SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME
Fatty Nitrogen Derived Cationics

SPONSORED CHEMICALS

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
Trimethyloctadecylammonium chloride (CAS No. 112-03-8)
Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (CAS No. 61789-77-3)
Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (CAS No. 68391-05-9)
Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, chlorides (CAS No. 68002-59-5)
Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates (CAS No. 68002-58-4)
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (CAS No. 61789-81-9)
Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides (CAS No. 67784-77-4)
Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichlorides (CAS No. 68607-29-4)

SUPPORTING CHEMICALS

Tricetylmethyl ammonium chloride (TMAC) (CAS No. 52467-63-7)
Didecyldimethylammonium chloride (DDAC) (CAS No. 7173-51-5)
Alkyl (C_{12-16}) dimethylbenzylammonium chloride (ADBAC) (CAS No. 68424-85-1)

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SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

The High Production Volume (HPV) Challenge Program[1] is 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 sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do 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. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[3].

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to "bin" chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,4] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[5] guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT's existing chemicals review process. These hazard characterizations are technical documents intended to support 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. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,6]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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[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. HPV Chemicals Hazard Characterization website (http://www.epa.gov/hpvis/abouthc.html).
[4] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[5] OECD. Guidance on the Development and Use of Chemical Categories; http://www.oecd.org/dataoecd/60/47/1947509.pdf.
[6] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

SCREENING-LEVEL HAZARD CHARACTERIZATION
Fatty Nitrogen Derived Cationics Category

Introduction

The sponsor, American Chemistry Council's (ACC) Fatty Nitrogen Derivatives (FND) Panel Cationics Task Group, submitted a Test Plan and Robust Summaries to EPA for the FND Cationics Category on December 20, 2001. EPA posted the submission on the ChemRTK Web site on January 25, 2002 (http://www.epa.gov/chemrtk/pubs/summaries/fatnitro/c13407tc.htm). EPA comments on the original submissions were posted to the website on October 21, 2002. Public comments were also received and posted to the website. The sponsor submitted revised documents on September 4, 2003 which were posted to the ChemRTK website on October 28, 2003. The FND cationics category consists of the following sponsored and supporting chemicals:

Sponsored Chemicals:

Dodecyltrimethylammonium chloride	CAS No. 112-00-5
Hexadecyltrimethylammonium chloride	CAS No. 112-02-7
Quaternary ammonium compounds, trimethyltallow alkyl, chlorides	CAS No. 8030-78-2
Trimethyloctadecylammonium chloride	CAS No. 112-03-8
Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides	CAS No. 61789-77-3
Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides	CAS No. 68391-05-9
Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, chlorides	CAS No. 68002-59-5
Quaternary ammonium compounds, dimethylditallow alkyl, chlorides	CAS No. 68783-78-8
Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates	CAS No. 68002-58-4
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride	CAS No. 61789-80-8
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates	CAS No. 61789-81-9
Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides	CAS No. 67784-77-4
Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride	CAS No. 68607-29-4

Supporting Chemicals:

Tricetylmethyl ammonium chloride (TMAC)	CAS No. 52467-63-7
Didecyldimethylammonium chloride (DDAC)	CAS No. 7173-51-5
Alkyl (C_{12-16}) dimethylbenzylammonium chloride (ADBAC)	CAS No. 68424-85-1

This screening-level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. 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. The structures of the sponsored chemicals are included in the Appendix. Summary tables of SIDS endpoint data are included in the document. The screening-level hazard characterization for environmental and human health toxicity is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Category Justification

The 13 quaternary (quats) ammonium chlorides or sulfates consist of four mono-alkyl chain quats, seven di-alkyl chain quats, one tri-alkyl chain quat and one dimeric mono-alkylpentamethyl compound. The category is based on the structural and functional similarities of cationic surfactants and their similar physicochemical properties, biodegradability, aquatic toxicity, mammalian toxicity and environmental disposition patterns. All compounds in the FND cationics category are structurally similar to Group 1[7] compounds in EPA's Office of Pesticide Program (OPP) clustering scheme for toxicity in support of pesticide re-registration of the quaternary ammonium compounds under FIFRA. EPA agrees with the sponsor's category justification.

Representative structures of category chemicals and supporting chemicals and their 9th Chemical Index (CI) names are presented in Figure 1.

Justification for Supporting Chemicals

The sponsor has submitted data for three other structurally similar supporting substances to address endpoints for the category members. The supporting substances are tricetylmethyl ammonium chloride (TMAC, CAS No. 52467-63-7, a tri-alkyl chain quat), didecyldimethylammonium chloride (DDAC, CAS No. 7173-51-5, a di-alkyl chain quat) and dimethylbenzylammonium chloride (ADBAC, CAS No. 68424-85-1, a benzyl mono-alkyl chain quat). DDAC was designated by EPA's OPP as a representative member of Group 1[7] in support of pesticide re-registering of quaternary ammonium compounds under FIFRA (http://www.epa.gov/pesticides/reregistration/ddac). The sponsor also stated that the toxicological profile of the proposed supporting chemical ADBAC (designated a Group 2[8] member by OPP http://www.epa.gov/pesticides/reregistration/adbac) is similar to that of DDAC. EPA agrees that the use of TMAC and DDAC data is appropriate. However, EPA did not agree that data for ADBAC are appropriate for the human health endpoints, due to significant differences in structure between this chemical and the category members. Data are appropriately extrapolated from the supporting chemicals, TMAC and ADBAC to address ecological toxicity data gaps and from TMAC and DDAC to address human health effects data gaps.

In its comments dated October 16, 2002, EPA recommended that CAS No. 68607-29-4 be tested to address the reproductive/developmental toxicity endpoints for the mono-alkyl category members. In its response to comments dated September 4, 2003, the Sponsor replied that "a limited-scope reproductive screening study on one of the FND Cationic Category chemicals will not further the understanding of potential human health hazards to these chemicals" and that "Detailed evaluations over multigenerations have not reported concern for reproductive effects". EPA finds this response to be reasonable (perhaps overly conservative) and based on the submitted data and category guidance (http://www.epa.gov/chemrtk/pubs/general/categuid.htm), EPA considers that the human health toxicity of all category members has been adequately addressed under the HPV Challenge program.

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[7] The Group 1 Quat Cluster is a group of structurally similar quaternary ammonium compounds (quats) that are characterized by having a positively charged nitrogen covalently bonded to two alkyl group substituents (at least one C_8 or longer) and two methyl substituents. These quats are salts with the positively charged nitrogen (cation) balanced by a negatively charged molecule (anion). The anion for the quats in this cluster is chloride or bromide.

[8] The Group 2 Quat Cluster is a group of structurally similar quaternary ammonium compounds (quats) that are characterized by having positively charged nitrogen covalently bonded to three alkyl group substituents and a benzyl substituent. These quats are salts with the positively charged nitrogen (cation) balanced by a negatively charged molecule (anion). The most common anion for the quats in this cluster is chloride. However, other anions, such as saccharinate and bromide are also used.

Summary-Conclusion

The log K_{ow} values of the FND cationic members indicate that their potential to bioaccumulate is expected to be low. The FND cationic members are not readily biodegradable indicating that they have the potential to persist in the environment.

The evaluation of available toxicity data for fish, aquatic invertebrates and aquatic plants indicate the potential hazard of FND cationic members to aquatic organisms is high.

The acute oral toxicity for FND cationic members is low to moderate. Acute dermal toxicity of FND cationic members is low while acute inhalation toxicity of the supporting chemical is high. FND cationic members are corrosive to skin and eye of rabbits; however, they are not dermal sensitizers based on supporting substance studies. Repeated exposures via the diet to FND cationic members and supporting substances resulted in decreased body weight and weight gain, increased adrenal and liver weights, increased histiocytic hyperplasia in the mesenteric lymph nodes and decreased total cholesterol levels at the doses tested. Repeated exposures via the dermal application of FND cationic members and supporting substances resulted in a range of skins effects (e.g., erythema, edema, atonia and desquamation) at treatment sites. However, no treatment-related systemic toxicity was evident following repeated exposures via the dermal route for FND cationic members or supporting substances at the doses tested. Two-generation reproduction toxicity studies for supporting substances showed reduced parental and pup body weights and body weight gain; however, no effects were seen on reproductive parameters. No treatment-related effects were seen on the reproductive organs during macroscopic or microscopic examinations in repeated-dose toxicity studies for FND cationic members. Developmental effects were not noted via dermal exposure to FND cationic members. Developmental toxicity studies via oral route for a supporting substance resulted in a decrease in fetal body weight, an increased number of dead fetuses and an increased incidence of skeletal variations. Other developmental oral (gavage) toxicity studies for FND cationic members and supporting substances indicated no treatment-related effects at doses tested. FND cationic members did not induce gene mutations in bacteria and mammalian cells. One FND cationic member (CAS No. 8030-78-2) showed a three-fold increase in mutation frequency in *S. typhimurium* in one assay but was negative in a second test. FND cationic members did not induce chromosomal aberrations *in vitro* or *in vivo*. One FND cationic member (CAS No. 112-00-5) and one supporting chemical (CAS No. 7173-51-5) did not induce unscheduled DNA synthesis when tested with male rat hepatocytes. The supporting chemical (CAS No. 7173-51-5) did not show evidence of carcinogenicity in rats and mice.

The potential health hazard of the FND cationic category is low to moderate based on the results of repeated-dose and reproductive and developmental toxicity.

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1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical properties and environmental fate data submitted is provided in Table 1. For the purpose of the screening-level hazard characterization, the review and summary of these data was limited to the octanol-water partition coefficient and biodegradation endpoints as indicators of bioaccumulation and persistence, respectively.

Octanol-Water Partition Coefficient

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)

Log K_{ow}: 1.22 (estimated)

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)

Log K_{ow}: 3.23 (estimated)

Trimethyloctadecylammonium chloride (CAS No. 112-03-8)

Log K_{ow}: 4.17 (estimated)

Tricetylmethyl ammonium chloride (TMAC; CAS No. 52467-63-7, Supporting Chemical)

Log K_{ow}: 17.9 (estimated)

Didecyldimethyl-ammonium chloride (DDAC; CAS No. 7173-51-5, Supporting Chemical)

Log K_{ow}: 4.66 (estimated)

Biodegradation

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
In a non-guideline study of aerobic biodegradation using resident bacteria in river water as inoculum, approximately 35% of the test substance had degraded in 10 days.
Dodecyltrimethylammonium chloride is not readily biodegradable.

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
In two separately conducted Closed Bottle tests using activated sludge as inoculum, 65 and 46% of the test substance had degraded after 28 days. Sixty-five percent degradation in one test was a borderline response for positive biodegradation. Therefore, using a weight-of-evidence approach, the test substance is considered as not readily biodegradable.
Hexadecyltrimethylammonium chloride is not readily biodegradable.

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
In three separately conducted Closed Bottle tests using activated sludge as inoculum, 40 to 53% of the test substance degraded after 28 days.
Quaternary ammonium compounds, trimethyltallow alkyl, chlorides is not readily biodegradable.

Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)
In a Closed Bottle test using activated sludge as inoculum, 9% of the test substance degraded after 28 days.
Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides is not readily biodegradable.

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
In a CO_2 evolution method using activated sludge as inoculum, 0% of the test substance had degraded after 28 days (0 − 35% after 20 to 49 days).
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride is not readily biodegradable.

Tricetylmethyl ammonium chloride (TMAC; CAS No. 52467-63-7, Supporting Chemical)
In a Closed Bottle test using activated sludge as inoculum, 0% of the test substance degraded after 32 days.
Tricetylmethyl ammonium chloride is not readily biodegradable.

Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride (CAS No. 68607-29-4)
In a Closed Bottle test using activated sludge as inoculum, 0% of the test substance degraded after 182 days.
Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride is not readily biodegradable.

Conclusion: The log K_{ow} values of the FND cationic members indicate that their potential to bioaccumulate is expected to be low for the mono- and tri- alkyl chain quats and high for the di-alkyl chain quats. The FND cationic members are not readily biodegradable indicating that they have the potential to persist in the environment.

Table 1. Summary of Physical-Chemical Properties and Environmental Fate Data

Endpoints	Dodecyltrimethyl-ammonium chloride (112-00-5)	Hexadecyltrimethyl ammonium chloride (112-02-7)	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (8030-78-2)	Trimethyloctadecylammonium chloride (112-03-8)	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)	Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (68391-05-9)	Quaternary ammonium compounds, di-C_{14-18}-alkyl dimethyl, chlorides (68002-59-5)	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (68783-78-8)
Melting Point (°C)	182 (e)	213 (e)	No data 223 (RA)	223 (e)	No data 50-60 (RA)	No data 50-60 (RA)	No data 50-60 (RA)	No data 50-60 (RA)
Boiling Point Range (°C)	454 (e)	500 (e)	No data 523 (RA)	523 (e)	No data 535 (RA)	No data 535 (RA)	No data 535 (RA)	No data 535 (RA)
Vapor Pressure (hPa at 25°C)	9.3×10^{-9} (e)	2.8×10^{-10} (e)	No data 5.4×10^{-11} (RA)	5.4×10^{-11} (e)	No data 2.3×10^{-11} (RA)	No data 2.3×10^{-11} (RA)	No data 2.3×10^{-11} (RA)	No data 2.3×10^{-11} (RA)
Log K_{ow}	1.22 (e)	3.23 (e)	No data 4.17 (RA)	4.17 (e)	No data 4.66 (RA)	No data 4.66 (RA)	No data 4.66 (RA)	No data 4.66 (RA)
Water Solubility (mg/L at 25°C)	1795 (e)	16.3 (e)	No data 1.76 (RA)	1.76 (e)	No data <0.001 (RA)	No data <0.001 (RA)	No data <0.001 (RA)	No data <0.001 (RA)
Direct Photodegra-dation	28.5×10^{-12} (e)	34×10^{-12} (e)	No data 37×10^{-12} (RA)	37×10^{-12} (e)	No data 46.3×10^{-12} (RA)	No data 46.3×10^{-12} (RA)	No data 46.3×10^{-12} (RA)	No data 46.3×10^{-12} (RA)
Indirect (OH^-) Photodegradation ($t_{1/2}$)	4.5 (e)	3.9 (e)	No data 3.5 (RA)	3.5 (e)	No data 5.5 (RA)	No data 5.5 (RA)	No data 5.5 (RA)	No data 5.5 (RA)
Stability in Water (Hydrolysis) ($t_{1/2}$)	Data Gap	Data Gap	Data Gap	Data Gap	No data 175 d (RA)	No data 175 d (RA)	No data 175 d (RA)	No data 175 d (RA)
Fugacity (Level III Model)	(e)	(e)	No data	(e)	No data	No data	No data	No data
Air (%)	< 1	< 1	< 1	< 1	< 0.1	< 0.1	< 0.1	< 0.1
Water (%)	99.8	98.5	83.3	83.3	78.9	78.9	78.9	78.9
Soil (%)	< 1	< 1	< 1	< 1	< 0.1	< 0.1	< 0.1	< 0.1
Sediment (%)	< 1	< 1.5	16.7 (RA)	16.7	21.1 (RA)	21.1 (RA)	21.1 (RA)	21.1 (RA)
Biodegradation at 28 days (%)	**35% (10 d) (m) Not readily biodegradable**	**65% (m) 48% (m) Not readily biodegradable**	**48% (m) 53% (m) 40% (m) Not readily biodegradable**	No data Not readily biodegradable (RA)	**9% (m) Not readily biodegradable**	No data Not readily biodegradable (RA)	No data Not readily biodegradable (RA)	No data Not readily biodegradable (RA)

Table 1. Summary of Physical-Chemical Properties and Environmental Fate Data (Continued)								
Endpoints	**Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates (68002-58-4)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (61789-80-8)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (61789-81-9)**	**Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides (67784-77-4)**	**Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride (68607-29-4)**	**Tricetylmethyl ammonium chloride(TMAC ;Supporting Chemical) (52467-63-7)**	**Didecyldimethyl-ammonium chloride (DDAC; Supporting Chemical) (7173-51-5)**	**Dimethylbenzyl-ammonium chloride (ADBAC; Supporting Chemical) (68424-85-1)**
Melting Point (°C)	No data 50-60 (RA)	**50 – 60 (m)**	No data 50-60 (RA)	No data 46.0-53.5 (RA)	No data 223 (RA)	**46.0 – 53.5 (m)** 350 (e)	229 (e)	241 (e)
Boiling Point Range (°C)	No data 535 (RA)	No data 535 (RA)	No data 535 (RA)	No data 121.5 (RA)	No data 523 (RA)	**121.5 (m)**[1] 848 (e)	535 (e)	561 (e)
Vapor Pressure (hPa at 25°C)	No data 2.3×10^{-11} (RA)	No data 2.3×10^{-11} (RA)	No data 2.3×10^{-11} (RA)	No data 1.8 (RA)	No data 5.4×10^{-11} (RA)	**1.8 (m)**[2] 3×10^{-21} (e)	2.3×10^{-11} (e)	3.5×10^{-12} (e)
Log K_{ow}	No data 4.66 (RA)	No data 4.66 (RA)	No data 4.66 (RA)	No data 17.9 (RA)	No data 4.17 (RA)	17.9 (e) > 5.9 (e)[3]	**0 (m)** 4.66 (e)	3.91 (e)
Water Solubility (mg/L at 25°C)	No data <0.001 (RA)	**<0.001 (m)**	No data <0.001 (RA)	No data <10 (RA)	No data 1.76 (RA)	**< 10 (m)**	**700 (m)** 0.55 (e)	2.2 (e)
Direct Photodegra-dation	No data 46.3×10^{-12} (RA)	No data 46.3×10^{-12} (RA)	No data 46.3×10^{-12} (RA)	No data 92.4×10^{-12} (RA)	No data 37×10^{-12} (RA)	92.4×10^{-12} (e)	46.3×10^{-12} (e)	4.3×10^{-11} (e)
Indirect (OH^-) Photodegradation ($t_{1/2}$)	No data 5.5 (RA)	No data 5.5 (RA)	No data 5.5 (RA)	No data 2.8 (RA)	No data 3.5 (RA)	2.8 (e)	5.5 (e)	5.9 (e)
Stability in Water (Hydrolysis) ($t_{1/2}$)	No data 175 d (RA)	No data 175 d (RA)	No data 175 d (RA)	Data Gap	Data Gap		**194 d** **175 d**	

Fugacity (Level III Model)	No data	No data	No data	No data	No data			
Air (%)	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Water (%)	78.9	78.9	78.9	4.8	4.7	4.8	78.9	4.7
Soil (%)	< 0.1	< 0.1	< 0.1	< 0.1	94.7	< 0.1	< 0.1	94.7
Sediment (%)	21.1 (RA)	21.1 (RA)	21.1 (RA)	95.2 (RA)	0.5 (RA)	95.2	21.1	0.5
Biodegradation (%) 28 days	No data Not readily biodegradable (RA)	**0% (m) Not readily biodegradable**	No data Not readily biodegradable (RA)	No data Not readily biodegradable (RA)	**0% (m) Not readily biodegradable**	**0% (m) Not readily biodegradable**		

(m) = measured data (i.e., derived from experiment); (e) = estimated data (i.e., derived from modeling); RA = Read Across; [1]Measured value may be affected by impurities; [2]Value considered as inaccurate based on structure of chemical and high vapor pressure is likely due to solvent impurities; [3]Estimated according to Guideline OCED 107

2. Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
Atlantic salmon (*Salmo salar*) were exposed to test substance (test concentrations not specified) under static conditions for 96 hours.
96-h LC_{50} = 6.0 mg/L

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
Atlantic salmon (*Salmo salar*) were exposed to test substance (test concentrations not specified) under static conditions for 24 hours.
24-h LC_{50} = 0.07 mg/L

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
Fathead minnows (*Pimephales promelas*) were exposed to the test substance (test concentrations not specified) under static-renewal conditions for 96 hours. (http://www.epa.gov\ecotox)
96-h LC_{50} = 0.08 mg/L

Trimethyloctadecylammonium chloride (CAS No. 112-03-8)
Atlantic salmon (*Salmo salar*) were exposed to test substance (test concentrations not specified) under static conditions for 96 hours.
96-h LC_{50} = 0.07 mg/L

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
(1) Bluegill sunfish (*Lepomis macrochirus*) were exposed to test substance (test concentrations not specified) under static conditions for 96 hours. Mortality was 0%.
96-h LC_{50} = 0.62 – 3.0 mg/L

(2) Sheepshead minnows (*Cyprinidon variegatus*) were exposed to test substance (test concentrations not specified) under static conditions for 96 hours.
96-h LC_{50} = 24 mg/L

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
(1) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance at nominal test concentrations of 0, 0.56, 1.0, 1.8, 3.2 and 5.6 mg/L under static conditions for 96 hours.
96-h LC_{50} = 1.33 mg/L

(2) Rainbow trout (*Salmo gairdneri*) were exposed to the test substance at nominal test concentrations of 0, 1.0, 1.8, 3.2, 5.6 and 10 mg/L under static conditions for 96 hours.
96-h LC_{50} = 4.22 mg/L

(3) Rainbow trout (*Salmo gairdneri*) were exposed to the test substance at nominal test concentrations of 0, 0.7, 1.2, 2.0, 3.5, 6.0 and 10 mg/L under static conditions for 96 hours.
96-h LC_{50} = 3.4 mg/L

(4) Various freshwater fish were exposed to the test substance (test concentrations not specified) under static conditions for 96 hours.
96-h LC_{50} = 1.7 – 2.6 mg/L (*Salmo gairdneri*)
96-h LC_{50} = 0.29 – 0.558 mg/L (*Pimephales promelas*)
96-h LC_{50} = 0.56 – 14 mg/L (*Lepomis macrochirus*)

Didecyldimethylammonium chloride (DDAC; CAS No. 7173-51-5, Supporting Chemical)
Various freshwater and saltwater fish species were exposed to the measured test substance concentrations (test concentrations not specified) under static and/or flow-through conditions for 96-hours.
96-h LC_{50} (bluegill sunfish, *Lepomis macrochirus*) **= 0.32 mg/L**
96-h LC_{50} (coho salmon, *Oncorhynchus kisutch*) **= 1.0 mg/L**
96-h LC_{50} (rainbow trout, *Oncorhynchus mykiss*) **= 0.66 mg/L**
96-h LC_{50} (fathead minnow, *Pimephales promelas*) **= 0.19 mg/L**
96-h LC_{50} (coho salmon, *Oncorhynchus kisutch*) **= 0.424 mg/L**
96-h LC_{50} (rainbow trout, *Oncorhynchus mykiss*) **= 0.466 mg/L**
96-h LC_{50} (fathead minnow, *Pimephales promelas*) **= 0.195 mg/L**

Tricetylmethyl ammonium chloride (TMAC; CAS No. 52467-63-7, Supporting Chemical)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance at test concentrations of 0, 2.29, 7.72, 12.5, 20.1, 59.4 and 110.8 mg/L (measured) under semi-static conditions for 96 hours.
96-h LC_{50} ≈ 14.5 mg/L

Dimethylbenzylammonium chloride (ADBAC;CAS No. 68424-85-1, Supporting Chemical)
(1) Fathead minnow (*Pimephales promelas)* were exposed to the test substance at (test concentrations not specified) under static-renewal conditions for 96 hours.
96-h LC_{50} = 0.280 mg/L

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance (test concentrations not specified) under flow-through conditions for 96 hours.
96-h LC_{50} = 0.515 mg/L

(3) Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance (test concentrations not specified) under static-renewal conditions for 96 hours.
96-h LC_{50} = 0.923 mg/L

(4) Sheepshead minnow (*Cyprinidon variegatus*) were exposed to the test substance (test concentrations not specified) under static-renewal conditions for 96 hours.
96-h LC_{50} = 0.860 mg/L

Acute Toxicity to Aquatic Invertebrates

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
(1) Water fleas (*Ceriodaphnia sp.*) were exposed to the test substance (test concentrations not specified) in Acton Lake (Ohio) water under static conditions for 48 hours.
48-h EC_{50} = 0.39 mg/L

(2) Water fleas (*Ceriodaphnia sp.*) were exposed to the test substance (35% purity) at nominal test concentrations of 0, 0.05, 0.10, 0.20, 0.30, 0.40 and 0.60 mg/L in Ohio River water under static conditions for 48 hours. Concentrations of 0.40 mg/L and higher resulted in 100% mortality.
48-h EC_{50} = 0.345 mg/L

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
Water fleas (*Daphnia magna*) were exposed to the test substance (test concentrations not specified) under flow through conditions for 48 hours.
48-h EC_{50} = 0.010 mg/L

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
(1) Water fleas (*Daphnia magna*) were exposed to the test substance at measured initial test concentrations of 0, 35, 39, 57.7, 87.5, 129.6, 162.1 and 214.2 µg/L in White River (Indiana) water under static conditions for 48 hours.
48-h EC_{50} = 0.099 mg/L

(2) Water fleas (*Daphnia magna*) were exposed to the test substance at measured initial test concentrations of 0, 3.3, 5.3, 9.0, 10.6, 15.7, 17.4 and 29.5 µg/L and repeat test concentrations of 0, 4.4, 6.0, 8.9, 12.1, 14.5 and 22.9 µg/L in laboratory blended water under static conditions for 48 hours.
48-h EC_{50} = 0.013 mg/L

(3) Water fleas (*Daphnia magna*) were exposed to the test substance at measured initial test concentrations of 0, 2.8, 3.9, 5.9, 8.9, 14.3, 19.6 and 29.2 µg/L and repeat test concentrations of 0, 3.9, 6.1, 8.6, 11.8, 14.4, 24.3 and 37.9 µg/L in Southwest well water under static conditions for 48 hours.
48-h EC_{50} = 0.017 mg/L

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
(1) Water fleas (*Daphnia magna*) were exposed to the test substance (test concentrations not specified) in reconstituted water (two tests) and well water under static conditions for 48 hours.
48-h EC_{50} = 0.19 – 0.48 mg/L (reconstituted water)

(2) Water fleas (*Ceriodaphnia sp.*) were exposed to the test substance (test concentrations not specified) in Ohio River water under static conditions for 48 hours.
48-h EC_{50} = 0.54 − 1.23 mg/L

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
Water fleas (*Daphnia magna*) were exposed to the test substance (test concentrations not specified) in 12 acute toxicity tests using laboratory-prepared water, well water and/or river water under static conditions for 48 hours.
48-h EC_{50} = 0.065–3.6 mg/L

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) Water fleas (*Daphnia magna*) were exposed to the test substance (test concentrations not specified) under static conditions for 48 hours in two separate studies.
48-h EC_{50} = 0.018 – 0.160 mg/L

(2) Mysid shrimp (*Mysidosis bahia*) were exposed to the test substance (test concentrations not specified) under static conditions for 96 hours.
96-h EC_{50} = 0.069 mg/L

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, Supporting Chemical)
Water fleas (*Daphnia magna*)were exposed to the test substance (86% purity) at test concentrations of 0, 0.92, 0.157, 0.281, 0.512 and 0.802 mg/L (measured) under static conditions for 48 hours.
48-h EC_{50} = 0.11 mg/L

Dimethylbenzylammonium chloride, ADBAC (CAS No. 68424-85-1, Supporting Chemical)
(1) Water flea (*Daphnia magna*) were exposed to test substance (95-96% purity) (measured concentrations not specified) under static-renewal conditions for 48 hours.
48-h EC_{50} = 0.0059 mg/L

(2) Mysid shrimp (*Mysidosis bahia)* were exposed to the test substance (81% purity) (test concentrations not specified) under static-renewal conditions for 96 hours.
96-h EC_{50} = 0.092 mg/L

Toxicity to Aquatic Plants

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
(1) Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance at test concentrations of 0, 0.6, 1.0, 4.2, 9.9 and 16.4 mg/L (measured) in filtered Little Miami River water under static conditions for 96 hours. Acidic methanol was used as a carrier solvent in the toxicity test due to the low water solubility of the test substance.
96-h EC_{50} = 1.12 mg/L

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
(1) Green algae (*Pseudokirchneriella* subcapitata) were exposed to the test substance (test concentrations not specified) in three separate tests under static conditions for 96 hours.
96-h ErC_{50} = 0.026 – 0.21 mg/L

(2) Green algae (*Scenedesmus pannonicus*) were exposed to the test substance (test concentrations not specified) in two separate tests under static conditions for 96 hours.
96-h ErC_{50} = 0.05 – 1.8 mg/L

(3) Green algae (*Chlorella vulgaris*) were exposed to test substance (test concentrations not specified) in two separate tests under static conditions for96 hours.
96-h ErC_{50} = 0.27 – 0.4 mg/L

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) Green algae (*Chorella sp.*) were exposed to the test substance (test concentrations not specified) under static conditions for 72 hours. Test substance at concentrations greater than 3 mg/L suppressed plant growth after 72 hours.
72-h ErC50 = 3 – 5 mg/L

(2) Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance (test concentrations not specified) in natural surface water under static conditions for 96 hours.
96-h EC_{50} = 0.073 mg/L

(3) Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance (test concentrations not specified) under static conditions for 96 hours.
96-h EC_{50} = 0.014 mg/L

Tricetylmethyl ammonium chloride (TMAC; CAS No. 52467-63-7, Supporting Chemical)
Green algae (*Pseudokirchneriella subcapitata*) were exposed to nominal test concentrations (measured concentrations in parentheses) of 0, 0.035 (0.01), 0.071, 0.142 (0.03), 0.283 and 0.566 (0.38) mg/L under static conditions for 96 hours.
96-h EC_{50} = 0.177 mg/L

Chronic Toxicity to Aquatic Species

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
(1) Water fleas (*Daphnia magna*) were exposed to the test substance at measured concentrations of 0, 0.0357, 0.0534, 0.0683, 0.0991, 0.1223 and 0.3093 mg/L in White River (Indiana) water under semi-static conditions for 21 days. Mortality increased significantly at 0.3093 mg/L and total young produced decreased significantly at 0.1223 mg/L.
21-d LC_{50} = 0.19 mg/L
21-d LOEC = 0.1223 mg/L
21-d NOEC = 0.0991 mg/L

(2) Water fleas (*Daphnia magna*) were exposed to the test substance at measured concentrations of 0, 0.0016, 0.0031, 0.0068, 0.0146, 0.0306 and 0.0608 mg/L in well water under semi-static conditions for 21 days. Mortality increased significantly at 0.060 mg/L and total young produced decreased 0.0146 mg/L.
21-d LC_{50} = 0.023 mg/L
21-d LOEC = 0.0146 mg/L
21-d NOEC = 0.0068 mg/L

Tricetylmethyl ammonium chloride (TMAC; CAS No. 52467-63-7, Supporting Chemical)
Water fleas (*Daphnia magna*) were exposed to the test substance at concentrations of 0.0, 0.01, 0.02 (0.0238 measured), 0.04, 0.08 (0.0888 measured), 0.16 (0.173 measured) and 0.32 mg/L under semi-static conditions for 21 days.
21-d LOEC (mortality/reproduction) = 0.128 mg/L
21-d NOEC (mortality/reproduction) = 0.064 mg/L

Dimethylbenzylammonium chloride (ADBAC; CAS No. 68424-85-1, Supporting Chemical)
(1) Fathead minnows (*Pimephales promelas*) were exposed to the test substance (test concentrations not specified) in a fish early life stage study under daily static-renewal conditions for 34 days.
LOEC = 0.076 mg/L
NOEC = 0.032 mg/L
MATC = 0.0494 mg/L

(2) Water fleas (*Daphnia magna*) were exposed to the test substance (30% purity) (test concentrations not specified) under static conditions for 21 days.
21-d LOEC = Not established
21-d NOEC = 0.00415 mg/L

Conclusion: The evaluation of available toxicity data for fish, aquatic invertebrates and aquatic plants indicate that the potential hazard of the category members to aquatic organisms is high.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data								
Endpoints	**Dodecyltrimethyl ammonium chloride (112-00-5)**	**Hexadecyltrimethylammonium chloride (112-02-7)**	**Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (8030-78-2)**	**Trimethyloctadecylammonium chloride (112-03-8)**	**Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)**	**Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (68391-05-9)**	**Quaternary ammonium compounds, di-C_{14-18}-alkyl dimethyl, chlorides (68002-59-5)**	**Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (68783-78-8)**
Fish 96-h LC_{50} (mg/L)	**6.0 (m)**	**0.07 (24-h) (m)**	**0.08 (m)**	**0.07 (m)**	No data 0.280 − 0.320 (RA)	No data 0.280 − 0.320 (RA)	No data 0.280 − 0.320 (RA)	**0.62 − 24 (m)**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**0.39 (m) 0.35 (m) 0.23 (m)**	**0.010 (m) 0.067 (m)**	**0.018 − 0.099(m)**	No data 0.0059 (RA)	No data 0.0059 (RA)	No data 0.0059 (RA)	No data 0.0059 (RA)	**0.19 – 0.48 (m) 0.54–1.23 (m) 1.23 (m) 0.22 (96-h) (m)**
Aquatic Plants 96-h EC_{50} (mg/L)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	**1.12 (m)**
Chronic Toxicity to Aquatic Species (mg/L)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	**21-d Daphnia NOEC = 0.0068 – 0.0991 LOEC = 0.0146 − 0.1223 (m)**	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data (Continued)								
Endpoints	**Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates (68002-58-4)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (61789-80-8)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (61789-81-9)**	**Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides (67784-77-4)**	**Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride (68607-29-4)**	**Tricetylmethyl ammonium chloride (TMAC; Supporting Chemical) (52467-63-7)**	**Didecyldimethyl-ammonium chloride (DDAC; Supporting Chemical) (7173-51-5)**	**Dimethylbenzyl-ammonium chloride (ADBAC; Supporting Chemical) (68424-85-1)**
Fish 96-h LC_{50} (mg/L)	No data 0.280 − 0.320 (RA)	**1.33 (m) 4.22 (m) 3.4 (m) 0.29 – 3.2 (m)**	No data 0.280 − 0.320 (RA)	No data 0.280 − 0.320 (RA)	No data 0.280 − 0.320 (RA)	**~ 14.5 (m)**	**0.195−0.466 (flow-through) (m) 0.190–1.00 (static) (m)**	**0.280 - 0.320 (m) 0.923 (static)(m) 0.860 (static) (m)**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No data 0.0059 (RA)	**0.065 – 3.2 (m)**	No data 0.0059 (RA)	No data 0.0059 (RA)	No data 0.0059 (RA)	**0.11 (m)**	**0.037 (m) 0.010 − 0.160 (m)**	**0.0059 (m) 0.092 (96-h) (m)**
Aquatic Plants 96-h EC_{50} (mg/L)	No data 0.177 (RA)	0.026 – 1.8 (m)	No data 0.177 (RA)	No data 0.177 (RA)	No data 0.177 (RA)	**0.177 (96-h) (m)**	**3.0–5.0 (m) 0.073 (m) 0.014 (m)**	−
Chronic Toxicity to Aquatic Species (mg/L)	No Data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA))	No Data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No Data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No Data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	No Data 21-d Daphnia NOEC = 0.064 LOEC = 0.128 (RA)	**21-d Daphnia NOEC = 0.064 LOEC = 0.128 (m)**	−	**Fish early life stage MATC = 0.0494 (m) 21-d Daphnia NOEC = 0.00415 LOEC = NE (m)**

(m) = measured data (i.e., derived from experiment); (e) = estimated data (i.e., derived from modeling); NE = Not established; RA = Read Across; − Data not needed for supporting chemical.

3. Human Health Effects

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

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
(1) Sprague Dawley CD rats (5/sex/dose) were administered the test substance (24.7% aqueous solution) via gavage at 0.19, 0.26, 0.36, 0.51, 0.71 or 1.0 mL/kg-bw (approximately 190, 260, 360, 510, 710 or 1000 mg/kg-bw) and observed for 14 days. Mortality occurred at and above 360 mg/kg-bw.
LD_{50} = 490 mg/kg-bw

(2) Sprague Dawley CD rats (5/sex/dose) were administered the test substance (37.35% aqueous solution) via gavage at 290, 400, 560, 780, 1090, 2140 or 3000 mg/kg-bw and observed for 14 days. Mortality occurred at and above 560 mg/kg-bw.
LD_{50} = 560 mg/kg-bw

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
Swiss-Webster mice (5/sex/dose) were administered 300 to 600 mg/kg-bw of the test substance via gavage and observed for seven days. Treatment-related mortality was 30% at 400 mg/kg-bw and 100% at 600 mg/kg-bw. All deaths occurred within 96 hours of dosing. Treatment-related effects were ataxia and loss of righting reflex. No abnormalities were noted during gross necropsy.
400 < LD_{50} < 600 mg/kg-bw

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
Sprague-Dawley CFY rats (5/sex/dose) were administered the test substance via gavage at 1000, 1260, 1587 or 2000 mg/kg-bw and observed for 14 days. Treatment-related clinical signs included hunched posture, lethargy, piloerection, decreased respiratory rate and diarrhea. Additional clinical signs at 1260 mg/kg-bw and above included ataxia, tip-toe gait, ptosis, pallor of the extremities, increased lacrimation, chromodacryorrhea, diuresis, occasional body tremors, emaciation and staining around the snout. Necropsy of decedents revealed abnormally red lungs, dark livers, hemorrhage and ulceration of the gastric mucosa and congestion of the small intestines. Necropsy of surviving animals revealed white raised areas on the non-glandular region of the stomach or general white thickening of this region.
LD_{50} = 1260 mg/kg-bw

Trimethyloctadecylammonium chloride (CAS No. 112-03-8)
Mice (ddY strain; 10/dose, sex distribution not specified) were administered the test substance (doses not specified) via gavage and observed for 14 days. Treatment-related clinical signs included hypoactivity and diarrhea. Necropsy findings included congestion of the brain and kidneys.
LD_{50} = 633 mg/kg-bw (males)
LD_{50} = 536 mg/kg-bw (females)

Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (CAS No. 61789-77-3)
Sprague-Dawley rats (8/sex/dose) were administered the test substance via gavage at 270, 430, 670, 1050, 1310, 2050 or 3200 mg/kg-bw and observed for 14 days. Treatment-related clinical signs included dose-dependent increases in incidence and duration were diarrhea, yellow-stained abdomen, red stains around the nose and mouth, ataxia and decreased limb tone. Hypoactivity was observed at and above 430 mg/kg-bw. At necropsy, lung abnormalities were seen at all doses and stomach adhesions to surrounding organs, cardiac thickening and enlarged, brown spleen at 1310 mg/kg-bw and above.
LD_{50} = 960 mg/kg-bw (combined)

Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (CAS No. 68391-05-9)
Sprague-Dawley rats (females, variable number/dose) were administered the test substance via gavage at 3846, 5000, 6500, 8450 or 10,985 mg/kg-bw and observed for at least four days (duration of observation period not specified). Treatment-related clinical signs included piloerection, hypoactivity, diarrhea, ptosis, high carriage, ataxia, chromodacryorrhea and decreased limb tone.
LD_{50} = 4700 mg/kg-bw

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
Sprague-Dawley rats (5 males/dose) were administered the test substance as a 1:10 aqueous dilution via gavage at 1.00, 2.15, 4.64, 10.0 and 21.5 ml/kg-bw (approximately 1000, 2150, 4640, 10,000 and 21,500 mg/kg-bw) and observed for 14 days. Treatment-related clinical signs included diarrhea stains and one rat with serosanguineous stain around the eye. Necropsies revealed no gross abnormalities.
LD_{50} > ~ 2150 mg/kg-bw

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
(1) Fischer rats (5/sex/dose) were administered the test substance via gavage at 500 mg/kg-bw and observed for 14 days. Treatment-related clinical signs included leg weakness that cleared by day two.
LD_{50} > 500 mg/kg-bw

(2) Swiss-Webster mice (5/sex/dose) were administered the test substance via gavage at 576 mg/kg-bw and observed for seven days. There were no observed clinical signs or mortality. Necropsy results were not reported.
LD_{50} > 576 mg/kg-bw

(3) Beagle dogs (3/sex/dose) were administered the test substance via gavage at 432 mg/kg-bw and observed for seven days. There were no observed clinical signs or mortality. Necropsy results were not reported.
LD_{50} > 432 mg/kg-bw

Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride (CAS No. 68607-29-4)
Wistar rats (5/sex/dose) were administered the test substance via gavage at 0.50, 0.63, 0.79, 1.00 or 1.26 ml/kg-bw (125, 157.5, 197.5, 250 or 315 mg/kg-bw, respectively) and observed for 14 days. Mortality occurred within 48 hours of dosing. Other treatment-related clinical signs included abnormal gait, piloerection, decreased motor activity and loss of corneal reflex. All surviving animals appeared normal by two days after dosing. There were no gross lesions observed at necropsy.
LD_{50} = 205 mg/kg-bw

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) Rats (5/sex/dose; strain not specified) were administered the test substance (65% purity) via gavage at 0, 100, 200, or 400 mg/kg-bw for females and 0, 100, 200, 283, 336, or 400 mg/bw-kg for males and observed for 14 days. Clinical signs of toxicity included sluggishness, lacrimation, diarrhea, and brown stains on the periurogenital fur, emaciation. Deaths occurred at 1 to 4 days. Survivors recovered at 2 to 5 days. Discolored, hemorrhaged stomachs, red to brown intestines, dark red livers and fluid-filled thoracic cavities were mainly seen during necropsy of rats that died. No remarkable gross lesions were seen during necropsy of survivors. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LD_{50} = 262 mg/kg-bw (combined)

(2) Rats (5/sex/dose; strain not specified) were administered the test substance (80% purity) via gavage at 100, 200, 300 or 500 mg/kg-bw and observed for 14 days. The major clinical signs during the observation period included urine and fecal stains, saliva discharge and stains, dried red stains on muzzle and around the eyes, eye squinting, piloerection, ataxia, body tremors, labored and shallow respiration, slight to severe depression, viscous red blood-like discharge from the mouth, bloated appearance to the abdomen and spasms in the abdominal area. With the exception of one animal, all animals that survived the observation period exhibited no gross pathologic findings during necropsy. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LD_{50} = 238 mg/kg-bw (combined)

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, Supporting Chemical)
Sprague-Dawley rats (1/sex/dose) were administered the test substance (40% w/v in mineral oil) via gavage at 2000, 2600, 3400, 4400, 5700, 7400, 9600, 12,500 or 16,300 mg/kg-bw and observed for seven days. There was no mortality at any dose. Treatment-related clinical signs included diarrhea, rough coat, decreased motor activity and lethargy. There were no visible treatment-related macroscopic lesions observed at necropsy.
LD_{50} > 16,300 mg/kg-bw

Acute Inhalation Toxicity

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
Albino rats (10 males, strain not specified) were exposed to the test substance (1:29 distilled water) via inhalation at 180 mg/L for one hour and observed for 14 days. Treatment-related clinical signs included preening, excessive masticatory (chewing) movements, excessive salivation stains, lacrimation, serosanguineous stains around the nose and labored respiration. All animals appeared normal one day after dosing.
LD_{50} (1h) > 180 mg/L

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
Rats (5/sex/dose, strain not specified) were exposed to the test substance (50% purity) via inhalation at 0.05, 0.09, 0.13, 0.25 or 4.54 mg/L for 4 hours or 1.36 mg/L for 2 hours and observed for 14 days. At necropsy, no gross lesions were observed in 48 of the 60 test rats. Abnormalities of the liver, ear, skin, urinary bladder, kidneys, stomach, intestine, cecum, and lungs were noted.. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LD_{50} = 0.07 mg/L

Acute Dermal Toxicity

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
New Zealand White rabbits (3/sex) were administered the undiluted test substance dermally at 4.3 ml/kg-bw (approximately 4300 mg/kg-bw) onto intact or abraded skin under occluded conditions for 24 hours and observed for 14 days. Two males and one female died on day 8, 13 and 5, respectively. Treatment-related clinical signs included decreased food consumption and defecation, weight loss, depressed reflexes, body cold to touch, clear fluid around nose, mouth, chin and front limbs. One male and female had tilted heads and reddened nictitating membranes and eyelids. In addition, slight to severe erythema, moderate or severe edema and whitening of the exposed skin area, atonia, moderate or marked coriaceous skin and fissuring were also observed. Desquamation was observed in one animal. Necropsy of treatment-related deaths showed brown/liquid fecal material around the anal area, back legs and colons, lungs adhered to chest wall, lungs white and filled with white granular pockets, enlarged gall bladder and brownish/clear fluid around nose, mouth, chin and front limbs. There were no visible lesions observed during necropsy of the surviving animals.
LD_{50} ~ 4300 mg/kg-bw

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
In two separate studies, New Zealand White rabbits (3/sex) were administered the undiluted test substance at 4.0 or 4.7 mL/kg-bw (approximately 4000 or 4700 mg/kg-bw) onto intact or abraded skin under occluded conditions for 24 hours and observed for 14 days.
At 4000 mg/kg-bw, all animals died within three to eight days. Treatment-related clinical signs included decreased food consumption or defecation, increased respiration and heart rate, ataxia, depression, excessive salivation, reduced motor reflexes, hyperexcitability when handled and moderate to severe skin irritation**.** At necropsy, dark discolored pituitary (red to purple) and dilation of blood vessels in the skin, gastrointestinal tract, the surface of the brain, renal and posterior vena cava were seen.
At 4700 mg/kg-bw, 5 of 6 rabbits died between 24 hours and 11 days. Treatment-related clinical signs included depressed reflexes, cold and drooping ears, intermittent tremors, hunched posture, wet fur around the mouth, side of head and front paws, decreased food consumption and defecation, weight loss, severe erythema, edema, atonia and marked coriaceous skin after two days. At necropsy, gas-filled, distended large intestines, very thin stomach wall and lungs red and adhered to the chest wall were seen. Surviving animals exhibited clear fluid in the abdominal cavity and depleted body fat stores during necropsy.
LD_{50} < 4000 mg/kg-bw

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
Rabbits (5/sex/dose, strain not stated) were administered the undiluted test substance (65% purity) dermally at 2000, 2830 or 4000 mg/kg-bw and observed for 14 days. Four rabbits died within 3 to 3.5 hours; most deaths occurred at 2 to 7 days. Skin reactions included erythema, edema, necrosis, ulceration, ecchymoses, fissuring, alopecia, desquamation, and scabs. Signs of systemic toxicity were sluggishness, prostration, diarrhea, and persistent weight loss (with emaciation in some animals). Necropsy revealed dark red lungs, hemorrhaged intestines, gas or liquid-filled intestines, dark purple thymus, and purple and enlarged kidneys. Gross lesions at necropsy of survivors included dark red lungs, enlarged spleen, tan or purple kidneys, an excessive amount of blood in the kidneys, and a trace amount of blood in the urine). (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LD_{50} > 2930 mg/kg-bw (combined)

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, Supporting Chemical)
New Zealand Albino rabbits (3/sex/dose) were administered the test substance (85% purity) dermally at 2000 mg/kg-bw onto intact or abraded skin under occluded conditions for 24 hours and observed for 14 days. There were no mortalities. Treatment-related effects were severe erythema, moderate edema, moderate atonia, slight desquamation, moderate fissuring and eschar and exfoliation. At necropsy, skin effects observed were minimal to slight erythema and moderate exfoliation and eschar. No other significant lesions were noted.
LD_{50} > 2000 mg/kg-bw

Repeated-Dose Toxicity

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
New Zealand White rabbits (5/sex/dose) were administered the test substance (54.5% in aqueous isopropanol) dermally on to the abraded skin at 0 and 10 mg/kg-bw/day for 6.5 – 7 hours/day, 5 days/week for 28 days. Erythema (slight to moderate) and fissuring were the only signs of dermal irritation noted in all rabbits at 10 mg/kg-bw/day that subsided after day 17. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy or histopathology (except for treated areas of the skin).
NOAEL = 10 mg/kg-bw/day (based on no systemic effects at only dose tested)

Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (CAS No. 68391-05-9)
New Zealand White rabbits (3/sex/dose, 28 days or 5/sex/dose, 91 days) were administered the test substance (69.8% in aqueous isopropanol) dermally at 0 and 10 mg/kg-bw/day for 4 hours/day, 5 days/week for 28 or 91 days. Skin irritation such as erythema, edema, atonia, desquamation and fissuring occurred at moderate severity at all doses. After week 3, all treated rabbits had skin irritation. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy or histopathology (except for treated areas of the skin).
NOAEL = 10 mg/kg-bw/day (based on no systemic effects at only dose tested)

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
(1) New Zealand White rabbits (5/sex/dose) were administered the test substance (78.2% in water/isopropanol) dermally at 10 or 140 mg/kg-bw/day for 6 hours/day, 5 days/week for 91 days. At the 140 mg/kg-bw/day, erythema and edema, with associated skin changes (not stated), were observed during the first 2 weeks of the study. These skin effects subsided over the next 2 weeks, and during the last 9 weeks of the study, only slight erythema, edema, desquamation and fissuring were consistently observed. In the 10 mg/kg-bw/day group, erythema was observed during the first 4 weeks of the study. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy or histopathology (except for treated areas of the skin) at either dose.
NOAEL = 140 mg/kg-bw/day (based on no systemic effects at highest dose tested)

(2) Beagle dogs (4/sex/dose) were administered the test substance (purity not specified) in the diet at 0, 14, 140 and 2800 ppm (approximately 0, 0.5, 5 and 100 mg/kg-bw/day, respectively) for 90 days. There were no treatment-related effects on body weights, body weight gains, food consumption, urinalysis, hematology and clinical chemistry parameters. There were no differences in organ weights and gross or microscopic findings among the control and treated groups.
NOAEL > 100 mg/kg-bw/day (based on no effects at highest dose tested)

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (CAS No. 61789-81-9)
Sprague-Dawley rats (5/sex/dose) were administered the test substance in the diet at 0, 0.25, 0.5 and 10% (approximately 0, 170, 365 and 750 mg/kg-bw/day, respectively) for a total of 22 weeks. There were no treatment-related clinical signs or ophthalmologic effects. An initial decrease in weight gain was noted at 750 mg/kg-bw/day. At 13 weeks, the mean serum glutamic pyruvic transaminase (SGPT) activity was increased at the 365 and 750 mg/kg-bw/day doses. The albumin (ALB) values and the albumin/globulin ratios (A/G) in males at 750 mg/kg-bw/day were also increased markedly. The mean absolute and relative (to body weight) adrenal weights increased at all doses in females and in the 365 and 750 mg/kg-bw/day doses in males. The absolute and relative liver weights were also increased at all doses in females. Treatment-related microscopic changes in the mesenteric and pulmonary lymph nodes, adrenal glands and liver were seen at all doses. The incidence of all treatment-related microscopic changes was similar in rats of all groups necropsied after 13 and 22 weeks of treatment.
LOAEL ~ 170 mg/kg-bw/day (based on increased adrenal and liver weights in females and associated histopathological changes)
NOAEL = Not established.

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, Supporting Chemical)
Sprague-Dawley rats (6/sex/dose) were administered the test substance (86.0% purity) in the diet at 0, 40, 200 and 1000 mg/kg-bw/day for 28 days. Food consumption, body weight gains and food utilization were unaffected by treatment. Blood chemistry examination revealed a slight increase in serum glutamic pyruvic transaminase (SGPT) activity in animals receiving 1000 mg/kg-bw/day when compared to controls. Hematology parameters, organ weights and macroscopic pathology were unaffected by treatment. Histopathological examination revealed marked increases in histiocytic hyperplasia in the mesenteric lymph nodes in male and female rats receiving 1000 mg/kg-bw/day. A few animals at 200 mg/kg-bw/day were also affected; although the group incidence was not significantly different from the control.
LOAEL = 200 mg/kg-bw/day (based on histiocytic hyperplasia in the mesenteric lymph nodes)
NOAEL = 40 mg/kg-bw/day

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) Rats (10/sex/dose) were administered the test substance (80.8% purity) via the diet at 0, 6.2, 18.5, 36.8, 60.7 and 175.4 mg/kg-bw/day for males and 0, 7.5, 22.3, 44.4, 74.3 and 225.5 mg/kg-bw/day for females for 13 weeks. High-dose animals showed increased mortality, decreased mean body weights, body weight gain and food consumption and an increased incidence of gross pathological observations and non-neoplastic lesions, including higher incidence of glycogen depletion in the liver and contracted spleens. Additionally, high-dose females showed sinus erythrocytosis and lymphoid hyperplasia of mesenteric lymph nodes. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LOAEL (males) = 175.4 mg/kg-bw/day (based on increased mortality and effects on body weights, liver and spleen)
NOAEL (males) = 60.7 mg/kg-bw/day
LOAEL (females) = 225.5 mg/kg-bw/day (based on increased mortality and effects on body weight, liver, spleen and lymph nodes)
NOAEL (females) = 74.3 mg/kg-bw/day

(2) Sprague-Dawley rats (15/sex/dose) were administered the test substance (80.8% purity) dermally at 0, 2, 6 and 12 mg/kg-bw/day for 6 hours/day, 5 days/week for 13 weeks. Treatment-related toxicity was limited to treated skin of 6 mg/kg-bw/day females and 12 mg/kg-bw/day males and females. The clinical and gross findings (erythema, edema, exfoliation, excoriation and ulceration) were confirmed by histopathological examination, where increased incidence of hyperkeratosis, acanthosis, dermatitis and ulceration were noted beginning after 5 days of exposure. No treatment-related effects were noticed in mortality, weight gain, food consumption or systemic toxicity. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
NOAEL = 12 mg/kg-bw/day (based on no systemic toxicity at the highest dose tested)
LOAEL = 6 mg/kg-bw/day (based on skin effects)
NOAEL = 2 mg/kg-bw/day

(3) CD-1 mice (60/sex/dose) were administered the test substance (80.8% purity) via the diet at 0, 100, 500 or 1000 ppm (approximately 0, 15.0, 76.3 or 155.5 mg/kg-bw-day for males and 0, 18.6, 93.1 or 193.1 mg/kg-bw/day for females) for 78 weeks. Treatment-related effects were decreased mean body weights and body weight gains. No treatment-related effects were noted in the incidence of clinical signs, deaths, gross and histopathological observations. Hematological values were comparable among all study groups. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LOAEL = 155.5/193.1 mg/kg-bw/day (males/females, based on decreased in mean body weights and body weight gains)
NOAEL = 76.3/93.1 mg/kg-bw/day (males/females)

(4) Beagle dogs (4/sex/dose) were administered the test substance in the diet at 0, 5, 15 or 50 mg/kg-bw/day for 90 days. High-dose males and females experienced marked decrease in body weight gain, food consumption, and food efficiency.
LOAEL = 50 mg/kg-bw/day (based on decreased body weight gain, food consumption, and food efficiency)
NOAEL = 15 mg/kg-bw/day

(5) Beagle dogs (4/sex/dose) were administered the test substance (80.8% purity) orally at 0, 3, 10, or 20/30 mg/kg-bw/day for 1 year. A dose of 30 mg/kg-bw/day was not well tolerated and was discontinued on day 31, dosing was resumed on day 36 at 20 mg/kg-bw/day. No treatment-related deaths occurred during the study. The treatment-related clinical signs (soft/mucoid feces, emesis) were observed frequently in high-dose animals. Hematology or urinalysis results were normal. Total cholesterol levels were significantly decreased in the high-dose females. Gross and histopathological findings did not reveal any treatment-related effects. EPA's OPP established a LOAEL of 20 mg/kg-bw/day based decreased total cholesterol levels in females and a NOAEL of 10 mg/kg-bw/day. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LOAEL = 20 mg/kg-bw/day (based on decreased total cholesterol levels)
NOEAL = 10 mg/kg-bw/day

Reproductive Toxicity

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (CAS No. 61789-80-8)
In a 90-day repeated-dose toxicity study in beagle dogs described previously, there were no treatment-related effects during the gross or microscopic evaluations of the reproductive organs.

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (CAS No. 61789-81-9)
In a 22-week repeated-dose toxicity study in Sprague-Dawley rats described previously, there were no treatment-related effects during the gross or microscopic evaluations of the reproductive organs.

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Sporting Chemical)
In a two-generation reproductive study, Sprague-Dawley rats (28/sex/dose) were administered the test substance (80.8% purity.) in the diet at 0, 300, 750 and 1500 ppm (0, 20, 50 or 103 mg/kg-bw/day for males and 0, 24, 61 or 122 mg/kg-bw/day for females, respectively). No adverse reproductive effects were observed at any dose. Parental toxicity observed at 1500 ppm (113 mg/kg-bw/day) was limited to body weight reduction, weight gain depression and decreased food consumption. Postnatal toxicity seen at 1500 ppm (113 mg/kg-bw/day) was reduced pup body weights. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)

LOAEL (parental toxicity) = ~ 113 mg/kg-bw/day (1500 ppm) (based on decreased body weight, weight gain and food consumption)
NOAEL (parental toxicity) = ~ 56 mg/kg-bw/day (750 ppm)
NOAEL (reproductive toxicity) = 113 mg/kg-bw/day (1500 ppm) (based no effects at the highest dose tested)
LOAEL (offspring toxicity) = ~ 113 mg/kg-bw/day (1500 ppm) (based on decreased body weights)
NOAEL (offspring toxicity) = ~ 56 mg/kg-bw/day (750 ppm)
Developmental Toxicity

Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
Pregnant New Zealand White rabbits (13/dose) were administered the test substance (35% purity) via gavage at 0, 2, 8 and 24 mg/kg-bw/day on days 6–18 of gestation. An examination of the uterus, including the number corpora lutea, implantations, and resorptions was conducted. Two thirds of the fetuses were examined for skeletal and one third was examined for visceral abnormalities. No maternal, developmental or fetal treatment-related effects were observed at any dose.
NOAEL (maternal/developmental toxicity) = 24 mg/kg-bw/day (based on no effects at highest level tested)

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
Pregnant New Zealand White rabbits (20/dose) were administered the test substance (~25% purity) dermally at 0, 10, 20 and 40 mg/kg-bw/day on days 7–18 of gestation. Two control animals and one animal each at 20 and 40 mg/kg-bw/day died but cause of death could not be determined during necropsy. Two of the does that died aborted prior to death (one control and one at 20 mg/kg-bw/day). Two additional abortions occurred, one each at 20 and 40 mg/kg-bw/day. Skin irritation was observed at all doses with the severity and duration of erythema, edema, desquamation, atonia and coriaceousness increased in a dose-dependent manner. No treatment-related maternal body weight or food intake effects were noted. A slight increase in congested lungs was observed at 40 mg/kg-bw/day during necropsy. The incidence of fetal malformations and genetic developmental variation in the treated groups was comparable to that of the control group. No treatment-related developmental effects were noted.
NOAEL (maternal/developmental toxicity) = 40 mg/kg-bw/day (based on no effects at the highest dose tested)

Trimethyloctadecylammonium chloride (CAS No. 112-03-8)
Pregnant Sprague-Dawley rats (20/dose) were administered the test substance dermally at 0, 0.9, 1.5 and 2.5% (approximately 0, 4.5, 7.5 and 12.5 mg/kg-bw/day on days 6–15 of gestation. There were no signs of toxicity, deaths or treatment-related macroscopic pathology changes in internal organs. The incidence and severity of local dermal reactions were dose related. There was no marked or consistent treatment-related difference in weight gain, although marginally lower weight gains during the dosing period were observed in all treated groups. There was no marked effect on food or water consumption. Litter values assessed by litter size, post-implantation loss, litter and mean fetal weights and the embryonic and fetal development were not affected by treatment with the test substance. There were no significant developmental differences from concurrent control values with respect to the incidence of malformations and anomalies in fetuses or litters. The types of malformation or anomalies observed were comparable to the types of abnormalities recorded among concurrent or historical control values.
NOAEL (maternal/developmental toxicity) = 12.5 mg/kg-bw/day (based on no effects at the highest dose tested)

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
Pregnant Sprague-Dawley rats (25/dose) were administered the test substance via gavage at 0, 100 and 500 mg/kg-bw/day or in the diet at 508 mg/kg-bw/day on days 6–13 or 6–18 of gestation, respectively. Depressed body weight gains during gestation were noted in the group that received the test substance in the diet; food consumption values also were less in this group than in the group that received control feed. No treatment-related maternal adverse effects were noted on pregnancy and mortality rates. An increase in resorptions was observed for the 100 mg/kg-bw/day gavage group compared to the control group (7.1% vs. 2.1%), but this was within historical data values for the laboratory. There were no treatment-related effects noted on fetal parameters or on degree of ossification or malformations.
NOAEL (maternal/developmental toxicity) (gavage) = 500 mg/kg-bw/day (based on no effects at the highest dose tested)
NOAEL (developmental toxicity) (diet) = 508 mg/kg-bw/day (based on no effects at the only dose tested)

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (CAS No. 61789-81-9)
Pregnant Sprague-Dawley rats (25/dose) were administered the test substance via gavage (in 15% isopropanol) at 0, 100 and 500 mg/kg-bw/day or at 475 mg/kg-bw/day in the diet (0.55% purity.) on days 6–13 or 6–18 of gestation, respectively. No treatment-related maternal adverse effects were noted on pregnancy and mortality rates. An increase in resorptions was observed for the 500 mg/kg-bw/day gavage group compared to the control group (8.9% vs. 2.1%), but this was within historical data values for the laboratory. There were no treatment-related effects on fetal parameters or on degree of ossification or malformations.
NOAEL (maternal/developmental toxicity) (gavage) = 500 mg/kg-bw/day (based on no effects at the highest dose tested)
NOAEL (maternal/developmental toxicity) (diet) = 475 mg/kg-bw/day (based on no effects at the highest dose tested)

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, supporting chemical)
(1) Pregnant New Zealand White rabbits (16/dose) were administered the test substance (80.8% purity.) via gavage at 0, 1, 3 and 10 mg/kg-bw/day on days 6–18 of gestation. Maternal toxicity was evident at the mid and high doses and was seen as hypoactivity, labored and/or audible respiration and decreased body weight gain during the dosing period. At 10.0 mg/kg-bw/day, there was an increased incidence of mortality. Developmental effects included increased incidence of fetal mortality and reduced fetal body weight per litter at 10.0 mg/kg-bw/day. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LOAEL (maternal toxicity) = 3 mg/kg-bw/day (based on reductions in body weight gain, hypoactivity, labored/audible respiration and mortality)
NOAEL (maternal toxicity) = 1 mg/kg-bw/day
LOAEL (developmental toxicity) = 10 mg/kg-bw/day (based on increased mortality, decreased fetal body weight and an increased number of dead fetuses)
NOAEL (developmental toxicity) = 3 mg/kg-bw/day

(2) Pregnant Sprague-Dawley rats (25/dose) were administered the test substance (80.8% purity) via gavage at 0, 1, 10 and 20 mg/kg-bw/day on days 6–15 of gestation. Treatment-related maternal effects observed at 10 and 20 mg/kg-bw/day were of audible respiration and low food efficiency. Treatment-related decreases in body weight gain and corrected body weight gain were also observed at the high dose during gestation and for several days after the dosing period. Treatment-related developmental effects at the high dose were increased incidences of skeletal variations (split anterior arch of the atlas, poorly ossified thoracic centrum, bilobed thoracic centrum, unilateral short rib, poorly ossified parietal, and poorly ossified sternebrae). (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
LOAEL (maternal toxicity) = 10 mg/kg-bw/day (based on decreased body weight gain, low food efficiency and audible respiration)
NOAEL (maternal toxicity) = 1 mg/kg-bw/day
LOAEL (developmental toxicity) = 20 mg/kg-bw/day (based on an increased incidence of skeletal variations)
NOAEL (developmental toxicity) = 10 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

In vitro
Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
(1) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, were exposed to the test substance up to 0.4 µL/plate in the presence and absence of metabolic activation. Cytotoxic concentration was 0.1 µL/plate.
Dodecyltrimethylammonium chloride was not mutagenic in this assay.

(2) Mouse lymphoma L5178Ycells were exposed to the test substance at concentrations ranging from 0.0038 to 0.16 µL/plate in the presence and absence of metabolic activation. Cytotoxic concentrations were 0.01 µL/mL without metabolic activation and 0.1 µL/mL with metabolic activation. Positive and negative controls were used and responded appropriately. There was no significant increase in mutant frequency over the average mutant frequency of the solvent control.
Dodecyltrimethylammonium chloride was not mutagenic in this assay.

Hexadecyltrimethylammonium chloride (CAS No. 112-02-7)
S. typhimurium strains TA98 and TA100, were exposed to the test substance at concentrations ranging from 0.05 to 10.0 µg/plate in the presence and absence of metabolic activation. Cytotoxic concentration was 5.0 µg/plate without metabolic activation.
Hexadecyltrimethylammonium chloride was not mutagenic in this assay.

Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS No. 8030-78-2)
(1) *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to the test substance (concentrations not specified) in the presence and absence of metabolic activation.
Quaternary ammonium compounds, trimethyltallow alkyl, chlorides was not mutagenic in this assay.

(2) *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to the test substance up to 500 µg/plate in the presence and absence of metabolic activation. Cytotoxic concentration was 500 µg/plate. The test substance produced a three-fold increase in back mutations at 50 µg/plate with TA1538 with and without S9 activation.
Quaternary ammonium compounds, trimethyltallow alkyl, chlorides may be considered mutagenic in this assay.

Trimethyloctadecylammonium chloride (CAS No. 112-03-8)
S. typhimurium strains TA98 and TA100 were exposed to the test substance (concentrations not specified) in the presence and absence of metabolic activation.
Trimethyloctadecylammonium chloride was not mutagenic in this assay.

Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (CAS No. 61789-77-3)
S. typhimurium strains TA98, TA100, TA1535 and TA1537 were exposed to the test substance at concentrations ranging from 0.1 up to 33.3 µg/plate of test substance, in the presence and absence of metabolic activation. Cytotoxic concentrations were 100 µg/plate in the presence of metabolic activation and 33.3 µg/plate in the absence of metabolic activation. Positive and negative controls responded appropriately.
Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides was not mutagenic in this assay.

Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (CAS No. 61789-81-9)
S. typhimurium strains TA97, TA98, TA100 and TA1535 were exposed to the test substance up to 10,000 µg/plate in the presence and absence of metabolic activation.
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates was not mutagenic in this assay.

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to the test substance at concentrations ranging from 3.9 to 1000 µg/plate of test substance, in the presence and absence of metabolic activation. Cytotoxic concentrations were ≥ 65.5 µg/plate without metabolic activation and at 125 or 250 µg/plate with metabolic activation. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride was not mutagenic in this assay.

(2) Chinese hamster ovary cells were exposed to the test substance at concentrations ranging from 1.0 to 40 µg/mL of test substance in the presence and absence of metabolic activation. Positive and negative controls responded appropriately. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride was not mutagenic in this assay.

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, supporting chemical)
S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538, and *Escherichia coli*, WP2uvrA were exposed to the test substance at concentrations ranging from 333 to 5500 µg/plate *in* the presence and absence of metabolic activation. Moderate precipitation was seen at 3333 and 5500 µg/plate and slight precipitate was seen at 333 µg/plate. Positive and negative controls responded appropriately.
Tricetylmethyl ammonium chloride was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
Chinese hamster ovary cells were exposed to the test substance at concentrations ranging from 1 to 16 µg/mL of test substance in the presence and absence of metabolic activation. Positive and negative controls responded appropriately. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride did not induce chromosomal aberrations in this assay.

In vivo
Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
In a bone marrow cytogenetic assay, Sprague-Dawley rats (5/sex/dose) were administered the test substance via gavage at 0, 16, 53.3 and 160 mg/kg-bw/day for 5 days followed by an intraperitoneal injection of colchicines approximately 20 hours after the last treatment to arrest cells in metaphase. Bone marrow cells were examined for structural chromosomal aberrations.
Dodecyltrimethylammonium chloride did not induce chromosomal aberrations in this assay.

Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (CAS No. 68783-78-8)
In a bone marrow micronucleus test, male mice (8/dose) were administered two doses 24 hours apart of the test substance via gavage at 0, 50, 500 and 1000 mg/kg-bw/day. Mice were sacrificed 24 hours after the second dose. Bone marrow cells were harvested and one thousand polychromatic erythrocytes were scored for micronuclei from each mouse. There were no statistically significant differences in the mean micronuclei of the test groups compared to the negative control group.
Quaternary ammonium compounds, dimethylditallow alkyl, chlorides did not induce chromosomal aberrations in this assay.

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
In a bone marrow cytogenetic assay, groups of rats were administered a single dose of the test substance via gavage at 600 mg/kg-bw, then sacrificed at 6, 24 or 48 hours post-dose. Bone marrow cells were examined for chromosomal aberrations. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride did not induce chromosomal aberrations in this assay.

Tricetylmethyl ammonium chloride, TMAC (CAS No. 52467-63-7, Supporting Chemical)
In a bone marrow cytogenetic test, Sprague-Dawley rats (10/sex) were administered a single dose of the test substance via gavage at 5000 mg/kg-bw. There was no indication of bone marrow toxicity, as evidenced by the absence of inhibition of mitosis. No statistically significant increases in percentage of aberrant cells were observed in the treated groups, regardless of sex or bone marrow harvest time.
Tricetylmethyl ammonium chloride did not induce chromosomal aberrations in this assay.

Genetic Toxicity – Other

In vitro
Dodecyltrimethylammonium chloride (CAS No. 112-00-5)
In an unscheduled DNA synthesis (UDS) assay, rat primary hepatocytes were exposed to the test substance at concentrations ranging from 0.004 to 0.1 µL/mL. Cytotoxic concentrations were above 0.048 µL/mL. There was no indication that the test substance induced UDS. Positive and negative controls responded appropriately.
Dodecyltrimethylammonium chloride was not mutagenic in this assay.

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
In an unscheduled DNA synthesis (UDS) assay, primary cultures of rat hepatocytes were exposed to the test substance at concentration ranging from 0.05 to 10 µg/mL. There was no indication that the test substance induced UDS. (docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride was not mutagenic in this assay.

Additional Information

Carcinogenicity

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
(1) In a combined chronic toxicity/carcinogenicity study, Sprague-Dawley CD rats (60/sex/dose) were administered the test substance (80.8% purity.) in the diet at 0, 300, 750 or 1500 ppm (approximately 0, 13, 32 or 64 mg/kg-bw/day, respectively, for males and 0, 16, 41 or 83 mg/kg-bw/day, respectively, for females) for 2 years. High-dose animals showed slight (<10%) but statistically significant decreases in mean body weight during the study. Treatment-related effects included increased incidence of sinusoidal blood, hemosiderosis and histiocytosis in the mesenteric lymph nodes in high dose animals. In addition, a treatment-related increase in the incidence of interstitial cell adenomas in testes was reported, but the incidences were within the historical incidence range. The maximum tolerated dose was achieved in this study for carcinogenicity testing based on slight but statistically significant decrease in mean body weight (<10%) and some histopathological changes. There was no other evidence of carcinogenicity in this study. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)

(2) In a carcinogenicity study, CD-1 mice (60/sex/dose) were administered the test substance in the diet (80.8% purity.) at 0, 100, 500 or 1000 ppm (approximately 0, 15.0, 76.3 or 155.5 mg/kg-bw/day, respectively, for males and 0, 18.6, 93.1 or 193.1 mg/kg-bw/day, respectively, for females) for 78 weeks. No treatment-related mortality or clinical signs, gross and histopathological observations were observed. Hematological values were comparable among all study groups. There was no evidence of carcinogenicity in this study. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)

Skin Irritation

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
One male rabbit was administered the test substance (80% purity) dermally for 4 hours. Signs of severe irritation persisted 24 hours following application. Changes noted in the coloration and/or texture of the skin included coriaceousness, blanching, green-brown discoloration, brown/dark red discoloration, and necrosis. Due to the evidence of corrosion exhibited in this animal at the 24-hour reading, this study was terminated without testing additional animals. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride is corrosive to rabbit's skin.

Eye Irritation

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
One male rabbit was instilled the test substance (80%) into the eye for 1 hour. The total irritation score for the single animal was 94 out of 110 maximum at the one-hour interval. The test material produced extreme corneal opacity, iritis and conjunctival irritation after 1 hour. The eye of this animal also appeared misshapen. Due to the evidence of corrosion exhibited in this single animal, the study was terminated following the 1-hour reading without testing additional animals. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride is corrosive to rabbit's eye.

Sensitization

Didecyldimethylammonium chloride, DDAC (CAS No. 7173-51-5, Supporting Chemical)
Guinea pigs (20/dose) were administered the test substance (80% purity) at 0.25, 0.5 or 0.75% w/w once a week for 3 weeks during induction phase. The challenge dose was 0.1% over 27 days. A control group of 10 guinea pigs, not induced, received challenge dose of 0.1% w/w. Erythema scores ranged from 0.05 to 0.10 in the test animals and from 0.05 to 0.20 in the controls. A positive response was not observed in any of the test or control animals. (Docket link for EPA-HQ-OPP-2006-0338 at http://www.epa.gov/pesticides/reregistration/ddac)
Didecyldimethylammonium chloride is not a sensitizer.

Conclusion: The acute oral toxicity for FND cationic members of this category is low to moderate. Acute dermal toxicity of FND cationic members is low while acute inhalation toxicity of the supporting chemical is high. FND cationic members are corrosive to skin and eye of rabbits; however, they are not dermal sensitizers based on supporting substance studies. Repeated exposures via the diet to FND cationic members and supporting substances resulted in decreased body weight and weight gain, increased adrenal and liver weights, increased histiocytic hyperplasia in the mesenteric lymph nodes and decreased total cholesterol levels at the doses tested. Repeated exposures via the dermal application of FND cationic members and supporting substances resulted in a range of skin effects (e.g., erythema, edema, atonia and desquamation) at treatment sites. However, no treatment-related systemic toxicity was evident following repeated exposures via the dermal route for FND cationic members or supporting substances at the doses tested. Two-generation reproduction toxicity studies for supporting substances showed reduced parental and pup body weights and body weight gain; however, no effects were seen on reproductive parameters. No treatment-related effects were seen on the reproductive organs during macroscopic or microscopic examinations in repeated-dose toxicity studies for FND cationic members. Developmental effects were not noted via dermal exposure to FND cationic members. Developmental toxicity studies via oral route for a supporting substance resulted in a decrease in fetal body weight, an increase number of dead fetuses and an increase incidence of skeletal variations. Other developmental oral (gavage) toxicity studies for FND cationic members and supporting substances indicated no treatment-related effects at doses tested. FND cationic members did not induce gene mutations in bacteria and mammalian cells. One FND cationic member (CAS No. 8030-78-2) showed a three-fold increase in mutation frequency in *S. typhimurium* in one assay but was negative in a second test. FND cationic members did not induce chromosomal aberrations *in vitro* or *in vivo*. One FND cationic member (CAS No. 112-00-5) and one supporting chemical (CAS No. 7173-51-5) did not induce unscheduled DNA synthesis when tested with male rat hepatocytes. The supporting chemical (CAS No. 7173-51-5) did not show evidence of carcinogenicity in rat and mice.

The potential health hazard of the FND cationic category is low to moderate based on the results of repeated-dose and reproductive and developmental toxicity.

Table 3. Summary of Human Health Data								
Endpoints	**Dodecyltrimethyl ammonium chloride (112-00-5)**	**Hexadecyltrimethylammonium chloride (112-02-7)**	**Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (8030-78-2)**	**Trimethyloctadecylammonium chloride (112-03-8)**	**Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)**	**Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (68391-05-9)**	**Quaternary ammonium compounds, di-C_{14-18}-alkyl dimethyl, chlorides (68002-59-5)**	**Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (68783-78-8)**
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**490** **560**	**< 400 LD_{50} < 600**	**1260**	**633** **536**	**960**	**4700**	No data 238 (RA)	**> ~ 2150**
Acute Inhalation Toxicity LD_{50} (mg/L)					No data 0.07 (RA)	No data 0.07 (RA)	No data 0.07 (RA)	No data 0.07 (RA)
Acute Dermal Toxicity LC_{50} (mg/kg-bw)	No data <4000 (RA)	**~ 4300**	**< 4000**	No data <4000 (RA)	No data > 2930 (RA)	No data > 2930 (RA)	No data > 2930 (RA)	No data > 2930 (RA)
Repeated-Dose Toxicity (Oral) NOAEL/ LOAEL (mg/kg-bw/day)	–	**–**	**–**	**–**	No data (rat) NOAEL 60/74 (m/f) LOAEL = 175/226 (m/f) (RA)	No data (rat) NOAEL 60/74 (m/f) LOAEL = 175/226 (m/f) (RA)	No data (rat) NOAEL 60/74 (m/f) LOAEL = 175/226 (m/f) (RA)	No data (rat) NOAEL 60/74 (m/f) LOAEL = 175/226 (m/f) (RA)
Repeated-Dose Toxicity (Dermal) NOAEL/ LOAEL (mg/kg-bw/day)	No data NOAEL = 10 (RA)	**NOAEL = 10** **(only dose tested)**	No data NOAEL = 10 (RA)	No data NOAEL = 10 (RA)	No data NOAEL = 10 (RA)	**NOAEL = 10** **(only dose tested)**	–	–
Reproductive Toxicity	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	(No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)
Developmental Toxicity (Oral) (mg/kg-bw/day) **Maternal** **Developmental**	**NOAEL = 24** hdt **NOAEL = 24** hdt	No data NOAEL = 24 hdt NOAEL = 24 hdt RA	No data NOAEL = 24 hdt NOAEL =24 hdt RA	No data NOAEL = 24 hdt NOAEL = 24 hdt RA	No data (rabbit) NOAEL = 1 LOAEL = 3 (rabbit) NOAEL = 3	No data (rabbit) NOAEL = 1 LOAEL = 3 (rabbit)	No data (rabbit) NOAEL = 1 LOAEL = 3 (rabbit)	(gavage) **NOAEL = 500** hdt (gavage) **NOAEL = 500** hdt

Table 3. Summary of Human Health Data								
Endpoints	**Dodecyltrimethyl ammonium chloride (112-00-5)**	**Hexadecyltrimethylammonium chloride (112-02-7)**	**Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (8030-78-2)**	**Trimethyloctadecylammonium chloride (112-03-8)**	**Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)**	**Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (68391-05-9)**	**Quaternary ammonium compounds, di-C_{14-18}-alkyl dimethyl, chlorides (68002-59-5)**	**Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (68783-78-8)**
					LOAEL = 10 (RA)	NOAEL = 3 LOAEL = 10 (RA)	NOAEL = 3 LOAEL = 10 (RA)	(diet) **NOAEL = 508** hdt
Developmental Toxicity (Dermal) (mg/kg-bw/day) **Maternal** **Developmental**	–	**NOAEL = 40 hdt** **NOAEL = 40 hdt**	–	**NOAEL = 12.5 hdt** **NOAEL = 12.5 hdt**	–	–	–	–
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Negative**	**Equivocal**	**Negative**	**Negative**	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)

Table 3. Summary of Human Health Data								
Endpoints	**Dodecyltrimethyl ammonium chloride (112-00-5)**	**Hexadecyltrimethylammonium chloride (112-02-7)**	**Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (8030-78-2)**	**Trimethyloctadecylammonium chloride (112-03-8)**	**Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (61789-77-3)**	**Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides (68391-05-9)**	**Quaternary ammonium compounds, di-C_{14-18}-alkyl dimethyl, chlorides (68002-59-5)**	**Quaternary ammonium compounds, dimethylditallow alkyl, chlorides (68783-78-8)**
Genetic Toxicity – Chromosomal Aberrations *In vivo*	**Negative**	**Negative**	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)
Genetic Toxicity – Other Endpoints DNA Effects	**Negative (UDS)**	No data Negative (RA)	No data Negative (RA))	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)
Carcinogenicity								
Skin Irritation	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)
Eye Irritation	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)
Sensitization	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)

Table 3. Summary of Human Health							
Endpoints	**Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates** **(68002-58-4)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride** **(61789-80-8)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (61789-81-9)**	**Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides (67784-77-4)**	**Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride** **(68607-29-4)**	**Tricetylmethyl ammonium chloride (TMAC; Supporting Chemical) (52467-63-7)**	**Didecyldimethyl-ammonium chloride (DDAC; Supporting Chemical)** **(7173-51-5)**
Acute Oral Toxicity LD_{50} (mg/kg-bw)	No data 238 (RA)	**> 500** **> 576** **> 432**	No data 238 (RA)	No data 238 (RA)	**205**	**> 16,300**	**238** **262**
Acute Inhalation Toxicity LC_{50} (mg/L)	No data 0.07 (RA)	**> 180 (1h)**	No data 0.07 (RA)	–	–	**–**	**0.07**
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	No data > 2930 (RA)	No data > 2930 (RA)	No data > 2930 (RA)	No data > 2000 (RA)	No data <4000 (RA)	**> 2000**	**> 2930**
Repeated-Dose Toxicity (Oral) NOAEL/ LOAEL (mg/kg-bw/day)	No data (rat) NOAEL 60/74 (m/f) LOAEL = 175/226 (m/f) (RA)	(dog) **NOAEL = 100** **hdt**	**NOAEL = NE** **LOAEL ~ 170**	No data NOAEL = 40 LOAEL = 200 (RA)	**–**	**NOAEL = 40** **LOAEL = 200**	**(rat)** **NOAEL 60/74 (m/f)** **LOAEL = 175/226** **(m/f)** **(dog)** **NOAEL = 10** (dog) **LOAEL = 20** (dog) **(mouse)** **NOAEL = 76**/93 (m/f) **LOAEL = 156/193** **(m/f)**
Repeated-Dose Toxicity (Dermal) NOAEL/ LOAEL (mg/kg-bw/day)	–	(rabbit) **NOAEL = 140 (hdt)**	**–**	–	No data NOAEL = 10 (RA)	**–**	**(rat)** **NOAEL (systemic) = 12 (hdt)** **NAOEL (dermal) = 2** **LOAEL = 6**

Table 3. Summary of Human Health							
Endpoints	**Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates** **(68002-58-4)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride** **(61789-80-8)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (61789-81-9)**	**Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides (67784-77-4)**	**Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride** **(68607-29-4)**	**Tricetylmethyl ammonium chloride (TMAC; Supporting Chemical) (52467-63-7)**	**Didecyldimethyl-ammonium chloride (DDAC; Supporting Chemical)** **(7173-51-5)**
Reproductive Toxicity	No data NOAEL = 56 LOAEL = 113 (RA)	No effects were seen on reproductive organs in the repeated-dose toxicity study in dogs.	No effects were seen on reproductive organs in the repeated-dose toxicity study in rats.	No data NOAEL = 56 LOAEL = 113 (RA)	No data NOAEL = 56 LOAEL = 113 (RA)	–	**NOAEL = 56** **LOAEL = 113**
Developmental Toxicity (mg/kg-bw/day) **Maternal** **Developmental**	No data (rabbit) NOAEL = 1 LOAEL = 3 (RA) (rabbit) NOAEL = 3 LOAEL = 10 (RA)	No data (rabbit) NOAEL = 1 LOAEL = 3 (RA) (rabbit) NOAEL = 3 LOAEL = 10 (RA)	(gavage) **NOAEL = 500 (hdt)** (diet) **NOAEL = 475 (hdt)** (gavage) NOAEL = 500 (hdt) (diet) **NOAEL = 475 (hdt)**	No data (rabbit) NOAEL = 1 LOAEL = 3 (RA) (rabbit) NOAEL = 3 LOAEL = 10 (RA)	No data NOAEL = 24 hdt (RA) NOAEL = 24 hdt (RA)	–	**(rabbit)** **NOAEL =1** **LOAEL = 3** **(rat)** **NOAEL = 1** **LOAEL = 10** **(rabbit)NOAEL = 3** **LOAEL = 10** (rat) **NOAEL = 10** **LOAEL = 20**

Table 3. Summary of Human Health							
Endpoints	**Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates (68002-58-4)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride (61789-80-8)**	**Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates (61789-81-9)**	**Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides (67784-77-4)**	**Quaternary ammonium compounds, pentamethyltallow alkyltrimethylene-di-, dichloride (68607-29-4)**	**Tricetylmethyl ammonium chloride (TMAC; Supporting Chemical) (52467-63-7)**	**Didecyldimethyl-ammonium chloride (DDAC; Supporting Chemical) (7173-51-5)**
Genetic Toxicity – Gene Mutation *In vitro*	No data Negative (RA)	No data Negative (RA)	**Negative**	No data Negative (RA)	No data Negative (RA)	**Negative**	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vivo*	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	**Negative**	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	**Negative**
Genetic Toxicity – Other Endpoints DNA Effects	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	**Negative (UDS)**
Carcinogenicity	–	–	–	–	–	–	**No evidence of carcinogenicity (rat/mice)**
Skin Irritation	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	**Corrosive**
Eye Irritation	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	No data Corrosive (RA)	**Corrosive**
Sensitization	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	No data Not a sensitizer (RA)	**Not a sensitizer**

Measured data in bold text; RA = Read Across; NE = not established; hdt = highest dose tested; UDS = unscheduled DNA synthesis; − Data for this endpoint not needed.

4. Hazard Characterization

The log K_{ow} values of the FND cationic members indicate that their potential to bioaccumulate is expected to be low. The FND cationic members are not readily biodegradable indicating that they have the potential to persist in the environment.

The evaluation of available toxicity data for fish, aquatic invertebrates and aquatic plants indicate that the potential hazard of FND cationic members to aquatic organisms is high.

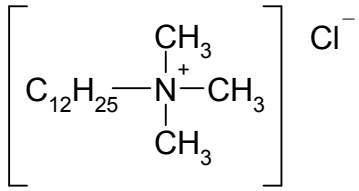
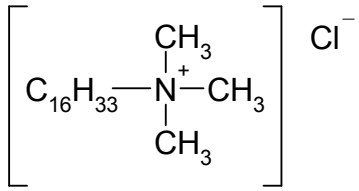
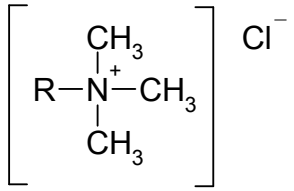
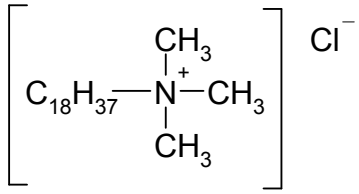
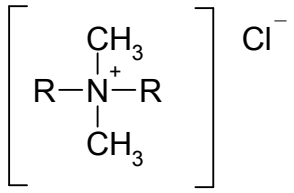
The acute oral toxicity for FND cationic members is low to moderate. Acute dermal toxicity of FND cationic members is low while acute inhalation toxicity of the supporting chemical is high. FND cationic members are corrosive to skin and eye of rabbits; however, they are not dermal sensitizers based on supporting substance studies. Repeated exposures via the diet to FND cationic members and supporting substances resulted in decreased body weight and weight gain, increased adrenal and liver weights, increased histiocytic hyperplasia in the mesenteric lymph nodes and decreased total cholesterol levels at the doses tested. Repeated exposures via the dermal application of FND cationic members and supporting substances resulted in a range of skins effects (e.g., erythema, edema, atonia and desquamation) at treatment sites. However, no treatment-related systemic toxicity was evident following repeated exposures via the dermal route for FND cationic members or supporting substances at the doses tested. Two-generation reproduction toxicity studies for supporting substances showed reduced parental and pup body weights and body weight gain; however, no effects were seen on reproductive parameters. No treatment-related effects were seen on the reproductive organs during macroscopic or microscopic examinations in repeated-dose toxicity studies for FND cationic members. Developmental effects were not noted via dermal exposure to FND cationic members. Developmental toxicity studies via oral route for a supporting substance resulted in a decrease in fetal body weight, an increase number of dead fetuses and an increase incidence of skeletal variations. Other developmental oral (gavage) toxicity studies for FND cationic members and supporting substances indicated no treatment-related effects at doses tested. FND cationic members did not induce gene mutations in bacteria and mammalian cells. One FND cationic member (CAS No. 8030-78-2) showed a three-fold increase in mutation frequency in *S. typhimurium* in one assay but was negative in the second test. FND cationic members did not induce chromosomal aberrations *in vitro* or *in vivo*. One FND cationic member (CAS No. 112-00-5) and one supporting chemical (CAS No. 7173-51-5) did not induce unscheduled DNA synthesis when tested with male rat hepatocytes. The supporting chemical (CAS No. 7173-51-5) did not show evidence of carcinogenicity in rat and mice.

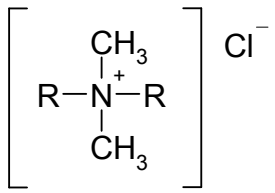
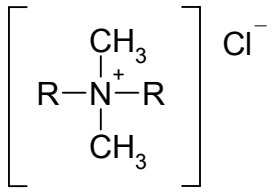
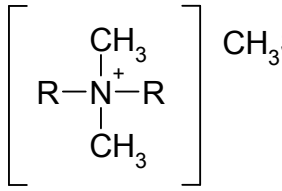
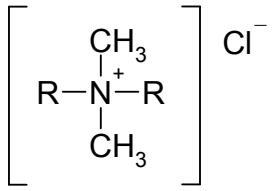
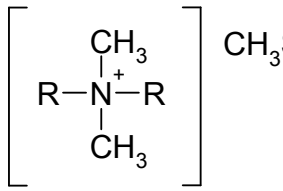
The potential health hazard of the FND cationic category is low to moderate based on the results of repeated-dose and reproductive and developmental toxicity.

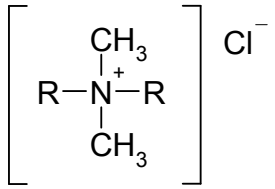
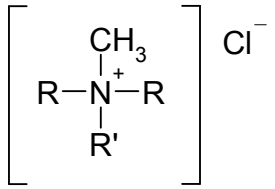
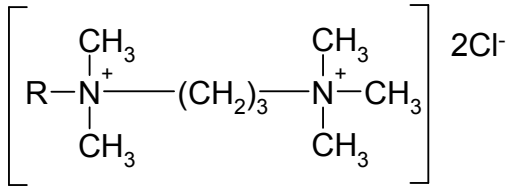
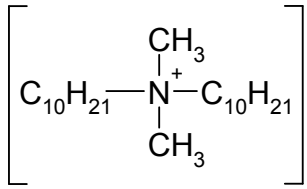
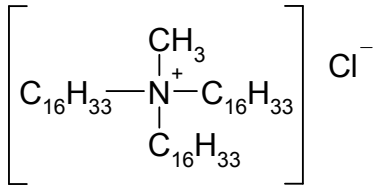
5. Data Gaps

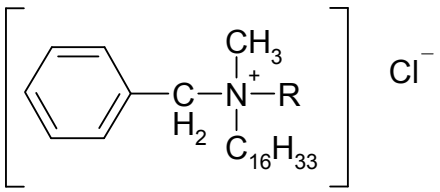
No data gaps were identified under the HPV Challenge Program.

Appendix

Fatty Nitrogen Derived Cationics Category		
CAS No.	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
112-00-5	Dodecyltrimethylammonium chloride [9th CI Name: 1-Dodecanaminium, N,N,N-trimethyl-, chloride]	 $C_{15}H_{34}ClN$
112-02-7	Hexadecyltrimethylammonium chloride [9th CI Name: 1-Hexadecanaminium, N,N,N-trimethyl-, chloride]	 $C_{19}H_{42}ClN$
8030-78-2	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides [9th CI Name: Quaternary ammonium compounds, trimethyltallow alkyl, chlorides]	 R = tallow alkyl $C_{21}H_{44}ClN$
112-03-8	Trimethyloctadecylammonium chloride [9th CI Name: 1-Octadecanaminium, N,N,N-trimethyl-, chloride]	 $C_{21}H_{44}ClN$
61789-77-3	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides [9th CI Name: Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides]	 R = coco alkyl $C_{26}H_{56}ClN$

68391-05-9	Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides [9th CI Name: Quaternary ammonium compounds, di-C_{12-18}-alkyldimethyl, chlorides]	 R = C_{12}-C_{18} alkyl $C_{32}H_{68}ClN$
68002-59-5	Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, chlorides [9th CI Name: Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, chlorides]	 R = C_{14}-C_{18} alkyl $C_{30}H_{64}ClN$
68002-58-4	Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates [9th CI Name: Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, Me sulfates]	 R = C_{14}-C_{18} alkyl $C_{31}H_{67}NO_4S$
68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides [9th CI Name: Quaternary ammonium compounds, dimethylditallow alkyl, chlorides]	 R = tallow alkyl $C_{37}H_{74}ClN$
61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates [9th CI Name: Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates]	 R = hydrogenated tallow alkyl $C_{38}H_{80}ClN$

61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chloride [9th CI Name: Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chlorides]	 R = hydrogenated tallow alkyl $C_{38}H_{80}ClN$
67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides [9th CI Name: Quaternary ammonium compounds, bis(hydroxyethyl) methyltallow alkyl, chlorides]	 R = hydroxyethyl R' = tallow alkyl $C_{43}H_{88}ClNO_{12}$
68607-29-4	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride [9th CI Name: Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichlorides]	 $C_{26}H_{56}Cl_2N_2$
SUPPORTING CHEMICALS		
7173-51-5	Didecyldimethylammonium chloride (DDAC) [9th CI Name: 1-Decanaminium, N-decyl-N,N-dimethyl-, chloride]	 $C_{22}H_{48}ClN$
52467-63-7	Tricetylmethylammonium chloride (TMAC) [9th CI Name: 1-Hexadecanaminium, N,N-dihexadecyl-N-methyl-, chloride]	 $C_{49}H_{102}ClN$

68424-85-1	Alkyl (C_{12-16}) dimethylbenzylammonium chloride (ADBAC) [9th CI Name: Quaternary ammonium compounds, benzyl-C_{12-16}-alkyldimethyl, chlorides]	 R = C_{12}-C_{16} alkyl $C_{23}H_{42}ClN$