

SCREENING-LEVEL HAZARD CHARACTERIZATION Fatty Nitrogen Derived Imidazoline Derivatives Category

SPONSORED CHEMICALS (See Section 1)

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

Chemical Abstract Service Registry Number (CASRN)	Sponsored 72749-55-4 72623-72-4 61791-39-7 68442-97-7 65817-50-7
	Supporting 68122-86-1
Chemical Abstract Index Name	See Section 1
Structural Formula	See Section 1
Summary	
<p>Members of the fatty nitrogen derived (FND) amides imidazoline derivatives category are liquid mixtures possessing negligible vapor pressure; these substances are dispersible in water. The category is subdivided into three subcategories: subcategory I, 1-(amidoethyl) imidazolines; subcategory II, 1-(2-hydroxyethyl) imidazolines; and subcategory III, 1-(aminoalkyl) imidazolines. Members of the imidazoline derivatives category are expected to possess low mobility in soil. Volatilization is considered low for all category members. The rate of hydrolysis is unknown; however, imidazoline derivatives are susceptible to hydrolysis under alkaline conditions and elevated temperatures resulting in the formation of their respective amide. The rate of atmospheric photooxidation is considered rapid for the imidazoline derivatives; however, this is not expected to be an important environmental fate process since these substances are not expected to exist in the vapor phase in the atmosphere. Members of subcategory I (1-(amidoethyl) imidazolines) possess moderate persistence (P2) and low bioaccumulation potential (B1). Members of subcategory II (1-(2-hydroxyethyl) imidazolines) and subcategory III (1-(aminoalkyl) imidazolines) possess moderate persistence (P2) and high bioaccumulation potential (B3); however, the dispersible nature of these substances makes the assessment of bioaccumulation uncertain.</p>	
<u>Human Health Hazard</u>	
<i>Subcategory I: 1-(Amidoethyl) Imidazolines</i>	
<i>Available data for supporting chemical, CASRN 68122-86-1 were used to address data gaps for the 1-(Amidoethyl) Imidazolines subcategory using a read-across approach.</i>	
<p>Acute oral toxicity for the 1-(amidoethyl) imidazolines subcategory is low in rats. A 13-week dietary study showed significant increases in relative liver weights in male and female rats at 2200 mg/kg-bw/day; the NOAEL for systemic toxicity was 730 mg/kg-bw/day. A 13-week dietary study in dogs showed no signs of systemic toxicity, resulting in a NOAEL of 1635 mg/kg-bw/day (highest dose tested). In a prenatal developmental toxicity study, dams treated via oral gavage on gestation days 6-15 showed no treatment-related effects on maternal (food consumption, body weight gain, gravid uterine weight) or developmental parameters (number of implantations, viable offspring, fetal body weight). The NOAEL for maternal/developmental toxicity was 1000 mg/kg-day (highest dose tested). No reproductive toxicity studies were</p>	

available; however, an evaluation of testes (weight and histopathology) in the 13-week rat study showed no effects up to the highest dose tested. CASRN 68122-86-1 was irritating to rabbit skin. It did not induce gene mutations or chromosomal aberrations when tested *in vitro*.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

No data were provided for this subcategory; however, studies taken from the Re-registration Eligibility Decision (RED) document (<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>) are described in this hazard characterization. Acute oral and dermal toxicity of CASRN 61791-39-7 is low in rats and rabbits, respectively. A prenatal developmental toxicity study in rats showed decreased food consumption and body weight gain in dams gavaged at or above 65 mg/kg/day during gestation days 6-15. Clinical signs, including excessive salivation and staining in the anogenital region were observed at or above 15 mg/kg-day; a NOAEL for maternal toxicity was not established. No treatment-related effects were reported for any of the developmental parameters examined in this study; the NOAEL for developmental toxicity was 100 mg/kg-day (highest dose tested). No reproductive toxicity studies were available. CASRN 61791-39-7 was irritating to rabbit skin and eyes. It did not induce gene mutations or chromosomal aberrations when tested *in vitro*.

Subcategory III: 1-(Aminoalkyl) Imidazolines

Acute oral toxicity for the 1-(Aminoalkyl) Imidazolines subcategory is low in rats. This substance is irritating to rabbit skin. No adequate toxicity data were provided to assess the repeated-dose/reproductive/developmental toxicity, gene mutation or chromosomal aberrations endpoints.

Hazard to the Environment

Subcategory I: Alkylated Dihydroimidazolium Compounds

The potential hazard of CASRN 72749-55-4 to aquatic organisms could not be evaluated because no data on aquatic toxicity endpoints were available.

Subcategory II: Alkylated Dihydroimidazoles

For the alkylated dihydroimidazoles, the 96-hour LC₅₀ for fish is 0.23 mg/L, and the 48-h EC₅₀ for aquatic invertebrates is 1.5 mg/L. Chronic toxicity to aquatic invertebrates and toxicity to aquatic plants could not be evaluated because no data were available for this endpoint.

Human Health Data Gaps

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

The repeated-dose/reproductive toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory III: 1-(Aminoalkyl) Imidazolines

The repeated-dose/reproductive/developmental toxicity, gene mutation and chromosomal aberrations endpoints were identified as data gaps under the HPV Challenge Program.

Environmental Data Gaps

Subcategory I: Alkylated Dihydroimidazolium Compounds

The acute toxicity to fish and aquatic invertebrates, chronic toxicity to aquatic invertebrates and toxicity to aquatic plants endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory II: Alkylated Dihydroimidazoles

The chronic toxicity to aquatic invertebrates and toxicity to aquatic plants endpoints were identified as data gaps under the HPV Challenge Program.

The sponsor, The American Chemistry Council's Fatty Nitrogen Derivatives Panel Amides Task Group, submitted a Test Plan and Robust Summaries to EPA for the Fatty Nitrogen Derived (FND) Amides category dated November 27, 2001 (actual posting date on the EPA website not known). Following initial comments by EPA dated June 27, 2002 (posted on July 3, 2002), the sponsor submitted revisions on September 16, 2004 (posted October 18, 2004). This revision subdivided the original submission into five separate submissions (FND Amides, FND Amphoterics, FND Imidazoline Derivatives and two single chemicals). This Hazard Characterization will focus on the FND Imidazoline Derivative category. Important submission history information is provided on the ChemRTK HPV Challenge Web site (<http://www.epa.gov/oppt/chemrtk/pubs/summaries/fantdrad/c13319tc.htm>). EPA comments specific to the FND Imidazoline Derivatives category are dated October 2, 2007 (posting date of October 18, 2007).

Category Justification

The sponsor's rationale for grouping these substances in one category is based on proposed similarities in structural features and surfactant properties. The sponsor submits that a similar toxicity profile may be expected for category members and proposes a read-across approach using data provided for one or more substances to support the rest of the category.

EPA does not accept this category justification, as the sponsor's claim of comparable toxicity has not been demonstrated. These substances exhibit considerable variation in imidazoline ring substituents which may affect toxicity. In order to evaluate the potential for human health effects, EPA recommends that the FND Imidazoline Derivatives category be divided into the following subcategories:

Subcategory I: 1-(Amidoethyl) Imidazolines. This subcategory includes two sponsored substances, imidazolium compounds, 2-(C17 & C17-unsat. alkyl)-1[2-(C18 & C18-unsat.amido ethyl]-4,5-dihydro-1-methyl-, methyl sulfates (CASRN 72749-55-4) and amides, C14-18, N-[2-(C13-17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]- (CASRN 72623-72-4). A supporting substance, imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1) is also included in this subcategory. These chemicals have higher molecular weights (561 – 644), as well as enhanced surfactant and hydrophobic properties which may affect absorption. Two of the chemicals in this group are quaternary ammonium salts. The influence of this chemical moiety (non-dissociable positive charge) on toxicity has not been adequately addressed; however, EPA agrees that a read-across approach for the sponsored and supporting chemicals is acceptable within this subcategory.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines. This subcategory consists of a single sponsored chemical, 1H-imidazole-1-ethanol, 4,5-dihydro-,2-nortall-oil alkyl derivatives (CASRN 61791-39-7), which is expected to have a metabolic profile that is unique for this category. The absence of toxicity data demonstrating comparable toxicity precludes grouping with other members of the FND Imidazoline Derivatives category.

Subcategory III: 1-(Aminoalkyl) Imidazolines. This subcategory includes two chemicals, 1H-imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 68442-97-7) and 1,2-ethanediamine, N-(2-aminoethyl)-N'-[2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-

1-yl]ethyl- (CASRN 65817-50-7). These sponsored chemicals contain the most hydrophilic substituents and the only primary amines in the FND Imidazoline Derivatives category. They exhibit significant differences in surfactant properties (when compared to other category members) that are expected to influence toxicity. As such, it is recommended that these substances be considered separately; however, EPA agrees that a read-across approach to characterize aquatic and human health toxicity is acceptable within this subcategory.

To address ecotoxicity, EPA recommends the FND Imidazoline Derivatives category be separated into the following subcategories:

Subcategory I: Alkylated Dihydroimidazolium Compounds. This subcategory has one sponsored substance, imidazolium compounds, 2-(C17 & C17-unsat. alkyl)-1[2-(C18 & C18-unsaturated amido) ethyl]-4,5-dihydro-1-methyl-, methyl sulfates (CASRN 72749-55-4). This chemical is a quaternary ammonium salt.

Subcategory II: Alkylated Dihydroimidazoles. This subcategory includes four sponsored chemicals, amides, C14-18,N-[2-(C13 -1-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]- (CASRN 72623-72-4), 1H-imidazole-1-ethanol,4,5-dihydro-2-nortall-oil alkyl derivatives (CASRN 61791-39-7), 1H-imidazole-1-ethanamine, 4,5-dihydro-,2-nortall-oil alkyl derivatives (CASRN 68442-97-7) and 1,2-ethanediamine, N-(2-aminoethyl)-N'-[2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl] ethyl (CASRN 65817-50-7).

Justification for Supporting Chemicals

Although few data are provided in the robust summaries, EPA agrees that the supporting substance, imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1), is a reasonable choice for read across in subcategory I, based on structural similarities with the two sponsored members of this subcategory.

A Re-registration Eligibility Decision (RED) document exists for 1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7). This document can be found at the following website: (<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>). It contains additional studies that have been included in this hazard characterization.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2004 Test Plan and Robust Summary:

These substances are formed by the reaction of fatty acids with ethylenediamine derivatives (diethylenetriamine, N-(2-hydroxyethyl)ethylenediamine and tetraethylenepentamine), yielding various amides which are subsequently dehydrated to form the stable imidazoline derivative. These insoluble or “dispersible” substances are not pure materials, being comprised of mixtures and reaction products of natural oils and/or long-chain hydrocarbons that vary with producer and

starting material. The alkyl chain components are generally reacted from natural products such as coconut, soya, tallow and pine oils. Purity of test article, when noted in the Robust Summaries, ranged between 37 – 90%. Chemical structures of the FND imidazoline derivatives are depicted in Table 1.

Table 1: Fatty Nitrogen Derived Imidazoline Derivatives Category		
Chemical Abstract Index Name	CASRN	Representative Structure
Imidazolium compounds, 2-(C17 & C17-unsatd. alkyl)-1-[2-(C18 & C18-unsatd. amido)ethyl]-4,5-dihydro-1-methyl, methyl sulfates	72749-55-4	
Amides, C14 – 18, N-[2-(C13 – 17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]-	72623-72-4	
Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Me sulfates	68122-86-1	
1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivs.	61791-39-7	
1H-Imidazole-1-ethanamine, 4,5-dihydro-,2-nortall-oil alkyl derivatives	68442-97-7	
1,2-Ethanediamine, N1-(2-aminoethyl)-N2-[2-[2-(8Z)-8-heptadecen-1-yl-4,5-dihydro-1H-imidazol-1-yl]ethyl-]	65817-50-7	
<p>The sponsor did not provide a comprehensive distribution for tall oil fatty acids. The HPV test plan for tall oil fatty acid provides the following distribution: 48% oleic acid; 42% linoleic acid; 2% stearic acid; and 1% palmitic acid.</p> <p>In the test plan, the sponsor stated that tallow fatty acids typically consist of 35-46% oleic acid; 20-37% palmitic acid; 14-21% stearic acid; 4-10% linoleic acid; 3-9% palmitoleic acid; 1-6% myristic acid and 0-3% linolenic acid.</p>		

1.2 Physical-Chemical Properties

The physical-chemical properties of the FND Imidazoline derivatives category are summarized in Table 2. These substances are liquid mixtures that possess negligible vapor pressure and are dispersible in water.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

According to the 2006 IUR submissions, the FND Imidazoline category had an aggregated production and/or import volume in the U.S. between 12 million and 70.5 million pounds.

- CASRN 61791-39-7: 1 to <10 million pounds;
- CASRN 68442-97-7: 10 to <50 million pounds;
- CASRN 72749-55-4: <500,000 pounds; and
- CASRN 68122-86-1: 1 to <10 million pounds.

CASRN 65817-50-7 and 72623-72-4 were not reported in the 2006 IUR.

CASRN 61791-39-7: Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include oil and gas extraction as corrosion inhibitors; anti-scaling agents and other basic organic chemical manufacturing as corrosion inhibitors and anti-scaling agents. Non-confidential commercial and consumer uses for this chemical include "other".

CASRN 68442-97-7: Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as surface active agents, intermediates and "other"; pesticide and other agricultural chemical manufacturing as surface active agents; support activities for mining as photosensitive chemicals. Non-confidential commercial and consumer uses of this chemical include "other".

CASRN 72749-55-4: Industrial processing and use information, as well as commercial and consumer uses for the chemical were claimed confidential.

CASRN 68122-86-1: Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include soap and cleaning compound manufacturing as surface active agents. Commercial and consumer uses were claimed to be confidential.

Table 2. Physical-Chemical Properties of Fatty Nitrogen Derived (FND) Amides Imidazoline Derivatives Category¹

Property	Subcategory I: 1-(Amidoethyl) imidazolines			Subcategory II: 1-(2-Hydroxyethyl) imidazolines	Subcategory III: 1-(Aminoalkyl) imidazolines	
	Imidazolium cmpds 2-(C17 & C17-unsatd alkyl) - 1-[2-(C18&C18 - unsatd amido) ethyl]-4,5-dihydro- 1-methyl, methyl sulfates	Amides, C14-18, N- [2-(C13-17- alkyl-4,5- dihydro-1H- imidazol-1- yl)ethyl]	Imidazolium cmpds, 4,5-dihydro-1-methyl - 2-nortallow alkyl-1-(2- tallow amidoethyl) methyl sulfates (Supporting chemical)	1H-Imidazole-1- ethanol, 4,5- dihydro-, 2-nortall- oil alkyl derives.	1H-Imidazole- 1-ethanamine, 4,5-dihydro-,2- nortall-oil alkyl derivs.	1,2-Ethanediamine, N1-(2-aminoethyl) - N2-[2-[2-(8Z)-8- heptadecen-1-yl-4,5- dihydro-1H- imidazol-1-yl]ethyl]-
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Molecular Weight	739 (typical)	506 (typical)	632 (typical)			435.75
Physical State	Clear yellow liquid ²		Viscous yellow paste ³	Dark viscous liquid ⁴		Light to dark yellow liquid ³
Melting Point (°C)	No data	No data	No data	No data	No data	No data
Boiling Point (°C)	>300 (estimated) ^{5,6}	>300 (estimated) ^{5,6}	>300 (estimated) ^{5,6}	>200 at 20 mm Hg (measured) ⁷ ; >300 (estimated) ^{5,6}	>300 (estimated) ^{5,6}	>300 (estimated) ^{5,6}
Vapor Pressure (mmHg) at 25°C	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵
Water Solubility (mg/L)	50 (measured; indicates dispersion rather than solution) ²	Dispersible	Dispersible	Dispersible	Dispersible	Dispersible
Dissociation Constant (pK _a)	Not applicable	12.2 (estimated)	Not applicable	12.5 (estimated); 9.1 (estimated)	12.5 (estimated)	12.5 (estimated); 8.9 (estimated); 9.9 (estimated); 9.6 (estimated)

Table 2. Physical-Chemical Properties of Fatty Nitrogen Derived (FND) Amides Imidazoline Derivatives Category¹

Property	Subcategory I: 1-(Amidoethyl) imidazolines			Subcategory II: 1-(2-Hydroxyethyl) imidazolines	Subcategory III: 1-(Aminoalkyl) imidazolines	
	Imidazolium cmpds 2-(C17 & C17-unsatd alkyl) - 1-[2-(C18&C18 - unsatd amido) ethyl]-4,5-dihydro- 1-methyl, methyl sulfates	Amides, C14-18, N- [2-(C13-17- alkyl-4,5- dihydro-1H- imidazol-1- yl)ethyl]	Imidazolium cmpds, 4,5-dihydro-1-methyl - 2-nortallow alkyl-1-(2- tallow amidoethyl) methyl sulfates (Supporting chemical)	1H-Imidazole-1- ethanol, 4,5- dihydro-, 2-nortall- oil alkyl derives.	1H-Imidazole- 1-ethanamine, 4,5-dihydro-,2- nortall-oil alkyl derivs.	1,2-Ethanediamine, N1-(2-aminoethyl) - N2-[2-[2-(8Z)-8- heptadecen-1-yl-4,5- dihydro-1H- imidazol-1-yl]ethyl]-
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Henry's Law Constant (atm-m ³ /mole)	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵	<1.0×10 ⁻¹⁰ (estimated) ⁵
Log K _{ow} ⁸	Not applicable due to dispersibility	Not applicable due to dispersibility	Not applicable due to dispersibility	Not applicable due to dispersibility	Not applicable due to dispersibility	Not applicable due to dispersibility

¹ American Chemistry Council. Fatty Nitrogen Derivatives Panel. September 16, 2004. Revised Test Plan and Robust Summary of Fatty Nitrogen Derived Amides Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/fantdrad/c13319tc.htm> as of April 1, 2010.

² National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Australia. September 1999. Full Report on Varisoft 360.

³ Ash, M.; Ash, I. 2000. Handbook of Individual Surfactants, 3rd edition, Volume 2. Synapse Information Resources, Endicott, NY.

⁴ Flick, E.W. 1993. Industrial Surfactants. 2nd edition. Noyes Publications, Park Ridge, NJ.

⁵ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of April 1, 2010.

⁶ Expected to decompose prior to boiling.

⁷ EPA Registration Eligibility Decision for Alkyl imidazole (Date 06/1995). Case# 3010 PC# 046609.

⁸ Tolls, J.; Sijm, D. 2000. Estimating properties of surface active chemicals. In: Handbook of Property Estimation for Chemicals. Boethling R.S.; Mackay, D. (editors.). Chapter 17. Lewis Publishers, Boca Raton, FL. pp. 419–446.

2.2 Environmental Exposure and Fate

All members of the fatty nitrogen derived (FND) amides imidazoline derivatives are expected to possess low mobility in soil. Limited biodegradation data are available for the category members. A commercial substance known as SURFAM P-12B (CASRN 68122-86-1; Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl) Me sulfate) was degraded approximately 5% using secondary effluent from a municipal wastewater treatment facility as inoculum. Imidazolium compounds, 2-(C17 and C17-unsaturated alkyl)-1-[2-(C18 and C18-unsaturated amido)ethyl]-4,5-dihydro-1-methyl, Me sulfates (CASRN 72749-55-4) achieved 7.2% of its theoretical biochemical oxygen demand in 28 days using the modified Sturm test (OECD 301B). A commercial product known as Varisoft 475, which is largely composed of CASRN 72749-55-4 was also not readily biodegradable using a CO₂ evolution test. Volatilization is expected to be low for all category members. The rate of hydrolysis is not known; however, it has been determined that imidazoline derivatives are susceptible to hydrolysis under alkaline conditions and elevated temperatures resulting in the formation of their respective amide. The members of the 1-(amidoethyl) imidazolines (subcategory A) are expected to possess moderate persistence (P2) and low bioaccumulation potential (B1). The substances in subcategory B (1-(2-hydroxyethyl) imidazolines) and subcategory C (1-(aminoalkyl) imidazolines) possess moderate persistence (P2) and high bioaccumulation potential (B3); however, the dispersible nature of these substances makes the assessment of bioaccumulation uncertain. The environmental fate properties are provided in Table 3

Table 3. Environmental Fate Characteristics of Fatty Nitrogen Derived (FND) Amides Imidazoline Derivatives Category¹						
Property	Subcategory I: 1-(Amidoethyl) Imidazolines			Subcategory II: 1-(2-droxyethyl) Imidazolines	Subcategory III: 1-(Aminoalkyl) Imidazolines	
	Imidazolium cmpds, 2-(C17 and C17- unsat'd. alkyl)-1-[2- (C18 & C18-unsatd. amido)ethyl]-4,5- dihydro-1-methyl, Me sulfates	Amides, C14-18, N- [2-(C13-17- alkyl-4,5- dihydro-1H- imidazol-1- yl)ethyl	Imidazolium cmpds, 4,5-dihydro-1-methyl- 2-nortallow alkyl-1-(2- tallow amido ethyl), Me sulfates (Supporting chemical)	1H-Imidazole-1- ethanol, 4,5- dihydro-, 2- nortall-oil alkyl derivs.	1H- Imidazole-1- ethanamine 4,5-dihydro- , 2-nortall-oil alkyl derivs.	1,2-Ethane diamine, N1-(2- aminoethyl)-N2- [2-[2-(8Z)-8- heptadecen-1-yl- 4,5-dihydro-1H- imidazol-1-yl] ethyl]
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Photodegradation Half-life	0.6 hours (estimated) ²	1 hour (estimated) ²	0.6 hours (estimated)	0.8 hours (estimated) ²	0.7 hours (estimated) ²	0.4 hours (estimated) ²
Hydrolysis Half- life	No change in pH of buffered solutions at pH 4, 7, and 9; imidazoline derivatives are susceptible to hydrolysis at pH >8 ³	No data	No data	No data	No data	No data
Biodegradation	7.2% after 28 days (not readily biodegradable) ⁴ BOD/COD = 0.19 after 30 days (not readily iodegradable) ⁴ ; 5% after 20 days (not readily biodegradable) ⁵	No data	No data	No data	No data	No data
Bioaccumulation factor	BCF = 10.7 (measured in bluegills exposed to Varisoft 475); BAF = 206 (estimated) ²	BAF = 130 (estimated) ²	BAF = 85 (estimated) ²	BAF = 1.6×10 ⁴ (estimated)	BAF = 2.2×10 ⁵ (estimated)	BAF = 7.6×10 ⁵ (estimated)

Property	Subcategory I: 1-(Amidoethyl) Imidazolines			Subcategory II: 1-(2-droxyethyl) Imidazolines	Subcategory III: 1-(Aminoalkyl) Imidazolines	
	Imidazolium cmpds, 2-(C17 and C17- unsat'd. alkyl)-1-[2- (C18 & C18-unsatd. amido)ethyl]-4,5- dihydro-1-methyl, Me sulfates	Amides, C14-18, N- [2-(C13-17- alkyl-4,5- dihydro-1H- imidazol-1- yl)ethyl	Imidazolium cmpds, 4,5-dihydro-1-methyl- 2-nortallow alkyl-1-(2- tallow amido ethyl), Me sulfates (Supporting chemical)	1H-Imidazole-1- ethanol, 4,5- dihydro-, 2- nortall-oil alkyl derivs.	1H- Imidazole-1- ethanamine 4,5-dihydro- , 2-nortall-oil alkyl derivs.	1,2-Ethane diamine, N1-(2- aminoethyl)-N2- [2-[2-(8Z)-8- heptadecen-1-yl- 4,5-dihydro-1H- imidazol-1-yl] ethyl]
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Log K _{oc}	10.3 (estimated) ²	8.0 (estimated) ²	9.8 (estimated) ²	5.1 (estimated) ²	6.2 (estimated) ²	6.9 (estimated) ²
Fugacity (Level III Model) ²						
Air	<0.1	0.1	<0.1	<0.1	<0.1	<0.1
Water	1.3	16.0	1.3	17.3	3.2	1.6
Soil	29.8	79.2	30.6	59.9	34.7	40.2
Sediment	68.9	4.7	68.2	22.8	62.0	58.2
Persistence ⁶	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation ⁶	B1 (low)	B1 (low)	B1 (low)	B3 (high)	B3 (high)	B3 (high)

¹ American Chemistry Council. Fatty Nitrogen Derivatives Panel. September 16, 2004. Revised Test Plan and Robust Summary of Fatty Nitrogen Derived Amides Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/fantdrad/c13319tc.htm> as of April 1, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of April 1, 2010.

³ Tyagi, R.; Tyagi, V.K.; Pandey, S.K. 2007. Imidazoline and its derivatives: An overview. *J. Oleo Sci.* 56(5):211–217.

⁴ National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Australia. September 1999. Full Report on Varisoft 360.

⁵ Data obtained for imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Me sulfates (CASRN 68122-86-1).

⁶ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Subcategory I: 1-(Amidoethyl) Imidazolines

Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1, supporting chemical)

(1) Albino rats (5/sex/dose; strain not specified) were administered CASRN 68122-86-1 (90% active ingredient) via oral gavage at 5000 mg/kg and observed for 14 days. No mortality was reported in this study.

LD₅₀ > 5000 mg/kg

(2) Male and female rats (5/sex/dose; strain not specified) received a single dose of CASRN 68122-86-1 (percent active ingredient not specified) via oral gavage at 7.0, 7.5, 8.0, 8.5 or 9.0 mL/kg-day and observed for up to 14 days. Significant mortality occurred within 12 hours of treatment. No other details were provided in the robust summary.

LD₅₀ ~ 8.45 mL/kg

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7)

Sprague-Dawley rats (5/sex/dose) received a single dose of CASRN 61791-39-7 (percent active ingredient not specified) via oral gavage at 100, 1750 or 3000 mg/kg and observed for up to 15 days. This information is taken from the EPA review found at the following website:

(<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

LD₅₀ = 1932 mg/kg (males and females)

Subcategory III: 1-(Aminoalkyl) Imidazolines

1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 68442-97-7)

Sprague-Dawley rats (5/sex/dose) were administered CASRN 68442-97-7 (percent active ingredient not specified) via oral gavage at 5000 mg/kg and observed for up to 15 days.

Significant mortality (60%) occurred in this study.

LD₅₀ < 5000 mg/kg

Acute Dermal Toxicity

Subcategory I: 1-(Amidoethyl) Imidazolines

No data were submitted for this endpoint.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortallow-alkyl derivatives (CASRN 61791-39-7)

New Zealand white rabbits (5/sex) were administered CASRN 61791-39-7 as a single topical application at 2000 mg/kg-bw. All animals survived until study termination (day 15). This information is taken from the EPA review found at the following website:

(<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

LD₅₀ > 2000mg/kg (males and females)

Subcategory III: 1-(Aminoalkyl) Imidazolines

No data were submitted for this endpoint.

Repeated-Dose/Reproductive Toxicity

Subcategory I: 1-(Amidoethyl) Imidazolines

Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow-alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1, supporting chemical)

(1) Beagles (4/sex/dose) received CASRN 68122-86-1 (~76.6% in isopropyl alcohol) via dietary administration at 0, 4000, 12000 or 40,000 ppm in a 13-week repeated-dose toxicity study. The actual doses received in the diet were ~142, 366 and 1322 mg/kg-bw/day for males and ~144, 632 and 1948 mg/kg-bw/day for females. Decreased food consumption observed in all treatment groups, most likely reflects decreased palatability in the treated diet. A significant decrease in body weight was observed in one male and one female at the highest dose. Study authors attributed observed decreases in mean cholesterol levels at or above 366 mg/kg-bw/day to decreased food intake. Macroscopic lesions (type not specified) were observed in all treatment groups; however, these lesions were not dose-related. Other findings reported in this study include significantly increased relative adrenal gland weight in females treated at 144 mg/kg-bw/day and significantly decreased relative pituitary gland weight in males and females at 1322 and 144 mg/kg-bw/day, respectively (level of significance not specified). These effects most likely reflect biological variation. No treatment-related histopathology was observed.

NOAEL ~ 1635 mg/kg-bw/day (males and females)

(2) Rats (10/sex/dose; strain not specified) received CASRN 68122-86-1 (37% active ingredient) via dietary administration at 0, 0.03, 0.3, 1 or 3% (~ 0, 22, 220, 730 or 2200 mg/kg-bw/day) for 13 weeks. The lungs, heart, liver, kidneys, spleen and testes were removed and weighed. Portions of each organ, as well as tissues taken from the adrenal, pancreas, thyroid, brain, stomach, and intestines were examined microscopically. Significant increases in relative liver weights were observed in females treated at 22, 220 or 2200 mg/kg-bw/day and in males treated at 2200 mg/kg-bw/day. In females, absolute kidney weight increased at or above 730 mg/kg-bw/day and relative spleen weight increased at doses up to 730 mg/kg-bw/day. Study authors indicate lower than average liver and kidney weights for controls (relative to recent historical data) as a potential mitigating factor.

NOAEL (reproductive) > 2200mg/kg-bw/day (highest dose tested)

LOAEL (systemic toxicity) ~ 2200 mg/kg-bw/day (increased weights of multiple organs)

NOAEL (systemic toxicity) ~ 730 mg/kg-bw/day

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

No data were submitted for this endpoint.

Subcategory III: 1-(Aminoalkyl) Imidazolines

No data were submitted for this endpoint.

Developmental Toxicity

Subcategory I: 1-(Amidoethyl) Imidazolines

Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1, supporting chemical)

In a prenatal developmental toxicity test, pregnant Sprague-Dawley rats (25/dose) were administered CASRN 68122-86-1 (~76.6% active ingredient in isopropyl alcohol) via oral gavage at 100, 300 or 1000 mg/kg-day during gestation days (GD) 6-15. Control animals received Milli-Q water at a volume equivalent to that used at the highest dose. One female treated at 300 mg/kg-day became moribund and was sacrificed on GD10. The rate of pregnancy (88-100%) did not vary significantly with treatment. There were no treatment-related effects on maternal (food consumption, body weight gain or gravid uterine weight) or developmental (number of implantations, viable offspring, fetal body weight) parameters. No treatment-related malformations or developmental anomalies were noted in this study.

NOAEL (maternal and developmental) >1000 mg/kg-day (highest dose tested)

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortallow oil alkyl derivatives (CASRN 61791-39-7)

In a prenatal developmental toxicity study, Pregnant Sprague-Dawley rats (24/dose), were administered CASRN 61791-39-7 (~85% active ingredient in corn oil vehicle) via oral gavage at 0, 15, 65, or 100 mg/kg/day during GD 6-15. Mortality (two dams) occurred at the highest dose. Clinical signs of toxicity, including excessive salivation, labored breathing, rales and staining of the anogenital region occurred at or above 15 mg/kg/day. Significant decreases in food consumption (~14%) and maternal body weight gain (~55%) were observed in dams treated at or above 65 mg/kg/day (level of significance not specified). The mean number of viable offspring was comparable among control and treated groups. No treatment-related effects on fetal body weight or sex ratio were observed; however, dose-related increases in mean pre-implantation loss and fetal resorptions were reported at or above 65 mg/kg/day. In addition, one dam treated at 65 mg/kg/day and another treated at 100 mg/kg/day delivered litters which showed extensive ocular and skeletal malformations. Study authors attributed these effects to maternal toxicity. No other details were provided. This summary is taken from the EPA review found at the following website: (<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

LOAEL (maternal) = 15 mg/kg/day (clinical signs of toxicity)

NOAEL (maternal) = Not established

NOAEL (developmental) > 100 mg/kg-day (highest dose tested)

Subcategory III: 1-(Aminoalkyl) Imidazolines

No data were submitted for this endpoint.

Genetic Toxicity – Gene Mutation
In vitro

Subcategory I: 1-(Amidoethyl) Imidazolines

Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1, supporting chemical)

(1) In a reverse-mutation assay, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed to CASRN 68122-86-1 in the presence or absence of metabolic activation at concentrations of 0.05, 0.1, 0.5, 1.0, 2.0, 4.0 and 8.0 µl per plate. Cytotoxicity was evident in all strains at 4.0 µl per plate. Positive and Negative control responses were not indicated in the robust summary. No mutagenic effects were observed with this test substance.

CASRN 68122-86-1 was not mutagenic in this assay.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7)

Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100, were exposed to CASRN 61791-39-7 at 0, 1.0, 3.3, 10, 33 and 100µg/plate in the presence or absence of metabolic activation. Cytotoxicity was apparent at 100µg/plate; however, none of the doses tested induced an increase in the number of revertant colonies. Positive and negative controls responded accordingly. No mutagenic effects were observed when tested up to cytotoxic concentrations. This summary is taken from the EPA review found at the following website: (<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

CASRN 61791-39-7 was not mutagenic in this assay.

Subcategory III: 1-(Aminoalkyl) Imidazolines

No data were submitted for this endpoint.

Genetic Toxicity – Chromosomal Aberrations
In vitro

Subcategory I: 1-(Amidoethyl) Imidazolines

Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (CASRN 68122-86-1, supporting chemical)

Chinese hamster ovary cells were exposed to CASRN 68122-86-1 at concentrations ranging from 15.0 to 199µg/mL in the presence of metabolic activation and from 3.74 to 74.8µg/mL in the absence of metabolic activation. Cytotoxicity was observed in the presence and absence of metabolic activation at 49.9µg/ml and 37.4µg/mL, respectively. CASRN 68122-86-1 was considered negative for inducing chromosomal aberrations in CHO cells under both non-activation and activation conditions of this assay. Positive and negative control responses were not provided in the robust summary.

CASRN 68122-86-1 did not induce chromosomal aberrations in this assay.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7)

Chinese hamster ovary cells were exposed to CASRN 61791-39-7 at concentrations of 0, 0.0013, 0.0025, 0.005, 0.01 and 0.02 µl/mL in the absence of metabolic activation or 0, 0.0065, 0.013, 0.025, 0.05 and 0.1 µl/mL in the presence of metabolic activation. Positive and negative controls responded accordingly. CASRN 61791-39-7 did not induce chromosomal aberrations when tested up to the cytotoxic concentrations (0.01 µl/mL/-S9; 0.05 µl/mL/+S9). This summary is taken from the EPA review found at the following website:

(<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

CASRN 61791-39-7 did not induce chromosomal aberrations in this assay.

Subcategory III: 1-(Aminoalkyl) Imidazolines

No data were submitted for this endpoint.

Additional Information

Skin irritation

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7)

New Zealand white rabbits (3/sex) were administered CASRN 61791-39-7 (neat) via dermal application to clipped, intact skin under semi-occluded conditions for four hours. Severe dermal irritation characterized by persistent edema, erythema and eschar formation (primary dermal irritation index = 5.0) were observed in treated animals. This summary is taken from the EPA review found at the following website: (<http://www.epa.gov/oppsrrd1/REDS/3010red.pdf>).

CASRN 61791-39-7 was severely irritating to rabbit skin.

Subcategory III: 1-(Aminoalkyl) Imidazolines

1-H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 68442-97-7)

New Zealand white rabbits (sex/dose not specified) were administered CASRN 68442-97-7 via dermal exposure to intact skin under semi-occluded conditions. Corrosive effects (ulceration and severe eschar formation) were observed in all treated animals at 48 hours post-treatment.

CASRN 68442-97-7 was severely irritating to rabbit skin.

Eye irritation

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall-oil alkyl derivatives (CASRN 61791-39-7, supporting chemical)

A New Zealand white rabbit (female) was administered CASRN 61791-39-7 via topical application to the conjunctival sac. The untreated contralateral eye served as a control. Severe ocular irritation characterized by corneal opacity, conjunctival irritation with blistering and extreme swelling were observed at 24 hours post-treatment. Although this study only involved

treatment of one rabbit, it was otherwise well-conducted. It is the Agency's opinion that additional eye irritation studies would be of little added value. This summary is taken from the EPA review found at the following website: (<http://www.epa.gov/oppsrrd1/REDs/3010red.pdf>). **CASRN 61791-39-7 was a severe eye irritant in rabbits.**

Conclusion:

Subcategory I: 1-(Amidoethyl) Imidazolines

Acute oral toxicity for the 1-(amidoethyl) imidazolines subcategory is low in rats. A 13-week dietary study showed significant increases in relative liver weights in male and female rats at 2200 mg/kg-bw/day; the NOAEL for systemic toxicity was 730 mg/kg-bw/day. A 13-week dietary study in dogs showed no signs of systemic toxicity, resulting in a NOAEL of 1635 mg/kg-bw/day (highest dose tested). In a prenatal developmental toxicity study, dams treated via oral gavage on gestation days 6-15 showed no treatment-related effects on maternal (food consumption, body weight gain, gravid uterine weight) or developmental parameters (number of implantations, viable offspring, fetal body weight). The NOAEL for maternal/developmental toxicity was 1000 mg/kg/day (highest dose tested). No reproductive toxicity studies were available; however, an evaluation of testes weights in the 13-week rat study showed no effects up to the highest dose tested. CASRN 68122-86-1 was irritating to rabbit skin. This chemical did not induce gene mutations or chromosomal aberrations when tested *in vitro*.

Subcategory II: 1-(2-Hydroxyethyl) Imidazolines

No data were provided for this subcategory; however, studies taken from the Re-registration Eligibility Decision (RED) document (<http://www.epa.gov/oppsrrd1/REDs/3010red.pdf>) are described in this hazard characterization. Acute oral and dermal toxicity of CASRN 61791-39-7 is low in rats and rabbits, respectively. A prenatal developmental toxicity study in rats showed decreased food consumption and body weight in dams gavaged at 65 mg/kg/day during gestation days 6-15. Clinical signs, including excessive salivation and staining in the anogenital region were observed at or above 15 mg/kg/day; the NOAEL for maternal toxicity was 15 mg/kg/day. No treatment-related effects were reported for any of the developmental parameters examined in this study; the NOAEL for developmental toxicity was 100 mg/kg/day (highest dose tested). No reproductive toxicity studies were available. CASRN 61791-39-7 was irritating to rabbit skin and eyes. It did not induce gene mutations or chromosomal aberrations when tested *in vitro*.

Subcategory III: 1-(Aminoalkyl) Imidazolines

Acute oral toxicity for the 1-(Aminoalkyl) Imidazolines subcategory is low in rats. This substance is irritating to rabbit skin. No adequate toxicity data were provided to assess the repeated-dose/reproductive/developmental toxicity, gene mutation or chromosomal aberrations endpoints

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data

Subcategory	I			II	III	
Endpoints	Imidazolium compounds, 2-(C17 & C17-unsat. alkyl)-1[2-(C18 & C18-unsat. amido)ethyl]-4,5-dihydro-1-methyl-, methyl sulfates	Amides, C14 – 18, N-[2-(C13 – 17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]-	Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (Supporting chemical)	1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortallow oil alkyl derivatives	1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortallow oil alkyl derivatives	1,2-Ethanediamine, N-(2-aminoethyl)-N'-[2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl]ethyl
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Acute Oral Toxicity LD₅₀ (mg/kg)	No Data > 5000 (RA)	No Data > 5000 (RA)	> 5000	1932	< 5000	No Data < 5000 (RA)
Acute Dermal Toxicity LD₅₀ (mg/kg)	No Data	No Data	No Data	>2000	No Data	No Data
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No Data LOAEL = 2200 NOAEL = 730 (RA)	No Data LOAEL = 2200 NOAEL = 730 (RA)	LOAEL = 2200 NOAEL = 730	No Data	No Data	No Data
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No Data (RA)	No Data (RA)	No effects were seen following evaluation of reproductive organs in a 13-wk oral repeated-dose toxicity study in rats.	No Data	No Data	No Data
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) Maternal Developmental	No Data >1000 (RA)	No Data >1000 (RA)	>1000	LOAEL = 15 NOAEL = Not established NOAEL =100	No Data	No Data

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data						
Subcategory	I			II	III	
Endpoints	Imidazolium compounds, 2-(C17 & C17-unsat. alkyl)-1[2-(C18 & C18-unsat. amido)ethyl]-4,5-dihydro-1-methyl-, methyl sulfates	Amides, C14 – 18, N-[2-(C13 – 17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]-	Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl)-, methyl sulfate (Supporting chemical)	1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives	1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall oil alkyl derivatives	1,2-Ethanediamine, N-(2-aminoethyl)-N'-[2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl]ethyl
CASRN	72749-55-4	72623-72-4	68122-86-1	61791-39-7	68442-97-7	65817-50-7
Genetic Toxicity – Gene Mutation <i>In vitro</i>	No Data	No Data	Negative	Negative	No Data Negative (RA)	No Data Negative (RA)
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	No Data	No Data	Negative	Negative	No Data	No Data
Additional Information Skin Irritation Eye Irritation	-	-	-	Irritating Irritating	Irritating -	No Data Irritating (RA)

Measured data indicated in bold test; (RA) = Read Across; (hdt) = Highest Dose Tested; (-) = Endpoint not addressed

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 5. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

Subcategory I: Alkylated Dihydroimidazolium Compounds

No experimental data were provided for this endpoint.

Subcategory II: Alkylated Dihydroimidazoles

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives (CASRN 61791-39-7)

Fathead minnows (*Pimephales promelas*) were exposed to Miramine TO-DT (92% 1H-imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives [CASRN 61791-39-7] and 8% amines, N-tallow alkyltrimethylenedi-, acetates [CASRN 61791-54-6]) at nominal concentrations of 0, 0.056, 0.10, 0.18, 0.32 or 0.56 mg/L under static conditions for 96 hours. At 48 hours, 100% mortality was reported at the two highest concentrations (0.32 and 0.56 mg/L), and 5% mortality was reported at 0.18 mg/L (TSCATS submission #OTS538410).

96-h LC₅₀ = 0.23 mg/L

Acute Toxicity to Aquatic Invertebrates

Subcategory I: Alkylated Dihydroimidazolium Compounds

No experimental data were provided for this endpoint.

Subcategory II: Alkylated Dihydroimidazoles

1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives (CASRN 61791-39-7)

Water fleas (*Daphnia magna*) were exposed to 1H-imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives at nominal concentrations of 0, 1.3, 2.2, 3.6, 6.0 or 10 mg/L under static conditions for 48 hours. At the start of the test, the test solutions at the highest two exposure concentrations (6.0 and 10 mg/L) were reported to be slightly cloudy. Concentrations \geq 3.6 mg/L resulted in 100% mortality. Immobilization was observed in surviving daphnids at 2.2 mg/L.

48-h EC₅₀ = 1.5 mg/L

Toxicity to Aquatic Plants

Subcategory I: Alkylated Dihydroimidazolium Compounds

No experimental data were provided for this endpoint.

Subcategory II: Alkylated Dihydroimidazoles

No experimental data were provided for this endpoint.

Conclusion:

Subcategory I: Alkylated Dihydroimidazolium Compounds

The potential hazard of CASRN 72749-55-4 to aquatic organisms could not be evaluated because no data on aquatic toxicity endpoints were available.

Subcategory II: Alkylated Dihydroimidazoles

For the alkylated dihydroimidazoles, the 96-hour LC₅₀ for fish is 0.23 mg/L, and the 48-h EC₅₀ for aquatic invertebrates is 1.5 mg/L. Chronic toxicity to aquatic invertebrates and toxicity to aquatic plants could not be evaluated because no data were available for this endpoint.

Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program Environmental Effects – Aquatic Toxicity Data					
Subcategory	I	II			
Endpoints	Imidazolium compounds, 2-(C17 & C17-unsat. alkyl)-1[2-(C18 & C18-unsat. amido)ethyl]-4,5-dihydro-1-methyl-, methyl sulfates (72749-55-4)	Amides, C14 – 18, N-[2-(C13 – 17-alkyl-4,5-dihydro-1H-imidazol-1-yl)ethyl]- (72623-72-4)	1H-Imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives (61791-39-7)	1H-Imidazole-1-ethanamine, 4,5-dihydro-, 2-nortall oil alkyl derivatives (68442-97-7)	1,2-Ethanediamine, N-(2-aminoethyl)-N'-2-(8Z)-8-heptadecenyl-4,5-dihydro-1H-imidazol-1-yl]ethyl (65817-50-7)
Fish 96-h LC₅₀ (mg/L)	No data	RA 0.23	0.23	RA 0.23	RA 0.23
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	No data	RA 1.5	1.5	RA 1.5	RA 1.5
Aquatic Plants 96-h EC₅₀ (mg/L)	No data	No data	No data	No data	No data

Measured data indicated in bold test; (RA) = Read Across