfates		644*
61791-39-7	1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives		351
68442-97-7	1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall oil alkyl derivatives		350
72623-72-4	Amides, C14-18, N-[2-(C13-17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]		561
65817-50-7	1,2-Ethanediamine, N-(2-aminoethyl)-N'-{2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl} ethyl		379
68122-86-1	<i>Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl) Me sulfate</i>		640*

* Estimated molecular weight without the salt.

Text Table E: Molecular Formula and Molecular Weight of the Category III FND Amides Chemicals

CAS RN	Name	Molecular Formula	Molecular Weight
61789-39-7	1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, chlorides, sodium salts		374*
*61789-40-0	1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, inner salt (betaine)		374
693-33-4	1-Hexadecanaminium, N-(carboxymethyl)-N,N-dimethyl-, inner salt		327
4292-10-8	<i>1-Propanaminium, N-(carboxymethyl)-N,N-dimethyl-3-[1-oxododecyl]amino]-, inner salt</i>		342
70851-07-9	<i>Amides, coco, N-[3-(dimethylamino)propyl], alkylation products with chloroacetic acid, sodium salt</i>		ND

ND = Cannot be determined.

* Estimated molecular weight without the salt.

Text Table F: Molecular Formula and Molecular Weight of the Individual FND Amides Chemicals

CAS RN	Name	Molecular Formula	Molecular Weight
68131-13-5	Naphthenic acids, reaction products with diethylenetriamine		ND
68132-46-7	Fatty acids, tall oil, compounds with triethanolamine		ND

ND = Cannot be determined.

Rationale for the FND Amides Structure-Based Chemical Categories

The members of the FND Amides chemicals are large molecules with surfactant properties. The FND chemical family (amines, cationics, amides, nitriles) is comprised of long-chain alkyl substituents most frequently from natural oils and fats. The following table summarizes the long-chain alkyl substituents found in the FND Amides Category chemicals:

Alkyl Substituents for Production of FND Amides		
Identifier	Chain Length(s) or Average	Degree of Unsaturation
Dodecane	12	None
C12-C18	Not specified	None
C13-C17	Not specified	None
C14-C18	Not specified	None
C17 and C17-unsaturated	17	Not specified
Heptadecenyl	17	1
C18 and C18-unsaturated	18	Not specified
Octadecane (Stearyl)	18	None
Octadecenyl (Olea)	18	1
Tall-oil (Pine)	C17: 7% C17: 34% C18: 46% Others: 13%	2 (non-conjugated) 2 (conjugated) None Not specified
Coco (Coconut)	C6: 0-1% C8: 5-9% C10: 5-10% C12: 44-53% C14: 13-19% C16: 8-11% C18: 1-3% C16: 0-1% C18: 5-8% C18: 1-3%	None None None None None None None 1 1 2
Tallow, hydrogenated ^a	C14: 1-6% C16: 23-46% C18: 49-67%	None None None
Tallow	C14: 1-6% C16: 20-37% C18: 14-21% C16: 3-9% C18: 35-46% C18: 4-10% C18: 0-3%	None None None 1 1 2 3
Soya (Soy bean)	C16: 7-11% C18: 2-7% C20: 0-2% C18: 20-30% C18: 43-56% C18: 8-14%	None None None 1 2 3

^a Percentages assume 100% hydrogenation of the unsaturated tallow chains.

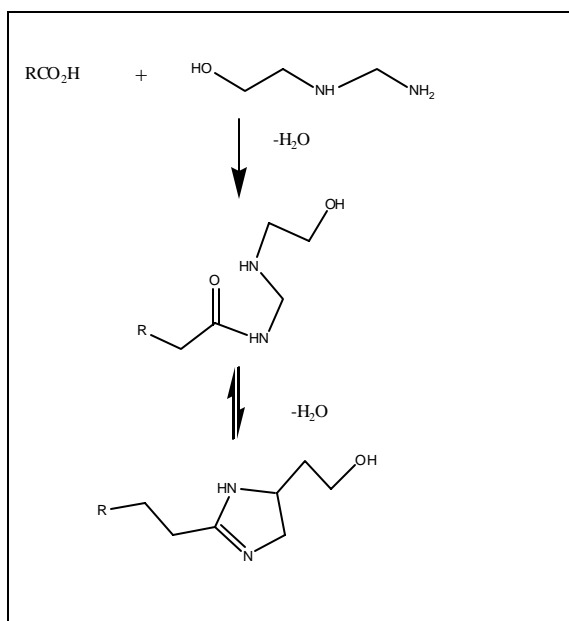
Based on an analysis of data across the FND chemicals, including the chemicals in the FND Amides Categories as well as FND amines, cationics and nitriles (submitted in separate Test Plans under the HPV Challenge Program), the chain length and degree of unsaturation in the FND chemicals have been shown to not significantly impact fate and effects of these chemicals. The following discussion describes the interrelationship of the chemicals within and among the various FND Amide Categories:

Category I FND Amides: Subcategory 1 – Fatty Acid Amides: The three chemicals in the subcategory and the supporting chemical are very similar. Stearamide and Oleamide differ only in a double bond in the alkyl chain of Oleamide (molecular weights of 283 and 281, respectively). Erucamide has four additional saturated carbon atoms in the alkyl chain but is otherwise identical to Oleamide. As noted above, hydrogenated tallow (primarily C16 and C18 saturated) is similar to the saturated defined alkyl derivatives. It should be noted that, although the three HPV chemicals have “defined” chain length substituents, they are most commonly produced from natural oils and are not “pure” substances. The primary functional group for this subcategory is an unsubstituted nitrogen (-C-O-NH₂).

Category I FND Amides: Subcategory 2 – Fatty Alkanolamides: The eight chemicals in this subcategory are similar to the chemicals in Subcategory 1 with the nitrogen substituted with one or two ethanol moieties. “Reaction products” with diethanolamine (OH-(CH₂)₂-N-(CH₂)₂-OH) are identical to the bishydroxyethyl chemicals except for their synthesis pathways that lead to more complex mixtures. The primary functional group in the subcategory is the mono- (OH-(CH₂)₂-N-) or di- (OH-(CH₂)₂-N-(CH₂)₂-OH) hydroxy functional nitrogen.

Category I FND Amides: Subcategory 3 – Fatty Acid Reaction Products with Amines: This subcategory is comprised of amides formed by the reaction with amines and the long-chain alkyl components (primarily tall oil from pine). The functional groups within this subcategory are alkyl substituted nitrogen, (-N-CH₂-CH₂-N-)_x.

Category II: FND Imidazoline Derivatives: The following shows the typical reaction used to form the FND Imidazoline Derivatives:



The Imidazoline ring is formed in a reversible reaction with water to stabilize the molecule (e.g. in cold environments). The five HPV chemicals in the category are all very similar with variable alkyl substituents. The supporting chemical (CAS RN 68122-86-1) is essentially the salt form of the HPV chemical, CAS RN 72623-72-4.

Category III: FND Amphoterics: The FND Amphoterics in the Amides Category are similar to the quaternary ammonium FND Cationic chemicals (submitted by ACC FND as a separate category) and have similar properties. The chemicals are charged species, forming either a quaternary amine inner salt (e.g. betaine), zwitter ions, or salts of zwitter ions. The three HPV chemicals and the two supporting chemicals are very similar in structure and function.

Individual Chemicals:

Naphthenic acids, reaction products with diethylenetriamine: Naphthenic acids are composed predominately of alkyl-substituted cycloaliphatic carboxylic acids with smaller amounts of acyclic aliphatic (paraffinic or fatty) acids. The cycloaliphatic acids include single rings and fused multiple rings. Naphthenic acids occur naturally in the oxygen rich fraction of crude petroleum. The classes and proportions of individual naphthenic acids in the overall mix vary according to the origin of the crude oil. Naphthenic acids are only slightly soluble in water. In performance, they resemble other fatty acids. Thus, they are included with the FND Amides chemicals.

Fatty acids, tall oil, compounds with triethanolamine: Although this trialkyl amide substituted product was not placed in one of the FND Amides Categories, the product is structurally similar to the other chemicals in the FND Amides Category. Therefore, there are no structural alerts nor are there any foreseeable breakdown products that would suggest this

product would present a fate/effects profile different from the other FND Amides chemicals or the FND family of chemicals as a whole.

Read-Across Approach:

Model Data: The complex mixtures common to the FND Amides Categories limit the ability to determine model estimates for the typical endpoints in the HPV program (physical/chemical properties, photodegradation, hydrolysis, and fugacity). In addition, the model values that can be generated are, at best, rough estimates because all of the FND Amides Chemicals are mixtures. Therefore, read-across from the available model data to all of the chemicals in the three Categories and the individual chemicals that cannot be modeled is considered appropriate to provide estimates for these endpoints.

Category I: The goal of subcategorizing is to aid in the description and evaluation of Category I as a whole. It is considered appropriate to read-across from other Subcategories. The approach to the Test Plan for the FND Amides Category I chemicals is, therefore, to provide the available information which shows that each of the Subcategories fits the overall pattern of fate and toxicity for the FND Amides Category I, the other FND Amides, and the FND family of chemicals in general. It is not necessary or appropriate to consider the Category or the Subcategories as having “ends” (e.g. based on alkyl chain length). That is, there is no pattern of increasing or decreasing environmental fate or toxicity among these chemicals. Rather, there is a consistency of response across the entire Category. The three subcategories within Category I represent a continuum of functional groups (i.e. unsubstituted, hydroxy substituted and alkyl substituted nitrogen). As with all FND chemicals, differences in the long-chain alkyl constituents do not significantly impact fate and effects. Test Plan development within the HPV construct focuses on ensuring that these functional groups do not impart unpredictable fate or toxicity based on the broad database from the FND family. Since there is no such unpredictability among the functional groups, it is appropriate to read-across within and among the subcategories.

Categories II and III: The chemicals within each category are considered to be structurally and functionally similar and, therefore, a value for an endpoint for one or more chemicals in the Category is considered to be adequate to support the other chemicals in the Category. Further, the similarity of these chemicals to the other FND chemicals (amides, amines, cationics, and nitriles) provides for use of data from the entire family of FND chemicals in support of the overall conclusions. As noted for Category I, proposed testing focuses on ensuring that there is no unpredictable fate or toxicity based on the broad database for the FND family of chemicals.

Individual Chemicals: Although the individual chemicals are not part of a Category, read-across from the family of FND Amides and other FND chemicals is considered appropriate when determination of specific endpoints or modeling cannot be performed for the HPV chemical. In addition, as discussed herein, the FND Amides Chemicals are all considered to be toxic to aquatic organisms and read-across to the larger database is appropriate for the two individual chemicals within the FND Amide group.

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

Approach to Evaluate the Database for the FND Amides Categories

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

1. The chemical names and CAS RNs of the 29 HPV FND Amides chemicals supported by the ACC FND Panel, Amides Task Group (Task Group) were provided.
2. The names of six supporting chemicals and their CAS registry numbers, considered similar to the members of the proposed FND Amides Chemical Categories, were also provided by the Task Group.
3. Published and unpublished reports were obtained as available from the members of the FND Amides 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 reports considered relevant by the Panel were obtained to help establish the full extent and nature of the published literature for the 29 FND Amides Category and 6 supporting chemicals.
5. Each of the reports obtained was reviewed 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. Where possible, estimates for physical/chemical properties and environmental fate values were developed for the HPV and supporting chemicals by using recommended approaches for developing Structure Activity Relationships (SAR).
8. Where possible, Level III fugacity modeling was performed to estimate transport and distribution into environmental compartments for the HPV and supporting chemicals.
9. Robust summaries were generated for the SAR data.

Use of Structure Activity Relationships for the FND Amides Category

Approaches recommended in the EPA document on the use of SAR in the HPV Chemicals Challenge Program were employed in the assessment of the FND Amides Category (U. S. EPA, 1999b). The models employed were those included in EPISuite™ including the Mackay-type fugacity-based modeling.

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

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

(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 RN. 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,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: $t_{1/2} = 0.693/[(k_{\text{phot}} \times \text{HO}\bullet) \times (12\text{-hr}/24\text{-hr})]$.

Estimation of Environmental Distribution

The Level III Mackay-type, fugacity-based models were obtained from the Trent University 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,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.

Modeling Information Specific to the FND Amide Chemicals

Estimations of physical properties, environmental fate and distribution, and ecotoxicity were possible (i.e. there were definable structures) for 8 of the 22 HPV and supporting chemicals in the FND Amides Category I. However, even for these "definable" structures, they at best, only represent the mixtures in these products and the model estimates should be considered with caution. No chemicals in Category II could be modeled. One chemical in Category III could be modeled. Neither of the individual chemicals could be modeled. Since the FND Amides

chemicals are considered to be released into wastewater treatment systems consistent with their use patterns, releases to soil and air were considered to be minor avenues of entry for FND Amides chemicals into the environment. Therefore, for fugacity modeling, all input was assumed to be into surface water using the chemical specific parameters, where available, to obtain estimates of the chemical distributions between environmental compartments.

Physical/Chemical Properties Data

The available data are provided as follows:

Category	Data Summary	Test Plan	Robust Summary Appendix
FND Amides Category I	Table 2a	Table 5a	A1
FND Amides Category II	Table 2b	Table 5b	A2
FND Amides Category III	Table 2c	Table 5c	A3
Individual chemicals	Table 2d	Table 5d	None Available

Measurement of physical/chemical properties for chemicals with surfactant properties is complicated by their behavior in test systems and the environment. For example, measurement of the octanol/water partition coefficient ($\log K_{ow}$) is confounded by the ability of the FND Amide chemicals to emulsify octanol/water solutions. As such, the resulting values are inaccurate and of limited utility for determining environmental fate and effects. Similarly, measurements such as melting point and boiling point do not identify key characteristics of the molecules and therefore provide minimal information. In addition, since these products are mixtures and degrade prior to boiling, they do not meet the criteria specified in the OECD Guideline for testing of these endpoints. The large size of the molecules makes these chemicals non-volatile and the determination of a precise value for vapor pressure is beyond the scope of the OECD guidelines that measure only to 10^{-7} hPa.

As described above, where possible, the estimation program EPIWIN version 3.05 was used to derive estimates of physical/chemical properties. As with actual measurement, prediction of physical/chemical properties for surfactants is complicated. As explained above, the $\log K_{ow}$, a key determinant in the models, is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior of chemicals with surfactant properties. The data are, therefore, of limited value in estimating environmental fate and toxicity. The SAR estimates are based on structure and can be made only for substances for which a structure can be defined. Thus, model data were generated for 8 of the 21 HPV and supporting chemicals in FND Amides Category I. No chemicals in Category II could be modeled. One chemical in Category III could be modeled. Neither of the individual chemicals could be modeled.

Melting Point - Category I and III: The available data or model estimates are presented in the appropriate tables. However, all of the FND Amides chemicals in the three Categories and single chemicals are mixtures. Therefore, they have no true melting point (i.e. each component of the mixture melts at a different temperature). In addition, OECD Guideline 102 is inappropriate for determining melting point of these of chemicals with variable composition (e.g. resulting from the use of natural oils) stating: *The melting point of a substance is considerably*

affected by impurities. Similarly, values from the models should be considered to represent only one of several components in these products.

Melting Point - Category II and Individual Chemicals: No reported or modeled data are available. However, all of the FND Amides chemicals in the three Categories and single chemicals are mixtures that vary with producer and starting materials. Therefore, they have no true melting point (i.e. each component of the mixture melts at a different temperature). In addition, OECD Guideline 102 is inappropriate for determining melting point of chemicals with variable composition (e.g. resulting from the use of natural oils) stating: *The melting point of a substance is considerably affected by impurities.*

Boiling Point - Category I and III: The available data or model estimates are presented in the appropriate tables. However, all of the FND Amides chemicals in the three Categories and single chemicals contain long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Therefore, no true boiling point exists. In addition, OECD Guideline 103 is inappropriate for determining boiling point of these types of chemicals stating: *The methods described in this guideline can be applied to liquid and low-melting substances, provided that they do not undergo chemical change, e.g. auto-oxidation, rearrangement, degradation, etc., below the boiling point.* Similarly, values from the models should be considered to represent only one of several components in these products.

Boiling Point - Category II and Individual Chemicals: No reported or modeled data are available. However, all of the FND Amides chemicals in the three Categories and single chemicals contain long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Therefore, no true boiling point exists. In addition, OECD Guideline 103 is inappropriate for determining boiling point of these types of chemicals stating: *The methods described in this guideline can be applied to liquid and low-melting substances, provided that they do not undergo chemical change, e.g. auto-oxidation, rearrangement, degradation, etc., below the boiling point.*

Vapor Pressure - Category I/III: The available data or model estimates are presented in the appropriate tables. However, all of the FND Amides chemicals in the three Categories and single chemicals are large complex molecules with long-chain hydrocarbons that are non-volatile. OECD Guideline 104 is inappropriate for determining vapor pressure for these types of chemicals. The lowest measurable value for the methods specified in the guideline is 10^{-5} Pa (10^{-7} hPa) using the gas saturation method. All of the FND Amide chemicals are predicted and would be expected to be lower than this value. Lastly, the primary use of vapor pressure in the HPV program is for determining environmental fate (i.e. fugacity) using MacKay-type modeling. This model is insensitive to vapor pressures below approximately 10^{-4} hPa giving essentially the same predicted environmental distribution with vapor pressures over many orders of magnitude below this value. Further, values from the models should be considered to represent only one of several components in these products.

Vapor Pressure - Category II and Individual Chemicals: No reported or modeled data are available. However, all of the FND Amides chemicals in the three Categories and single chemicals are large complex molecules with long-chain hydrocarbons that are non-volatile. OECD Guideline 104 is inappropriate for determining vapor pressure for these types of chemicals. The lowest measurable value for the methods specified in the guideline is 10^{-5} Pa

(10^{-7} hPa). All of the FND Amide chemicals are predicted and would be expected to be lower than this value. Lastly, the primary use of vapor pressure in the HPV program is for determining environmental fate (i.e. fugacity) using MacKay-type modeling. This model is insensitive to vapor pressures below approximately 10^{-4} hPa giving essentially the same predicted environmental distribution with vapor pressures over many orders of magnitude below this value.

Partition Coefficient ($\log K_{ow}$) - Category I and III: The available data or model estimates are presented in the appropriate tables. An inherent property of chemicals with surfactant properties such as these is that they accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Therefore, the accurate measurement of the $\log K_{ow}$ of any chemical with surfactant properties is difficult. Even if such measurements were made accurately, the $\log K_{ow}$ is not an appropriate value by which to predict the partitioning behavior of the FND Amides chemicals in the environment because of the tendency of surfactants to partition at lipid/aqueous interfaces. In addition, the OECD Guidelines (107/117) for determination of the Partition Coefficient indicate that neither method is applicable to “surface-active materials” (Guideline 107) or “surface-active agents” (Guideline 117). Similarly, values from the models should be considered to represent only one of several components in these products.

Partition Coefficient ($\log K_{ow}$) - Category II and Individual Chemicals: No reported or modeled data are available. An inherent property of chemicals with surfactant properties is that they accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Therefore, the accurate measurement of the $\log K_{ow}$ of any chemical with surfactant properties is difficult. Even if such measurements were made accurately, the $\log K_{ow}$ is not an appropriate value by which to predict the partitioning behavior of the FND Amides chemicals in the environment because of the tendency of surfactants to partition at lipid/aqueous interfaces. In addition, the OECD Guidelines (107/117) for determination of the Partition Coefficient indicate that neither method is applicable to “surface-active materials” (Guideline 107) or “surface-active agents” (Guideline 117).

Water Solubility – Category I: The available data or model estimates are presented in the appropriate table. Long-chain (> C18) hydrocarbons are insoluble in water. The chemicals in the FND Amides Category I are formed from these long-chain hydrocarbons and the functional groups, (unsubstituted nitrogen for Subcategory 1, hydroxy functional nitrogen for Subcategory 2, and alkyl functional nitrogen for Subcategory 3) do not increase the solubility to a measurable extent. Because the natural oils used for production of the chemicals are comprised of long-chain hydrocarbons, a read-across from the available information is reasonable for the entire Category. Therefore, the FND Category I chemicals are considered to be insoluble (i.e. solubility much less than 1 ppb). In addition, none of FND Amides chemicals are pure substances and OECD Guideline 105 states: *This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile.* Therefore, the Guideline is not appropriate for the determination of water solubility of these types of chemicals. Similarly, values from the models should be considered to represent only one of several components in these products.

Water Solubility – Category II: The available data are presented in the appropriate table. These chemicals are considered to be “insoluble” or “dispersible” as noted in Table 2b [no published

information is available]. In addition, these chemicals are not pure substances being comprised of mixtures of reaction products of natural oils and/or long-chain hydrocarbons that vary with producer and starting materials. OECD Guideline 105 states: *This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile.* Therefore, the Guideline is not appropriate for the determination of water solubility of these types of chemicals.

Water Solubility – Category III: The available model estimate is presented in the appropriate table. The FND Amphoteric chemicals are completely water soluble resulting from the ionic charges. Company literature and product information indicate high water solubility but no specific solubility values are available. The HPV chemicals, however, are mixtures of long-chain alkyl groups that vary with producer and starting materials. OECD Guideline 105 states: *This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile.* Therefore, the Guideline is not appropriate for the determination of water solubility of these types of chemicals. Similarly, the value from the model should be considered to represent only one of several components in this product.

Water Solubility – Individual Chemicals: The available data are presented in the appropriate table. These chemicals are considered to be “insoluble” as noted in Table 2d [no published information is available]. In addition, these chemicals are not pure substances being comprised of reaction products of naphthenic acids or tall oil. OECD Guideline 105 states: *This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile.* Therefore, the Guideline is not appropriate for the determination of water solubility of these types of chemicals.

Additional Testing – Physical/Chemical Properties

Category I: No additional testing is proposed for any endpoint.

Category II: No additional testing is proposed for any endpoint.

Category III: No additional testing is proposed for any endpoint.

Individual Chemicals: No additional testing is proposed for any endpoint.

See page 14 for a discussion of the read-across approach for these endpoints.

Environmental Fate Data

The available data are provided as follows:

Category	Data Summary	Test Plan	Robust Summary Appendix
FND Amides Category I	Table 3a	Table 6a	A1
FND Amides Category II	Table 3b	Table 6b	A2
FND Amides Category III	Table 3c	Table 6c	A3
Individual chemicals	Table 3d	Table 6d	None Available

Photodegradation – All FND Amides: Models for atmospheric photodegradation were used, where possible, according to EPA guidelines. However, due to the lack of volatility, the fugacity models predict virtually no occurrence of the FND Amides chemicals in air, which is consistent with the very low vapor pressures. Nonetheless, modeling of the HPV and supporting chemicals indicates that they would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 1.1 to 4.7 hours for the Category I chemicals and 3.2 hours for the Category III chemical that could be modeled). Values from the models should be considered to represent only one of several components in these products.

Water Stability (Hydrolysis) – Category I, III and Individual Chemicals: These FND Amide chemicals do not have hydrolyzable groups and, therefore, abiotic hydrolysis is not a pathway for degradation in the environment. Consistent with this knowledge, 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.

Water Stability (Hydrolysis) – Category II: As noted above, the FND Imidazoline Derivatives in this category are produced to provide stability (e.g. at low temperatures) but can be hydrolyzed to their respective amide from which they are formed. Thus, hydrolysis is a key feature for these chemicals. The rate of hydrolysis is important to the understanding of the environmental fate and toxicity of these chemicals. Therefore, hydrolysis testing for this group of chemicals is required prior to defining approaches to other environmental fate and effects evaluations.. The similarity of the chemicals allows for one chemical (CAS RN 72749-55-4) to be tested to support the category (also see read-across discussion on page 14).

Environmental Distribution - Category I: An estimation of the transport and distribution in environmental media (percent in air, water, soil and sediment) of the FND Amides Category I chemicals that could be modeled was made. All releases (using the 1000 kg/hr default) were considered to be to the water compartment. Distribution to air and soil were < 1% while distribution to the water compartment varied from 5 to 99% with the remainder in the sediment. Values from the models should be considered to represent only one of several components in these products.

Environmental Distribution - Category III: An estimation of the transport and distribution in environmental media (percent in air, water, soil and sediment) of the FND Amides Category III

chemical that could be modeled was made. All releases (using the 1000 kg/hr default) were considered to be to the water compartment. Distribution to air, sediment and soil were < 1% while distribution to the water compartment was > 99%. Values from the models should be considered to represent only one of several components in these products.

Environmental Distribution - Category II and Individual Chemicals: These FND Amides could not be modeled and no environmental distribution was obtained. Using read-across from other FND chemicals provides an estimate of the likely distribution. Assuming the primary release to the water compartment, the sediment would be expected to be the principle reservoir for the low solubility chemicals. The remainder would be expected to remain in the water compartment with little partitioning to the air or soil.

Biodegradation – Category I

Subcategory 1 (Fatty Acid Amides): Oleamide (CAS RN 301-02-0) and the supporting tallow amide derivative (CAS RN 61790-31-6) were “readily” biodegradable in standard OECD test protocols. Erucamide (CAS RN 112-84-5), however, was “inherently” degradable attaining 27 and 43% degradation after 28 and 140 days, respectively at a concentration of 10 mg/L.

Subcategory 2 (Fatty Alkanolamides): Two chemicals were tested in standard OECD studies that showed “ultimate” (77%; CAS RN 120-40-1) and “inherent” (52%; CAS RN 68603-42-9) biodegradation. A third study (CAS RN 68140-00-1) simulating a treatment facility indicated the test substance would be rapidly degraded (92% with a 3 hour retention time). The supporting chemical (CAS RN 68155-06-6) was “readily” biodegradable in a standard test.

Subcategory 3 (Fatty Acid Reaction Products with Amines): A study with CAS RN 68910-93-0 showed “inherent” biodegradation of the test substance.

SUMMARY: The data available for the FND Amides Category I chemicals indicate that single alkyl substituents of C18 or less are rapidly degraded. Longer single alkyl group substitutions and/or multiple long-chain alkyl substituents result in slower “inherent” biodegradability. The available data across the Subcategories, therefore, are adequate to define and support Category I as a whole. No additional testing is proposed.

Biodegradation – Category II: No biodegradation studies for the FND Imidazoline Derivatives (HPV chemicals) were identified. A study with the supporting chemical (CAS RN 68122-86-1) showed minimal degradation, thought to result from degradation of a contaminant, after 20 days. It is likely that the nature and rate of the hydrolysis of these chemicals to the amide (and non-cyclic) form will impact the biodegradation of the chemicals. Upon completion of the hydrolysis determinations (see above), appropriate tests to establish biodegradability will be proposed. The similarity of the chemicals allows for one chemical (CAS RN 72749-55-4) to be tested to support the category (also see read-across discussion on page 14).

Biodegradation – Category III: One of the HPV chemicals (CAS RN 61789-40-0) has been tested in a standard OECD guideline study. In five different procedures, the chemical was determined to be “readily” biodegradable. In a study simulating a treatment facility, the test substance was rapidly degraded (97% with a 3-hour retention time). In addition, the two

supporting chemicals (CAS RNs 4292-10-8 and 70851-07-9) were shown to be “readily” biodegradable. Based on these data, the chemicals in this Category can be considered to be “readily” biodegradable. No additional testing is proposed.

Biodegradation – Individual Chemicals: No biodegradation data are available for the individual chemicals. Testing according to OECD Guidelines is proposed for both chemicals.

Ecotoxicity Data

Aquatic Toxicity – All FND Amides: The FND Amides chemicals in the three Categories and the two individual chemicals all have surfactant properties and should be considered to be toxic (EC₅₀ and LC₅₀ values of < 10 mg/L) to aquatic species under conditions that allow contact of the chemicals with the organisms. The water solubility of the chemicals does not impact the toxicity except as it relates to the ability to conduct tests appropriately to obtain exposure of the test species. This toxicity is common not only to the FND Amides chemicals but also to the FND Amines, Cationics, and Nitriles Categories that have been submitted in the HPV Challenge program separately. Further, the high toxicity is consistent with that of a large body of surfactants (e.g. alcohol ethoxylates, alkylphenol ethoxylates, sodium lauryl sulfate, and others). The available data for the FND Amides chemicals are provided in the appropriate Tables. For screening purposes, read-across is adequate for the chemicals without tests (also see read-across discussion on page 14) and the FND Amides chemicals, as with surfactants in general, are considered toxic to aquatic organisms.

Aquatic Toxicity – Category II: The ability of the parent chemicals to hydrolyze to the amide in this Category requires further investigation. Studies to complete the aquatic toxicity screening profile for CAS RN 61791-39-7 for acute fish and algae toxicity (this chemical has been shown to have an EC₅₀ value of 1.5 mg/L for daphnia) will be conducted following completion of the hydrolysis studies (see above).

Human Health-Related Data

The available data are provided as follows:

Category	Data Summary	Test Plan	Robust Summary Appendix
FND Amides Category I	Table 4a	Table 7a	A1
FND Amides Category II	Table 4b	Table 7b	A2
FND Amides Category III	Table 4c	Table 7c	A3
Individual chemicals	Table 4d	Table 7d	None Available

Acute Toxicity – All FND Amides: All of the acute oral and dermal toxicity data available for the FND Amides indicate that these chemicals are of limited toxicity with LD₅₀ values > 1.5 g/kg and > 2 g/kg, respectively. Two inhalation studies with Category I chemicals indicate local effects (irritation), but no systemic toxicity at high concentrations. These data are consistent with the acute toxicity of the other FND chemicals (amines, cationics, nitriles) described and submitted in the HPV Challenge Program in separate Categories. Thus, there is a large body of

data supporting the conclusion that all of these FND supported chemicals are of low acute toxicity. No further testing is proposed.

Repeated dose toxicity

Category I: Repeated dose toxicity studies were available for 3 (CAS RNs 112-84-5, 120-40-1 and 68140-00-1) of the 22 chemicals in this category. The reported no observed adverse effect level (NOAEL) for CAS RN 112-84-5 was 7500 mg/kg/day (animals dosed via gavage with 10 doses each day for five days followed by a 23-day observation period). In 90-day feeding studies (CAS RNs 120-40-1 and 68140-00-1), the NOAELs were determined to be 50 and > 750 mg/kg/day, respectively. These 90-day studies indicated no organ specific or overt toxicity. For CAS RN 120-40-1, effects of general weight loss and other nonspecific responses were observed at the higher doses.

Category II: Two repeated dose toxicity studies were available for the supporting chemical, CAS RN 68122-86-1. In a 13-week dietary study in dogs, the only effects noted were slightly altered hematology measurements at the high dose of 40,000 ppm (approximately 1300 and 1950 mg/kg/day for males and females, respectively) and decreased cholesterol in males from the mid-dose group (12,000 ppm; 366 mg/kg/day) and males and females from the high-dose group. The NOAEL was considered to be the low dose of 4000 ppm (approximately 143 mg/kg/day for both sexes). In a 91-day rat study, the NOAEL was greater than 2200 mg/kg/day.

Category III: Repeated dose toxicity tests were available for CAS RN 61789-40-0. The NOAELs were 250 mg/kg/day (based on the presence of gastritis at 500 and 1000 mg/kg/day) in a 90-day study and 500 mg/kg/day in a 28-day subchronic study (based on similar gastric lesions at 1000 mg/kg/day). In addition, a LOAEL of 300 mg/kg/day (the lowest dose tested) was determined in a 7-day gavage study based primarily on clinical signs in females that included compound-colored urine, soft feces and nasal discharge.

Individual Chemicals: No data were located for repeated dose toxicity.

Genetic Toxicity (*in vitro/in vivo*)

Category I: *In vitro* genetic toxicity studies (bacterial reverse mutation assay) for 10 of the 22 chemicals in this Category indicated the chemicals are not mutagenic in this assay, as would be expected based on the structures and molecular weights.

Category II: *In vitro* mutagenicity tests, including bacterial reverse mutation, CHO cytogenetics, and Unscheduled DNA Synthesis assays, were available for the supporting chemical, CAS RN 68122-86-1, and indicated no mutagenic or clastogenic activity.

Category III: *In vitro* mutagenicity assays (bacterial reverse mutation assay) were available for CAS RN 61789-40-0 and indicated no mutagenic activity. In addition, an *in vivo* mouse micronucleus assay was negative for this chemical.

Individual Chemicals: No data were available for mutagenicity screening assays.

Reproductive/Developmental Toxicity

Category I: Evaluation of potential reproductive effects are satisfied by the histological evaluation of reproductive organs in the 90-day repeated dose toxicity studies for CAS RNs 120-40-1 and 68140-00-1. 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 > 1000 and > 750 mg/kg/day, respectively, which were the highest doses tested.

A developmental toxicity study was conducted for one chemical in Subcategory 2 (CAS RN 68603-42-9). No effects were observed, and the rat maternal and developmental NOAELs were greater than the highest dose tested of 1000 mg/kg/day.

Category II: Evaluation of potential reproductive effects are satisfied by the histological evaluation of reproductive organs in the 13-week repeated dose toxicity study for CAS RN 68122-86-1. No effects on the gonads or other reproductive organs were observed at any dose level in this study. Thus the NOAEL for reproductive screening was > 1322 mg/kg/day, the highest dose tested.

Developmental toxicity studies were conducted for CAS RN 68122-86-1. No effects were observed and thus the rat maternal and developmental NOAELs were greater than the highest dose tested of 1000 mg/kg/day. In addition, a probe study conducted to help set doses for the definitive developmental toxicity study, indicated no maternal or fetal toxicity up to the highest dose of 1875 mg/kg/day.

Category III: Toxicity to reproduction was satisfactorily screened in the two repeated dose toxicity studies for CAS RN 61789-40-0 by histological evaluation of the reproductive organs. No effects were observed at any dose in either study and the NOAEL for reproductive screening for each study was > 1000 mg/kg/day.

A developmental toxicity study was conducted for CAS RN 693-33-4. The NOAEL was established as 50 mg/kg/day for maternal toxicity and 150 mg/kg/day for developmental toxicity. Effects in the fetuses at the highest dose of 250 mg/kg/day were considered biologically significant but related to maternal toxicity.

Individual Chemicals: No data were available for reproductive or developmental toxicity.

Related FND Chemicals: In evaluating potential toxicity of the FND Amides chemicals, it is also useful to review the available data for the related FND Cationic 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 no mutagenic activity 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 Amides chemicals will not pose significant toxicity to humans.

Additional Testing – Human Health-Related Studies

Category I: The consistency of the available data for most endpoints with the large body of data for the FND family as a whole, allows for read-across throughout the Category and within and between Subcategories (also see read-across discussion on page 14). One exception is the lack of a valid chromosomal aberration test. A chromosome aberration test with CAS RN 142-78-9, the lowest molecular weight chemical in Category I, is proposed. No other testing is proposed.

Category II: The consistency of the available data for most endpoints with the large body of data for the FND family as a whole allows for read-across throughout the Category (also see read-across discussion on page 14). One exception is the lack of a valid chromosomal aberration test. A chromosome aberration test with CAS RN 61791-39-7, the lowest molecular weight chemical in Category II, is proposed. No other testing is proposed.

Category III: The consistency of the available data for all of the endpoints with the large body of data for the FND family as a whole allows for read-across throughout the Category (also see read-across discussion on page 14). No testing is proposed.

Individual Chemicals: Although Naphthenic acids, reaction products with diethylenetriamine (CAS RN 68131-13-5) and Fatty acids, tall oil, compounds with triethanolamine (CAS RN 68132-46-7) were not considered to adequately fit in one of the three FND Amides categories, the chemicals do not contain major structural alerts nor are there any foreseeable breakdown products of concern. Therefore, these chemicals are not expected to result in toxicology profiles significantly different from the other FND Amides or FND chemicals in general. This conclusion allows for read-across to acute toxicity data (Table 7d) from the other FND Amides as well as the other FND chemicals. Due to the lack of supporting data, OECD Guideline 471 and 473 testing for mutagenicity, and OECD Guideline 422 testing for repeated dose and reproductive/developmental screening are proposed for both. In addition to providing information on the individual chemicals, these studies are expected to further support the overall evaluation of the FND Amides group of chemicals.

References

- 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. 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. 2000. User's Guide for AOPWIN, Version 1.9. 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. 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>.

Table 1a
Structures of FND Amides Category I Chemicals^a

Subcategory 1: Fatty Acid Amides	
$\text{CH}_3(\text{CH}_2)_{16}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ <p align="center">Stearamide 124-26-5</p>	$\text{CH}_3(\text{CH}_2)_7-\text{CH}=\text{CH}-(\text{CH}_2)_7-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ <p align="center">Oleamide 301-02-0</p>
$\text{CH}_3(\text{CH}_2)_7-\text{CH}=\text{CH}-(\text{CH}_2)_{11}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ <p align="center">Erucamide 112-84-5</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ <p align="center">R = Hydrogenated Tallow</p> <p align="center"><i>Amides, tallow, hydrogenated</i> 61790-31-6</p>
Subcategory 2: Fatty Alkanolamides	
$\text{CH}_3(\text{CH}_2)_{10}-\overset{\text{O}}{\parallel}{\text{C}}-\underset{\text{H}}{\text{N}}-(\text{CH}_2)_2-\text{OH}$ <p align="center">Dodecanamide, N-(2-hydroxyethyl)- 142-78-9</p>	$\text{CH}_3(\text{CH}_2)_{10}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p align="center">Dodecanamide, N,N-bis(2-hydroxyethyl)- 120-40-1</p>
$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p align="center">R = Coconut Oil</p> <p align="center">Amides, coco, N,N-bis(hydroxyethyl) 68603-42-9</p>	$\text{CH}_3(\text{CH}_2)_7-\text{HC}=\text{CH}-(\text{CH}_2)_7-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p align="center">Oleamide, N,N-bis(2-hydroxyethyl)- 93-83-4</p>
$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p align="center">R = Tall Oil</p> <p align="center">Amides, tall-oil fatty, N,N-bis(hydroxyethyl) 68155-20-4</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p align="center">R = Soya Bean Oil</p> <p align="center">Amides, soya, N,N-bis(hydroxyethyl) 68425-47-8</p>

Table 1a (continued)

$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-(\text{CH}_2)_2-\text{OH}$ <p>R = Coconut Oil</p> <p>Amides, coco, N-(hydroxyethyl) 68140-00-1</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p>R = Coconut Oil</p> <p>Coconut oil, reaction products with diethanolamine** 8051-30-7</p>
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C} \\ \backslash \\ \text{O}^- \end{array}$ $\text{HO}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{N}^+-\text{CH}_2-\text{CH}_2-\text{OH}$ <p>R = Coconut Oil</p> <p>Fatty acids, coco, compounds with diethanolamine 61790-63-4</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}-[(\text{CH}_2)_2\text{OH}]_2$ <p>R = C₁₂ - C₁₈</p> <p>Amides, C12-18, N,N-bis(hydroxyethyl) 68155-06-6</p>
<p>Subcategory 3: Fatty Acid Reaction Products with Amines</p>	
$\text{C}_{17}\text{H}_{35}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\overset{\text{O}}{\parallel}{\text{C}}-\text{C}_{17}\text{H}_{35}$ <p>Octadecanamide, N,N'-ethylenebis 110-30-5</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-[\text{NH}-\text{CH}_2-\text{CH}_2]_2-\text{NH}-\text{R}'$ <p>R = Tall Oil R' = H or Tall Oil</p> <p>Fatty acids, tall-oil, reaction with diethylenetriamine** 61790-69-0</p>

Table 1a (continued)

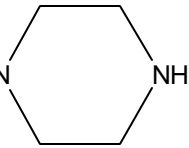
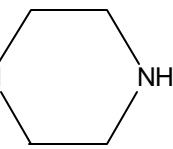
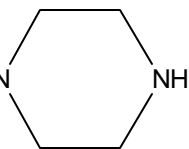

$R-C(=O)-NH-[(CH_2)_2-NH]_3-(CH_2)_2-NH_2$ <p style="text-align: center;">...</p> $R-C(=O)-[NH-CH_2-CH_2]_2-N-C(=O)-R$ <p style="text-align: center;">R = Tall Oil</p> <p style="text-align: center;">Fatty acids, tall-oil, reaction products with tetraethylenepentamine** 68953-36-6</p>	$R-C(=O)-NH-CH_2-CH_2-N$  $R-C(=O)-[NH-CH_2-CH_2]_3-NH_2$ <p style="text-align: center;">R = Tall Oil</p> <p style="text-align: center;">Fatty acids, tall-oil, reaction with polyethylenepolyamines** 68910-93-0</p>
$R-C(=O)-NH-CH_2-CH_2-N$  $R-C(=O)-[NH-CH_2-CH_2]_3-NH_3^+ \quad CH_3COO^-$ <p style="text-align: center;">R = Tall Oil</p> <p style="text-align: center;">Fatty acids, tall-oil, reaction with polyethylenepolyamine acetates (essentially acetates of CAS RN 68910-93-0)** 64754-93-4</p>	$R-C(=O)-NH-CH_2-CH_2-N$  <p style="text-align: center;">R = Tall Oil</p> <p style="text-align: center;">Fatty acids, tall-oil, low boiling, reaction products with 1-piperzineethanamine** 71820-35-4</p>

Table 1a (continued)

$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-(\text{CH}_2)_3-\underset{\text{CH}_3}{\text{N}}-\text{CH}_3$ <p>R = Coconut Oil</p> <p>Amides, coco, N-[3-(dimethylamino)propyl] ** 68140-01-2</p>	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-[\text{NH}-\text{CH}_2-\text{CH}_2]_x-\text{NH}-\text{R}'$ <p>● $\text{C}_{12}\text{H}_{25}$--SO_3H</p> <p>R = Tall Oil R' = H, Tall Oil</p> <p><i>Fatty acids, tall-oil, reaction products with polyalkylenepolyamines, dodecylbenzenesulfonates**</i> 68910-87-2</p>
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Shaded cells with name and CAS RN in italics are supporting chemicals.

^a Note that in the naming convention used for the FND Amides chemicals, the carbon in the carbonyl group is one of the carbons in the alkyl chain when R or R' is used to designate the alkyl chain (e.g. when R=C₁₈ with a carbonyl group, the structure is C₁₇-C=O).

** Reaction products are diverse in their potential structures.

Example 1: for CAS RN 68953-36-6, the structures shown represent two of several products that are generated by different processes yielding one, two or three moles of fatty acid reacted with one mole of amine (the final products will also be mixtures of these reaction products).

Example 2: for CAS RN 68910-93-0, the reaction product mixture is highly dependent on the polyamine starting material that is used to react with tall oil fatty acid (TOFA). In one process, the polyamine material is approximately 20% triethylenetetramine (TETA), 20% ethylene dichloride-ammonia condensation product, and 60% 1-(2-aminoethyl) piperazine (this mixture being assigned the CAS RN 71820-35-4). The piperazine yields the ring structure as shown above. One commercial product contains 60% of the CAS RN 71820-35-4 mixture with the balance a TOFA/TETA material and unreacted ethylene dichloride-ammonia condensation product. Other commercial products may not contain any of the piperazine and may have a second TOFA reacted with the polyamine (i.e. -NHR' where R' = H or TOFA). For the acetate salts (CAS RN 64754-93-4), when the piperazine mixture is employed, only the TOFA/TETA is in the salt form.

Table 1b

Structures of FND Amides Category II (Imidazoline Derivatives) Chemicals^a

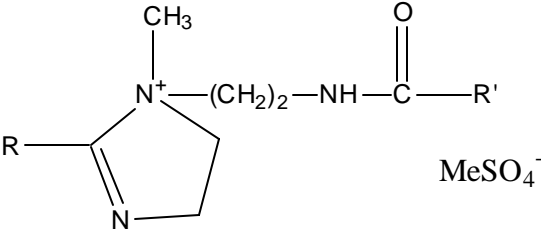
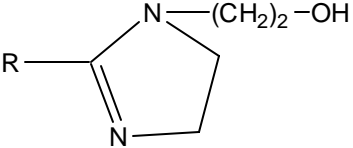
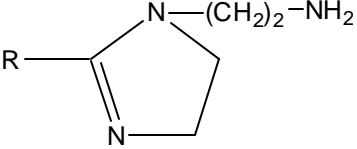
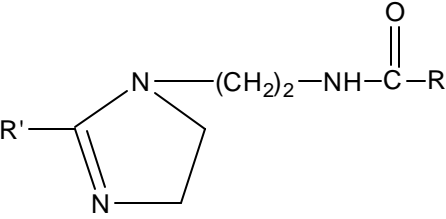
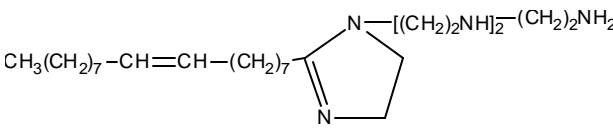
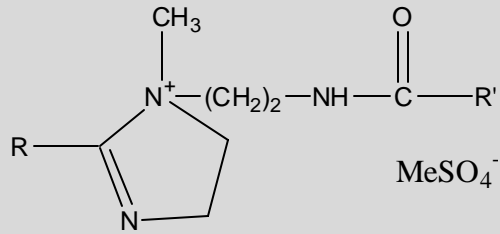
 <p>R = C₁₇ & C₁₇ Unsaturated R' = C₁₈ & C₁₈ Unsaturated</p> <p>Imidazolium cmpds., 2-(C17&C-17-unsat. Alkyl)-1[2-(C18 & C18-unsat. amido) ethyl]-4,5-dihydro-1-methyl, Me sulfates 72749-55-4</p>	 <p>R =Nortall Oil</p> <p>1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives 61791-39-7</p>
 <p>R =Nortall Oil</p> <p>1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall oil alkyl derivatives 68442-97-7</p>	 <p>R = C₁₄ & C₁₈ R' = C₁₃ & C₁₇</p> <p>Amides, C14-18, N-[2-(C13-17-alkyl)-4,5-dihydro-1H-imidazol-1-yl]ethyl] 72623-72-4</p>

Table 1b (continued)

Structures of FND Amides Category II (Imidazoline Derivatives) Chemicals^a

 <p>CH₃(CH₂)₇-CH=CH-(CH₂)₇-N-[(CH₂)₂NH]₂-(CH₂)₂NH₂</p> <p>1,2-Ethanediamine, N-(2-aminoethyl)-N'-{2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl} ethyl 65817-50-7</p>	 <p><i>R = Nortallow</i> <i>R' = Tallow</i></p> <p><i>Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl) Me sulfate</i> 68122-86-1</p>
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Shaded cells with name and CAS RN in italics are supporting chemicals.

^a Note that in the naming convention used for the FND Amides chemicals, the carbon in the carbonyl group is one of the carbons in the alkyl chain when R or R' is used to designate the alkyl chain (e.g. when R=C₁₈ with a carbonyl group, the structure is C₁₇-C=O).

Table 1c
Structures of FND Amides Category III
(FND Amphoteric (N-carboxymethyl substituted) Chemicals^a)

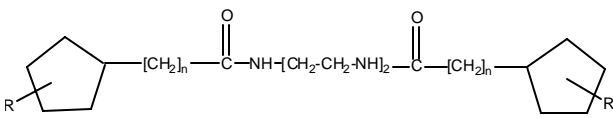
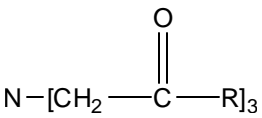
$\left[\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}-(\text{CH}_2)_3-\text{N}^+ \begin{array}{l} \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array} -\text{CH}_2-\text{COO}^- \end{array} \right] \bullet \text{NaCl}$ <p>R = Coconut Oil</p> <p>1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, chlorides, sodium salts 61789-39-7</p>	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}-(\text{CH}_2)_3-\text{N}^+ \begin{array}{l} \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array} -\text{CH}_2-\text{COO}^- \end{array}$ <p>R = Coconut Oil</p> <p>1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivatives, inner salt (betaine) 61789-40-0</p>
$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3(\text{CH}_2)_{14}-\text{C}-\text{N}^+ \begin{array}{l} \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array} -\text{CH}_2-\text{COO}^- \end{array}$ <p>1-Hexadecanaminium, N-(carboxymethyl)-N,N-dimethyl-, inner salt 693-33-4</p>	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3(\text{CH}_2)_{10}-\text{C}-\text{NH}-(\text{CH}_2)_3-\text{N}^+ \begin{array}{l} \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array} -\text{CH}_2-\text{COO}^- \end{array}$ <p><i>1-Propanaminium, N-(carboxymethyl)-N,N-dimethyl-3-[(1-oxododecyl)amino]-, inner salt</i> 61789-39-7 4292-10-8</p>
$\left[\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{N} \begin{array}{l} \\ \text{H} \end{array} -(\text{CH}_2)_3-\text{N}^+ \begin{array}{l} \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array} -\text{CH}_2\text{COO}^- \end{array} \right] \bullet \text{NaCl}$ <p>R = Coconut Oil</p> <p><i>Amides, coco, N-[3-(dimethylamino)propyl], alkylation products with chloroacetic acid, sodium salt**</i> 70851-07-9</p>	

Shaded cells with name and CAS RN in italics are supporting chemicals.

^a Note that in the naming convention used for the FND Amides chemicals, the carbon in the carbonyl group is one of the carbons in the alkyl chain when R or R' is used to designate the alkyl chain (e.g. when R=C₁₈ with a carbonyl group, the structure is C₁₇-C=O).

** See footnote to Table 1a regarding reaction products.

Table 1d
Structures of FND Amides Individual Chemicals^a

 <p align="center">R = Multiple alkyl groups or fused cycloaliphatic rings</p> <p align="center">Naphthenic acids, reaction products with diethylenetriamine 68131-13-5</p>	 <p align="center">R = Tall Oil</p> <p align="center">Fatty acids, tall oil, compounds with triethanolamine** 68132-46-7</p>
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^a Note that in the naming convention used for the FND Amides chemicals, the carbon in the carbonyl group is one of the carbons in the alkyl chain when R or R' is used to designate the alkyl chain (e.g. when R=C₁₈ with a carbonyl group, the structure is C₁₇-C=O).

** See footnote to Table 1a regarding reaction products.

**Table 2a: Category I – FND Amides
 Physical/Chemical Properties Data/Model Results**

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
Subcategory 1: Fatty Acid Amides					
124-26-5	109	250 – 251	0.004	6.70	insoluble
301-02-0	76	415	1.2 E-006	6.48	insoluble
112-84-5	183 80 ^a	461	8.3 E-8	8.44	0.0005
<i>61790-31-6</i>					
Subcategory 2: Fatty Alkanolamides					
142-78-9	154	404	6.6 E-9	3.24	43.9
120-40-1	38.7	431	6.7 E-9	2.89	insoluble
68603-42-9					
93-83-4	204	504	5.9 E-13	5.62	0.08
68155-20-4					
68425-47-8					
68140-00-1					
8051-30-7					
61790-63-4					
<i>68155-06-6</i>	<i>154</i>	<i>419</i>	<i>1 E-9</i>	<i>2.39</i>	<i>158</i>
Subcategory 3: Fatty Acid Reaction Products with Amines					
110-30-5	323	736	8 E-18	14	2 E-10
61790-69-0					Insoluble ^a
68953-36-6					Insoluble ^a
68910-93-0					Insoluble ^a
64754-93-4					Insoluble ^a
71820-35-4					
68140-01-2					
<i>68910-87-2</i>					

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.

Shaded cells with CAS RN and data in italics are supporting chemicals.

^a Based on company literature.

**Table 2b: Category II – FND Imidazoline Derivatives
 Physical/Chemical Properties Data/Model Results**

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
72749-55-4					
61791-39-7					Dispersible ^a
68442-97-7					Insoluble ^a
72623-72-4					
65817-50-7					
<i>68122-86-1</i>					

Regular font indicates data obtained from appropriate models as described in the text.
 Shaded cells with CAS RN and data in italics are supporting chemicals.

^a Based on company literature.

**Table 2c: Category III - FND Amphoteric (N-carboxymethyl substituted)
 Physical/Chemical Properties Data/Model Results**

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
61789-39-7					
61789-40-0					
693-33-4	243	566	2.4 E-12	2.44	171
<i>4292-10-8</i>					
<i>70851-07-9</i>					

Regular font indicates data obtained from appropriate models as described in the text.
 Shaded cells with CAS RN and data in italics are supporting chemicals.

**Table 2d: FND Amides Individual Chemicals
 Physical/Chemical Properties Data/Model Results**

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K _{ow})	Water Solubility (mg/l)
68131-13-5					Insoluble ^a
68132-46-7					Insoluble ^a

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

^a Based on company literature.

**Table 3a: Category I – FND Amides
 Environmental Fate and Ecotoxicity Data/Model Results**

CAS RN	Photodegradation ($\text{cm}^3/\text{molecule}\cdot\text{sec}$ for k_{phot})	Stability in Water	Transport & Distribution ^a	Biodegradation	Acute/Prolonged Tox. to Fish LC_{50} (mg/l)	Acute Tox. to Invertebrates EC_{50} (mg/l)	Toxicity to Aquatic Plants EC_{50} (mg/l)	Chronic Tox. to Aquatic Invertebrates EC_{50} (mg/l)
Subcategory 1: Fatty Acid Amides								
124-26-5	$k_{\text{phot}} = 27 \text{ E-12}$ $t_{1/2} = 4.7 \text{ hr}$	NC	air: < 1% water: 13% soil: < 1% sediment: 87%					
301-02-0	$k_{\text{phot}} = 80 \text{ to } 88 \text{ E-12}$ $t_{1/2} = 1.5 \text{ to } 1.6 \text{ hr}$	NC	air: < 1% water: 14% soil: < 1% sediment: 86%	80% ThOD in 28 d				
112-84-5	$k_{\text{phot}} = 86 \text{ to } 93 \text{ E-12}$ $t_{1/2} = 1.4 \text{ to } 1.5 \text{ hr}$	NC	air: < 1% water: 5% soil: < 1% sediment: 95%	15 and 43% ThOD in 28 and 140 d, respectively; 27% ThOD in 28 d	NOEC > 0.105 mg/l (28 days)			NOEC = 0.080
<i>61790-31-6</i>				<i>73% ThOD in 28 d</i>				

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

Regular font without footnote indicates data obtained from appropriate models as described in the text.

Shaded cells with CAS RN and data in italics are supporting chemicals.

NC = Not calculable.

^a Water was assumed to be the primary route of entry into the environment.

Table 3a: Category I – FND Amides (continued)
Environmental Fate and Ecotoxicity Data/Model Results

CAS RN	Photodegradation (cm ³ /molecule-sec for k_{phot})	Stability in Water	Transport & Distribution ^a	Biodegradation	Acute/Prolonged Tox. to Fish LC ₅₀ (mg/l)	Acute Tox. to Invertebrates EC ₅₀ (mg/l)	Toxicity to Aquatic Plants EC ₅₀ (mg/l)	Chronic Tox. to Aquatic Invertebrates EC ₅₀ (mg/l)
Subcategory 2: Fatty Alkanolamides								
142-78-9	$k_{\text{phot}} = 31 \text{ E-12}$ $t_{1/2} = 4.2 \text{ hr}$	NC	air: < 1% water: 98% soil: < 1% sediment: 1%					
120-40-1	$k_{\text{phot}} = 49 \text{ E-12}$ $t_{1/2} = 2.6 \text{ hr}$	NC	air: < 1% water: 99% soil: < 1% sediment: 1%	77% ThCO₂ in 28 d				
68603-42-9				51.8% ThOD in 28 d	6.7	3.3 2.15^b 2.64^b		
93-83-4	$k_{\text{phot}} = 111 \text{ to}$ 118 E-12 $t_{1/2} = 1.1 \text{ to } 1.2 \text{ hr}$	NC	air: < 1% water: 34% soil: < 1% sediment: 66%		2.6			
68155-20-4								
68425-47-8								
68140-00-1				92% DOC			1.1	
8051-30-7								
61790-63-4								
<i>68155-06-6</i>	<i>$k_{\text{phot}} = 48 \text{ E-12}$</i> <i>$t_{1/2} = 2.7 \text{ hr}$</i>	<i>NC</i>	<i>air: < 1%</i> <i>water: 99%</i> <i>soil: < 1%</i> <i>sediment: 0.5%</i>	84% ThOD in 28 d				

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

Regular font without footnote indicates data obtained from appropriate models as described in the text.

Shaded cells with CAS RN and data in italics are supporting chemicals.

NC = Not calculable.

^a Water was assumed to be the primary route of entry into the environment.

^b Replicate values from same study.

Table 3a: Category I – FND Amides (continued)
Environmental Fate and Ecotoxicity Data/Model Results

CAS RN	Photodegradation (cm ³ /molecule-sec for k _{phot})	Stability in Water	Transport & Distribution ^a	Biodegradation	Acute/Prolonged Tox. to Fish LC ₅₀ (mg/l)	Acute Tox. to Invertebrates EC ₅₀ (mg/l)	Acute Toxicity to Aquatic Plants EC ₅₀ (mg/l)	Chronic Tox. to Aquatic Invertebrates EC ₅₀ (mg/l)
Subcategory 3: Fatty Acid Reaction Products with Amines								
110-30-5	k _{phot} = 70 E-12 t _{1/2} = 1.8 hr	NC	air: < 1% water: 5% soil: < 1% sediment: 95%					
61790-69-0								
68953-36-6								
68910-93-0				30 - 40% ThOD in 126 d	0.43			
64754-93-4								
71820-35-4						0.30		
68140-01-2								
<i>68910-87-2</i>								

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

Regular font without footnote indicates data obtained from appropriate models as described in the text.

Shaded cells with CAS RN and data in italics are supporting chemicals.

NC = Not calculable.

^a Water was assumed to be the primary route of entry into the environment.

**Table 3b: Category II – FND Imidazoline Derivatives
 Environmental Fate and Ecotoxicity Data/Model Results**

CAS RN	Photodegradation (cm³/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution ^a	Biodegradation	Acute/Prolonged Tox. to Fish LC₅₀ (mg/l)	Acute Tox. to Invertebrates EC₅₀ (mg/l)	Acute Toxicity to Aquatic Plants EC₅₀ (mg/l)	Chronic Tox. to Aquatic Invertebrates EC₅₀ (mg/l)
72749-55-4								
61791-39-7						1.5		
68442-97-7								
72623-72-4								
65817-50-7								
<i>68122-86-1</i>				<i>5% BOD in 20 d</i>	<i>59</i>			

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

Shaded cells with CAS RN and data in italics are supporting chemicals.

^a Water was assumed to be the primary route of entry into the environment.

**Table 3c: Category III – FND Amphetics (N-carboxymethyl substituted)
 Environmental Fate and Ecotoxicity Data/Model Results**

CAS RN	Photodegradation (cm ³ /molecule-sec for k _{phot})	Stability in Water	Transport & Distribution ^a	Biodegradation	Acute/Prolonged Tox. to Fish LC ₅₀ (mg/l)	Acute Tox. to Invertebrates EC ₅₀ (mg/l)	Acute Toxicity to Aquatic Plants EC ₅₀ (mg/l)	Chronic Tox. to Aquatic Invertebrates EC ₅₀ (mg/l)
61789-39-7					0.23			
61789-40-0				³ 93% ThCO ₂ in 28 d; 86% degraded in 28 d; 71% ThCO ₂ in 35 d; » 100% DOC in 28 d; » 100% DOC in 28 d; 97% DOC removed (3 h hydraulic retention time); Anaerobic - » 56% degraded in 56 d	2.0 2.0 6.73 NOEC = 0.16 (28 d)	21.5 6.40 1.1 NOEC = 0.9 (21 d)	E_bC₅₀ = 30^c and E_rC₅₀ = 48; EC₅₀ = 0.55; EC₅₀ = 0.55; NOEC = 0.96 (72 hr)	
693-33-4	k _{phot} = 40 E-12 t _{1/2} = 3.2 hr	NC	air: < 1% water: > 99% soil: < 1% sediment: 0.5%			2.5		

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

Regular font without footnote indicates data obtained from appropriate models as described in the text.

Shaded cells with CAS RN and data in italics are supporting chemicals.

NC = Not calculable.

^a Water was assumed to be the primary route of entry into the environment.

^c E_bC₅₀ is the EC₅₀ based on growth (biomass); E_rC₅₀ is the EC₅₀ based on growth rate.

**Table 4a: Category I – FND Amides
 Human Health-Related Data**

CAS RN	Acute Oral Toxicity LD ₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD ₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
Subcategory 1: Fatty Acid Amides							
124-26-5	> 10				Not mutagenic (Ames)		
301-02-0	12.4 ml/kg				Not mutagenic (Ames)		
112-84-5	> 5			7500 ^a	Not mutagenic (Ames)		
<i>61790-31-6</i>	<i>> 5</i>						
Subcategory 2: Fatty Alkanolamides							
142-78-9					Not mutagenic (Ames)		
120-40-1	> 3.5; > 5 ml/kg		> 2	50 ^b	Not mutagenic (Ames)	> 1000 ^b	^c
68603-42-9	> 5; > 5; > 5		> 2				Rat maternal and developmental > 1000 ^a
93-83-4							

Shaded cells with CAS RN and data in italics are supporting chemicals.

^a Animals dosed (gavage) 10 times a day for five days followed by a post-dose period of 23 days.

^b 90-Day rat oral feeding study; histological evaluation of reproductive organs is adequate for SIDS reproductive screening. Toxicity to reproduction evaluation shown in robust summary for repeated dose toxicity.

^c Data for CAS RN 68603-42-9 are appropriate since CAS RN 120-40-1 is a major component (44 – 53%).

Table 4a: Category I – FND Amides (continued)
Human Health-Related Data

CAS RN	Acute Oral Toxicity LD ₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD ₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
Subcategory 2: Fatty Alkanolamides (continued)							
68155-20-4		Sensory and pulmonary irritant at 86 to 219 mg/m ³					
68425-47-8							
68140-00-1	> 5; 7.4; > 5 ^d ; > 5 ml/kg		> 2	> 750 ^b	Not mutagenic (Ames)	> 750 ^b	
8051-30-7							
61790-63-4							
<i>68155-06-6</i>	<i>> 10 (Males)</i>				<i>Not mutagenic (Ames)</i>		<i>e</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

^b 90-Day rat oral feeding study; histological evaluation of reproductive organs is adequate for SIDS reproductive screening. Toxicity to reproduction evaluation shown in robust summary for repeated dose toxicity.

^d The LD₅₀ of the original solution (10%) was > 50 ml/kg.

^e CAS RNs 68155-06-6 (C12 - C18) and 68603-42-9 (C8 - 16) are very similar and the developmental toxicity study is considered to represent both compounds.

Table 4a: Category I – FND Amides (continued)
Human Health-Related Data

CAS RN	Acute Oral Toxicity LD ₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD ₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
Subcategory 3: Fatty Acid Reaction Products with Amines							
110-30-5		At 112 mg/m ³ no deaths and mild and transient inflammatory response in the lung			Not mutagenic (Ames)		
61790-69-0							
68953-36-6							
68910-93-0							
64754-93-4							
71820-35-4	3.61 (Male) 4.26 (Female); > 5				Not mutagenic (Ames – 2 studies)		
68140-01-2							
<i>68910-87-2</i>					<i>Not mutagenic (Ames)</i>		

Shaded cells with CAS RN and data in italics are supporting chemicals.

**Table 4b: Category II – FND Imidazoline Derivatives
 Human Health-Related Data**

CAS RN	Acute Oral Toxicity LD ₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD ₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
72749-55-4							
61791-39-7							
68442-97-7	< 5 (60% died at 5 g/kg)						
72623-72-4							
65817-50-7							
<i>68122-86-1</i>	<i>> 5; 8.45 ml/kg</i>			<i>143^e > 2200^f</i>	<i>Not Mutagenic (Ames); CHO Cyto-genetics (Neg); UDS (Neg)</i>	<i>> 1322^g</i>	<i>Maternal and developmental > 1000^h</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

^e 13-Week dietary toxicity study in dogs.

^f 91-Day feeding study in rats.

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

^h Developmental toxicity study in rats. A probe study conducted prior to the definitive study indicated no maternal or fetal toxicity at the highest dose of 1875 mg/kg/day (see Robust Summary in Appendix A).

**Table 4c: Category III – FND Amphetics (N-carboxymethyl substituted)
 Human Health-Related Data**

CAS RN	Acute Oral Toxicity LD ₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD ₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
61789-39-7							
61789-40-0	> 1.8 (Males) ⁱ 2.6 ^j 1.5 ^k > 1.5 g/kg ^l		> 2 g/kg ^m	250 ⁿ 500 ^o LOAEL = 300	Not Mutagenic (Ames – 4 studies); <i>In vivo</i> Mouse Micro-nucleus – (Neg)	> 1000 ⁿ > 1000 ^o	
693-33-4							Maternal = 50 Developmental = 150 ^p
<i>4292-10-8</i>							
<i>70851-07-9</i>							

Shaded cells with CAS RN and data in italics are supporting chemicals.

- ⁱ Value is in ml/kg of a 35.6% aqueous solution; none of 5 males died, all 5 females died; therefore, an LD₅₀ for females was not established. (See Robust Summary 74, Appendix A)
- ^j LD₅₀ of the original solution (30% aqueous) was 8.55 g/kg.
- ^k LD₅₀ of the original solution (30% aqueous) was 4.9 g/kg.
- ^l Study was conducted with 5 g/kg of a solution containing 31% active ingredient.
- ^m Acute dermal toxicity study in rats.
- ⁿ 90-Day rat oral gavage study; histological evaluation of reproductive organs is adequate for SIDS reproductive screening. (Toxicity to reproduction evaluation shown in robust summary for repeated dose toxicity.)
- ^o 28-Day rat oral gavage study; histological evaluation of reproductive organs is adequate for SIDS reproductive screening. (Toxicity to reproduction evaluation shown in robust summary for repeated dose toxicity.) A range-finding study (Appendix A) was also reviewed with a LOAEL determined to be 300 mg/kg/day based on clinical signs.
- ^p Dose selection study is included as a Robust Summary in Appendix A.

**Table 4d: FND Amides Individual Chemicals
Human Health-Related Data**

CAS RN	Acute Oral Toxicity LD₅₀ (g/kg)	Acute Inhalation Toxicity	Acute Dermal Toxicity LD₅₀ (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
68131-13-5							
68132-46-7							

**Table 5a: Proposed Test Plan for Category I – FND Amides
 Physical/Chemical Properties**

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility
Subcategory 1: Fatty Acid Amides					
124-26-5	A	A	M	M	A
301-02-0	A	M	M	M	A
112-84-5	M	M	M	M	M
<i>61790-31-6</i>	<i>(1)</i>	<i>(2)</i>	<i>(3)</i>	<i>(4)</i>	<i>(5)</i>
Subcategory 2: Fatty Alkanolamides					
142-78-9	M	M	M	M	M
120-40-1	A	M	M	M	A
68603-42-9	(1)	(2)	(3)	(4)	(5)
93-83-4	M	M	M	M	M
68155-20-4	(1)	(2)	(3)	(4)	(5)
68425-47-8	(1)	(2)	(3)	(4)	(5)
68140-00-1	(1)	(2)	(3)	(4)	(5)
8051-30-7	(1)	(2)	(3)	(4)	(5)
61790-63-4	(1)	(2)	(3)	(4)	(5)
<i>68155-06-6</i>	<i>M</i>	<i>M</i>	<i>M</i>	<i>M</i>	<i>M</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill endpoint.

M – Model data available. NOTE: Values from the models should be considered to represent only one of several components in these products.

Use of these model values is, at best, a crude estimate of the endpoint.

- (1) This material is a mixture and has no true melting point (i.e. each component of the mixture melts at a different temperature). Determination of this endpoint is not applicable.
- (2) This material contains long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Determination of this endpoint is not applicable.
- (3) This material is a large complex molecule with long-chain hydrocarbons that are non-volatile. Determination of this endpoint is not applicable.
- (4) This material has surfactant properties and will accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Determination of this endpoint is not applicable.
- (5) This material is a mixture and has no single value for water solubility. Determination of this endpoint is not applicable.

Table 5a: Proposed Test Plan for Category I – FND Amides (continued)
Physical/Chemical Properties

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility
Subcategory 3: Fatty Acid Reaction Products with Amines					
110-30-5	M	M	M	M	M
61790-69-0	(1)	(2)	(3)	(4)	(5)
68953-36-6	(1)	(2)	(3)	(4)	(5)
68910-93-0	(1)	(2)	(3)	(4)	(5)
64754-93-4	(1)	(2)	(3)	(4)	(5)
71820-35-4	(1)	(2)	(3)	(4)	(5)
68140-01-2	(1)	(2)	(3)	(4)	(5)
<i>68910-87-2</i>	<i>(1)</i>	<i>(2)</i>	<i>(3)</i>	<i>(4)</i>	<i>(5)</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

M – Model data available. NOTE: Values from the models should be considered to represent only one of several components in these products.

Use of these model values is, at best, a crude estimate of the endpoint.

- (1) This material is a mixture and has no true melting point (i.e. each component of the mixture melts at a different temperature). Determination of this endpoint is not applicable.
- (2) This material contains long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Determination of this endpoint is not applicable.
- (3) This material is a large complex molecule with long-chain hydrocarbons that are non-volatile. Determination of this endpoint is not applicable.
- (4) This material has surfactant properties and will accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Determination of this endpoint is not applicable.
- (5) This material is a mixture and has no single value for water solubility. Determination of this endpoint is not applicable.

**Table 5b: Proposed Test Plan for Category II – FND Imidazoline Derivatives
Physical/Chemical Properties**

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility
72749-55-4	(1)	(2)	(3)	(4)	(5)
61791-39-7	(1)	(2)	(3)	(4)	(5)
68442-97-7	(1)	(2)	(3)	(4)	(5)
72623-72-4	(1)	(2)	(3)	(4)	(5)
65817-50-7	(1)	(2)	(3)	(4)	(5)
<i>68122-86-1</i>	<i>(1)</i>	<i>(2)</i>	<i>(3)</i>	<i>(4)</i>	<i>(5)</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

- (1) This material is a mixture and has no true melting point (i.e. each component of the mixture melts at a different temperature). Determination of this endpoint is not applicable.
- (2) This material contains long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Determination of this endpoint is not applicable.
- (3) This material is a large complex molecule with long-chain hydrocarbons that are non-volatile. Determination of this endpoint is not applicable.
- (4) This material has surfactant properties and will accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Determination of this endpoint is not applicable.
- (5) This material is a mixture and has no single value for water solubility. Determination of this endpoint is not applicable.

**Table 5c: Proposed Test Plan for Category III – FND Amphetics (N-carboxymethyl substituted)
 Physical/Chemical Properties**

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility
61789-39-7	(1)	(2)	(3)	(4)	(5)
61789-40-0	(1)	(2)	(3)	(4)	(5)
693-33-4	M	M	M	M	M
<i>4292-10-8</i>	<i>(1)</i>	<i>(2)</i>	<i>(3)</i>	<i>(4)</i>	<i>(5)</i>
<i>70851-07-9</i>	<i>(1)</i>	<i>(2)</i>	<i>(3)</i>	<i>(4)</i>	<i>(5)</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

M – Model data available. NOTE: Values from the models should be considered to represent only one of several components in these products.

Use of these model values is, at best, a crude estimate of the endpoint.

- (1) This material is a mixture and has no true melting point (i.e. each component of the mixture melts at a different temperature). Determination of this endpoint is not applicable.
- (2) This material contains long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Determination of this endpoint is not applicable.
- (3) This material is a large complex molecule with long-chain hydrocarbons that are non-volatile. Determination of this endpoint is not applicable.
- (4) This material has surfactant properties and will accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Determination of this endpoint is not applicable.
- (5) This material is a mixture and has no single value for water solubility. Determination of this endpoint is not applicable.

Table 5d: Proposed Test Plan for FND Amides Individual Chemicals
Physical/Chemical Properties

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility
68131-13-5	(1)	(2)	(3)	(4)	(5)
68132-46-7	(1)	(2)	(3)	(4)	(5)

- (1) This material is a mixture and has no true melting point (i.e. each component of the mixture melts at a different temperature). Determination of this endpoint is not applicable.
- (2) This material contains long-chain hydrocarbons that degrade at much lower temperatures than those at which they would be expected to boil. Determination of this endpoint is not applicable.
- (3) This material is a large complex molecule with long-chain hydrocarbons that are non-volatile. Determination of this endpoint is not applicable.
- (4) This material has surfactant properties and will accumulate at the interface between hydrophobic and hydrophilic phases rather than equilibrating between the two phases. Determination of this endpoint is not applicable.
- (5) This material is a mixture and has no single value for water solubility. Determination of this endpoint is not applicable.

**Table 6a: Proposed Test Plan for Category I – FND Amides
 Environmental Fate and Ecotoxicity**

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants	Chronic Tox. to Aquatic Invertebrates
Subcategory 1: Fatty Acid Amides								
124-26-5	M	(6)	M	R	R	R	R	
301-02-0	M	(6)	M	A	R	R	R	
112-84-5	M	(6)	M	A	A	R	R	A
<i>61790-31-6</i>	<i>R</i>	<i>(6)</i>	<i>R</i>	<i>A</i>	<i>R</i>	<i>R</i>	<i>R</i>	
Subcategory 2: Fatty Alkanolamides								
142-78-9	M	(6)	M	R	R	R	R	
120-40-1	M	(6)	M	A	R	R	R	
68603-42-9	R	(6)	R	A	A	A	R	
93-83-4	M	(6)	M	R	A	R	R	
68155-20-4	R	(6)	R	R	R	R	R	
68425-47-8	R	(6)	R	R	R	R	R	
68140-00-1	R	(6)	R	A	R	R	A	
8051-30-7	R	(6)	R	R	R	R	R	
61790-63-4	R	(6)	R	R	R	R	R	
<i>68155-06-6</i>	<i>M</i>	<i>(6)</i>	<i>M</i>	<i>A</i>	<i>R</i>	<i>R</i>	<i>R</i>	
Subcategory 3: Fatty Acid Reaction Products with Amines								
110-30-5	M	(6)	M	R	R	R	R	
61790-69-0	R	(6)	R	R	R	R	R	
68953-36-6	R	(6)	R	R	R	R	R	
68910-93-0	R	(6)	R	A	A	R	R	
64754-93-4	R	(6)	R	R	R	R	R	
71820-35-4	R	(6)	R	R	R	A	R	
68140-01-2	R	(6)	R	R	R	R	R	
<i>68910-87-2</i>	<i>R</i>	<i>(6)</i>	<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>	

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill endpoint.

M – Model data available. NOTE: Values from the models should be considered to represent only one of several components in these products. Use of these model values is, at best, a crude estimate of the endpoint.

R – Read-across as described in text (page 14).

(6) This material does not have hydrolyzable groups and, therefore, abiotic hydrolysis is not a pathway for degradation in the environment. Determination of this endpoint is not applicable.

**Table 6b: Proposed Test Plan for Category II – FND Imidazoline Derivatives
 Environmental Fate and Ecotoxicity**

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
72749-55-4	R	Test OECD 111	R	Test OECD 301	R	R	R
61791-39-7	R	R	R	R	Test OECD 203	A	Test OECD 201
68442-97-7	R	R	R	R	R	R	R
72623-72-4	R	R	R	R	R	R	R
65817-50-7	R	R	R	R	R	R	R
<i>68122-86-1</i>	<i>R</i>	<i>R</i>	<i>R</i>	<i>A</i>	<i>A</i>	<i>R</i>	<i>R</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill endpoint.

R – Read-across as described in text (page 14)

**Table 6c: Proposed Test Plan for Category III - FND Amphetics (N-carboxymethyl substituted)
 Environmental Fate and Ecotoxicity**

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
61789-39-7	R	(6)	R	R	A	R	R
61789-40-0	R	(6)	R	A	A	A	A
693-33-4	M	(6)	M	R	R	A	R
<i>4292-10-8</i>	<i>R</i>	<i>(6)</i>	<i>R</i>	<i>A</i>	<i>R</i>	<i>R</i>	<i>A</i>
<i>70851-07-9</i>	<i>R</i>	<i>(6)</i>	<i>R</i>	<i>A</i>	<i>R</i>	<i>R</i>	<i>R</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill endpoint.

M – Model data available.

R – Read-across as described in text (page 14).

(6) This material does not have hydrolyzable groups and, therefore, abiotic hydrolysis is not a pathway for degradation in the environment.

Determination of this endpoint is not applicable.

**Table 6d: Proposed Test Plan for FND Amides Individual Chemicals
Environmental Fate and Ecotoxicity**

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
68131-13-5	R	(6)	R	Test OECD 301	R	R	R
68132-46-7	R	(6)	R	Test OECD 301	R	R	R

R – Read-across as described in text (page 14).

(6) This material does not have hydrolyzable groups and, therefore, abiotic hydrolysis is not a pathway for degradation in the environment. Determination of this endpoint is not applicable.

**Table 7a: Proposed Test Plan for Category I – FND Amides
 Human Health-Related**

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity	Genetic Toxicity	Toxicity to Reproduction	Developmental Toxicity
Subcategory 1: Fatty Acid Amides							
124-26-5	A			R	A (Ames)	R	R
301-02-0	A			R	A (Ames)	R	R
112-84-5	A			A	A (Ames)	R	R
<i>61790-31-6</i>	<i>A</i>			<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>
Subcategory 2: Fatty Alkanolamides							
142-78-9	R			R	A (Ames) Test OECD 473	R	R
120-40-1	A		A	A	A (Ames)	A	R
68603-42-9	A		A	R	R	R	A
93-83-4	R			R	R	R	R
68155-20-4	R	A		R	R	R	R
68425-47-8	R			R	R	R	R
68140-00-1	A		A	A	A (Ames)	A	R
8051-30-7	R			R	R	R	R
61790-63-4	R			R	R	R	R
<i>68155-06-6</i>	<i>A</i>			<i>R</i>	<i>A (Ames)</i>	<i>R</i>	<i>R</i>
Subcategory 3: Fatty Acid Reaction Products with Amines							
110-30-5	R	A		R	A (Ames)	R	R
61790-69-0	R			R	R	R	R
68953-36-6	R			R	R	R	R
68910-93-0	R			R	R	R	R
64754-93-4	R			R	R	R	R
71820-35-4	A			R	A (Ames)	R	R
68140-01-2	R			R		R	R
<i>68910-87-2</i>	<i>R</i>			<i>R</i>	<i>A (Ames)</i>	<i>R</i>	<i>R</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill the endpoint.

R – Read-across as described in text (page 14).

**Table 7b: Proposed Test Plan for Category II - FND Imidazoline Derivatives
 Human Health-Related**

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity	Genetic Toxicity	Toxicity to Reproduction	Developmental Toxicity
72749-55-4	R			R	R	R	R
61791-39-7	R			R	Test OECD 473	R	R
68442-97-7	A			R	R	R	R
72623-72-4	R			R	R	R	R
65817-50-7	R			R	R	R	R
<i>68122-86-1</i>	<i>A</i>			<i>A</i>	<i>A (Ames; CHO; UDS)</i>	<i>A</i>	<i>A</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill the endpoint.

R – Read-across as described in text (page 14).

**Table 7c: Proposed Test Plan for Category III - FND Amphoteric (N-carboxymethyl substituted)
 Human Health-Related**

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity	Genetic Toxicity	Toxicity to Reproduction	Developmental Toxicity
61789-39-7	R			R	R	R	R
61789-40-0	A		A	A	A (Ames; MMN)	A	R
693-33-4	R			R	R	R	A
<i>4292-10-8</i>	<i>R</i>			<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>
<i>70851-07-9</i>	<i>R</i>			<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>

Shaded cells with CAS RN and data in italics are supporting chemicals.

A – Adequate data exist to fill the endpoint.

R – Read-across as described in text (page 14).

MMN – Mouse micronucleus study.

**Table 7d: Proposed Test Plan for FND Amides Individual Chemicals
Human Health-Related**

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity	Genetic Toxicity	Toxicity to Reproduction	Developmental Toxicity
68131-13-5	R			Test OECD 422	Test OECD 471 Test OECD 473	Test OECD 422	Test OECD 422
68132-46-7	R			Test OECD 422	Test OECD 471 Test OECD 473	Test OECD 422	Test OECD 422

R – Read-across as described in text.