Trimethoxysilyl Quaternary Ammonium Chloride Preliminary Work Plan

Registration Review: Initial Docket Case Numbers 3148, 5100, 5113

March 2013

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Date: 3-27-2013

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1 Introduction

This document is the Environmental Protection Agency's (EPA or "the agency") Preliminary Work Plan (PWP) for the Trimethoxysilyl Quaternary Ammonium Chloride (QAC) Case. The PWP document explains what EPA's Office of Pesticide Programs knows about trimethoxysilyl QACs, highlighting anticipated data and assessment needs, identifying the types of information that would be especially useful to the agency in conducting the review, and providing an anticipated timeline for completing trimethoxysilyl QACs' review.

Initially, this Registration Review was scheduled to address only 1-octadecanaminium-N, N-dimethyl-N-[3-(trihydroxysilyl) propyl] chloride (PC code 107403). However, because of their similar use patterns as well as chemical, physical, toxicological, environmental fate, and ecotoxicity characteristics, this document also addresses three other silyl QACs: 1-octadecanaminum-N-N-dimethyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 107401); 1-tetradecanaminum-N-N-dimethyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 107409); and 1-decanaminium-N,N-didecyl-N-methyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 169160). The September 2007 RED (http://www.epa.gov/oppsrrd1/REDs/trimethoxysilyl-quats-red.pdf) addressed these simultaneously because of the similarities described above. In light of the similarities described above, the agency is grouping these active ingredients together and merging them into the Trimethoxysilyl QAC Registration Review case pursuant to 40 CFR Part 155.42(a) and 40 CFR Part 155.42(b)(4).

The registration review process was designed to include a public participation component to solicit input from interested stakeholders. The agency intends, by sharing this information in the docket, to inform the public of what it knows about trimethoxysilyl QACs and what types of new data or other information would be helpful for the agency to receive as it moves toward a decision on trimethoxysilyl QACs. The agency encourages all interested stakeholders to review the PWP and to provide comments and additional information that will help the agency's decision-making process for this chemical.

1.1 Statutory and Regulatory Authority

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides distributed or sold in the United States generally must be registered by the U.S. Environmental Protection Agency (USEPA, EPA, or the agency) based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at http://www.epa.gov/oppsrrd1/registration_review/.

The agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for

registration. The regulations governing registration review begin at 40 CFR 155.40. The agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial comment period, the agency will develop and commit to a Final Work Plan (FWP) and anticipated schedule for the Trimethoxysilyl QAC Case.

Documents associated with this registration review can be viewed at http://www.regulations.gov in docket EPA-HQ-OPP-2013-0095, EPA-HQ-OPP-2013-0096 and EPA-HQ-OPP-2013 -0085. Below is a summary of the issues relevant to this registration review case.

Table 1 - Summary of Anticipated Risk Assessments and Data Needs for the Trimethoxysilyl QACs

Risk Assessment	Assessment Necessary to Support Registration Review	Date of Most Recent Assessment	Type of Assessment Required (New/Updated)	Data Anticipated as Needed (See Table 6 for more detail about anticipated data needs)
Dietary (food)	No (see 3.2.1)	N/A	N/A	None
Dietary (drinking water)	Yes (see 3.2.2)	N/A	New	Two-generation reproductive toxicity[1] Developmental toxicity[1]
Occupational Handler	Yes	2007 RED	New	Occupational exposure data Inhalation toxicity study
Residential Handler	Yes	2007 RED	Updated	Indoor exposure data Inhalation toxicity study
Residential Post Application - Incidental Oral and Dermal, Inhalation	No (see 3.3)	N/A	None	None
Aggregate	Yes	N/A	New	Residential handler inhalation exposure Inhalation toxicity study
Cumulative	No (see 3.4)	N/A	No	None
Tolerance Review	No (see 1.5.2)	N/A	New	None
Ecological	Yes	N/A	New	Chronic daphnia study Aquatic plant toxicity Sediment toxicity Leaching from treated shingles and fascia board

N/A = Not applicable

[1] These studies are expected to be required but may be waived depending on the outcome of the required environmental fate studies. If the environmental fate studies reveal that human exposure via drinking water is negligible, a waiver may be justified.

Table 2 - Anticipated Registration Review Schedule

Anticipated Activity	Target Date[2]	Completion Date
Phase 1: Opening the Docket		
Open Docket and 60-Day Comment Period for Preliminary Work Plan	2013-03	2013-03-20
Close Public Comment Period	2013-05	
Phase 2: Case Development		
Issue Final Work Plan	2013-09	
Issue Data Call-In (DCI)	2014-09	
Receive Data to be Considered in Risk Assessment	2016-09	
Open 30-Day Public Comment Period for Preliminary Risk Assessment(s)	2018-03	
Close Public Comment Period	2018-04	
Phase 3: Registration Review Decision and Implementation		
Open 60-Day Public Comment Period for Proposed Decision	2018-09	
Close Public Comment Period	2018-11	
Issue Final Decision	2019-03	
Begin Post-Decision Follow-up	2019	
Total (years)	6	

1.2 Case Overview

Initially, this Registration Review was scheduled to address only 1-octadecanaminium-N, N-dimethyl-N-[3-(trihydroxysilyl) propyl] chloride (PC code 107403). However, because of their similar use patterns as well as chemical, physical, toxicological, environmental fate, and ecotoxicity characteristics, this document also addresses three other silyl QACs: 1-octadecanaminum-N-N-dimethyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 107401); 1-tetradecanaminum-N-N-dimethyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 107409); and 1-decanaminium-N,N-didecyl-N-methyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code 169160). The September 2007 RED (http://www.epa.gov/oppsrrd1/REDs/trimethoxysilyl-quats-red.pdf) addressed these simultaneously because of the similarities described above. According to the 2011-2014 public Registration Review schedule, case 3148 and 5113 were planned to begin in fiscal year 2015. To ensure the public is able to locate information associated with case 3148, case 5100 and case 5113, EPA has created and will maintain a separate docket for each case. All EPA documents relevant to the three cases will be posted in all the three dockets.

This case will be referred to as the trimethoxysilyl quaternary ammonium chlorides (trimethoxysilyl QACs). As a result of this grouping and merger, the trimethoxysilyl QACs case will now include:

1. Case 3148: 1-Octadecanaminium-N, N-dimethyl-N-(3-(trimethoxysilyl) propyl) chloride (PC code 107401) and 1-Decanaminium-N-decyl-N-methyl-N-[3-(trimethoxysilyl) propyl] chloride (PC code 169160).

[2] The anticipated schedule will be revised as necessary (*e.g.*, on any need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

2. Case 5100: 1-Octadecanaminium-N, N-dimethyl-N-[3-(trihydroxysilyl) propyl] chloride (PC code 107403); and

3. Case 5113: 1-Tetradecanaminium-N, N-dimethyl-N-[3-(trimethoxysilyl) propyl] chloride (PC code 107409)

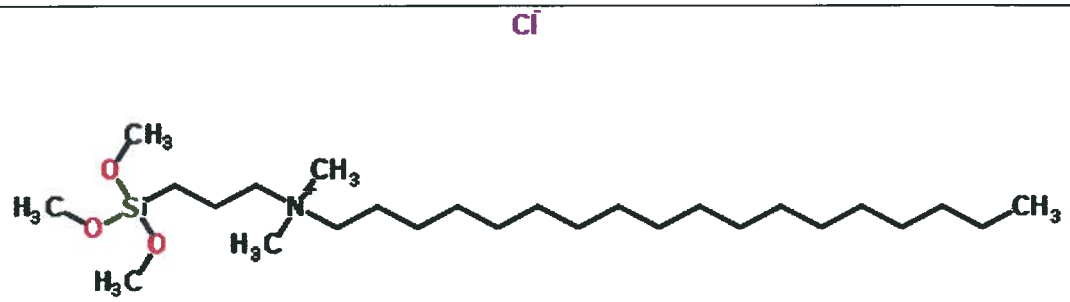
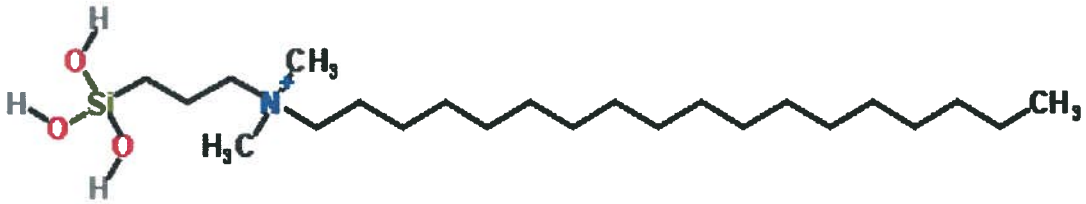
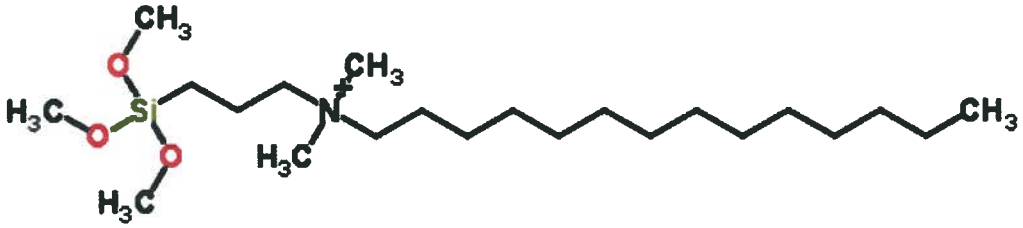
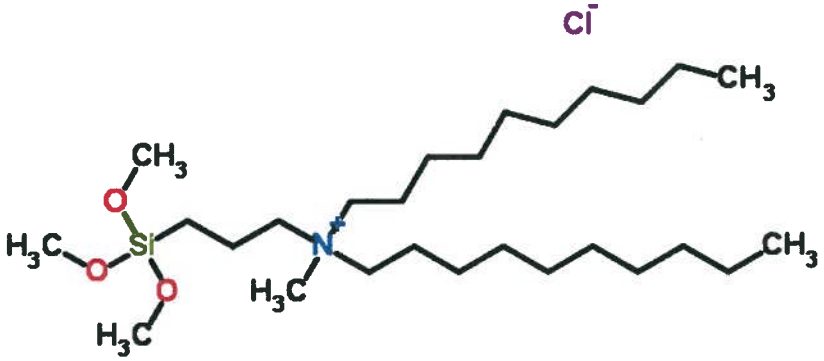
The dockets for the trimethoxysilyl QAC (Case 3148, Case 5100, Case 5113) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2013-0095; EPA-HQ-OPP-2013-0096; EPA-HQ-OPP-2013 -0085.

1.3 Chemical Identification and Properties

Table 3 presents the four active ingredients to be assessed in Case 3148, 5100 and 5113: 1-Octadecanaminium- N, N-dimethyl-N-[3-(trimethoxysilyl) propyl] chloride (PC Code: 107401), 1-Octadecanaminium-N,N-dimethyl-N-[3-(trihydroxysilyl)propyl] chloride (PC Code: 107403), 1-Tetradecanaminium-N,N-dimethyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code: 107409), 1-Decanaminium-N-decyl-N-methyl-N-[3-(trimethoxysilyl)propyl] chloride (PC Code: 169160). These four active ingredients are considered to be toxicologically and ecologically equivalent for the purposes of registration review; and except where otherwise noted, the four active ingredients in these cases will be referred to collectively as "trimethoxysilyl QACs".

Table 3 - Chemical Identification of Trimethoxysilyl QACs

Chemical Name	1-Octadecanaminium, N, N-dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	1-Tetradecanaminium, N, N-dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	1-Decanaminium, N-decyl-N-methyl-N-[3-(trimethoxysilyl] propyl)-, chloride	1-Octadecanaminium-N, N-dimethyl-N-[3-(trihydroxysilyl) propyl]-chloride
Common Name	3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride	Dimethyltetradecyl [3-(trimethoxysilyl) propyl] ammonium chloride	N,N-Didecyl-N-methyl-3-(trimethoxysilyl) propanaminium chloride	3-(trihydroxysilyl) propyl dimethyl octadecyl ammonium chloride
Classification	Silicone Quaternary Ammonium Chloride Salt			
PC Code	107401	107409	169160	107403
CAS No.	27668-52-6	41591-87-1	68959-20-6	199111-50-7
Molecular Formula	$C_{26}H_{58}ClNO_3Si$	$C_{22}H_{50}ClNO_3Si$	$C_{27}H_{60}ClNO_3Si$	$C_{23}H_{52}ClNO_3Si$
Molecular Weight	496.30 g/mol	440.17 g/mol	510.31 g/mol	454.20 g/mol
Tolerances	None	None	None	None
Incidents	None	None	None	None
PC Code	Molecular structures for the Trimethoxysilyl Quaternary Ammonium Chloride Compounds			

107401	 1-Octadecanaminium, N,N-dimethyl-N-[3(trimethoxysilyl)propyl]-, chloride
107403	 1-octadecananminium-N,N-dimethyl-N-[3-(trihydroxysilyl)propyl]-, chloride
107409	 1-Tetradecanaminium, N, N-dimethyl-N-[3(trimethoxysilyl)propyl]-, chloride
169160	 1-Decanaminium, N-decyl-N-methyl-N-[3-(trimethoxysilyl)propyl]-, chloride

The trimethoxysilyl QACs product chemistry information relevant to risk assessment is summarized in Table 4 and details of the environmental fate properties are discussed in Appendix B.

Table 4 - Physicochemical Properties for Trimethoxysilyl QACs

Guideline No. Physical and Chemical Properties	1-Octadecanaminium, N,N-dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	1-Tetradecanaminium, N, N dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	N,N-Didecyl-N-methyl-3-(trimethoxysilyl) propanaminium chloride	1-ocatdecanaminium-N,N-dimethyl-N-[3-(trihydroxysilyl) propyl]-chloride
830.1650 Description of Formulation Process	Confidential Business Information (CBI)	CBI	CBI	CBI
830.6302 Color	Pale yellow to off White Light brown	Clear yellowish	Light to dark amber	Clear
830.6303 Physical State	Liquid	Liquid	Liquid	Liquid
830.6304 Odor	Characteristic Silane odor	Characteristic Silane odor	Characteristic Silane odor	Characteristic Silane odor
830.6313 Stability to normal and elevated temperature, metals/metal ions	Stable			
830.6314 Oxidation/ Reduction:	Does not contain oxidizing/reducing agents			
830.7000 pH	5.3 to 6.9 at 20C (5% aqueous) 4.7(5% aqueous)	6.9 (5% solution)	6.91 (1% solution)	6.5 – 7.5
830.7050 UV/Visible Absorption	Not applicable because the chemical structure shows that it will not absorb in the UV spectral region. No UV absorbing chromophore.			
830.7200 Melting point	Not applicable, it is a liquid.			
830.7220 Boiling point	617° C (EPI Suite v4.1)	570 °C (EPI Suite v4.1)	628° C (EPI Suite v4.1)	702°C (EPI Suite v4.1)
830.7300 Density	0.841 to 0.859 g/ml	0.878 g/ml	0.865 g/ml	1.0 g/ml
830.7370 Dissociation Constant in water	As a cationic quaternary ammonium salt, it will completely ionize in an aqueous solution.			
830.7550 Partition coefficient (*n*-octanol/ water) Log *K*ow	4.90 (EPI Suite v4.1)	2.93(EPI Suite v4.1)	5.39(EPI Suite v4.1)	1.95 (EPI Suite v4.1)

Guideline No. Physical and Chemical Properties	1-Octadecanaminium, N,N-dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	1-Tetradecanaminium, N, N dimethyl-N-[3-(trimethoxysilyl) propyl]-, chloride	N,N-Didecyl-N-methyl-3-(trimethoxysilyl) propanaminium chloride	1-ocatdecanaminium-N,N-dimethyl-N-[3-(trihydroxysilyl) propyl]-chloride
830.7840 Solubility in water	At room temperature, the product is miscible in all proportions with water.			
830.7950 Vapor pressure	5.8×10^{-14} mm Hg at 25°C (EPI Suite v4.1)	1.74×10^{-12} mm Hg at 25°C (EPI Suite v4.1)	2.46×10^{-14} mm Hg at 25°C (EPI Suite v4.1)	1.85×10^{-21} mm Hg at 25°C (EPI Suite v4.1)

1.4 Use/Usage Description

1.4.1 Registrations

There are 39 products containing 1-Octadecanaminium, N,N-dimethyl-N-(3-(trimethoxysilyl) propyl)-chloride (PC Code 107401) as an active ingredient. The percent active ingredient (ai) ranges from 0.5 percent to 84 percent and the formulations include liquid, soluble concentrate and ready to use solution. There are 17 products containing 1-Octadecanaminium, N,N-dimethyl-N-[3-(trihydroxysilyl)propyl], chloride (PC Code 107403) as an ai. The percent ai ranges from 0.75 percent to 35.6 percent and the formulations include liquid, soluble concentrate, flowable concentrate and ready to use solution. There is currently one product containing 1-Tetradecanaminium, N,N-dimethyl-N-[3(trimethoxysilyl)propyl]-, chloride (PC Code 107409) as an ai. The percent ai is 40 percent and is a liquid formulation. There is currently one active product containing 1-Decanaminium, N-decyl-N-methyl-N-(3-(trimethoxysilyl)propyl)-, chloride (PC Code 169160) as an ai. The percent ai is 42 percent and it is a liquid formation.

1.4.2 Summary of Registered Uses

Table 5 presents a summary of the registered uses of trimethoxysilyl QACs that will be assessed in this registration review. Trimethoxysilyl QAC products can be applied using the following application methods: fogger, pump sprayer, pressure sprayer, trigger spray bottle, dip treatment, brush treatment, sponge treatment, pad surface treatment, foam applicator, washing machine, vat soak, mechanical mixer, carpet steam cleaner, open pour, painting with brush/roller and airless sprayer, and placement of treated sponges for nonpotable water treatment.

Table 5 - Summary of Trimethoxysilyl QAC Registered Uses

Use	Application Method	Application Rate (ai/wt of material, w/w)
Surface treatment of indoor nonfood contact organic and inorganic materials in homes and in commercial, industrial and institutional facilities such as wood, tile, glass, stone, bath rooms, floors, window sills, kitchens, *etc.*	Fogger, pressure sprayer, pump-up sprayer, carpet steam cleaner, dip treatment, brush, foaming apparatus, pad, trigger spray bottle	1,000-10,000 ppm
Surface treatment of outdoor building materials including roofing and exterior walls made of wood, stone, brick, metal, tile, *etc.*	Pressure sprayer, pump-up sprayer, dip treatment, pad, brush, foaming apparatus	1,000-10,000 ppm
Preservative treatment by incorporating into material during manufacture of paints, coatings, lattices, plastics, rubbers, grouts, mastics, emulsions, *etc.*	Mechanical mixer (open pour)	1,000-10,000 ppm
Textiles, fibers, and cordage in raw form or finished including fabrics, diapers, sheets, rugs, draperies, clothing, tents, rope, shoes, face gear, sails, upholstery, *etc.*	Pressure sprayer, pump-up sprayer, dip treatment, pad, brush, foaming apparatus, washing machine, carpet steam cleaner	1,000-10,000 ppm
Concrete (added in water when mixing concrete)	Mechanical mixer (open pour)	1,000-10,000 ppm
Surfaces and fabrics in automobiles, taxis, recreational vehicles, *etc.* including tires	Pressure sprayer, pump-up sprayer, dip treatment, pad, brush, foaming apparatus	1,000-10,000 ppm
Air filters and materials, nonfood conveyor belts	Pressure sprayer, pump-up sprayer, dip treatment, pad, brush, foaming apparatus	1,000-10,000 ppm
Commercial and residential paints	Brush/roller and airless sprayer	1,000-10,000 ppm

1.4.3 Usage Information

Usage information is not available for the trimethoxysilyl QACs. The Kline Biocides Report for 2004/2005 (Kline, 2005) does not include the trimethoxysilyl QACs.

1.5 Regulatory History

The trimethoxysilyl QACs are registered as bacteriostatic, algaestatic, and fungistatic compounds. The first products containing1-Decanaminium, N-decyl-N-methyl-N-[3-(trimethoxysilyl] propyl)-, chloride as an ai were registered in 1960. The first products containing 1-Octadecanaminium, N, N-dimethyl-N-[3(trimethoxysilyl) propyl]-, chloride as an ai were registered in 1992. The first products containing 1-Octadecanaminium-N, N-dimethyl-N-[3-(trihydroxysilyl) propyl]-chloride as an ai were registered in 2003. The first products containing 1-Tetradecanaminium, N, N-dimethyl-N-[3(trimethoxysilyl) propyl]-, chloride as an ai were registered in 2006.

The agency completed a Reregistration Eligibility Decision (RED) for Trimethoxysilyl Quaternary Ammonium Chloride in 2007. The post-RED data call-in (DCI) has not yet been issued.

1.5.1 Recent/Pending Regulatory Actions

There are no recent or pending regulatory actions for trimethoxysilyl QAC. EPA anticipates issuing the post-RED data call-in (DCI) in the near future.

1.5.2 Tolerance Information

EPA has not established a tolerance or tolerance exemption for residues of the trimethoxysilyl QACs in food. In addition, the Food and Drug Administration (FDA) has not established a food additive regulation and has not received a Food Contact Substance Notification for these compounds.

1.6 Incidents

1.6.1 Human Health

No trimethoxysilyl QAC human poisoning incidents have been reported in OPP's Incident Data System (IDS) from 1992 to the present.

1.6.2 Ecological

No trimethoxysilyl QAC ecological incidents have been reported in OPP's Incident Data System (IDS) from 1992 to the present.

2 Anticipated Data Needs

Table 6 presents a summary of the data anticipated as being needed to support this registration review.

Table 6 - Studies Anticipated to be Needed for the Registration Review of Trimethoxysilyl QACs

GLN	Study Name	Test Substance	Time Frame (Months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Studies Anticipated to be Required through the Registration Review DCI						
Special Study[1]	Special leaching study from roofing shingles and fascia board	TGAI[2]	12	Environmental fate	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
835.1230[3]	Leaching-adsorption-desorption (batch equilibrium)	TGAI[2]	12	Environmental Fate	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
835.4100[3]	Aerobic soil metabolism	TGAI[2]	12	Environmental Fate	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
835.4400[4]	Anaerobic aquatic metabolism	TGAI[2]	12	Environmental Fate	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
Special study	Whole sediment chronic toxicity, freshwater invertebrate (2 species: an amphipod[5]and a chironomid[5])	TGAI[6]	12	Ecological	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
Special study	Whole sediment chronic toxicity, marine invertebrate (an amphipod[7])	TGAI[6]	12	Ecological	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
850.4400 850.4550	Aquatic plant toxicity (non-vascular) 4 species: green algae, freshwater diatom[8], saltwater diatom[8], and a cyanobacteria[8]	TGAI[6]	12	Ecological	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
850.4500	Aquatic plant toxicity (vascular)	TGAI[6]	12	Ecological	Exterior surfaces (e.g., Treated shingles, walls, and fascia board)	Transport to the aquatic environment
870.3465	90-day inhalation toxicity study	TGAI	24	Occupational and Residential	Indoor and outdoor use sites treated such that respirable aerosols are likely to be generated	All scenarios below involving inhalation exposures (see 875.1300/875.1400).

GLN	Study Name	Test Substance	Time Frame (Months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
875.3700b[9]	Developmental Toxicity in Rabbits	TGAI	24	Dietary (drinking water)	Exterior surfaces (e.g., Treated shingles and fascia board)	Dietary exposures from drinking water.
870.3800[9]	Two-gen reproductive toxicity study	TGAI	24	Dietary (drinking water)	Exterior surfaces (e.g.,Treated shingles and fascia board)	Dietary exposures from drinking water.
875.1300 875.1400	Outdoor or Indoor Exposure, Inhalation	TGAI	24	Occupational and Residential	Indoor and outdoor uses[10]	Trigger pump sprayer, low pressure hand wand, high pressure hand wand, hand-held fogger, open pour, painting with brush/roller and airless sprayer.
875.1700	Product Use Information	TGAI	12	Occupational and Residential	All	All above scenarios.
Studies Expected to be Required through the Anticipated Post-RED DCI						
850.1010	Aquatic invertebrate acute toxicity, test, freshwater daphnids	TGAI	12	Ecological	Outdoor	Transport to the aquatic environment
850.1075	Fish acute toxicity test, freshwater and marine	TGAI	12	Ecological	Outdoor	Transport to the aquatic environment

[1] Residues in treated shingles may leach upon contact with rainwater. Because the label (53053-8) is not specific about the types of shingles to be treated, results from each potential treatment material (*i.e.*, asphalt, wood, *etc.*) are expected to be required to be submitted as well as results for wood used for fascia board. If the leaching data from treated roofing shingles and fascia board in this study indicate limited environmental exposure, then certain other anticipated environmental fate data requirements (GLN 835.1230, GLN 835.4100, GLN 835.4400, GLN 875.3700b, and GLN 870.3800) may be waived.

[2] Analytical monitoring would include both the parent and its alkyl quaternary ammonium degradate.

[3] Leached residues in treated shingles and fascia board may leach and move across lawns, where they have the potential for sorption and degradation in surface soil (835.1230). If the anticipated required soil/sediment sorption data indicate limited environmental exposure, then anticipated data needs for aerobic soil metabolism (835.4100) may be waived. Aerobic soil metabolism (835.4100) represents the sum of hydrolysis and microbial degradation in surface soil that is non-flooded and oxygenated.

[4] Anaerobic aquatic metabolism represents the fate of a compound in suspended and bottom sediment in water bodies. If leaching from treated roof shingles and fascia boards is minimal and sorption to soil and sediment indicates limited release into water, then anticipated data needs for anaerobic aquatic metabolism (835.4400) may be waived.

[5] EPA has published the following guidance: Methods for Measuring the Toxicity and Bioaccumulation of Sediment-Associated Contaminants with Freshwater Invertebrates, EPA 600/R-99/064 available on-line at http://water.epa.gov/polwaste/sediments/cs/freshfact.cfm.

[6] TGAI will rapidly form an alkyl quaternary ammonium group and insoluble silyl compounds by hydrolysis. Documentation of stable concentrations during study should be on the alkyl quaternary ammonium portion, not the parent.

[7] EPA has published agency-wide guidance: Method for Assessing the Chronic Toxicity of Marine and Estuarine Sediment-associated Contaminants with the Amphipod *Leptocheirus plumulosus* EPA 600/R-01/020 available on-line at http://water.epa.gov/polwaste/sediments/cs/leptofact.cfm.

[8] If the anticipated testing shows green algae, *Selenastrum capricornutum* IC_{50} and NOEC for trimethoxysilyl QACs are greater than 1.0 ppm or mg/L then anticipated aquatic plant testing for the freshwater diatom (*Navicula pelliculosa*), estuarine/marine diatom (*Skeletonema costatum*), and cyanobacteria (*Anabaena flos-aquae*) may be waived.

[9] If the anticipated environmental fate studies reveal that human exposure via drinking water is negligible, this anticipated data requirement may be waived.

[10] See Table 7 for specific exposure scenarios.

3 Human Health Risk Assessment

The agency anticipates the need to conduct a human health risk assessment for trimethoxysilyl QACs. The agency expects to require additional data for use in conducting the registration review (see Table 6).

3.1 Existing Toxicological Endpoints

EPA has not previously identified toxicological endpoints of concern for trimethoxysilyl QACs. The studies anticipated as being required through this registration review will allow the agency to establish the endpoints necessary to conduct risk assessment.

3.2 Dietary Exposure

3.2.1 Food

Human dietary exposure to trimethoxysilyl QAC residues is not expected to occur as there are no registered food uses. Approved uses involve preservation of materials and treatment of surfaces not intended for food contact. In addition, there are no oral hazard endpoints of concern identified. Residue chemistry data are not expected to be needed. Because dietary (food) exposure is not expected, dietary risk assessments reflecting exposures to trimethoxysilyl QACs in food are not expected to be conducted.

3.2.2 Drinking Water

EPA anticipates revisiting the need to conduct a drinking water assessment based on the results of the environmental fate and toxicity studies anticipated as being required to support this registration review. As noted above, the trimethoxysilyl QACs are registered for preservation of materials and treatment of surfaces. Due to the potential for trimethoxysilyl QACs to leach into water from treated materials and surfaces, there may be human exposure via drinking water. Treated materials and surfaces must be dried prior to their use which generally precludes pesticide residues from going down-the-drain. The trimethoxysilyl QACs form stable polymers that are also covalently bonded to the treated material (see Appendix B). Although some degradation and/or leaching from the treated material/surface may occur over time, the extent of such leaching is unknown. For this reason, environmental fate studies including two leaching studies, aerobic soil metabolism and anaerobic aquatic metabolism have been identified as being anticipated to be needed to support this registration review. No residue chemistry data are expected to be needed to characterize drinking water exposures. However, depending on the outcome of the anticipated environmental fate studies and toxicity studies (if needed based on environmental fate studies) that become required, an oral hazard endpoint of concern may be identified. If the anticipated environmental fate studies (particularly leaching) that become required indicate that contamination of drinking water is unlikely, the two toxicity studies may be waived. If there is an oral hazard of concern and if exposure to trimethoxysilyl QACs in drinking water is expected based on the new studies, a dietary drinking water risk assessment will be warranted.

3.3 Occupational and Residential Exposures

The agency anticipates the need to conduct occupational and residential assessments to support this registration review. Uses of trimethoxysilyl QACs that may result in occupational handler and residential handler/post application exposure are presented in Table 7. At the time of the RED, there were no toxicological endpoints of concern based on the review of the hazard data set. As a result, occupational and residential risk assessments were not conducted to support the RED. Dermal risk assessments were not conducted for short-, intermediate-, or long-term exposure based upon the lack of any adverse systemic effects resulting from doses up to and including a limit dose (1000 mg/kg) from an adequate dermal toxicity study. Although adverse systemic effects were not observed via other routes of exposure (*i.e.*, inhalation and incidental oral ingestion), the RED noted that the hazard database for these and other routes of exposure (*e.g.*, dietary) was incomplete and not well characterized.

For registration review, the agency does not anticipate the need to conduct a dermal risk assessment or an incidental oral ingestion toddler assessment. This is due to the lack of adverse systemic effects in adequate oral developmental toxicity and dermal toxicity studies at doses up to and including a limit dose of 1000 mg/kg/day in both studies. However, the agency cannot at this time adequately determine inhalation risks to handlers due to the lack of an inhalation toxicity study as well as inhalation exposure studies reflecting scenarios likely to generate aerosols such as fogging or painting with a brush/roller and an airless sprayer. Therefore, the likely occupational and residential inhalation exposure scenarios for which risk assessments are needed have been identified in Table 7.

The agency expects occupational and residential handler inhalation exposure from aerosolized sprays. Aerosolized spray may occur from treating textiles, carpets, roofing materials, tents, mattress pads, bathrooms, *etc.* via trigger pump spray, pressure sprayer, or fogging. Paint application using an airless sprayer and paint brush/roller would also generate aerosols. The RED specified that the fogging use was to be removed from labels. However, a fogging use still remains on some EPA-approved labels (*e.g.*, EPA Reg. Nos. 75174-2 and 83019-2). Unless labels are amended to remove the fogging use from their labels prior to risk assessment, the agency intends to assess fogging use. Finally, the agency plans to assess inhalation exposure via open-pour, dipping, soaking and brushing applications as well. Occupational and residential inhalation postapplication exposure is expected to be negligible since the vapor pressures of the trimethoxysilyl QACs are very low (all less than 1E-12 mm Hg) (EPA, 2012).

Residential postapplication exposure of toddlers may occur via mouthing treated surfaces or clothing and toys made out of treated fabric. However, as no adverse effects were observed in either maternal or offspring rats in an oral developmental toxicity study at a limit dose of 1000 mg/kg/day, toxicity via the oral route of exposure is very low; therefore, this scenario is not expected to be assessed (EPA, 2007). A listing of trimethoxysilyl QAC exposure scenarios that will need to be assessed for registration review is included in Table 7.

Table 7 - Occupational and Residential Exposure Scenarios for Trimethoxysilyl QACs

Scenario	Exposure Route(s)	Duration
Occupational Exposures		
Applying antimicrobial surface treatment using low pressure sprayer, trigger sprayers, sponge, brush and handheld fogger.	Inhalation	Short and Intermediate Term
Applying paints (containing in-can preservatives) using paint brush/roller and airless sprayer.	Inhalation	Short and Intermediate Term
Open pouring preservatives during manufacture of materials, dip treatments, concrete mixing, *etc.*	Inhalation	Short and Intermediate Term
Residential Exposures		
Applying antimicrobial surface treatment to hard surfaces, carpets, clothing, floors using low pressure sprayer, trigger sprayer, sponge, brush and handheld fogger.	Inhalation	Short and Intermediate Term
Applying paints (containing in-can preservatives) using paint brush/roller and airless sprayer.	Inhalation	Short and Intermediate Term

3.4 Aggregate and Cumulative Exposure

3.4.1 Aggregate Exposures

The agency anticipates conducting an aggregate assessment. Upon review of the required toxicity and exposure studies as well as reevaluation of existing studies, human exposure assessments via various sources and routes will be assessed for this registration review case. Any exposures expected to co-occur will be aggregated.

3.4.2 Cumulative Exposures

The agency does not intend to conduct a cumulative risk assessment. With respect to cumulative exposure, unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to the trimethoxysilyl QACs and any other substances and the trimethoxysilyl QACs do not appear to produce a toxic metabolite produced by other substances. For the purposes of

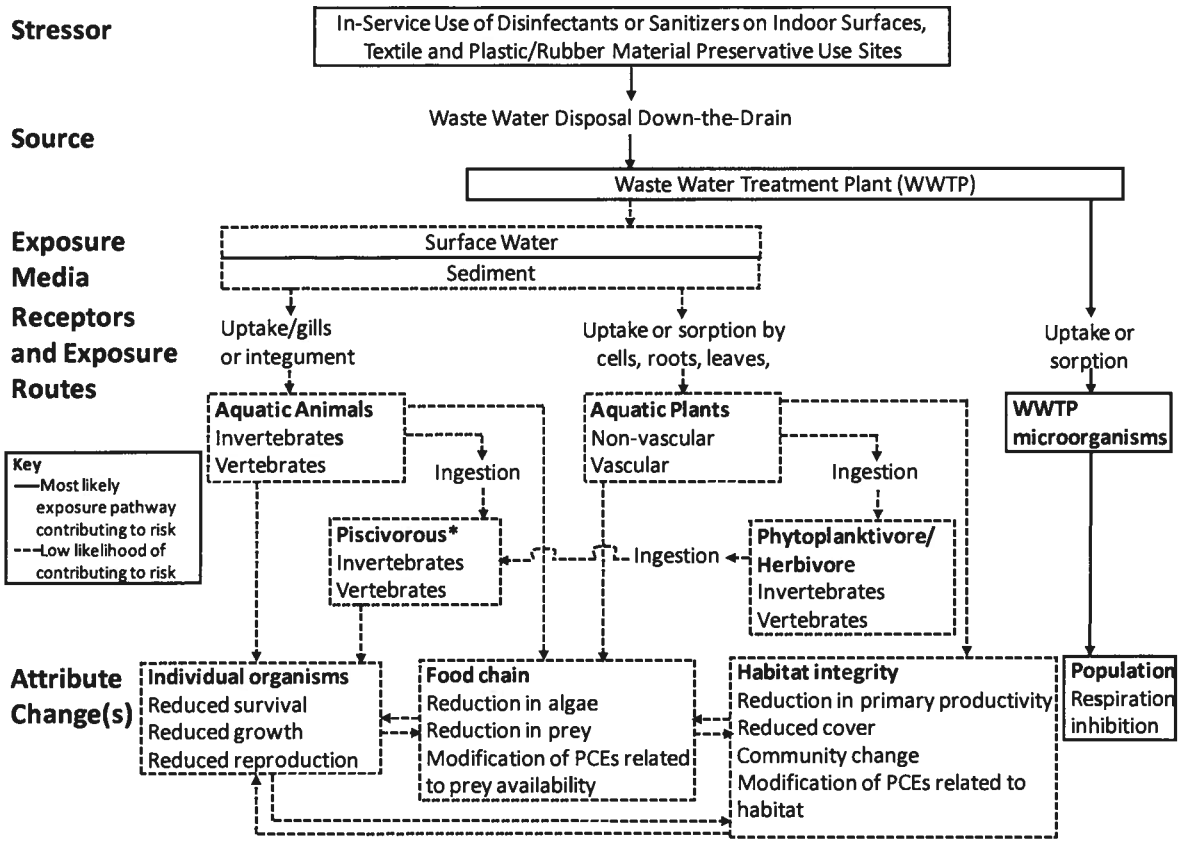
this registration review, therefore, EPA has not assumed that the trimethoxysilyl QACs have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs at http://www.epa.gov/pesticides/cumulative/.

4 Environmental Risk Assessment

The agency has not conducted an environmental risk assessment that supports a complete endangered species determination for the trimethoxysilyl QACs. Outdoor applications of the trimethoxysilyl QAC to exterior walls, sidewalks, roofing and siding may result in movement of the ai into the aquatic environment and exposure of terrestrial organisms. Because the material will quickly sorb to aquatic sediment and is stable, benthic organisms may be additionally exposed via sediment contact and ingestion. The risk assessment planned during registration review will allow the agency to determine whether the use of these trimethoxysilyl QACs has 'no effect' or 'may affect' federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use 'may affect' a listed species or its designated critical habitat, the agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services), as appropriate.

4.1 Environmental Conceptual Model Exposure Pathways

Based on the chemical/physical properties and environmental fate studies (Appendix B) and the uses in Table 5, the agency has developed conceptual models for the environmental exposure to the trimethoxysilyl QACs and their degradates. Figure 1 contains the conceptual model for the environmental exposure from the indoor uses as a sanitizer and disinfectant, and uses as a material preservative in textiles and plastic/rubber manufacturing process. Figure 2 contains the conceptual models for the outdoor/exterior uses on walls, sidewalks, siding and roofing materials. For the indoor and material preservative uses in Figure 1, all lines except for WWTP exposure are dashed indicating that the only potential exposure from these use patterns is to waste water treatment plants (WWTPs) and other exposures are not expected. These use patterns have the potential for releases down-the-drain but releases from WWTPs to surface waters are expected to be highly unlikely due to sorption and precipitation occurring prior to reaching the WWTP and removal in biosolids at WWTPs (Appendix B). The highest potential environmental exposure is based on the spray-on application to exterior wall surfaces, siding and roofing materials, which can result in leaching and runoff across lawns, sidewalks, and driveways. Additionally, spray drift might result in off-site drift adjacent to the application site and some potential exposure of terrestrial organisms. For the outdoor uses in Figures 3, the agency assumes that all routes of exposure are possible except for ingestion and bioconcentration by aquatic organisms and long-range transport from spray drift. Because of its electric charge and cell membrane activity, the major hydrolysis degradate, alkyl quaternary ammonium cation, is not expected to bioconcentrate in fish.



*As used here this term refers to animals (terrestrial or aquatic) that eat not just fish but any aquatic animal (*e.g.*, amphibians, mollusks, crustaceans, *etc.*)

Figure 1 - Conceptual model for environmental exposure to trimethoxysilyl QACs and its major degradates from indoor uses as a sanitizer and disinfectant, textile and plastic/rubber material preservative.

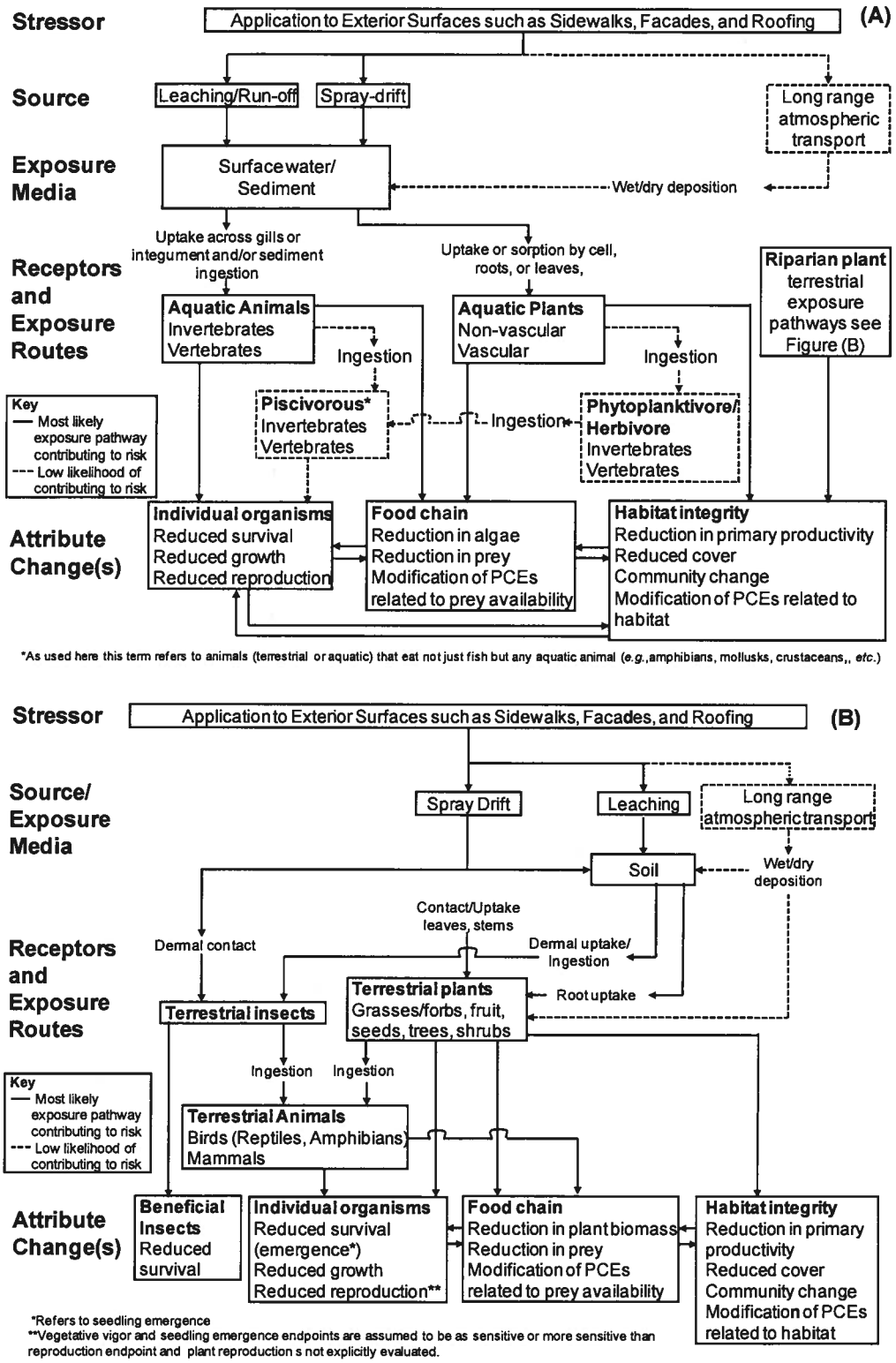


Figure 2 - Conceptual model for environmental exposure to trimethoxysilyl QACs and its major degradates from outdoor uses. (A) Aquatic exposure routes. (B) Terrestrial exposure routes.

4.2 Ecological Effects Assessment

Ecological effects data are used as measures of direct and indirect effects to aquatic and terrestrial organisms. Acute and chronic toxicity data from registrant-submitted studies conducted in accordance with the 850 OCSPP Harmonized Test Guidelines will be used to evaluate the potential direct and indirect effects of the trimethoxysilyl QAC to plants and animals. Relevant data from the open literature available in ECOTOX also may be used to evaluate potential direct and indirect effects.

4.2.1 Mode of Action

Like other quaternary ammonium compounds trimethoxysilyl QAC compounds are membrane-active agents, causing leakage of intracellular molecules leading to death.

4.2.2 Measures of Effect (Ecotoxicity Endpoints)

The available ecotoxicity data are summarized in Appendix C. The agency uses the most sensitive endpoints for assessing acute and chronic risks to each receptor group shown in conceptual models (Figures 1 and 3) to be evaluated in the risk assessment. Table 8 indicates the ecotoxicity data endpoints that will be used for the risk assessment and also indicates endpoints that are anticipated to be required but are not currently available.

Table 8 - Selected Endpoints and Data Gaps for Risk Assessment of Trimethoxysilyl QACs

Receptor Group	Test Material	Surrogate Species	Risk Scenario	Toxicity Endpoint	Source
Freshwater fish	TGAI[1]	Rainbow trout	Acute	96-h LC_{50} = 1.73 mg ai/L	MRID 41001120
			Chronic	Data waived[2]	NA
Freshwater invertebrates	TGAI[1]	Waterflea	Acute	48-h EC_{50} = 0.17 mg/L	MRID 00105187
			Chronic	Data required	NA
Estuarine/marine fish	TGAI[1]	Fish	Acute	Data waived[3]	NA
			Chronic	Data waived[3]	NA
Estuarine/marine invertebrates	TGAI[1]	Shrimp (mysid)	Acute	Data required	NA
			Chronic	Data waived[4]	NA
		Mollusk	Acute	Data required	NA
Benthic invertebrates	TGAI[1]	Freshwater (1 chironomid sp. and 1 amphipod sp.)	Chronic	Data required	NA
		Estuarine/marine (1 amphipod sp.)	Chronic	Data required	NA
Aquatic plants (nonvascular)	TGAI[1]	4 species[4]	IC_{50} and NOAEC	Data required for 4 species[5]	NA
Aquatic plants (vascular)	TGAI[1]	Duckweed	IC_{50} and NOAEC	Data required	NA
Birds	TGAI	Mallard	Acute	LD_{50} > 1590 mg ai/kg-bw	MRID 40385218

Receptor Group	Test Material	Surrogate Species	Risk Scenario	Toxicity Endpoint	Source
			Dietary	LC_{50} >5620 ppm ai	MRID 40385217
			Chronic	Data not required	NA
Mammals	TGAI	Lab. rat or mouse	Acute	LD_{50} >5000 mg ai/kg-bw	MRID 40385201
			Chronic	NOAEL >1000 mg ai/kg-bw/day	MRID 41339403

NA: not applicable

[1] Tested and expressed on TGAI basis but recognize that the compounds rapidly form an alkyl quaternary ammonium group and insoluble silyl compounds by hydrolysis.

[2] More sensitive freshwater species appears to be the invertebrate, *Daphnia magna*. Based on this relative toxicity and partitioning to sediment being the major exposure route, chronic testing with one species was considered sufficient to evaluate chronic risks to freshwater animals. Based on this relative toxicity and partitioning to sediment being the major exposure route data based on freshwater fish species was considered sufficient to characterize risk to estuarine/marine fish.

[3] Toxicity for other alkyl quaternary ammonium compounds (*e.g.*, DDAC and DDACB) show toxicity to estuarine/marine fish are comparable to freshwater species.

[4] Based on the non-specific mode-of-action and relative toxicity data for other alkyl ammonium compounds, chronic testing and the acute-to-chronic ratio derived from the freshwater invertebrate data will be used to characterize chronic risk for estuarine/marine invertebrates.

[5] A test with a freshwater diatom, an estuarine/marine diatom, green algae, and cyanobacterium are anticipated to be required. If the green algae study demonstrates detrimental effects do not occur at less than 1.0 ppm or mg/L, then the freshwater diatom, estuarine/marine diatom, and cyanobacteria data may be waived.

Freshwater Fish and Invertebrates

No additional data is required for freshwater fish. A chronic life cycle test for the daphnid is required because of the potential for chronic exposure from repeated applications and repeated rainfall events with associated leaching and runoff events. No chronic fish data is anticipated to be required because the more acutely sensitive freshwater taxon appears to be an invertebrate and given that sediment is expected to be the primary exposure route, chronic data for one species was considered sufficient. Chronic risks to freshwater fish will be put into context of the freshwater invertebrate data, and if further refinement or characterization is needed information based on the relative toxicity and acute-to-chronic ratio of other quaternary ammonium compounds can be used (*e.g.*, DDAC[3] and DDACB[4]).

Estuarine/Marine Fish and Invertebrates

No additional acute or chronic data is required for estuarine/marine fish. Toxicity for other alkyl quaternary ammonium compounds show toxicity to estuarine/marine fish are comparable to freshwater species (e.g., DDAC[3] and DDACB[4]). Because sediment is expected to be the primary exposure route for the use patterns of concern, data for freshwater fish was considered sufficient to characterize risk to estuarine/marine fish. Based on other quaternary ammonium compounds (e.g., DDAC[3] and DDACB[4]) and ecotoxicity models (Appendix C) for surfactants, mollusks may be more acutely sensitive to quaternary ammonium compounds than the other two required test species of a fish and a shrimp. An acute test with a mollusk is anticipated to be needed to assess risk.

[3] Didecyl dimethyl ammonium chloride, Case 3003, EPA docket EPA-HQ-OPP-2006-0338
[4] Didecyl dimethyl ammonium carbonate and bicarbonate Case 5014, EPA-HQ-OPP-2012-0651

Aquatic Plants

An algal Tier II study is expected to be required for three aquatic non-vascular species: one green algae (*Selenastrum capricornutum)*, one freshwater diatom (*Navicula pelliculosa)*, one estuarine/marine diatom (*Skeletonema costatum*), and one cyanobacteria *(Anabaena flos-aquae*) species. If the green algae results demonstrate that detrimental effects do not occur at less than 1.0 ppm (mg/L), then the freshwater diatom, estuarine/marine diatom, and cyanobacteria requirements would be waived. A Tier II study is expected to be required for one aquatic vascular species (*Lemna gibba*).

Sediment Toxicity

No data are available. Data are expected to be needed for freshwater and estuarine/marine benthic invertebrates potentially exposed in sediment, because any leachate transported to the aquatic environment from outdoor applications to roofing, facades, sidewalks and siding will sorb to aquatic sediment. The active ingredient is positively-charged and the sediment is negatively-charged. The negative electrical charge of the sediment will attract and sorb the positively-charged active ingredient.

Based on the half life of the hydrolyzed transformation product (quaternary ammonium group) being stable (*i.e.*, >10 days), chronic rather than acute sediment tests are expected to be required. For freshwater organisms, testing is expected to be required with 1 chironomid sp. and 1 amphipod sp. For estuarine/marine organisms, testing is expected to be required with 1 amphipod species.

4.3 Exposure Analysis Plan

4.3.1 Aquatic and Terrestrial Wildlife Exposure Estimates

Available OPP models will be used to derive aquatic exposure estimates (EECs) for use in the risk assessment. Models are available to provide EECs for leaching of trimethoxysilyl QACs from applications to roofing and siding and for down-the-drain estimates for uses that discharge into waste water treatment facilities. For other uses for which models are not available, exposure estimates cannot be quantified but will be considered subjectively.

4.3.2 Human Health Drinking Water Exposure Estimates

The agency does not expect significant contamination of drinking water because the trimethoxysilyl QACs form polymers that covalently bond to treated material and then degrade slowly to monomers (Green *et al*, 2011; de Buyl; see Appendix B). However, the rate of leaching from treated surfaces or materials is unknown. To determine the potential for human exposure to the trimethoxysilyl QACs via drinking water, leaching studies are anticipated to be required. Whether reproductive and developmental toxicity studies are required and whether a human drinking water assessment is conducted will depend on the outcome of the environmental fate studies

4.3.3 Screening Level Down-the-Drain Analysis

No screening Down-the-Drain analysis was conducted because releases of trimethoxysilyl QACs from WWTPs to the environment are not expected. Gorman (1995) shows a hydrolysis study conducted on 3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride (PC Code 107401) at pH 5, 7, and 9 that showed the half-lives of this chemical at all three pHs were very short: at pH 5, the half-life is 14.6 minutes; at pH 7, the half-life is 8 minutes, and at pH 9, the half-life is 3.8 minutes. Thus, hydrolytically, the trimethoxysilyl QACs are unstable and degrade within an hour. The degradation process would include the fissure of silyl moiety group from the rest of the trimethoxysilyl QACs, instantly converting into silicate (which precipitates out) and alkyl quaternary ammonium which will sorb to solids. The next step would be rapid degradation of alkyl groups (C_{10} to C_{14}) on the alkyl quaternary ammonium degradate and mineralization. Because of the inherent instability of the parent Trimethoxysilyl QACs and sorption (Appendix B) and biodegradation of the alkyl quaternary ammonium degradates, insignificant or no exposure to the parent or its toxic degradates will result from the down-the-drain exposure pathway.

4.4 Effects Analysis Plan

In addition to the required 850 OCSPP guideline studies, open literature studies will be identified through EPA's ECOTOXicology (ECOTOX) database[5]. This database employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The ECOTOX database will be searched for trimethoxysilyl QACs and alkyl quaternary ammonium compounds when the risk assessment for the trimethoxysilyl QACs is prepared. At that time, endpoints more sensitive than what is currently known will be reviewed from the open literature studies. Data from the ECOTOX run for the trimethoxysilyl QAC will be evaluated for possible quantitative and/or qualitative inclusion in the risk assessment in support of Registration Review.

5 Endocrine Disruptor Screening Program (EDSP)

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of the 2007 RED for the trimethoxysilyl QACs, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), trimethoxysilyl QAC is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

[5] http://cfpub.epa.gov/ecotox/ ECOTOX was created and is maintained by the USEPA, Office of Research and Development, and the National Health and Environmental Effects Research Laboratory's Mid-Continent Ecology Division.

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. Trimethoxysilyl QAC is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Accordingly, as part of registration review, EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for Trimethoxysilyl QAC.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

6 Guidance for Commenters

6.1 Preliminary Work Plan

The public is invited to comment on EPA's Preliminary Work Plan and rationale. The agency will carefully consider all comments as well as any additional information or data provided in a timely manner prior to issuing a final work plan for the trimethoxysilyl QAC registration review case.

6.1.1 Trade Irritants

Through the registration review process, the agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. The agency will work to harmonize tolerances and international maximum residue limits (MRLs) and may modify tolerance levels to do so, when possible. **Stakeholders are asked to comment** on any trade irritant issues resulting from lack of MRLs or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

6.1.2 Water Quality

Trimethoxysilyl QAC is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[6]. In addition, no Total Maximum Daily

[6] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

Loads (TMDL) have been developed for trimethoxysilyl QAC[7]. More information on impaired water bodies and TMDLs can be found at EPA's website[8]. **The agency invites submission of water quality data for this pesticide.** To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process*[9] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

6.1.3 Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to trimethoxysilyl QAC compared to the general population. **Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.**

6.1.4 Structure Activity Relationships

EPA must rely upon information of appropriate quality and reliability for each decision made by the agency. In the Office of Pesticide Programs (OPP), the evaluation process for a pesticide chemical traditionally begins with the applicant's submission of a set of studies conducted with the specific pesticide chemical of interest. The use of the results of such testing (measured data) is a logical, scientifically rigorous process that identifies the physical, chemical, and environmental fate properties of the pesticide, as well as the dose and endpoints at which an adverse effect can occur in various animal species.

Today, there is significant interest in alternative techniques, *i.e.*, techniques other than data generation that could significantly inform the agency's decision-making process. Recently, OPP has made increasing use of structure activity relationship (SAR) as part of its regulatory decision-making process. In the SAR process, a chemical's molecular structure is compared to that of other chemicals for which data are available. These structural similarities are then used to make predictive judgments about a chemical's physical, chemical, and biological properties. Thus, the chemical's physical, chemical, and biological properties are a function of (or directly related to) the chemical's molecular structure. Quantitative SAR is referred to as QSAR. To develop a QSAR, a selected set of measured data on a single physical, chemical, or biological property is used to derive a model (an equation) to predict the value of that property.

Since SAR assessments and QSAR modeling are another set of tools that are available to agency scientists, OPP has begun a process shift that envisions shifting from the current study-by-study approach to an approach in which the use of predicted data, generated using validated models, is

[7]http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[8] http://www.epa.gov/owow/tmdl/
[9] http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm

considered along with information from open literature and studies specifically generated under Part 161 requirements. All relevant information would be considered as part of a weight-of-the-evidence evaluation.

At this time, EPA believes that for certain endpoints, especially physical/chemical and fate properties, that SAR and QSAR might be effectively utilized to fulfill these data requirements for many antimicrobial pesticide chemicals. When considering biological properties, at this time, EPA believes that SAR and QSAR can be most effectively utilized in the evaluation of chemicals that exhibit lower toxicity for human health and/or ecotoxicity parameters. This is appropriate because the risk assessment for lower toxicity chemicals can be stream-lined, *i.e.*, a screening-level assessment procedure rather than multiple tiers of assessments with progressively more data requirements.

If stakeholders believe that submission of predicted data can fulfill one of the data needs for the Trimethoxysilyl QAC Case, then the agency invites submission of this information. The submitter would be expected to supply a rationale describing the utility of the information and provide documentation on the scientific validity of the information. The determination that the predicted data fulfills the data requirement would be at the sole discretion of the agency. Pre-submission consultation with the agency is encouraged.

6.1.5 Additional Information

Stakeholders are also specifically asked to provide available information and data that will assist the agency in refining its risk assessments, including any species-specific ecological effects determinations. The agency is interested in receiving the following information:

1. Confirmation on the following label information:
    A. Sites of application
    B. Formulations
    C. Application methods and equipment
    D. Maximum application rates
    E. Frequency of application, application intervals and maximum number of applications
    F. Geographic limitations on use
2. Use or potential use distribution
3. Use history
4. Usage/use information for non-agricultural uses (*e.g.*, materials preservation)
5. Typical application interval
6. State or local use restrictions
7. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the agency
8. Monitoring data

7 Next Steps

After the 60-day comment period closes in May 2013 the agency will review and respond to any comments received in a timely manner, and then issue a Final Work Plan for the Trimethoxysilyl QAC case.

8 References

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Appendix A Toxicology Profile

Acute Toxicity for Product Labeling

As listed in Table 9, acute toxicity data for a 50% formulation of 3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride show low acute toxicity for single exposures by the oral, dermal, and inhalation routes (Categories IV, III, and IV respectively). However, severe acute toxicity is observed with respect to skin and eye irritation of this active ingredient.

Table 9 - Acute Toxicity Studies for Trimethoxysilyl QACs

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100 (81-1)	40385201	Oral LD_{50} > 5000 mg/kg	IV
870.1200 (81-2)	40385201	Dermal LD_{50} > 2000 mg/kg	III
870.1300 (81-3)	Not Available	Inhalation LC_{50} > 2.0 mg/L (1 Hour)	IV
870.2400 (81-4)	403385201	Severe irritant to ocular tissue	I
870.2500 (81-5)	Not Available	Severe irritant to skin	I
870.3250	41339403	Dermal and Systemic NOAEL > 1000 mg/kg/day	Acceptable
870.3100	46280411	NOAEL ≥ 240 mg/kg/day (HDT)	Acceptable
870.3700	41438003	Maternal and Developmental NOAEL ≥ 1000 mg/kg/day	Acceptable
870.5100	46280412	No evidence of mutagenicity	Acceptable
870.5300	46280413	No evidence of mutagenicity	Acceptable
870.5375	46280414	No association with the induction of structural chromosomal aberration	Acceptable
	41296803	No evidence of compound inducted cytotoxicity	Acceptable

Subchronic Toxicity

There is one rat 90-day dermal study (MRID 41339403) in the toxicology database and this study is summarized below. In the 90-day subchronic dermal toxicity study, groups of 10 male and 10 female Sprague-Dawley rats were treated with 3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride (81.08%, Lot No. BN029263) at doses of 0, 100, 500, or 1000 mg/kg/day (doses based on range-finding study MRID 41339402). A vehicle control group was treated with 1000 mg/kg/day propylene glycol and an additional sham control group was

included in the study. Animals were treated by dermal occlusion for 6 hours/day, 5 days/week for 90 days. There were no treatment-related deaths or signs of systemic toxicity and no treatment-related effects on body weight, food consumption, hematology, and clinical chemistry.

Developmental Toxicity

In a developmental toxicity study in rats (MRID 41438003), 3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride (81.08% ai, in corn oil) was administered by gavage to pregnant Sprague-Dawley rats (25/sex/dose) on days 6 through 15 of gestation at dose levels of 0, 100, 300, and 1000 mg/kg/day. Group mean liver weight was increased 6% in maternal animals at 1000 mg/kg/day compared to vehicle control. There was no significant treatment related effect on body weights or food consumption in maternal animals. There were no significant treatment related effects on cesarean section observations or on the incidence of fetal skeletal or soft tissue malformations or variations at any dose level. Although maternal liver weight was increased by 7% at the 1000 mg/kg/day dose, this effect was not accompanied by any other signs of liver toxicity, and is thus not considered treatment-related. The maternal NOAEL is considered to be ≥1000 mg/kg/day, and the Maternal LOAEL is >1000 mg/kg/day. The developmental toxicity NOAEL is considered to be ≥1000 mg/kg/day, and the developmental toxicity LOAEL is >1000 mg/kg/day. This study is classified as acceptable and satisfies the guideline requirement (870.3700) for a developmental toxicity study in rats.

This rat study was the only developmental toxicity study available for the trimethoxysilyl QACs. Although no evidence of increased susceptibility of offspring was observed following in utero exposure up to and including a limit dose (1000 mg/kg/day), an additional developmental study in another species is anticipated to be needed to characterize the hazard of the trimethoxysilyl QACs potentially associated with chronic dietary exposure via drinking water. However, if the environmental fate studies (particularly leaching) that are anticipated to be required indicate that contamination of drinking water is unlikely, the second developmental toxicity study anticipated to be required may be waived.

Reproductive Toxicity

There is no reproductive toxicity study available. However, such a study is required to support uses that may result in human exposure via food or drinking water. As there is the potential for drinking water exposure to the trimethoxysilyl QACs, a two-generation reproductive toxicity study is anticipated to be needed for registration review. However, if the environmental fate studies (particularly leaching) that are anticipated to be required indicate that contamination of drinking water is unlikely, the reproductive toxicity study anticipated to be required may be waived.

Chronic Toxicity

No chronic toxicity studies are available, but none are needed. The database for chronic toxicity is adequate given the limited potential for chronic or long-term human exposures based on the approved uses of the trimethoxysilyl QACs.

Carcinogenicity

There is no carcinogenicity study available, but none is needed. There are no concerns for carcinogenicity for the trimethoxysilyl QACs based on the results of the mutagenicity studies and the lack of any systemic toxicity being observed in studies comprising the existing toxicity database; therefore, no carcinogenicity study is required.

Mutagenicity

The mutagenicity of the trimethoxysilyl QACs is fully characterized. For all of the compounds covered under this RED, there are a total of four acceptable mutagenicity studies, all of which demonstrate that the trimethoxysilyl QACs are negative for mutagenicity.

Appendix B Environmental Fate

Environmental Fate Properties

Environmental fate data reflecting testing of any trimethoxysilyl QACs were used as surrogate for all other trimethoxysilyl QACs because they are all expected to exhibit very similar behavior. The trimethoxysilyl QACs form stable polymers that are covalently bonded to the treated material and then degrade slowly to monomers (Green *et al*, 2011 and de Buyl). However, the rate of leaching from treated surfaces or materials is unknown. In water, any monomers will degrade quickly to the quaternary amine portion (active and water soluble) and the other silyl portion (inactive and insoluble) with half-lives of <1 hour (MRID 43811201). Sorption of the cationic portion of the molecule to soil and sediment will be the primary route of dissipation because soil and sediment are negatively-charged and opposite electrical charges attract. The silyl portion of the molecule will become part of the soil and sediment matrices because of their high silica content. As a result, the only significant aquatic exposure is likely to be in the bottom sediment with minimal water column exposure.

As a result of this rapid hydrolysis, the environmental exposure in surface water from WWTPs is based on the extent of sorption of the quaternary ammonium degradates to sludge. Three of the 4 compounds have estimated removal efficiencies of 82-90 % and one (PC Code 107409) has an estimated percent removal efficiency of 7.6 % (EPI-Suite 4.1).

Trimethoxysilyl QAC monomers will completely ionize in water at environmental pH values, and volatility and bioconcentration are expected to be minimal. A pKa is the pH in water where 50% of the compound is ionized and 50% is not ionized. The extent of ionization increases as the pH drops and decreases as the pH increases. Volatility from soil or water is not expected based on the vapor pressure and Henry's Law Constants of 1.85×10^{-21} to 1.74×10^{-12} mm Hg and 1.1×10^{-25} to 1×10^{-16} atm•m^3 mol^{-1}, respectively. Bioconcentration of the active portion will not be significant because of its removal in wastewater treatment plants by sludge sorption and the inactive portion will partition to sediment immediately.

Leaching from treated swimming pool and spa filters was not detected (LOD=49-60 ug/l). The treated media included sand, zeolite, and plastic fabric mesh (MRIDs 48851903, 47652806).

Appendix C Ecotoxicology Profile

Toxicity to Terrestrial Receptors

Avian acute-oral and dietary toxicity

There is one available avian acute oral study with a mallard duck and four avian dietary studies testing two species the mallard and Northern bobwhite quail. The available acute-oral and dietary toxicity studies categorize the trimethoxysilyl QAC as being practically nontoxic to birds (Table 10).

Table 10 – Avian Toxicity

Test Species	Test Material (% ai)	Toxicity	Toxicity Category	Source
Mallard (*Anas platyrhynchos*)	Trimethoxysilyl QACs (42%)	LC_{50} >5620 ppm (diet)	Practically nontoxic	MRID 40385217
		LD_{50} >1590 mg ai/kg bw	Not determined – but no more than slightly toxic	MRID 40385218
		LC_{50} >5620 ppm (diet)	Practically nontoxic	MRID 40385217
Northern bobwhite (*Colinus virginianus*)		LC_{50} > 5620 ppm (diet)	Practically nontoxic	MRID 40770106
		LC_{50} > 5620 ppm (diet)	Practically nontoxic	MRID 40385217

Mammals

The trimethoxysilyl QACs are practically nontoxic to small mammals (LD_{50} >5000 mg ai/kg). No chronic effects have been reported (NOAEL >1000 mg ai/kg/day). See Appendix A for more information on all available mammalian toxicity studies.

Nontarget Insects

Nontarget insect data are not required for the current use patterns.

Toxicity to Aquatic Receptors

Freshwater Fish

There are three available acute studies Appendix C categorize the trimethoxysilyl QACs as being moderately toxic to freshwater fish (LC_{50}s = 1.73 to 1.75 mg ai/L). Chronic data are not required because the trimethoxysilyl QACs will quickly sorb to aquatic sediment which minimizes the potential for chronic exposure in the water column.

There are three available acute studies The available acute toxicity studies categorize the trimethoxysilyl QAC as being moderately toxic to freshwater fish (Table 11). No chronic data are available.

Table 11 – Acute toxicity to freshwater fish

Test Species	Test Material (% ai)	Toxicity Endpoint (mg ai/L)	Toxicity Category	Source (MRID)
Rainbow Trout (*Oncorhynchus mykiss)*	Trimethoxysilyl QACs (42%)	96-hr LC_{50} = 1.73	Moderately toxic	41001120
		96-hr LC_{50} = 1.75	Moderately toxic	00105187
		96-hr LC_{50} = 1.75	Moderately toxic	00105187

Freshwater Invertebrates

There are three available acute studies for the waterflea (Table 12); these categorize the trimethoxysilyl QACs as being highly toxic to freshwater invertebrates (LC_{50}s = 0.17 to 0.19 mg ai/L). No chronic data are available.

Table 12 – Acute toxicity to freshwater invertebrates

Test Species	Test Material (% ai)	Toxicity Endpoint (mg ai/L)	Toxicity Category	Source (MRID)
Waterflea (*Daphnia magna*)	Trimethoxysilyl QACs (42%)	48-hr EC_{50} = 0.18	Highly toxic	41001120
		48-hr EC_{50} = 0.19	Highly toxic	00105187
		96-hr EC_{50} = 0.17	Highly toxic	00105187

Estuarine/Marine Fish and Invertebrates

No acute or chronic data are available.

Aquatic Plants

No data are available available.

Sediment Toxicity

No data are available.

Table 13 – Modeled toxicity data for alkyl quaternary ammonium surfactants

Endpoint	Mono alkyl quaternary ammonium compounds[1]		Di alkyl quaternary ammonium compound[1]	1-Decanaminium, N-decyl-methyl-N-[3-(trimethoxysilyl) propyl]-, chloride[1,2]	
	(C<16)	(C 18)	Avg 10 C chain	Silanes (alkoxy)	Neutral Organic SAR

Acute freshwater fish (96-h LC_{50} ppm)	1.778	2.10	53.7	0.090*	0.032*
Acute daphnia (48-h EC_{50} ppm)	1.778	2.692	5.8	4.95*	0.029*
Acute mollusk (EC_{50})	--	1.01	--	--	--
Green algae (96 hr EC_{50})	--	--	--	0.976*	0.119*
Fish Chv				0.0019	0.005*
Daphnia Chv				0.004*	0.009*
Green algae Chv				0.998*	0.080*

* Chemical may not be soluble enough to measure this predicted effect.

Chv (chronic value) from these models are equivalent to the maximum allowable toxicant concentration (MATC) which is equivalent to the geometric mean of the NOEC and LOEC. Since the NOEC is used in the agency's pesticide risk assessment, these values will underestimate risk as compared to the use of an NOEC.

[1] ECOSAR v1.1.1 surfactant special case.

[2] The more toxic of the four trimethoxysilyl QACs.