201-14171

Mariam_Azimi-Osman@americanchemistry.com on 12/23/2002 03:20:24 PM

To: oppt.ncic@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA
cc: Steven_Russell@americanchemistry.com, Jim_Keith@americanchemistry.com, Francis_Maher@americanchemistry.com

Subject: FND Amines Task Group Test Plan

Please find attached the following documents in submission of the "Test Plan" for the 29 chemicals sponsored by the ACC FND Panel Amines Task Group.

Cover Letter to Governor Whitman
FND Amines Test Plan
Appendix A
Appendix B

(See attached file: Cover Letter 122002.pdf)(See attached file: FND Amines Test Plan 122002 - Final.pdf)(See attached file: Appendix A 122002.pdf)(See attached file: Appendix B 122002.pdf)

Sincerely,
Mariam Azimi-Osman
Coordinator, CHEMSTAR
American Chemistry Council
1300 Wilson Boulevard
Arlington, VA 22209
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Cover Letter 122002 FND Amines Test Plan 122002 - Appendix A 122002 Appendix B 122002

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COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

2002 DEC 27 PM 12: 19

American Chemistry Council

December 23, 2002

Via U.S. Mail and E-Mail

Ms. Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program-Consortium No.

Dear Governor Whitman:

The Fatty Nitrogen Derivatives Panel Amines Task Group of the American Chemistry Council submits the subject documents to EPA's HPV Chemical Challenge Program as its test plan for a category covering 29 chemicals. The Amines Task Group includes the following member companies that are sponsoring these chemicals under the Voluntary HPV Chemical Challenge Program: Akzo Nobel Chemicals Inc.; Corsicana Technologies Inc.; Crompton Corporation; Goldschmidt Chemical Corporation; KAO Specialties Americas LLC; Procter and Gamble, Chemicals Division; Rhodia Inc.; and Tomah3 Products, Inc.

This submission includes the following documents:

(1) Fatty Nitrogen Derived Amines Category High Production Volume (HPV) Chemical Challenge – Assessment of Data Availability and Test Plan;
(2) Appendix A: Robust Summaries for Reliable Studies; and
(3) Appendix B: Robust Summaries for SAR Model Data.

This submission is also being sent electronically to the following e-mail addresses:

Oppt.ncic@epa.gov
Chem.rtk@epa.gov

Please be advised that the Task Group is considering the submission of a revised version of this test plan, along with additional robust study summaries, by no later than the end of March 2003. Additional study information has been received which could not be summarized by the end of 2002, and the Task Group anticipates that this information may suggest alterations to the current plan.

If you require additional information, please contact F. J. "Sonny" Maher, Fatty Nitrogen Derivatives Panel Manager at (703) 741-5605 or sonny_maher@americanchemistry.com.

Sincerely yours,

Courtney M. Price
CHEMSTAR, Vice President

Attachment

cc: Amines Task Group
Steve Russell, ACC
Jim Keith, ACC

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201-14171A

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

Assessment of Data Availability and Test Plan

Prepared for:

American Chemistry Council's
Fatty Nitrogen Derivatives Panel
Amines Task Group

Prepared by:

Toxicology/Regulatory Services, Inc.

December 20, 2002

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

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

Introduction

Surfactants have a long history of safe use and have been studied extensively for environmental fate and effects and human health effects. The Fatty Nitrogen Derived (FND) Amines Category chemicals have surfactant properties (e.g. form oil/water emulsions, toxic to aquatic species) and are used primarily in the production of commercial surfactants such as ethoxylated amine surfactants or as chemical intermediates (e.g. for the production of quaternary amines). Some typical applications of FND Amines Category chemicals and/or their derivatives are as degreasers, metal cleaners, metal working fluids, and industrial laundry cleaners.

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

The FND Amines Category is comprised of 29 chemicals with unique Chemical Abstracts Service Registry Numbers (CAS RN; see Text Table A). While these long-chain substituted amines are considered appropriately combined in a single category based on their similar properties and toxicity, for aid in review, the chemicals were placed in the following subcategories:

Subcategory I: Primary Alkylamines:
Four long-chain alkyloxy derivatives of propanamine (CAS RN 68784-38-3, 30113-45-2, 218141-16-3, and 151789-06-9) and six long-chain substituted amines (CAS RN 124-22-1, 143-27-1, 68037-91-2, 68155-38-4, 61790-18-9 and 68037-95-6).

Subcategory II: Dimethylalkylamines:
Five long-chain substituted dimethyl amines (CAS RN 112-75-4, 112-69-6, 124-28-7, 61788-95-2 and 61788-91-8).

Subcategory III: Dialkylmethylamines and Dialkylamines:
Six long-chain disubstituted amines and disubstituted methyl amines (CAS RN 7396-58-9, 67700-99-6, 68153-95-7, 4088-22-6, 61788-63-4 and 68783-24-4).

Subcategory IV: Alkyldiamines:
Four long-chain substitutes of propanediamine (CAS RN 151789-07-0, 68479-04-9, 61791-55-7 and 7173-62-8).

Subcategory V: Trialkylamines:
Two long-chain tri-substituted amines (CAS RN 68814-95-9 and 61790-42-9) and two long-chain substituted ethanol, 2,2'-iminobis-amines (CAS RN 61791-31-9 and 61791-44-4).

Data for five primary alkylamines (CAS RN 61788-45-2*, 124-30-1*, 61788-46-3*, 61790-33-8* and 112-90-3*) sponsored in the ICCA program by the European Oleochemicals and Allied Products Group (APAG) under the ICCA program (see Task Group letter to EPA dated November 9, 2001) that have similar structures to the Subcategory I chemicals are included in

this review. These chemicals are identified throughout this document by CAS RN and an "*" since they provide extensive supporting information to the FND Amines Category. In addition, nine additional supporting individual chemicals and an FDA-approved (used in toothpaste), two-chemical mixture, that are not part of the US HPV Chemical Challenge Program, but are structurally closely-related to the FND Amines Category chemicals, are included to provide supporting data for the category. These 15 chemicals are termed "supporting chemicals" throughout this document and are defined in Text Table A.

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

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
Subcategory I: Primary Alkylamines	
68784-38-3	1-Propanamine, 3-(C_{8-10}-alkyloxy) derivs.
30113-45-2	1-Propanamine, 3-(isodecyloxy)-
28701-67-9	*1-Propanamine, 3-(isodecyloxy)-, acetate*
218141-16-3	1-Propanamine, 3-(C_{9-11}-isoalkyloxy)derivs., C_{10} rich
68511-40-0	*1-Propanamine, 3-(tridecyloxy)-, branched*
151789-06-9	1-Propanamine, 3-(C_{11-14}-isoalkyloxy)derivs., C_{13} rich
124-22-1	Dodecylamine
143-27-1	Hexadecylamine[1]
68037-91-2	Amines, C_{14-18}-alkyl
*61788-45-2**	*Amines, hydrogenated tallow alkyl*
*124-30-1**	*Octadecylamine*
*61788-46-3**	*Amines, coco alkyl*
68155-38-4	Amines, C_{14-18} and C_{16-18}-unsatd. alkyl
*61790-33-8**	*Amines, tallow alkyl*
61790-18-9	Amines, soya alkyl
68037-95-6	Amines, C_{16-18} and C_{18}-unsatd. alkyl
*112-90-3**	*Cis-9-Octadecenylamine*
3151-59-5 + 36505-83-6	*Hexadecylamine hydrofluoride (Hetaflur)* *9-Octadecen-1-amine hydrofluoride*

[1] CAS RN 143-27-1 is officially listed as "Hetaflur Hexadecylamine"; CAS RN 3151-59-5 (Hexadecylamine hydrofluoride) is officially listed as "Hetaflur." It is assumed that the "Hetaflur" designation should be used with the hydrofluoride salt form of hexadecylamine (CAS RN 3151-59-5) and the "Hetaflur" designation has been removed for CAS RN 143-27-1 in this report to avoid confusion.

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
Subcategory II: Dimethylalkylamines	
112-18-5	*1-Dodecanamine, N,N-dimethyl*
112-75-4	1-Tetradecanamine, N,N-dimethyl
112-69-6	1-Hexadecanamine, N,N-dimethyl
124-28-7	1-Octadecanamine, N,N-dimethyl
61788-93-0	*Amines, coco alkyl dimethyl*
61788-95-2	Amines, (hydrogenated tallow alkyl)dimethyl
61788-91-8	Amines, dimethyl soya alkyl
28061-69-0	*Octadecen-1-amine, N,N-dimethyl*
Subcategory III: Dialkylmethylamines and Dialkylamines	
7396-58-9	1-Decanamine, N-decyl-N-methyl
67700-99-6	Amines, di-C_{14-18}-alkylmethyl
68153-95-7	Amines, di-C_{12-18}-alkyl
4088-22-6	1-Octadecanamine, N-methyl-N-octadecyl
61788-62-3	*Amines, dicoco alkylmethyl*
61788-63-4	Dihydrogenated tallow methylamine
61789-79-5	*Amines, bis(hydrogenated tallow alkyl)*
61789-76-2	*Amines, dicoco alkyl*
68783-24-4	Amines, ditallow alkyl
Subcategory IV: Alkyldiamines	
52898-18-7	*1,3-Propanediamine, N-(3-(dodecyloxy)propyl)*
151789-07-0	1,3-Propanediamine,N-(3-(C_{11-14}-isoalkyloxy)propyl)derivs., C_{13} rich
68479-04-9	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched
61791-55-7	Amines, N-tallow alkyltrimethylenedi-
7173-62-8	1,3-Propanediamine, N-(9Z)-octadecenyl-
Subcategory V: Trialkylamines	
68814-95-9	Amines, tri-C_{8-10}-alkyl-
61790-42-9	Amines, tris (hydrogenated tallow alkyl)
61791-31-9	Ethanol, 2,2'-iminobis-, N-coco alkyl derivs.
61791-44-4	Ethanol, 2,2'-iminobis-,N-tallow alkyl derivs.

* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

Structural Information for the FND Amines Category and Supporting Chemicals

The following table presents the molecular formula and molecular weight data for the chemicals with defined structures or structures for which a representative structure can be determined. The structures for these and the remaining chemicals in the FND Amines Category are provided in Table 1.

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

CAS RN	Name	Molecular Formula	Molecular Weight
Subcategory I: Primary Alkylamines			
68784-38-3	1-Propanamine, 3-(C_{8-10}-alkyloxy) derivs.	$C_{12}H_{27}NO$	201
30113-45-2	1-Propanamine, 3-(isodecyloxy)-	$C_{13}H_{29}NO$	215
218141-16-3	1-Propanamine, 3-(C_{9-11}-isoalkyloxy) derivs., C_{10} rich	$C_{13}H_{29}NO$	215
68511-40-0	*1-Propanamine, 3-(tridecyloxy)-, branched*	*$C_{16}H_{35}NO$*	*257*
151789-06-9	1-Propanamine, 3-(C_{11-14}-isoalkyloxy) derivs., C_{13} rich	$C_{16}H_{35}NO$	257
124-22-1	Dodecylamine	$C_{12}H_{27}N$	185
143-27-1	Hexadecylamine	$C_{16}H_{35}N$	241
*61788-45-2**	*Amines, hydrogenated tallow alkyl*		*263*
*124-30-1**	*Octadecylamine*	*$C_{18}H_{39}N$*	*270*
*61788-46-3**	*Amines, coco alkyl*		*200*
*61790-33-8**	*Amines, tallow alkyl*		*262*
61790-18-9	Amines, soya alkyl		*264*
*112-90-3**	*Cis-9-Octadecenylamine*	*$C_{18}H_{37}N$*	*267*
3151-59-5 *+36505-83-6*	*Hexadecylamine hydrofluoride (Hetaflur)* *9-Octadecen-1-amine hydrofluoride*	*$C_{16}H_{35}N.H\text{-}F$* *$C_{18}H_{37}N.H\text{-}F$*	*241*[a] *267*[a]
Subcategory II: Dimethylalkylamines			
112-18-5	*1-Dodecanamine, N,N-dimethyl*	*$C_{14}H_{31}N$*	*213*
112-75-4	1-Tetradecanamine, N,N-dimethyl	$C_{16}H_{35}N$	241
112-69-6	1-Hexadecanamine, N,N-dimethyl	$C_{18}H_{39}N$	270
124-28-7	1-Octadecanamine, N,N-dimethyl	$C_{20}H_{43}N$	298
61788-93-0	*Amines, coco alkyl dimethyl*		*228*
61788-95-2	Amines, (hydrogenated tallow alkyl)dimethyl		291
61788-91-8	Amines, dimethyl soya alkyl		292
28061-69-0	*Octadecen-1-amine, N,N-dimethyl*	*$C_{20}H_{41}N$*	*296*
Subcategory III: Dialkylmethylamines and Dialkylamines			
7396-58-9	1-Decanamine, N-decyl-N-methyl	$C_{21}H_{45}N$	312
4088-22-6	1-Octadecanamine, N-methyl-N-octadecyl	$C_{37}H_{77}N$	536
61788-62-3	*Amines, dicoco alkylmethyl*		*397*
61788-63-4	Dihydrogenated tallow methylamine		523
61789-79-5	*Amines, bis(hydrogenated tallow alkyl)*		*509*
61789-76-2	*Amines, dicoco alkyl*		*383*
68783-24-4	Amines, ditallow alkyl		507

Note: Average chain length or estimated chain length is used where appropriate; where no formula is provided, the molecular weight is that used by the industry to define the chemical.
Shaded cells with italic font indicate supporting chemicals.

* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[a] Molecular weight of the alkyl chain (excludes the hydrofluoride salt).

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

CAS RN	Name	Molecular Formula	Molecular Weight
Subcategory IV: Alkyldiamines			
52898-18-7	*1,3-Propanediamine, N-(3-(dodecyloxy)propyl)-*	*$C_{18}H_{40}N_2O$*	*301*
151789-07-0	1,3-Propanediamine, N-(3-(C_{11-14}-isoalkyloxy)propyl) derivs., C_{13} rich	$C_{19}H_{43}N_2O$	316
68479-04-9	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-branched	$C_{19}H_{42}N_2O$	315
61791-55-7	Amines, N-tallow alkyltrimethylenedi-		320
7173-62-8	1,3-Propanediamine, N-(9Z)-octadecenyl-	$C_{21}H_{44}N_2$	325
Subcategory V: Trialkylamines			
68814-95-9	Amines, tri-C_{8-10}-alkyl-	$C_{27}H_{57}N$	396
61790-42-9	Amines, tris (hydrogenated tallow alkyl)		752
61791-31-9	Ethanol, 2,2'-iminobis-, N-coco alkyl derivs.		302
61791-44-4	Ethanol, 2,2'-iminobis-,N-tallow alkyl derivs.		364

Note: Average chain length or estimated chain length is used where appropriate; where no formula is provided, the molecular weight is that used by the industry to define the chemical.
Shaded cells with italic font indicate supporting chemicals.

Rationale for the FND Amines Structure-Based Chemical Category

The members of the FND Amines category are large surfactant molecules. As such, they fall into an even larger family of surfactants, all of which have similar physical/chemical properties. The FND surfactants (amines, cationics, amides) employ either defined long-chain alkyl substituents or use natural oils. The following table summarizes the long-chain alkyl substituents found in the FND Amines Category Chemicals:

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

Identifier	Chain Length(s) or Average	Degree of Unsaturation
C8-C10 alkyl	9	None
Isodecyl	10	None
C9-C11 (C10 rich)	10	None
Dodecyl	12	None
C13 branched	13	None
C11-C14 (C13 rich)	13	None
Tetradecyl	14	None
Hexadecyl	16	None
C14-C18	Not specified	None
C12-C18	Not specified	None
C14-C18 and C16-C18 unsaturated	Not specified	Not specified
C16-C18 and C18-unsaturated	Not specified	Not specified

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

Identifier	Chain Length(s) or Average	Degree of Unsaturation
Octadecyl	18	None
Octadecenyl	18	1
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	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

Overall, the chain length and degree of unsaturation in the FND surfactants has no impact on fate and effects. These chemicals, by the nature of their surfactant properties, are toxic to aquatic organisms at low concentrations. A careful examination of the chemical structures (Table 1) shows a close relationship of all of the chemicals in the category. The following discussion highlights views on the intra- and inter-Subcategory chemicals.

Subcategory I - Primary Alkylamines: A number of the chemicals in the category are essentially identical or only differ in one or two carbons on the long-chain substituent. CAS RN 28701-67-9 (supporting) is the salt form of the HPV chemical CAS RN 30113-45-2 (isodecyloxy derivative of propanamine) and further, CAS RN 218141-16-3 is the same chemical since its carbon chain distribution, C9-C11, is C10 rich. Further, the other propanamine alkyloxy derivatives only differ by one to three carbons (CAS RN 68784-38-3, 68511-40-0 and 151789-06-9) on the alkyl chain. Thus, these six propanamine alkyloxy derivatives can be considered identical for purposes of hazard screening. The remaining alkane-substituted amines in Subcategory I have carbon chain distributions ranging from C12 to C18. Degradation of these molecules would clearly result in similar by-products and metabolites. While degradates of these molecules would not generate propanol, as might be expected for the propanamine alkyloxy derivatives, the overall degradation profile would be the same. Similarly, other than unsaturation of the alkyl chain, the unsaturated substituents including tallow (primarily C16 and C18 saturated and unsaturated) and soya (primarily C18 unsaturated) are identical to the saturated chain molecules.

Subcategory II - Dimethylalkylamines: Each of the Subcategory II chemicals has an identical or very similar corresponding primary alkylamine in Subcategory I. The addition of the dimethyl substituents would not be expected to result in recognizable differences in environmental fate or hazard assessments.

Subcategory III - Dialkylmethylamines and Dialkylamines: The chemicals in this Subcategory are similar to those in Subcategory II with the substitution of a longer chain length for one of the methyl groups (dialkylmethylamines) or with substitution of one methyl group and removal of one of the methyl groups (dialkylamines). These substitutions would not be expected to result in recognizable differences in environmental fate or hazard assessments since these substituents impart no structural alerts or unusual properties from the chemicals in the other subcategories.

Subcategory IV - Alkyldiamines: The three alkyloxy derivatives of propanediamine in this Subcategory (CAS RN 52898-18-7, 151789-07-0 and 68479-04-9) are essentially the same chemical with C12, C13 and C13-rich substituents. In addition, these alkyloxy derivatives and the two alkyldiamines in this Subcategory have corresponding alkylamines in the other subcategories. Degradation of these molecules, other than generation of an additional ammonia, would be identical to those of the corresponding monoamine.

Subcategory V - Trialkylamines: The two long-chain tri-substituted members of this category (CAS RN 68814-95-9 and 61790-42-9) are essentially equivalent to the dimethyl alkyl and dialkyl amines in Subcategory II or III. Replacing two of the long-chain substituents with ethanol would not result in structural alerts or potential degradation products of concern.

SUMMARY: The diversity of chemical structures for the FND Amines Category results from the need for different application properties and in manufacturing processes including the use of natural oils. This structural diversity does not result in chemicals with different structural alerts. To the contrary, based on the chemical structures and supported by the available ecotoxicity and mammalian toxicity data, these chemicals show consistent and predictable toxicity.

The goal of subcategorizing is to aid in the description and evaluation of the Category as a whole. It is considered appropriate to read-across from other subcategories when the data are consistent. As noted above, each of the chemicals within the Subcategories are structurally similar to chemicals in one or more other Subcategories. The approach to the Test Plan for the FND Amine Category chemicals is, therefore, to show that each of the Subcategories fits the overall pattern of fate and toxicity for the FND Amines Category and the FND surfactants in general. It is not necessary or appropriate to consider the Category or the Subcategories as having "ends" that, when tested, represent a continuum of structure. 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.

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

Approach to Evaluate the Database for the FND Amines Category

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

1. The chemical names and CAS RN of 34 HPV FND Amines Category chemicals supported by the American Chemistry Council Fatty Nitrogen Derivatives Panel, Amines Task Group (Task Group) were provided.
2. Five Primary Alkylamines (CAS RN 61788-45-2*, 124-30-1*, 61788-46-3*, 61790-33-8* and 112-90-3*) were removed from the original list since they were sponsored by the European Chemical Industry in the ICCA Program. As discussed above, these and 10 other chemicals of similar structure and function to the FND Amines Category chemicals were included as "supplementary" with supporting data. Therefore, there are a total of 29 HPV Sponsored chemicals in the category.
3. Available published and unpublished reports were obtained from the members of the FND Amines Task Group and other chemical industry companies; they were organized and reviewed to identify studies that could fulfill SIDS endpoints.
4. Pertinent databases[2] were searched and all relevant reports were obtained to establish the full extent and nature of the published literature for the 29 FND Amines Category and 15 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. Robust Summaries for the studies sponsored in the ICCA program included herein were accepted *a priori* from the European industry and were not generated from the original reports.
8. Where possible, estimates for physical/chemical properties, environmental fate and ecotoxicity values were developed by using appropriate Structure Activity Relationships (SAR).
9. Where possible, fugacity modeling was performed to estimate transport and distribution into environmental compartments for the HPV and supporting chemicals.
10. Robust summaries were generated for the SAR data.

Use of Structure Activity Relationships for the FND Amines Category

Approaches recommended in the EPA document on the use of structure activity relationship (SAR) in the HPV Chemicals Challenge Program were employed in the assessment of the FND Amines Category (U. S. EPA, 1999b). Several models were employed to support the review and assessment of the FND Amines Category chemicals. The models included several based on SAR, as well as Mackay-type fugacity-based modeling. The SAR models for physical properties were used to estimate boiling points, melting points, aqueous solubility, octanol-water partition coefficients and vapor pressures. Other SAR models were used to estimate hydroxyl radical

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

mediated atmospheric photo-oxidation and biodegradation potential. SAR models also were used to obtain estimates of acute toxicity to aquatic organisms.

Common Features of the Models

All of the models (except the Mackay-type models) require the input of a molecular structure to perform the calculations. The structure must be entered into the model in the form of a SMILES (Simplified Molecular Input Line Entry System) notation or string. SMILES is a chemical notation system used to represent a molecular structure by a linear string of symbols. The SMILES string allows the program to identify the presence or absence of structural features used by the submodels to determine the specific endpoint. The models contain files of structures and SMILES strings for approximately 100,000 compounds, accessible via CAS 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, and c).

Estimation of Environmental Fate Properties

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

The database that supports the modeling of water stability provides only for neutral organic compounds that have structures that can be hydrolyzed. Therefore, no model estimates for hydrolytic stability are available since the FND Amines Category chemicals do not have the necessary characteristics.

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

Estimation of Environmental Distribution

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

Estimation of Acute Aquatic Toxicity

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

Modeling Information Specific to the FND Amine Category

When CAS RN were included in the files of structures, the models described above were used for the FND Amines Category chemicals and the 15 supporting chemicals. Estimations of physical properties, environmental fate and distribution, and ecotoxicity were not possible for 20 of the 29 HPV chemicals in the FND Amines Category because they do not have single definable structures and/or were not available in the files of structures of the models. Model predictions were available for six of the supporting chemicals. The model did not provide estimates of stability in water for this class of chemicals because the model cannot calculate this parameter for chemicals that do not meet the criteria of neutral organic compounds with structures that can be hydrolyzed. Since the FND Amines Category chemicals are considered to be released into wastewater treatment systems consistent with their use patterns, release to soil and air were considered to be minor avenues of entry for FND Amines Category chemicals into the environment. Therefore, for fugacity modeling, all input was assumed to be into surface water using the chemical specific parameters to attain estimates of the chemical distributions between environmental compartments. The submodel for Cationic Surfactants was initially used for the ECOSAR model output (data included on Table 3). Subsequently, the model for Aliphatic Amines was examined. In a number of cases, the Aliphatic Amines calculations are much more similar to experimental values. Therefore, these values, where different, are included in Table 3 as well. In many cases the ECOSAR model indicated the chemicals were not toxic to aquatic organisms at predicted solubility. These are indicated on appropriate tables but are not discussed in this text.

Physical/Chemical Properties - Reliable Data and Correlation to SAR Estimates

The available reliable data and SAR estimates for physical/chemical properties of the FND Amines Category chemicals are presented in Table 2. Robust summaries for the reliable studies are provided in Appendix A and Robust Summaries for all of the SAR data are included in Appendix B. The Test Plan for Physical/Chemical Properties is outlined in Table 5.

Measurement of physical/chemical properties for surfactants 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 chemicals to emulsify octanol/water solutions. The resulting values are inaccurate and of limited utility for determining environmental fate and effects. Similarly, measurements such as melting points and boiling points provide minimal information since they do not identify key characteristics of the molecules. The large size of the molecules makes these chemicals non-volatile and the determination of a precise value for vapor pressure is difficult and of little practical use.

As described above, where possible, the physical/chemical property estimation program EPIWIN version 3.05 was used to derive estimates. The EPIWIN estimates must be interpreted with a great deal of professional judgment. As with actual measurement, prediction of physical/chemical properties for surfactants is complicated. The log K_{ow}, a key determinant in the models, is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior of surfactants. 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, a complete set of model data was generated for nine of the 29 HPV chemicals and six supporting chemicals that have discrete structures.

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

Subcategory I - Primary Alkylamines: EPIWIN predicted melting points ranged from approximately 28ºC to 93ºC. Three reported values, for CAS RN 124-22-1, 61788-45-2* and 124-30-1*, were the same as the model value suggesting that these reported values were also calculated. The reported value for CAS RN 112-90-3* of 21ºC was lower than the model value of 93ºC Reported values for the supporting chemical CAS RN 61790-33-8* were 34-40ºC and 25-30ºC. Model estimates made for boiling points ranged from 259ºC to 347ºC. Decomposition at 348ºC was reported for CAS RN 61788-45-2*.

As expected, based on extensive practical experience with these and similar large organic molecules, the reported and EPIWIN estimated vapor pressures were extremely low across the FND Amines Category, i.e. more than two orders of magnitude lower than water. The FND Amines Category chemicals are essentially nonvolatile, as is generally the case for molecules of this size and complexity.

Predicted or measured log K_{ow} values are of limited practical use for the FND Amines Category chemicals. An inherent property of surfactants 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 surfactant is notoriously 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 Amines Category chemicals in the

environment because of the tendency of surfactants to partition at lipid/aqueous interfaces. The EPIWIN estimated values for the octanol/water partition coefficient (log K_{ow}) ranged from 3.92 to approximately 8. No reported values were identified for the HPV chemicals. For supporting chemicals, a measured value for CAS RN 61790-33-8* was reported to be 7.5 and a range of values from >3.11 to 8.1 was reported for CAS RN 112-90-3*.

Reported water solubility for the primary alkylamines varies from insoluble to slightly soluble. Reported values for CAS RN 124-22-1 and 124-30-1* were 2000 and 1000 mg/l, respectively although a separate report for CAS RN 124-30-1* indicated it was insoluble. Other reported information indicated the chemicals were insoluble or very insoluble in water. Model predictions for water solubility also ranged from virtually insoluble (<< 0.1 mg/l) to slightly soluble (approximately 165 mg/l).

Subcategory II – Dimethylalkylamines: EPIWIN predicted melting points were 22ºC and 80ºC for the supporting chemicals that could be modeled. There is a reported value for CAS RN 112-18-5 of –15 to –20ºC compared to the model value of 22ºC and two reported values for CAS RN 124-28-7 of approximately 20 to 23ºC similar to the model value (23ºC). Model estimates for boiling point ranged from 260 to 346ºC. There are no reported boiling point values available for HPV or supporting chemicals.

EPIWIN estimated vapor pressures were very low across this FND Amines Subcategory and ranged from 0.000052 to 0.0159 hPa. There are no reported values available for HPV or supporting chemicals.

No reported values for the octanol/water partition coefficient (log K_{ow}) were identified for HPV or supporting chemicals. EPIWIN predicted values for log K_{ow} ranged from 5.44 to 8.39.

Model predictions for water solubility ranged from 0.0089 to 8.58 mg/l. HPV chemical, CAS RN 124-28-7 was reported as "not soluble."

Subcategory III – Dialkylmethylamines and Dialkylamines: EPIWIN predicted data were available for one HPV chemical that could be modeled (CAS RN 4088-22-6). The predicted melting point was 216ºC; the predicted boiling point was 543ºC. The estimated vapor pressure was 2.0×10^{-11} hPa and estimated partition coefficient (log K_{ow}) was 17. This chemical was insoluble with a predicted water solubility of 2×10^{-11} mg/l. The accuracy of all of these model values is highly questionable. No measured data were available.

Subcategory IV – Alkyldiamines: EPIWIN predicted data were available for two HPV chemicals that could be modeled (CAS RN 68479-04-9 and 7173-62-8). The melting points were 130 and 142ºC, respectively. The predicted boiling points were 380 and 402ºC, respectively. Estimated vapor pressures were 2.2×10^{-6} and 4.9×10^{-7} hPA, respectively. The partition coefficients (log K_{ow}) were predicted to be 5.37 and 7.47, respectively. Water solubility was low with predicted values of 2.6 and 0.037 mg/l, respectively. The accuracy of all of these model values is highly questionable. No measured data were available.

Subcategory V – Trialkylamines: No measured or model data were available for these chemicals.

Summary – Physical/Chemical Properties

Melting points and boiling points are of very limited value in determining the fate and toxicity of surfactant molecules. The available data and model predictions are considered adequate to define the typical ranges for these endpoints. In addition, these types of molecules tend to degrade rather than boil. Consistent with the size and nature of these molecules, measured and modeled vapor pressures are very low, and the FND Amines Category chemicals are considered to be essentially nonvolatile. As noted previously, measurement and prediction of physical/chemical properties for surfactants are complicated by their behavior in test systems and the environment, and the log K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior. The available estimates are considered of very minimal use and additional testing is not warranted. Water solubility estimates varied from slightly soluble to very insoluble. The majority of these chemicals are clearly insoluble in water and the chemicals in Subcategories I – IV are adequately represented as insoluble. The trialkyl substituted amines in Subcategory V would be expected to be insoluble based on similarity of structure with other members of the Category containing shorter-chain substituents. While the water solubility of the fatty acid diethanolamines (CAS RN 61791-31-9 and 61791-44-4) has not been evaluated, in testing for biodegradation (see Robust Summary for Biodegradation), it is clearly stated that CAS RN 61791-31-9 was not water soluble while CAS RN 61797-44-4 was soluble to 1 g/liter. Surfactants were required to generate emulsions necessary to complete the test for CAS RN 61791-31-9. Therefore, these chemicals are also insoluble or poorly soluble. Overall, it is noted that measurement and prediction of physical/chemical properties for surfactants are complicated by their behavior in test systems and the environment, including strong adsorption and absorption properties and surface tension activity. Although predictions vary, the data and knowledge of the chemicals support the conclusion that the FND Amines Category chemicals behave similarly from the perspective of physical/chemical properties.

Additional Testing – Physical/Chemical Properties

No additional testing (Table 5) is proposed for the Category based either on the inappropriateness of the endpoint (melting point, boiling point, partition coefficient) for these surfactant molecules or adequate information (vapor pressure, water solubility) to establish the characteristics across the category.

Environmental Fate and Ecotoxicity - Reliable Data and Correlation to SAR Estimates

The available reliable data and SAR estimates for the environmental fate and effects of the FND Amines Category chemicals are presented in Table 3. Robust summaries for the reliable studies are provided in Appendix A and Robust Summaries for all of the SAR data are included in Appendix B. The Test Plan for the Environmental Fate and Ecotoxicity Endpoints is summarized in Table 6.

Subcategory I – Primary Alkylamines: Models for atmospheric photodegradation were used according to EPA guidelines. However, the fugacity models predict virtually no occurrence of the FND Amines Category chemicals in air, which is consistent with the very low vapor pressures. None the less, 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 1.2 to 2.8 hours).

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. These types of surfactants are generally not hydrolysable.

An estimation of the transport and distribution of the FND Amines Category chemicals in environmental media (percent in air, water, soil and sediment) following entry into the environment via water is presented in Table 3. Distribution to air and soil were < 1% for all of the chemicals that could be modeled while distribution to the water compartment varied from 10 to 90% with the remainder in the sediment.

For biodegradation, guideline studies and studies similar to guidelines were available for six of the 18 FND Amines Category and supporting chemicals. For the HPV chemical for which measured data are available (CAS RN 124-22-1) the 28-day biodegradation was > 60% ThOD. For the supporting chemicals, the 28-day ThOD ranged from 44 to 75%. Overall, the Subcategory I chemicals are either readily biodegradable or attain degradation very close to meeting the "readily biodegradable" criteria.

One HPV (CAS RN 124-22-1) and four supporting chemicals (CAS RN 61788-45-2*, 61788-46-3*, 61790-33-8*, and 112-90-3*) were tested for acute toxicity to fish. The LC_{50} values ranged from 0.11 to 9.3 mg/l. Acute toxicity to aquatic invertebrates was determined for five of the supporting chemicals (CAS RN 61788-45-2*, 124-30-1*, 61788-46-3*, 61790-33-8*, and 112-90-3*). The EC_{50} values were all less than 1 mg/l with the lowest actually determined value being 0.09 mg/l. In addition, a study evaluating the toxicity of CAS RN 61788-46-3* to the larvae and pupae of four mosquito species indicated the chemical is moderately toxic with EC_{50} values ranging between 2.0 and 13.0 mg/l. Toxicity to aquatic plants was determined for these same five supporting chemicals and indicated these amine surfactants are highly toxic to algae (E_bC_{50} and E_rC_{50} values ranging from < 0.00075 to 0.17 mg/l). The ECOSAR model for cationic surfactants and for some of the aliphatic amines does not predict toxicity to aquatic organisms accurately when the chemicals are poorly soluble or insoluble in water. However, the prediction for acute fish toxicity for one of the chemicals in this Subcategory as an aliphatic amine, rather than as cationic surfactant, is similar to the experimental value (0.87 mg/l predicted vs 0.42 mg/l measured for CAS RN 124-22-1). Estimates for the toxicity to daphnia and algae similarly indicated a high order of toxicity for this chemical. Other estimates (CAS RN 30113-45-2 and 68511-40-0) indicate these chemicals are expected to be acutely toxic as well. While these model values are useful in support of the conclusion that the FND Amine Category chemicals are toxic to aquatic species, overall the model estimates are of little value because of the low solubility of the chemicals.

<u>Subcategory II</u> – Dimethylalkylamines: Modeling of three HPV and two supporting chemicals indicated they would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 1.0 to 1.4 hours). The model did not provide estimates of stability in water for this subclass of chemicals.

An estimation of the transport and distribution of the FND Amines Category chemicals in environmental media (percent in air, water, soil and sediment) following entry into the environment via water is presented in Table 3. Distribution to air and soil were < 1% for all of

the chemicals that could be modeled while distribution to the water compartment varied from 5 to 42% with the remainder in the sediment.

Measured data for biodegradation were available for the five HPV and three supporting chemicals in this Subcategory. Four of the five HPV chemicals (CAS RN 112-69-6, 124-28-7, 61788-95-2, and 61788-91-8) were considered to be readily biodegradable. The fifth HPV chemical (CAS RN 112-75-4) had a value of < 2% degradation after 28 days. This value is not scientifically justifiable based on all other tests of similar chemicals, and the assay is considered invalid by the FND Amines Task Group. For the supporting chemicals, the 28-day ThOD ranged from 50 to 81%. Overall, the chemicals in this Subcategory are either readily biodegradable or closely approach ready biodegradability.

Toxicity to fish was measured for six of the eight HPV and supporting chemicals with LC_{50} values all less than 1.0 mg/l. For toxicity to aquatic invertebrates, one HPV chemical (CAS RN 124-28-7) and one supporting chemical (CAS RN 112-18-5) had LC_{50}/EC_{50} values of 0.074 and 0.083 mg/l, respectively. CAS RN 112-18-5 was shown to be highly toxic to algae in three assays each yielding E_bC_{50} and E_rC_{50} values < 0.1 mg/l. In addition, a study with CAS RN 124-28-7 to establish algistatic and algicidal concentrations to two species of algae confirmed the high toxicity of this chemical to aquatic species (0.029 and 0.11 mg/l algistatic concentrations and >0.032 and 0.16 algicidal concentrations). Model values for toxicity to aquatic invertebrates (CAS RN 112-18-5 and 112-75-4) and algae (CAS RN 112-18-5) for aliphatic amines appeared to be relatively accurate with predicted EC_{50} values of 0.04 and 0.01 mg/l for daphnia and 0.26 mg/l for algae. Overall, however, as for the other subcategories, the model predictions (Table 3) were considered of little value due to the low water solubility of the chemicals.

<u>Subcategory III</u> – Dialkylmethylamines and Dialkylamines: Modeled data were available for one HPV chemical (CAS RN 4088-22-6). The model predicted rapid photodegradation ($t_{1/2}$ was 1.0 hour). Stability in water was not calculable by the model. The Level III fugacity model estimated that 5% of the chemical would be distributed to the water compartment and 95% distributed to sediment.

One HPV (CAS RN 61788-63-4) and one supporting chemical (CAS RN 61788-62-3) were shown to be readily biodegradable in high quality tests. In both of these assays, a surfactant was used in the assay to suspend the test chemical providing for adequate bioavailability. A lesser degree of biodegradation was measured for two supporting chemicals (CAS RN 61789-79-5 and 61789-76-2) with only 16% and 20% degradation observed respectively after 28 days. In the first test, no effort was made to suspend the test chemical in the solution and the second assay employed binding of the chemical to silica gel as a means of suspension. Due to the low water solubility and the ability of these types of chemicals to tenaciously bind to solids, the FND Amines Task Group considers the results of these studies were likely significantly impacted by lack of bioavailability.

A measured LC_{50} value for fish toxicity was determined to be 6.15 mg/l for the supporting chemical with CAS RN 61788-62-3. However, tests conducted for three other chemicals in the Subcategory (CAS RN 4088-22-6, 61788-63-4, and 61789-79-5) indicated much higher LC_{50} values of 100 to more than 1000 mg/l. In each of these latter studies, however, there was evidence that the test material was not soluble in the test solutions and no remedial action was taken to emulsify the test chemicals. Similarly, tests for acute toxicity to daphnia for CAS RN

61788-63-4 were confounded by solubility problems and yielded higher EC_{50} values (35.2 and 790 mg/l) than expected. Careful examination of the large numbers of acute toxicity to fish and aquatic invertebrate studies available for the FND Amines Category chemicals overall, indicates that when studies are carried out at low concentrations (generally less than 10 mg/l) and emulsions are made using additives, the toxicity to aquatic organisms is high with LC_{50}/EC_{50} values less than 10 mg/l. Therefore, the lower toxicity reported for the chemicals in this Subcategory is considered inaccurate. This conclusion is supported by the high toxicity observed in a well-conducted study for algae toxicity for CAS RN 61788-63-4 showing E_bC_{50} and E_rC_{50} values of 0.05 and 0.12 mg/l, respectively.

Subcategory IV – Alkyldiamines: Modeled data were available for two HPV chemicals (CAS RN 68479-04-9 and 7173-62-8). The model predicted rapid photodegradation ($t_{1/2}$ was ≤ 1 hour for both chemicals). Stability in water was not calculable by the model. The estimated transport and distribution of these chemicals was respectively 27% and 11% to water and 73 and 89% to sediment.

One HPV chemical (CAS RN 61791-55-7) was tested for biodegradability. In this test, 87% of the chemical was adsorbed in the sludge and 90% DOC elimination occurred in 3 hours. Based on data from the other chemicals in the FND Amines Category, biodegradation of these chemicals would be expected if procedures adequate to ensure bioavailability were employed.

Measured LC_{50}/EC_{50} values of 0.16 and 0.033 mg/l for fish and 0.132 and 0.021 mg/l for aquatic invertebrates were available for the HPV chemical, CAS RN 68479-04-9, and the supporting chemical, CAS RN 52898-18-7. No data were available for toxicity to aquatic plants. The ECOSAR model predicted aliphatic amine EC_{50} values for daphnia and plants for the HPV chemical CAS RN 68479-04-9 of 0.07 and 0.42mg/l, respectively which is similar to other measured and modeled data for chemicals in the FND Amines Category.

Subcategory V – Trialkylamines: No modeled data were available for chemicals in this Subcategory.

Measured biodegradation data were available for the two alkyl diethanolamines (CAS RN 61791-31-9 and 61791-44-4). In 28 days, there was 61% COD and 52% ThOD, respectively indicating these, like the other FND Amines in the category are readily or nearly readily biodegradable.

No data were available for toxicity to aquatic organisms.

Summary – Environmental Fate and Ecotoxicity

As anticipated in the EPA guidance for HPV chemicals, only model estimates were available for photodegradation and fugacity. The other exclusively modeled value, stability in water, could not be calculated for this category of chemicals. Atmospheric photodegradation was predicted to be rapid although fugacity models suggested very minimal distribution of these chemicals to the air. Predicted distribution of the chemicals in the environment was to water and sediment compartments based on the assumption that release of the chemicals to the environment is all via water. Extensive biodegradation testing across the Category indicated that the FND Amines Category chemicals are biodegradable, often meeting the "readily biodegradable" criteria. No additional biodegradation studies are proposed since there is no pattern or structural properties of

the chemicals within the Category and Subcategories to suggest that non-tested chemicals would behave differently. The substantial numbers of studies evaluating the aquatic toxicity of the FND Amine Category chemicals clearly indicate that these surfactants are highly toxic (LC_{50}/EC_{50} values generally < 1 mg/l) to aquatic organisms. Only when the chemicals are not adequately dispersed in the test medium are confounding values obtained. Furthermore, this high toxicity is consistent with the large numbers of tests conducted for other FND surfactants (amides, cationics) and for surfactants in general. Therefore, further testing of these chemicals for aquatic toxicity is considered of no value in a screening program such as the HPV Chemical Challenge. For the purpose of the program, all of the FND Amine Category chemicals can be considered highly toxic to aquatic species. Overall, the available data support the conclusion that the FND Amines Category chemicals possess similar environmental fate and ecotoxicity across the category.

Additional Testing – Environmental Fate and Ecotoxicity

No additional testing (Table 6) is proposed for the Category. The available model data are adequate for photodegradation, particularly in light of the very limited potential volatility of the FND Amines Category chemicals, and fugacity. These chemicals are not expected to exhibit hydrolysis under normal conditions. Adequate biodegradation data are available to indicate the chemicals in the Category are readily or nearly readily biodegradable. As noted above, additional testing for aquatic toxicity is unwarranted since all of the FND Amine Category chemicals, similar to other surfactants, can be considered highly toxic to aquatic organisms. Since biological treatment of chemicals such as those in the FND Amines Category is the normal and specified manner of disposal, the available data are adequate for the screening purposes of the HPV Chemical Challenge Program.

Human Health-Related Reliable Data

The human health effects data for SIDS endpoints of the 29 FND Amines Category chemicals and 15 supporting chemicals are presented in Table 4. Robust summaries for the reliable studies are provided in Appendix A. The Test Plan for human health related studies is presented in Table 7.

Subcategory I – Primary Alkylamines: The rat acute oral LD_{50} value for the HPV chemical, CAS RN 124-22-1, in two separate studies was 1020 and >2000 mg/kg indicating that the chemicals possess slight acute toxicity by the oral route. The value for mice was similar (1160 mg/kg). Results were similar for six supporting chemicals with LD_{50} values ranging from approximately 1000 to >5000 mg/kg. A rabbit acute dermal toxicity study for CAS RN 61788-46-3* gave an LD_{50} >2000 mg/kg. One acute inhalation study (CAS RN 61788-46-3*) indicated this chemical caused irritation but no lethality at 0.099 mg/l from a one-hour exposure.

Repeated dose toxicity studies were available for four supporting chemicals. In two chronic two-year dietary studies in rats for CAS RN 124-30-1* the NOAEL was approximately 50 mg/kg/day. In a one-year chronic dietary study in dogs for this chemical, the reported NOAEL was 3.0 mg/kg/day. In this study, the occurrence of "foamy" histiocytes in the mesenteric lymph nodes and abnormal appearance of the intestines was recorded. For CAS RN 61790-33-8*, a 4-week gavage study had an NOAEL of 12.5 mg/kg/day. A 14-day repeated dose skin study with minimal observations was reported with CAS RN 112-90-3* in rats. The chemical was irritating at all doses after several days of dosing with the lowest dose of 0.5% showing minimal irritation.

No necropsies were performed so this study is considered of supplemental value to establishing the irritant properties of the test chemical. For the mixture of hydrofluoride salts of hexadecylamine and octadecenamine (CAS RN 3151-59-5 + 36505-83-6), a 24-month rat study and a 2-year dog study were available. The NOAEL for both studies was 6.0 mg/kg/day. Non-specific effects on body weight, food consumption, clinical chemistry measurements and organ weights were observed at 30 mg/kg/day in the rat study. Enlarged intestinal lymph nodes with histological evidence of sinusoidal dilation with congestion and fibroplasias were observed at the high dose. Dogs could not tolerate a dose of 30 mg/kg/day and the high dose was reduced to 12 mg/kg/day after five weeks. Effects at the high dose were minimal, primarily related to decreased serum protein throughout the study.

Adequate Salmonella Reverse Mutation (Ames) assays for one of the FND Amines Category chemicals (CAS RN 143-27-1) and five of the supporting chemicals (CAS RN 68511-40-0, 124-30-1*, 61788-46-3*, 61790-33-8*, and 112-90-3*) were identified. All of the assays were negative. In two cases (CAS RN 124-30-1* and 61788-46-3*), toxicity was observed for the higher concentrations used in these studies thus limiting the number of concentrations available for evaluation. However, since the criteria for a positive test includes dose response and the concentrations that could be evaluated were as high as could have been tested, these studies are considered adequate. An *in vivo* mouse micronucleus assay for CAS RN 61790-33-8* was negative. A CHO/HGPRT gene mutation assay, a mouse lymphoma assay, a chromosome aberration assay and an *in vivo* cytogenetics assay were negative for CAS RN 112-90-3*.

Evaluations of potential reproductive effects were available for three supporting chemicals. For CAS RN 124-30-1*, reproductive organs were examined in both two-year toxicity studies with rats and the one-year toxicity study with dogs. No effects were seen in the reproductive organs at the highest doses tested (approximately 50 mg/kg/day for rats and 15 mg/kg/day for dogs). Reproductive and developmental screening for CAS RN 61790-33-8* was conducted in a study that followed OECD 421 guidelines. The parental and offspring NOAEL was 12.5 mg/kg based on body weight effects at the mid dose of 50 mg/kg/day. The high dose of 120 mg/kg/day was lethal. No effects on reproduction or developmental toxicity were observed. For the mixture of hydrofluoride salts of hexadecylamine and octadecenamine (CAS RN 3151-59-5 + 36505-83-6), in a Segment I, reproductive screening assay, male body weights were decreased at the highest dose (30 mg/kg/day) while no effects on offspring were noted. Results for two developmental toxicity studies were available for the supporting chemical, CAS RN 112-90-3*. The NOAEL for maternal toxicity in rats was 10 mg/kg/day and the corresponding value for rabbits was 3.0 mg/kg/day. No teratogenic or developmental toxicity was observed in either study at the highest doses tested. For the mixture (CAS RN 3151-59-5 + 36505-83-6), Segment II (teratology) studies in rats and rabbits and a Segment III (perinatal) study in rats were identified. Maternal body weights were decreased in the Segment II study for rats (NOAEL = 6.0 mg/kg/day) and rabbits (NOAEL not established). No developmental toxicity was observed in these studies and no effects on offspring or mothers was observed in the Segment III study (NOAELs = 30 mg/kg/day).

<u>Subcategory II</u> – Dimethylalkylamines: Rat acute oral toxicity LD_{50} data were available for the five HPV chemicals and two of three supporting chemicals in this Subcategory. Values ranged from approximately 800 to >2000 mg/kg indicating that the chemicals possess slight acute toxicity by the oral route. Acute dermal studies for the HPV chemicals (CAS RN 112-69-6, 124-28-7, and 61788-91-8) and supporting chemicals (CAS RN 112-18-5 and 61788-93-0)

yielded LD_{50} values ranging from approximately 3000 to 5000 mg/kg. These values indicate that these chemicals possess slight toxicity via the dermal route with doses of 3000 to 8000 mg/kg being lethal to some animals for the tested chemicals.

Salmonella Reverse Mutation (Ames) assays were conducted on three HPV chemicals (CAS RN 112-75-4, 112-69-6 and 124-28-7). These studies were conducted using only two strains of bacteria and do not adequately fulfill the HPV Chemical Challenge Program requirements. However, the results were negative adding support to the large weight of evidence that the FND Amines Category chemicals are unlikely to be mutagenic. An *in vivo* mouse micronucleus assay for supporting chemical, CAS RN 112-18-5, was negative.

No reproductive or developmental toxicity studies were identified for the chemicals in this Subcategory.

Subcategory III – Dialkylmethylamines and Dialkylamines: Two HPV (CAS RN 4088-22-6 and 61788-63-4) and two supporting (CAS RN 61788-62-3 and 61789-79-5) chemicals had reported acute oral LD_{50} values of >2000, >5000, or > 10000 mg/kg.

A 13-week dietary toxicity study was reported for CAS RN 4088-22-6. The dietary concentrations for this study were 0.15, 0.5, and 1.5% (approximately 130, 375 and 1000 mg/kg/day). This study reported extensive findings of 'foamy macrophages' in the intestinal mucosa and other organs including ovaries. This finding was dose related and occurred at all doses. The lymph nodes in the intestines were enlarged at all doses as well. No NOAEL was, therefore, established.

An adequate Salmonella Reverse Mutation (Ames) assay for CAS RN 4088-22-6 was negative.

Reproductive organs were examined in the 13-week dietary study with CAS RN 4088-22-6. The identification of 'foamy macrophages' in the ovaries of this study precludes a definition of a NOAEL. However, this finding is not considered related to reproductive toxicity per se and is likely related to clearance of the test material. However, finding these macrophages in the ovaries is not common for chemicals that have this type of lesion due to clearance. No developmental toxicity studies were identified for the chemicals in this Subcategory.

Subcategory IV – Alkyldiamines: Rat acute oral toxicity LD_{50} values (approximate 300 – 400 mg/kg) for the supporting alkyloxy derivatives of propanediamine, CAS RN 52898-18-7, indicated these chemicals are moderately toxic via the oral route. The acute oral toxicity LD_{50} value for the alkyldiamine HPV chemical (CAS RN 61791-55-7) in this Subcategory was >5000 mg/kg indicating that the alkyldiamines are relatively non-toxic by the oral route similar to the chemicals in the other subcategories.

Repeated dose toxicity data were not available for chemicals in this Subcategory.

An adequate Salmonella Reverse Mutation (Ames) assay for the supporting chemical, CAS RN 52898-18-7, was negative.

No reproductive or developmental toxicity studies were identified for the chemicals in this Subcategory.

Subcategory V – Trialkylamines: Rat acute oral toxicity LD_{50} data were available for the two diethanolamines (CAS RN 61791-31-9 and 61791-44-4) in this Subcategory. Values ranged from 1200 to >5000 mg/kg indicating that the chemicals possess slight to minimal acute toxicity by the oral route.

One acute inhalation study for this Subcategory (CAS RN 61791-44-4) was conducted. The study had an unusual design, testing heated test material with and without polypropylene aerosol. The study design and untoward results prohibited a clear definition of an LC_{50} since 100% of the animals with the polypropylene in the aerosol died while none died without the inert polymer. The authors speculate that the actual concentration of the test material may have been much higher than the nominal value in the polypropylene plus test material group. Based on the group exposed to the test chemical only, the inhalation LC_{50} was greater than the 0.08 mg/l tested (no deaths). However, this value is considered to be uncertain (FND Amines Task Group).

A 90-day dietary study in rats and dogs was reported for alkyl ethanolamine, CAS RN 61791-44-4. The NOAEL values were approximately 50 mg/kg/day and 13 mg/kg/day, respectively. In the dog study, the higher doses of 40 and 120 mg/kg/day were poorly tolerated with extensive emesis reported. Both of these studies reported the finding of "foamy macrophages" in the intestines of the animals at the higher doses, similar to that reported for the Subcategories I and III chemicals discussed above.

In vitro genetic assays were not available for chemicals in this Subcategory.

Evaluations of reproductive organs was made for the animals in the 90-day rat and dog studies (CAS RN 61791-44-4) meeting the requirements for the HPV screening for reproductive effects. No effects were observed at the highest doses tested (approximately 450 and 120 mg/kg/day, respectively). No developmental toxicity data were available for chemicals in this Subcategory.

Summary – Human Health-Related Data

Adequate acute oral LD_{50} studies were available throughout the category. They indicate slight to minimal acute toxicity for the majority of the FND Amines Category chemicals with moderate toxicity observed for the alkyloxy derivatives of propanediamine. Several acute dermal studies indicate these chemicals can be classified as minimally toxic. Acute inhalation studies did not result in deaths under normal exposure conditions for two chemicals. Repeated dose toxicity studies in Subcategories I, III, and V had similar NOAELs (12.5 to 50 mg/kg/day for rats and 3 or 13 mg/kg/day for dogs). Interestingly, one dog study in Subcategory I (CAS RN 124-30-1*) and the rat and dog studies from Subcategories III and V all reported 'foamy macrophages' in the intestines, this finding being associated with effects by which the NOAELs were established. These types of findings have been reported following oral consumption of white oils (Firriolo *et al.*, 1995; Shoda *et al.*, 1997). These lesions are thought to be related to clearance of these high molecular weight oils but are not associated with long-term effects. Enlargement and lesions in the intestinal lymph nodes in the chronic rat study with the hydrofluoride salt mixture (CAS RN 3151-59-5 + 36505-83-6) in Subcategory I were also observed. The occurrence of these lesions following exposure to the FND Amines Category chemicals suggests that they may behave similarly to high molecular weight oils. Available data indicate that the FND Amines Category chemicals are unlikely to be mutagenic and that they are not reproductive or developmental toxins.

Additional Testing – Human Health-Related Studies

In evaluating the needs for further testing of the FND Amines Category chemicals, it is useful to review the available data for the related FND Cationic and FND Amides Category chemicals. Acute oral toxicity studies (approximately 70 studies for 40 chemicals in the three categories) provide LD_{50} values from approximately 400 to 10,000 mg/kg with no apparent organ specific toxicity. Similarly, repeated dose toxicity studies (approximately 28 studies for 15 chemicals) provide NOAELs between 10 and 100 mg/kg/day for rats and slightly lower for dogs. More than 50 genetic toxicity studies (*in vitro* bacterial and mammalian cells as well as *in vivo* studies) indicated only one equivocally positive Salmonella Reverse Mutation assay among more than 30 chemicals tested. For reproductive evaluations, 12 studies evaluated reproductive endpoints and/or reproductive organs for 11 chemicals and 14 studies evaluated developmental toxicity for 12 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 Amines Category chemicals will not pose significant toxicity to humans. As noted previously, it is not appropriate to consider the FND Amines Category chemicals to represent a continuum of alkyl chain substitution. As outlined in Text Table C the minimal difference among the alkyl substituents and the large database for the FND Categories indicates that the structural differences in these large alkyl chains that do exist do not result in differences in toxicity or mutagenicity. Thus, there is no scientifically justifiable expectation that any of the alkylamines in the Category will result in significant toxicity not already established by tests with the HPV and supporting chemicals. The primary amines are well represented by the available data and additional substitutions for the chemicals in the other Subcategories serve to decrease bioavailability while providing no additional structural alerts to warrant selection for additional testing. Based on the consistent pattern of toxicity within and among the FND Categories, no additional testing is proposed for the FND Amines Category chemicals. Table 7 provides the Test Plan for the human health related endpoints.

References

Firriolo, J.M., C.F. Morris, G.W. Trimmer, L.D. Twitty, J.H. Smith and J.J. Freeman. 1995. Comparative 90-day feeding study with low-viscosity white mineral oil in Fischer-344 and Sprague-Dawley-derived CRL:CD rats. *Toxicologic Pathol* 23: 26-33.

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

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

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

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

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

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

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

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

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

Shoda T., K. Toyoda, C. Uneyama, K. Takada and M. Takahashi. 1997. Lack of carcinogenicity of medium-viscosity liquid paraffin given in the diet to F344 rats. *Food Chem Toxicol* 35: 1181-1190.

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

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

U. S. EPA. 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/sarfinl1.htm.

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

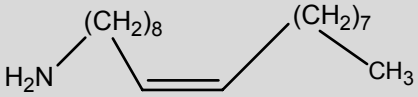
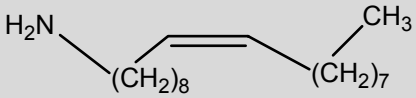
Table 1

Structures of FND Amines Category Chemicals

Subcategory I: Primary Alkylamines	
H_2N——$(CH_2)_3$——O——R **R = C_8 – C_{10} alkyl** 1-Propanamine, 3-(C_{8-10}-alkyloxy) derivs. 68784-38-3	H_2N——$(CH_2)_3$——O——$(CH_2)_7$—— 1-Propanamine, 3-(isodecyloxy)- 30113-45-2
H_2N $(CH_2)_3$ O——$(CH_2)_7$—— HO O *1-Propanamine, 3-(isodecyloxy)-, acetate* *28701-67-9*	H_2N——$(CH_2)_3$——O——R **R = C_9 – C_{11} isoalkyl, C_{10} rich** 1-Propanamine,3-(C_{9-11}-isoalkyloxy) derivs., C_{10} rich 218141-16-3
H_2N——$(CH_2)_3$——O——R **R = C_{13} alkyl, branched** *1-Propanamine, 3-(tridecyloxy)-, branched* *68511-40-0*	H_2N——$(CH_2)_3$——O——R **R = C_{11} – C_{14} isoalkyl, C_{13} rich** 1-Propanamine,3-(C_{11-14}-isoalkyloxy) derivs., C_{13} rich 151789-06-9
H_2N——$(CH_2)_{11}$——CH_3 Dodecylamine 124-22-1	H_2N——$(CH_2)_{15}$——CH_3 Hexadecylamine 143-27-1

Table 1 (continued)

Structures of FND Amines Category Chemicals

H_2N——R **R = C_{14} – C_{18} alkyl** Amines, C_{14-18}-alkyl 68037-91-2	H_2N——R **R = hydrogenated tallow alkyl** *Amines, hydrogenated tallow alkyl* *61788-45-2**
H_2N——$(CH_2)_{17}$——CH_3 *Octadecylamine* *124-30-1**	H_2N——R **R = coco alkyl** *Amines, coco alkyl* *61788-46-3**
H_2N——R **R = C_{14} – C_{18}- and C_{16} – C_{18}-unsaturated alkyl** Amines, C_{14-18} and C_{16-18}-unsatd. alkyl 68155-38-4	H_2N——R **R = tallow alkyl** *Amines, tallow alkyl* *61790-33-8**
H_2N——R **R = soya alkyl** Amines, soya alkyl 61790-18-9	H_2N——R **R = C_{16} – C_{18}- and C_{18}-unsaturated alkyl** Amines, C_{16-18} and C_{18}-unsaturated alkyl 68037-95-6
 *Cis-9-Octadecenylamine* *112-90-3**	H_2N——$(CH_2)_{15}$——CH_3 *Hexadecylamine hydrofluoride (Hetaflur)*[3] *3151-59-5*  *9-Octadecen-1-amine hydrofluoride*[3] *36505-83-6*

* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.
[3] Hydrofluoride salt not shown in structure.

Table 1 (continued)

Structures of FND Amines Category Chemicals

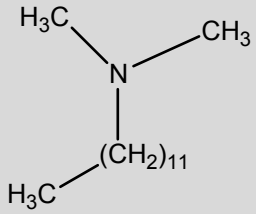
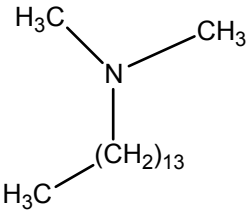
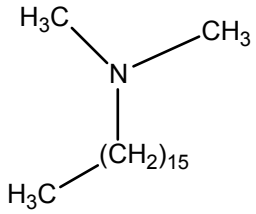
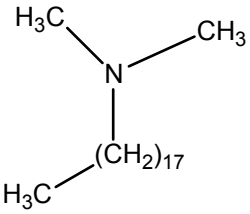
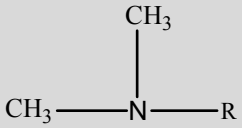
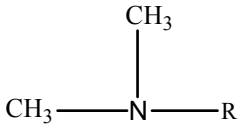
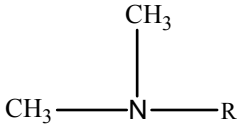
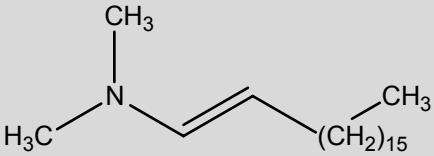
Subcategory II: Dimethylalkylamines	
 *1-Dodecanamine, N,N-dimethyl* *112-18-5*	 1-Tetradecanamine, N,N-dimethyl 112-75-4
 1-Hexadecanamine, N,N-dimethyl 112-69-6	 1-Octadecanamine, N,N-dimethyl 124-28-7
 **R = coco alkyl** *Amines, coco alkyl dimethyl* *61788-93-0*	 **R = hydrogenated tallow alkyl** Amines, (hydrogenated tallow alkyl)dimethyl 61788-95-2
 **R = soya alkyl** Amines, dimethyl soya alkyl 61788-91-8	 *Octadecen-1-amine, N,N-dimethyl* *28061-69-0*

Table 1 (continued)

Structures of FND Amines Category Chemicals

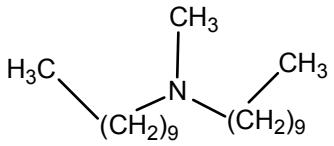
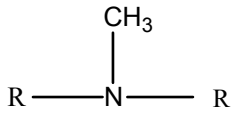
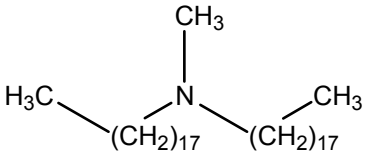
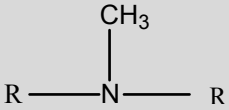
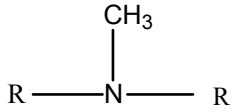
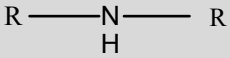
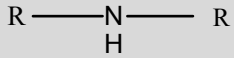
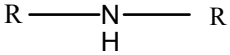
Subcategory III: Dialkylmethylamines and Dialkylamines	
 1-Decanamine, N-decyl-N-methyl 7396-58-9	 **R = C_{14} – C_{18} alkyl** Amines, di-C_{14-18}-alkylmethyl 67700-99-6
 R = C_{12} – C_{18} alkyl Amines, di-C_{12-18}-alkyl 68153-95-7	 1-Octadecanamine, N-methyl-N-octadecyl 4088-22-6
 **R = coco alkyl** *Amines, dicoco alkylmethyl* *61788-62-3*	 **R = hydrogenated tallow alkyl** Dihydrogenated tallow methylamine 61788-63-4
 **R = hydrogenated tallow alkyl** *Amines, bis(hydrogenated tallow alkyl)* *61789-79-5*	 **R = coco alkyl** *Amines, dicoco alkyl* *61789-76-2*
 **R = tallow alkyl** Amines, ditallow alkyl 68783-24-4	

Table 1 (continued)

Structures of FND Amines Category Chemicals

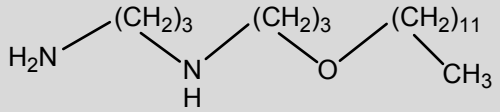
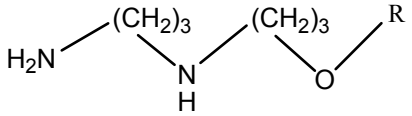
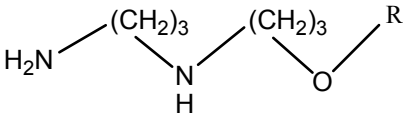
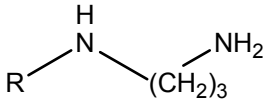
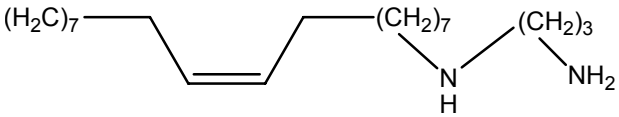
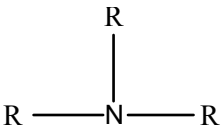
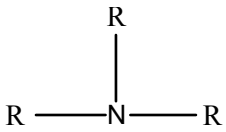
Subcategory IV: Alkyldiamines	
 *1,3-Propanediamine, N-(3-(dodecyloxy)propyl)* *52898-18-7*	 **R = C_{11} – C_{14}-isoalkyl derivs., C_{13} rich** 1,3-Propanediamine, N-(3-(C_{11-14}-isoalkyloxy)propyl)derivs., C_{13} rich 151789-07-0
 **R = C_{13} alkyl, branched** 1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched 68479-04-9	 **R = tallow alkyl** Amines, N-tallow alkyltrimethylenedi- 61791-55-7
 1,3-Propanediamine, N-(9Z)-octadecenyl- 7173-62-8	
Subcategory V: Trialkylamines	
 **R = C_8 – C_{10} alkyl** Amines, tri-C_{8-10}-alkyl- 68814-95-9	 **R = hydrogenated tallow alkyl** Amines, tris (hydrogenated tallow alkyl) 61790-42-9

Table 1 (continued)

Structures of FND Amines Category Chemicals

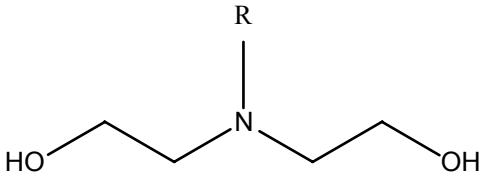
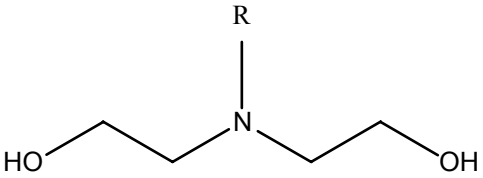
 **R = coco alkyl derivs.** Ethanol, 2,2'-iminobis-, N-coco alkyl derivs. 61791-31-9	 **R = tallow alkyl derivs.** Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs. 61791-44-4

Table 2

Physical/Chemical Properties Data for FND Amines Category Chemicals

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
Subcategory I: Primary Alkylamines					
68784-38-3					
30113-45-2	51	278	0.0035	3.92	165
28701-67-9					
218141-16-3					
68511-40-0	*81*	*322*	*0.00017*	*5.40*	*5.4*
151789-06-9					
124-22-1	**28.3** 28.3	**259** 259	 0.0081	 4.76	**2000** 45.1
143-27-1	 47	 323	 0.00013	 6.73	 0.48
68037-91-2					
*61788-45-2**	***52.9*** *52.9*	***348*** *347.8*	***0.000012*** *0.000087*	 *7.71*	 *0.049*
*124-30-1**	***52.9*** *52.9*	***347*** ***347*** *347*	***0.000012*** *0.000087*	 *7.71*	***1000*** ***not soluble*** *0.049*
*61788-46-3**					
68155-38-4					

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

Table 2 (continued)

Physical/Chemical Properties Data for FND Amines Category Chemicals

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
*61790-33-8**	***34 – 40*** ***25 – 30***	***200 – 230***	***< 1.3***	***7.5***	***insoluble***
61790-18-9					
68037-95-6					
*112-90-3**	***~21*** ***21*** *93*	***275- 344*** ***335*** *346*	***< 1.3*** ***0.00013***[4] *0.000037*	***7.5***[4] ***and 8.1***[4] ***7.5***[4] ***>3.11*** *7.50*	***(0.5 x 10^{-3})***[4] ***and*** ***(0.7 x 10^{-5})***[4] ***insoluble*** ***very insoluble*** *0.076*
3151-59-5 *+ 36505-83-6*					
Subcategory II: Dimethylalkylamines					
112-18-5	***-20 to -15*** *22*	*260*	*0.0159*	*5.44*	*8.58*
112-75-4	43	292	0.0020	6.42	0.88
112-69-6	63	321	0.00029	7.41	0.089
124-28-7	**22.9** **19.6 - 22.4** 22.9	346	0.00017	8.39	**not soluble** 0.0089
61788-93-0					
61788-95-2					
61788-91-8					
28061-69-0	*80*	*345*	*0.000052*	*8.25*	*0.012*

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[4] Estimated value.

Table 2 (continued)

Physical/Chemical Properties Data for FND Amines Category Chemicals

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
Subcategory III: Dialkylmethylamines and Dialkylamines					
7396-58-9					
67700-99-6					
68153-95-7					
4088-22-6	216	543	2.0×10^{-11}	17	2×10^{-11}
61788-62-3					
61788-63-4					
61789-79-5					
61789-76-2					
68783-24-4					
Subcategory IV: Alkyldiamines					
52898-18-7					
151789-07-0					
68479-04-9	130	380	2.2×10^{-6}	5.37	2.64
61791-55-7					
7173-62-8	142	402	4.9×10^{-7}	7.47	0.037
Subcategory V: Trialkylamines					
68814-95-9					
61790-42-9					
61791-31-9					
61791-44-4					

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

Table 3

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
Subcategory I: Primary Alkylamines							
68784-38-3							
30113-45-2	64 E-12 $t_{1/2}$ = 2.0 hr	not calculable	Air: <1% Water: 90% Soil: <1% Sediment: 10%		126 (3.5)	7.9 (0.33)	not calculable (1.21)
28701-67-9							
218141-16-3							
68511-40-0	*68 E-12* *$t_{1/2}$ = 1.9 hr*	*not calculable*	*Air: <1%* *Water: 26%* *Soil: <1%* *Sediment: 74%*		*not toxic at solubility* *(0.05)*	*3.24*	*not calculable* *(0.33)*
151789-06-9							
124-22-1	46 E-12 $t_{1/2}$ = 2.8 hr	not calculable	Air: <1% Water: 75% Soil: <1% Sediment: 25%	**> 60% ThOD in 28 d**	**0.42** 9.77 (0.87)	3.2 (0.09)	not calculable (0.45)
143-27-1	51 E-12 $t_{1/2}$ = 2.5 hr	not calculable	Air: <1% Water: 13% Soil: <1% Sediment: 87%		not toxic at solubility	not toxic at solubility (0.008)	not calculable (not toxic at solubility)

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[5] Water was assumed to be the exclusive route of entry into the environment.
[6] Original model calculations were made specifying the chemicals as "Cationic Surfactants"; a second calculation was made assuming the chemicals are Aliphatic Amines – the values for this second calculation are included in ( ) if different than for Cationic Surfactants.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
68037-91-2							
*61788-45-2**	*54 E-12* *$t_{1/2}$ = 2.4 hr*	*not calculable*	*Air: <1%* *Water: 10%* *Soil: <1%* *Sediment: 90%*	***75% ThOD in 28 d*** ***64% CO_2 in 28 d***	***0.88*** *not toxic at solubility*	***0.16*** ***<1.0*** *not toxic at solubility*	***96-hour:*** ***E_bC_{50}[7] = 0.012*** ***E_rC_{50}[7] = ~0.016*** *not calculable (not toxic at solubility)*
*124-30-1**	*54 E-12* *$t_{1/2}$ = 2.4 hr*	*not calculable*	*Air: <1%* *Water: 10%* *Soil: <1%* *Sediment: 90%*	***>60% ThOD in 12 d*** ***70% ThOD in 28 d***	 *not toxic at solubility*	***0.13*** *not toxic at solubility*	***E_bC_{50} = 0.062*** ***E_rC_{50} =0.12*** *not calculable (not toxic at solubility)*
*61788-46-3**				***56% ThOD in 28 d*** ***(74% in 42 d)*** ***58% $ThC0_2$ in 28 d***	***0.16*** ***0.24***	***0.045*** ***0.09*** ***Larvae = 2.0 – 3.0[8]*** ***Pupae = 3.5 – 13.0[8]***	***E_bC_{50} = 0.14*** ***E_rC_{50} =0.17*** ***96-hour:*** ***E_bC_{50} = 0.00075*** ***E_rC_{50} =0.0011***
68155-38-4							

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[7] E_bC_{50} is the EC_{50} based on growth (biomass); E_rC_{50} is the EC_{50} based on growth rate.
[8] Test performed on 4 strains of mosquito larvae and pupae; *C .p. quinquefasciatus, A. albimanus, A. aegypti, and A. nigromaculis.*

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
*61790-33-8**				***56% TCO_2 in 28 d*** ***>51% BOD in 28 d*** ***(~70% in 42 d)*** ***73% in 28 d***	***9.3*** ***>0.18 and <0.25***	***0.093*** ***0.09*** ***<0.25***	***E_bC_{50} = 0.052*** ***E_rC_{50} =0.059*** ***E_bC_{50} = 0.068*** ***E_rC_{50} =0.083***
61790-18-9							
68037-95-6							
*112-90-3**	*110 E-12* *$t_{1/2}$ = 1.2 hr*	*not calculable*	*Air: <1%* *Water: 11%* *Soil: <1%* *Sediment: 89%*	***> 60% ThOD in 12 d*** ***44% ThOD in 28 d*** ***(72% in 42 d)*** ***66% $ThC0_2$ in 28 d*** ***69% ThOD in 28 d***	***0.11*** *not toxic at solubility*	***0.011*** *not toxic at solubility*	***96-hour:*** ***E_bC_{50} =0.03*** ***E_rC_{50} =0.04*** *not toxic at solubility*
3151-59-5 + 36505-83-6							

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
Subcategory II: Dimethylalkylamines							
112-18-5	*93 E-12* *$t_{1/2}$ = 1.4 hr*	*not calculable*	*Air: <1%* *Water: 42%* *Soil: <1%* *Sediment: 58%*	***67% ThOD in 28 d*** ***72% TCO_2 in 29 d*** ***67% ThN-BOD in 28 d***	***0.57*** *not toxic at solubility*	***0.083*** *3.24* *(0.04)*	***E_bC_{50} = 0.056***[9] ***E_rC_{50} =0. 092*** ***E_bC_{50} = 0.034*** ***E_rC_{50} =0.056*** ***$E_bC_{50} \leq 0.0133$*** ***$E_rC_{50} \leq 0.0235$*** *not calculable* *(0.26)*
112-75-4	96 E-12 $t_{1/2}$ = 1.3 hr	not calculable	Air: <1% Water: 7% Soil: <1% Sediment: 93%	**≤ 2% COD in 28 d**[10]	**0.18** **> 0.01 and < 1.0** **>0.01 and < 0.1** **0.35** not toxic at solubility	not toxic at solubility (0.01)	not calculable (not toxic at solubility)

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].

[9] First four values are from a single study using two natural water sources.
[10] The scientific validity of this value is unjustifiable based on all other tests of similar chemicals. The assay is presumed to be invalid.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
112-69-6	99 E-12 $t_{1/2}$ = 1.3 hr	not calculable	Air: <1% Water: 5% Soil: <1% Sediment: 95%	**59% ThOD in 28 d (70% in 42 d)** **107% TCO_2 in 29 d**	**0.18** **>0.1 and <1.0** not toxic at solubility	not toxic at solubility	not calculable (not toxic at solubility)
124-28-7	102 E-12 $t_{1/2}$ = 1.3 hr	Not calculable	Air: <1% Water: 5% Soil: <1% Sediment: 95%	**91% TCO_2 at 0.2 mg/l in 7 d (79% at 2.0 mg/l in 7 d);** **118% TCO_2 at 10 mg/l in 40 d; and** **51% TCO_2 at 20 mg/l in 40 d** **49% TCO_2 in 28 d**	**0.18** **>0.1 and <1.0** not toxic at solubility	**LC_{50} = 0.074[11]** not toxic at solubility	**algistatic conc. = 0.029 or 0.11** **algicidal conc. > 0.032 or = 0.16[12]** not calculable (not toxic at solubility)
61788-93-0				***81% ThOD in 28 d*** ***69% ThOD in 28 d***	***>0.1 and <1.0***		
61788-95-2				**58% ThOD in 28d (66% in 42 d)**			

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[11] 96-hour LC_{50} value for Mysidopsis bahia
[12] The study was conducted on *Selenastrum capricornutum* and *Microcystis aeruginosa* with a 5-day exposure and a 9 day recover period. An EC_{50} was not determined.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
61788-91-8				**98% ThOD in 28 d**	**> 0.1 and < 1.0**		
28061-69-0	*126 E-12* *$t_{1/2}$ = 1.0 hr*	*not calculable*	*Air: <1%* *Water: 5%* *Soil: <1%* *Sediment: 95%*	***50% ThOD in 28 d (59% in 70 d)***	*not toxic at solubility*	*not toxic at solubility*	*not calculable (not toxic at solubility)*
Subcategory III: Dialkylmethylamines and Dialkylamines							
7396-58-9							
67700-99-6							
68153-95-7							
4088-22-6	134 E-12 $t_{1/2}$ = 1.0 hr	not calculable	Air: <1% Water: 5% Soil: <1% Sediment: 95%		**>100 and <500[13]** not toxic at solubility	not toxic at solubility	not calculable (not toxic at solubility)
61788-62-3				***82% ThOD in 28 d***	***6.15***		
61788-63-4				**75% ThOD in 28 d (85% in 40 d) 100% COD in 28 d**	**>1000[13]**	**35.2[13] 790[13]**	**E_bC_{50}= 0.05 E_rC_{50} =0.12**
61789-79-5				***16% O_2 in 28 d[13]***	***≥ 220 and ≤ 500[13]***		

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Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[13] The value(s) is(are) questionable due to the bioavailability of the test substance in this study.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
61789-76-2				***20% ThOD in 28 d[13] (18% in 42 d)[13]***			
68783-24-4							
Subcategory IV: Alkyldiamines							
52898-18-7					***0.033[14]***	***0.021[14]***	
151789-07-0[15]							
68479-04-9	154 E-12 $t_{1/2}$ = 1.0 hr	not calculable	Air: <1% Water: 27% Soil: <1% Sediment: 73%		**0.16** not toxic at solubility	**LC_{50} = 0.132** not toxic at solubility (0.07)	not calculable (0.42)
61791-55-7				**90% DOC elimination in 3 hrs; 87% adsorption in sludge**			
7173-62-8	193 E-12 $t_{1/2}$ = 0.7 hr	not calculable	Air: <1% Water: 11% Soil: <1% Sediment: 89%		not toxic at solubility	not toxic at solubility	not calculable (not toxic at solubility)

Note: Bold font indicates reliable data for which a Robust Summary is provided in Appendix A
Regular font indicates data obtained from appropriate models as described in the text and Appendix B.
Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[14] Test run with a formulated product – 51% primary amine and 49% secondary and tertiary amine.
[15] Chemical is essentially the same as CAS RN 68479-04-9.

Table 3 (continued)

Environmental Fate and Ecotoxicity Data for FND Amines Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution[5]	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)[6]	Acute Tox. to Invertebrates 48-hour EC_{50} (mg/l)[6]	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)[6]
Subcategory V: Trialkylamines							
68814-95-9							
61790-42-9							
61791-31-9				**61% COD in 28 d (62% in 42 d)**			
61791-44-4				**52% ThOD in 28 d (62% in 35 d)**			

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

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

Table 4

Human Health-Related Data for FND Amines Category Chemicals

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity *In vitro/ In vivo*	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
Subcategory I: Primary Alkylamines							
68784-38-3							
30113-45-2[16]							
28701-67-9	*1.46 (male)* *1.03 (female)*						
218141-16-3							
68511-40-0					*Negative (Ames)*		
151789-06-9[17]							
124-22-1	1.02 (rats) 1.16 (mice) >2.0 (rats)						
143-27-1					Negative (Ames) Negative (Ames)		
68037-91-2							
*61788-45-2**	*>5.0* *4.8* *>2.0*						

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[16] Chemical is essentially the same as CAS RN 28701-67-9.
[17] Chemical is essentially the same as CAS RN 68511-40-0.

Table 4 (continued)

Human Health-Related Data for FND Amines Category Chemicals

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity *In vitro/ In vivo*	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
*124-30-1**	*~1.0 (rat and mouse)* *>2.0* *>2.0*			*~25*[18] *~25*[19] *3.0*[20]	*Negative (Ames)* *Negative (Ames)* *Negative (Ames)*	*~25*[18] *~25*[19] *15*[20]	
*61788-46-3**	*1.24 (male)* *1.39 (female)* *>2.0 (male)* *2.82 (female)*	*>0.099*[21]	*>2.0*		*Negative (Ames)*		
68155-38-4							
*61790-33-8**	*>2.50 (male)* *>2.00 (female)* *2.23 (male)* *2.61 (female)*			*12.5*[22]	*Negative (Ames)* *Negative (In vivo rat micronucleus)*	*Parents = 12.5* *Offspring = 12.5* [23]	*Parents = 12.5* *Offspring = 12.5* [23]
61790-18-9							
68037-95-6							

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[18] Chronic (two-year) dietary toxicity study in rats. The NOAEL was 500 ppm (highest dose tested) estimated to be approximately 25 mg/kg/day. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.
[19] Chronic (two-year) dietary toxicity study in rats. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.
[20] Chronic (one-year) dietary toxicity study in dogs. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.
[21] Exposure period = 1 hour
[22] Four-week oral (gavage) toxicity study in rats.
[23] OECD 421 oral gavage study in rats.

Table 4 (continued)

Human Health-Related Data for FND Amines Category Chemicals

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity *In vitro/ In vivo*	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
*112-90-3**	*~2.0 (females)* *~ 1.18 (males)*			*See Robust Summary*[24]	*Negative (Ames)* *Negative (CHO/HGPRT gene mutation)* *Negative (mouse lymphoma)* *Negative (chrom. aberration)* *Negative (In vivo cytogenetic)*		*Maternal = 10; Developmental = 80 .*[25] *Maternal =3.0 ; Developmental =30*[26]
3151-59-5 + 36505-83-6				*6.0*[27] *6.0*[28]		*Parents =6.0* *Offspring = 30.0*[29]	*Maternal = 6.0* *Developmental = 30.0*[30] *Maternal = 1.2 (LOAEL)* *Developmental = 30.0*[31] *Maternal and Offspring = 30.0*[32]

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

[24] A 14-day dermal toxicity study with limited evaluations; not adequate for SIDS/HPV testing but provides data on the irritation of the chemical following repeated exposure.
[25] Developmental toxicity study in rats dosed via oral gavage at doses of 0, 10, 40 and 80 mg/kg.
[26] Developmental toxicity study in rabbits dosed via oral gavage at doses of 0, 3, 10 and 30 mg/kg/day.
[27] 24-Month feeding study in rats at doses of 1.2, 6.0 and 30.0 mg/kg/day.
[28] 2-Year study in dogs via oral gavage at doses of 1.2, 6.0 and 12.0 mg/kg/day.
[29] Segment I (Fertility and General Reproductive Performance) study in rats via oral gavage at doses of 1.2, 6.0 and 30.0 mg/kg/day.
[30] Two Segment II (Teratology) studies in rats were conducted at doses of 1.2, 6.0 and 30.0 mg/kg/day. Decreases in maternal body weight gains at 30.0 mg/kg/day in the confirmatory study.
[31] Segment II (Teratology) study in rabbits at doses of 1.2, 6.0 and 30.0 mg/kg/day. Maternal body weight decreased at the low dose.
[32] Segment III (Perinatal and Postnatal) study in rats at doses of 1.2, 6.0 and 30.0 mg/kg/day.

Table 4 (continued)

Human Health-Related Data for FND Amines Category Chemicals

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity *In vitro/ In vivo*	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
Subcategory II: Dimethylalkylamines							
112-18-5	*1.22* *0.79* *>0.63 and <1.26*		*~5.0*		*Negative (In vivo mouse micronucleus)*		
112-75-4	2.116 1.32				Negative (Ames)[33]		
112-69-6	0.80[34] >2.0 1.015		4.29[34]		Negative (Ames)[33]		
124-28-7	0.78 2.116		4.29[34]		Negative (Ames)[33]		
61788-93-0	*1.50 (male)* *1.30 (female)* *>1.0 and <1.25* *1.58[34]*		*4.29[34]*				
61788-95-2	>2.0						
61788-91-8	0.835[34]		3.0[34]				
28061-69-0							
Subcategory III: Dialkylmethylamines and Dialkylamines							
7396-58-9							
67700-99-6							
68153-95-7							

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[33] Evaluation with only two tester strains.
[34] Value is ml/kg.

Table 4 (continued)

Human Health-Related Data for FND Amines Category Chemicals

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity *In vitro/ In vivo*	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
4088-22-6	>2.0			LOAEL = 130[35]	Negative (Ames)	LOAEL = 130[35]	
61788-62-3	*>2.0*						
61788-63-4	>5.0						
61789-79-5	*>10.0 (males)*						
61789-76-2							
68783-24-4							
Subcategory IV: Alkyldiamines							
52898-18-7	*0.378 (male)* *0.299 (female)*				*Negative (Ames)*		
151789-07-0							
68479-04-9							
61791-55-7	>5.0						
7173-62-8							
Subcategory V: Trialkylamines							
68814-95-9							
61790-42-9							
61791-31-9	>5.0						
61791-44-4	1.50 (male) 1.20 (female) >2.0	See Robust Summary[36]		~50[37] 13[38]		~450[37] 120[38]	

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[35] 13-week dietary toxicity study in rats. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.
[36] A 4-hour exposure study was conducted that does not adequately define the LC_{50} for the chemical. The study provides additional data on the potential inhalation hazard.
[37] 90-day dietary toxicity study in rats . NOAEL was 500 ppm in the diet estimated to be approximately 50 mg/kg/day. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.
[38] 90-day dietary toxicity study in dogs. Dose of 40 and 140 mg/kg/day were poorly tolerated with extensive emesis. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.

Table 5

Proposed Test Plan for American Chemistry Council FND Amines Category Physical/Chemical Properties

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
Subcategory I: Primary Alkylamines					
68784-38-3	R	R	R	R	R
30113-45-2	**M**	**M**	**M**	**M**	**M**
28701-67-9	*R*	*R*	*R*	*R*	*R*
218141-16-3	R	R	R	R	R
68511-40-0	***M***	***M***	***M***	***M***	***M***
151789-06-9	R	R	R	R	R
124-22-1	**A (M)**	**A (M)**	**M**	**M**	**A (M)**
143-27-1	**M**	**M**	**M**	**M**	**M**
68037-91-2	R	R	R	R	R
*61788-45-2**	***A (M)***	***A (M)***	***A (M)***	***M***	***M***
*124-30-1**	***A (M)***	***A (M)***	***A (M)***	***M***	***A (M)***
*61788-46-3**	*R*	*R*	*R*	*R*	*R*
68155-38-4	R	R	R	R	R
*61790-33-8**	***A***	***A***	***A***	***A***	***A***
61790-18-9	R	R	R	R	R
68037-95-6	R	R	R	R	R
*112-90-3**	***A (M)***	***A (M)***	***A (M)***	***A (M)***	***A (M)***
3151-59-5 + 36505-83-6	***R***	***R***	***R***	***R***	***R***

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
A = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

Table 5 (continued)

Proposed Test Plan for American Chemistry Council FND Amines Category Physical/Chemical Properties

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
Subcategory II: Dimethylalkylamines					
112-18-5	***A (M)***	***M***	***M***	***M***	***M***
112-75-4	**M**	**M**	**M**	**M**	**M**
112-69-6	**M**	**M**	**M**	**M**	**M**
124-28-7	**A (M)**	**M**	**M**	**M**	**A (M)**
61788-93-0	*R*	*R*	*R*	*R*	*R*
61788-95-2	R	R	R	R	R
61788-91-8	R	R	R	R	R
28061-69-0	***M***	***M***	***M***	***M***	***M***
Subcategory III: Dialkylmethylamines and Dialkylamines					
7396-58-9	R	R	R	R	R
67700-99-6	R	R	R	R	R
68153-95-7	R	R	R	R	R
4088-22-6	**M**	**M**	**M**	**M**	**M**
61788-62-3	*R*	*R*	*R*	*R*	*R*
61788-63-4	R	R	R	R	R
61789-79-5	*R*	*R*	*R*	*R*	*R*
61789-76-2	*R*	*R*	*R*	*R*	*R*
68783-24-4	R	R	R	R	R

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
A = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.

Table 5 (continued)

Proposed Test Plan for American Chemistry Council FND Amines Category
Physical/Chemical Properties

CAS RN	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa)	Partition Coefficient (log K_{ow})	Water Solubility (mg/l)
Subcategory IV: Alkyldiamines					
52898-18-7	*R*	*R*	*R*	*R*	*R*
151789-07-0	R	R	R	R	R
68479-04-9	**M**	**M**	**M**	**M**	**M**
61791-55-7	R	R	R	R	R
7173-62-8	**M**	**M**	**M**	**M**	**M**
Subcategory V: Trialkylamines					
68814-95-9	R	R	R	R	R
61790-42-9	R	R	R	R	R
61791-31-9	R	R	R	R	R
61791-44-4	R	R	R	R	R

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
A = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.

Table 6

Proposed Test Plan for American Chemistry Council FND Amines Category Environmental Fate and Ecotoxicity

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)	Acute Tox. To Invertebrates 48-hour EC_{50} (mg/l)	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)
Subcategory I: Primary Alkylamines							
68784-38-3	R	R	R	R	R	R	R
30113-45-2	**M**	NC	**M**	R	**M**	**M**	**M**
28701-67-9	*R*	*R*	*R*	*R*	*R*	*R*	*R*
218141-16-3	R	R	R	R	R	R	R
68511-40-0	***M***	*NC*	***M***	*R*	***M***	***M***	***M***
151789-06-9	R	R	R	R	R	R	R
124-22-1	**M**	NC	**M**	**A**	**A (M)**	**M**	**M**
143-27-1	**M**	NC	**M**	R	**M**	**M**	**M**
68037-91-2	R	R	R	R	R	R	R
*61788-45-2**	***M***	*NC*	***M***	***A***	***A (M)***	***A (M)***	***A (M)***
*124-30-1**	***M***	*NC*	***M***	***A***	***M***	***A (M)***	***A (M)***
*61788-46-3**	*R*	*R*	*R*	***A***	***A***	***A***	***A***
68155-38-4	R	R	R	R	R	R	R
*61790-33-8**	*R*	*R*	*R*	***A***	***A***	***A***	***A***
61790-18-9	R	R	R	R	R	R	R
68037-95-6	R	R	R	R	R	R	R
*112-90-3**	***M***	*NC*	***M***	***A***	***A (M)***	***A (M)***	***A (M)***
3151-59-5 + 36505-83-6	*R*	*R*	*R*	*R*	*R*	*R*	***R***

Note: **Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].**
A = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.
NC = Model could not calculate a value.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.

Table 6 (continued)

Proposed Test Plan for American Chemistry Council FND Amines Category Environmental Fate and Ecotoxicity

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)	Acute Tox. To Invertebrates 48-hour EC_{50} (mg/l)	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)
Subcategory II: Dimethylalkylamines							
112-18-5	***M***	*NC*	***M***	***A***	***A (M)***	***A (M)***	***A (M)***
112-75-4	**M**	NC	**M**	**A**	**A (M)**	**M**	**M**
112-69-6	**M**	NC	**M**	**A**	**A (M)**	**M**	**M**
124-28-7	**M**	NC	**M**	**A**	**A (M)**	**A (M)**	**A (M)**
61788-93-0	*R*	*R*	*R*	***A***	***A***	*R*	*R*
61788-95-2	R	R	R	**A**	R	R	R
61788-91-8	R	R	R	**A**	**A**	R	R
28061-69-0	***M***	*NC*	***M***	***A***	***M***	***M***	***M***
Subcategory III: Dialkylmethylamines and Dialkylamines							
7396-58-9	R	R	R	R	R	R	R
67700-99-6	R	R	R	R	R	R	R
68153-95-7	R	R	R	R	R	R	R
4088-22-6	**M**	NC	**M**	R	**A (M)**	**M**	**M**
61788-62-3	*R*	*R*	*R*	***A***	***A***	*R*	*R*
61788-63-4	R	R	R	**A**	**A**	**A**	**A**
61789-79-5	*R*	*R*	*R*	***A***	***A***	*R*	*R*
61789-76-2	*R*	*R*	*R*	***A***	*R*	*R*	*R*
68783-24-4	R	R	R	R	R	R	R

Note: **Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].A** = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.
NC = Model could not calculate a value.

Table 6 (continued)

Proposed Test Plan for American Chemistry Council FND Amines Category Environmental Fate and Ecotoxicity

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute/Prolonged Tox. to Fish 96-hour LC_{50} (mg/l)	Acute Tox. To Invertebrates 48-hour EC_{50} (mg/l)	Toxicity to Aquatic Plants 72-hr. EC_{50} (mg/l)
Subcategory IV: Alkyldiamines							
52898-18-7	*R*	*R*	*R*	*R*	***A***	***A***	*R*
151789-07-0	R	R	R	R	R	R	R
68479-04-9	**M**	NC	**M**	R	**A (M)**	**A (M)**	**M**
61791-55-7	R	R	R	**A**	R	R	R
7173-62-8	**M**	NC	**M**	R	**M**	**M**	**M**
Subcategory V: Trialkylamines							
68814-95-9	R	R	R	R	R	R	R
61790-42-9	R	R	R	R	R	R	R
61791-31-9	R	R	R	**A**	R	R	R
61791-44-4	R	R	R	**A**	R	R	R

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
A = Adequate reported values
M = Adequate model data available
R = Read across from available data and/or experimental determination is considered inappropriate.
NC = Model could not calculate a value.

Table 7
Proposed Test Plan for American Chemistry Council FND Amines Category
Human Health-Related Data

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOEL (mg/kg/day)	Genetic Toxicity *In vitro/In vivo*	Toxicity to Reproduction	Developmental Toxicity NOEL
Subcategory I: Primary Alkylamines							
68784-38-3	R	R	R	R	R	R	R
30113-45-2	R	R	R	R	R	R	R
28701-67-9	***A***	*R*	*R*	*R*	*R*	*R*	*R*
218141-16-3	R	R	R	R	R	R	R
68511-40-0	*R*	*R*	*R*	*R*	***A (Ames)***	*R*	*R*
151789-06-9	R	R	R	R	R	R	R
124-22-1	**A**	R	R	R	R	R	R
143-27-1	R	R	R	R	**A (Ames)**	R	R
68037-91-2	R	R	R	R	R	R	R
*61788-45-2**	***A***	*R*	*R*	*R*	*R*	*R*	*R*
*124-30-1**	***A***	*R*	*R*	***A***	***A (Ames)***	***A***	*R*
*61788-46-3**	***A***	***A***	***A***	*R*	***A (Ames)***	*R*	*R*
68155-38-4	R	R	R	R	R	R	R
*61790-33-8**	***A***	*R*	*R*	***A***	***A (Both)***	***A***	***A***
61790-18-9	R	R	R	R	R	R	R
68037-95-6	R	R	R	R	R	R	R
*112-90-3**	***A***	*R*	*R*	*R*	***A (Both)***	*R*	***A***
3151-59-5 + 36505-83-6	***R***	*R*	*R*	*A*	***R***	*A*	***A***
Subcategory II: Dimethylalkylamines							
112-18-5	***A***	*R*	***A***	*R*	***A (Cyto)***	*R*	*R*
112-75-4	**A**	R	R	R	[39]	R	R
112-69-6	**A**	R	**A**	R	[39]	R	R
124-28-7	**A**	R	**A**	R	[39]	R	R
61788-93-0	***A***	*R*	***A***	*R*	*R*	*R*	*R*
61788-95-2	**A**	R	R	R	R	R	R

[39] Salmonella Reverse Mutation Assay in two tester strains was negative.

Table 7 (continued)
Proposed Test Plan for American Chemistry Council FND Amines Category
Human Health-Related Data

CAS RN	Acute Oral Toxicity (g/kg)	Acute Inhalation Toxicity (mg/l)	Acute Dermal Toxicity (g/kg)	Repeated Dose Toxicity NOEL (mg/kg/day)	Genetic Toxicity *In vitro/In vivo*	Toxicity to Reproduction	Developmental Toxicity NOEL
61788-91-8	**A**	R	**A**	R	R	R	R
28061-69-0	*R*	*R*	*R*	*R*	*R*	*R*	*R*
Subcategory III: Dialkylmethylamines and Dialkylamines							
7396-58-9	R	R	R	R	R	R	R
67700-99-6	R	R	R	R	R	R	R
68153-95-7	R	R	R	R	R	R	R
4088-22-6	**A**	R	R	**A**	**A (Ames)**	**A**	R
61788-62-3	*A*	*R*	*R*	*R*	*R*	*R*	*R*
61788-63-4	**A**	R	R	R	R	R	R
61789-79-5	*A*	*R*	*R*	*R*	*R*	*R*	*R*
61789-76-2	*R*	*R*	*R*	*R*	*R*	*R*	*R*
68783-24-4	R	R	R	R	R	R	R
Subcategory IV: Alkyldiamines							
52898-18-7	*A*	*R*	*R*	*R*	***A (Ames)***	*R*	*R*
151789-07-0	R	R	R	R	R	R	R
68479-04-9	R	R	R	R	R	R	R
61791-55-7	**A**	R	R	R	R	R	R
7173-62-8	R	R	R	R	R	R	R
Subcategory V: Trialkylamines							
68814-95-9	R	R	R	R	R	R	R
61790-42-9	R	R	R	R	R	R	R
61791-31-9	**A**	R	R	R	R	R	R
61791-44-4	**A**	R	R	**A**	R	**A**	R

Note: Shaded cells with CAS RN and data in italics are for supporting chemicals [non-HPV].
Reliable data for acute toxicity by any of the three routes of exposure are considered adequate under the EPA HPV Challenge Program.
A = Adequate reliable data
R = Endpoint fulfilled by category read-across from existing or proposed test data.
* These chemicals were removed from the original FND Amines Category because they are sponsored by APAG under the ICCA program.