UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

July 31, 2006

ACTION MEMORANDUM

SUBJECT: Inert Reassessments: Three Exemptions from the Requirement of a Tolerance for Alkyl Sulfates

FROM: Pauline Wagner, Chief Pauline Wagner 7/31/06
Inert Ingredient Assessment Branch
Registration Division (7505P

TO: Lois A. Rossi, Director
Registration Division (7505P)

I. FQPA REASSESSMENT ACTION

Action: Reassessment of three inert ingredient exemptions from the requirement of a tolerance. Current exemptions are to be maintained.

Chemical: See Table 1 below

Table 1. CFR Citation, CAS Registry Numbers and CAS Index Name for Alkyl Sulfates

40 CFR	Inert Ingredient	Limits	Uses	CAS Reg. No. and 9CI Names
180.910[a]	Alkyl (C_{8-18}) sulfate and its ammonium, calcium, isopropylamine, magnesium, potassium, sodium and zinc salts	None	Surfactants	(See Appendix A)
	Sodium salt of sulfated oleic acid		Surfactants; related adjuvants, of surfactants	None
180.930[b]	Alkyl (C_{8-18}) sulfate and its ammonium, calcium, magnesium, potassium, sodium, and zinc salts	None	Surfactant	(See Appendix A)

Use Summary: Alkyl sulfates are widely used as detergents in cleaning products and shampoos; emulsifying agents in creams and lotions; and wetting agents. As inert ingredients, alkyl sulfates are used as surfactants or adjuvants of surfactants in pesticide formulations.

List Classification Determination: Because EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to these chemicals when used as an inert ingredients in pesticide formulations, the List Classification for alkyl sulfates (as listed in Appendix A) will be List 4B.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the three exemptions from the requirement of a tolerance for the inert ingredients alkyl sulfates (as defined in Table 1), as well as the List Classification Determination described above. I consider the two exemptions from the requirement of a tolerance established in 40 CFR 180.910 and the one exemption from the requirement of a tolerance in 40 CFR 180.930 as listed to be reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois Rossi

Lois A. Rossi, Director
Registration Division

July 31, 2006

Date:

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

APPENDIX A

Alkyl sulfate 9CI Names and CAS Reg. Nos.	
Chemical Name	**CAS Reg. No.**
Sulfuric acid, mono-C12-15-alkyl esters, ammonium salts	68815-61-2
1-Tetradecanol, hydrogen sulfate (8CI, 9CI)	4754-44-3
Sulfuric acid, monoisononyl ester, sodium salt (9CI)	26856-96-2
Sulfuric acid, monoisodecyl ester, sodium salt (9CI)	68299-17-2
Sulfuric acid, mono-C12-16-alkyl esters, potassium salts	73296-90-9
Sulfuric acid, mono-C12-16-alkyl esters, sodium salts	73296-89-6
Sulfuric acid, mono-C10-16-alkyl esters, sodium salts	68585-47-7
Sulfuric acid, mono-C15-18-alkyl esters, sodium salts	68784-79-2
Sulfuric acid, mono-C12-15-alkyl esters, sodium salts	68890-70-0
Sulfuric acid, mono-C10-16-alkyl esters, potassium salts	68908-46-3
Sulfuric acid, mono-C9-13-alkyl esters, sodium salts	72906-11-7
Sulfuric acid, mono-C10-16-alkyl esters	68611-55-2
Sulfuric acid, monoisodecyl ester, sodium salt (9CI)	68299-17-2
1-Hexadecanol, hydrogen sulfate, potassium salt (8CI, 9CI)	7065-13-6
1-Tetradecanol, hydrogen sulfate, potassium salt (9CI)	13419-37-9
6-Tridecanol, 3,9-diethyl-, hydrogen sulfate, sodium salt (6CI, 7CI, 8CI, 9CI)	3282-85-7
4-Undecanol, 7-ethyl-2-methyl-, hydrogen sulfate, sodium salt (6CI, 7CI, 8CI, 9CI)	139-88-8
2-Decanol, hydrogen sulfate, sodium salt (8CI, 9CI)	32687-84-6
Sulfuric acid, mono-C>10-alkyl esters, sodium salts	68188-45-4
1-Hexadecanol, hydrogen sulfate, magnesium salt (9CI)	17018-84-7
4-Hexadecanol, hydrogen sulfate, ammonium salt (9CI)	59862-22-5
Sulfuric acid, mono(2-ethylhexyl) ester, ammonium salt (9CI)	70495-37-3
1-Tridecanol, hydrogen sulfate, potassium salt (9CI)	71317-43-6
1-Tetradecanol, hydrogen sulfate, magnesium salt (9CI)	25446-91-7
1-Tridecanol, hydrogen sulfate, magnesium salt (9CI)	71317-56-1
1-Hexadecanol, hydrogen sulfate, ammonium salt (9CI)	52304-21-9
1-Tridecanol, hydrogen sulfate, ammonium salt (9CI)	34506-45-1
Sulfuric acid, mono-C8-18-alkyl esters, sodium salts	68130-43-8
2-Decanol, hydrogen sulfate, sodium salt, (2R)- (9CI)	57689-21-1
Sulfuric acid, mono-C6-10-alkyl esters, ammonium salts	68187-17-7
Sulfuric acid, monooctyl ester, sodium salt (8CI, 9CI)	142-31-4
Sulfuric acid, monodecyl ester, sodium salt (8CI, 9CI)	142-87-0
Sulfuric acid, monooctyl ester, magnesium salt (9CI)	67633-86-7
Sulfuric acid, monododecyl ester, magnesium salt (8CI, 9CI)	3097-08-3
Sulfuric acid, monododecyl ester, compd. with 2-propanamine (1:1) (9CI)	3032-58-4
Sulfuric acid, monooctyl ester (8CI, 9CI)	110-11-2
Sulfuric acid, monododecyl ester, ammonium salt (8CI, 9CI)	2235-54-3
Sulfuric acid, monodecyl ester (8CI, 9CI)	142-98-3
Sulfuric acid, monooctadecyl ester (8CI, 9CI)	143-03-3

Chemical Name	CAS Reg. No.
Sulfuric acid monododecyl ester sodium salt (8CI, 9CI)	151-21-3
Sulfuric acid, monododecyl ester (8CI, 9CI)	151-41-7
1-Hexadecanol, hydrogen sulfate, sodium salt (9CI)	1120-01-0
Sulfuric acid, monooctadecyl ester, sodium salt (8CI, 9CI)	1191-50-0
1-Tridecanol, hydrogen sulfate, sodium salt (9CI)	30862-33-0
Sulfuric acid, mono-C8-18-alkyl esters, sodium salts	68130-43-8
Sulfuric acid, mono-C10-16-alkyl esters, magnesium salts	68081-97-0
Sulfuric acid, mono-C10-16-alkyl esters, ammonium salts	68081-96-9
Sulfuric acid, monooctyl ester, ammonium salt (9CI)	67633-88-9
Sulfuric acid, monooctyl ester, magnesium salt (9CI)	67633-86-7
Sulfuric acid, monodecyl ester, magnesium salt (8CI, 9CI)	25446-93-9
Sulfuric acid, monodecyl ester, calcium salt (8CI, 9CI)	25446-90-6
Sulfuric acid, monododecyl ester, compd. with 1-amino-2-propanol (1:1) (8CI, 9CI)	21142-28-9
Sulfuric acid, monooctadecyl ester, magnesium salt (8CI, 9CI)	13006-05-8
Sulfuric acid, monodecyl ester, potassium salt (8CI, 9CI)	7739-63-1
Sulfuric acid, monooctadecyl ester, ammonium salt (8CI, 9CI)	4696-46-2
Sulfuric acid, monodecyl ester, ammonium salt (9CI)	13177-52-1
Sulfuric acid, monododecyl ester, potassium salt (8CI, 9CI)	4706-78-9

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OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

July 31, 2006

MEMORANDUM

SUBJECT: Reassessment of Three Exemptions from the Requirement of a Tolerance for Alkyl Sulfates

FROM: Kerry Leifer
Inert Ingredient Assessment Branch
Registration Division (7505P)

and

Pauline Wagner, Chief
Inert Ingredient Assessment Branch
Registration Division (7505P)

TO: Lois Rossi, Director
Registration Division (7505P)

BACKGROUND

Attached is the science assessment for alkyl (C_{8-18}) sulfate and its ammonium calcium, isopropylamine, magnesium, potassium, sodium and zinc salts; and sodium salt of sulfated oleic acid, which, for the ease of reading, are collectively referred to as "alkyl sulfates" throughout this document. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of the alkyl sulfates. The purpose of this document is to reassess the three exemptions from the requirement of a tolerance for residues of alkyl sulfates when used as inert ingredients in pesticide formulations as required under the Food Quality Protection Act (FQPA).

EXECUTIVE SUMMARY

This document evaluates the three tolerance exemptions for alkyl sulfates for use as an inert ingredient in pesticide formulations applied to growing crops or raw agricultural commodities after harvest under 40 CFR 180.910 and applied to animals under 40 CFR 180.930. An inert ingredient is defined by the U.S. Environmental

Protection Agency (EPA) as any ingredient in a pesticide product that is not intended to affect a target pest.

The alkyl sulfates are anionic surfactants in which an aliphatic alcohol is sulfated and then neutralized with a base to most commonly produce the sodium salt and, less commonly, other salt forms such as the ammonium salt. The most widely used form of alkyl sulfate is sodium dodecyl sulfate. Alkyl sulfates are widely used as detergents in cleaning products and shampoos; emulsifying agents in creams and lotions; and wetting agents.

The data being considered in this reassessment are primarily data for the sodium dodecyl (C_{12}) or the sodium C_{12-15} alkyl sulfates. Because of the preponderant use of these alkyl sulfates (by far the most predominant commercial form of alkyl sulfates), the predictability of the homologous series, and the fact that these alkyl chain lengths are located in the mid-range of the alkyl sulfate series, these data will support the reassessment of the alkyl sulfates listed in the tolerance exemptions presented in Table 1.

The alkyl sulfates acute oral toxicity ranges from 1.4 to 7.8 g/kg in rats, with the toxicity decreasing with increases in the alkyl chain length of the alkyl sulfates. The main effect of acute oral exposure to alkyl sulfates is irritation to the stomach and GI tract due to their surfactant nature. The alkyl sulfates are all irritating to the skin and eyes with the longer alkyl chain length compounds having less of an effect than the shorter alkyl chain length compounds.

The primary effects of oral repeated dose dietary studies (28-day and 90-day) with alkyl sulfates are increased liver and kidney weights with some liver hypertrophy in male and female rats and increased testes weight in male rats at dose levels of approximately 250 mg/kg/day. The increased organ weights were seen in all repeated dose studies over the entire alkyl chain length range that was tested. A published oral developmental study reported slight developmental effects at maternally toxic doses of 600 mg/kg/day Mice were the most sensitive species in a series of developmental toxicity studies which also included rats and rabbits. There was no increased pre- or postnatal sensitivity in any of the tested species. Reliable genotoxicity assays both *in vitro* and *in vivo* were negative and several summaries of carcinogenicity studies reported negative results in rats.

Dietary (food and drinking water) and residential exposures (dermal and inhalation) of concern are not anticipated for the alkyl sulfates considering their ready biodegradation in the environment and their physical-chemical properties. Exposure from the inert ingredient use of the alkyl sulfates in pesticide products is expected to result in human exposure below any dose level that would produce an adverse effect.

Taking into consideration all available information on the alkyl sulfates, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to alkyl sulfates (as identified in Table 1) when used

as an inert ingredient in pesticide products when considering dietary exposure and all non-occupational sources of pesticide exposure for which there is reliable information. Overall, exposure due to the inert ingredient use of alkyl sulfates is expected to result in human exposure below any dose level that would produce an adverse effect. Therefore, it is recommended that the three exemptions from the requirement of a tolerance established for residues of alkyl sulfates can be considered reassessed as safe under section 408(q) of FFDCA.

Based on the results of laboratory toxicity testing, the ready biodegradability of alkyl sulfates in the environment, and the measured concentrations in surface waters, effects of concern to nontarget aquatic organisms resulting from the use of these substances as inert ingredients in pesticide formulations would occur only at extremely high use rates of alkyl sulfates. Acute effects to nontarget terrestrial animals, based on the rodent acute toxicity data, are unlikely. However, based on available developmental toxicity data, effects to nontarget terrestrial animals cannot be ruled out.

I. Introduction

This report provides a qualitative assessment for the alkyl sulfates, pesticide inert ingredients which have three exemptions from the requirement of a tolerance when used as surfactants in pesticide formulations applied to growing crops and raw agricultural commodities after harvest under 40 CFR 180.910 and applied to animals under 40 CFR180.930.

The alkyl sulfates are anionic surfactants in which an aliphatic alcohol is sulfated and then neutralized with a base to most commonly produce the sodium salt and, less commonly, other salt forms such as the ammonium salt. The alkyl sulfates are primarily derived from linear primary alcohols, usually from alcohol feedstocks that have a distribution of various alkyl chain lengths. Some alkyl sulfates also contain linear and mono-branched alkyl alcohol-derived moieties (e.g., 2-ethylhexyl alcohol-derived moiety) with the linear alcohol-derived moiety being the predominant species. In the tolerance exemptions that are being reassessed in this document, all of the alkyl sulfate salt counter ions, with the exception of the isopropylamine salt, are inorganic compounds.

II. Use Information

A. Pesticide Uses

The tolerance exemption expressions for the alkyl sulfates are provided in Table 1 below.

Table 1. CFR Citation, CAS Registry Numbers and CAS Index Name for Alkyl Sulfates

40 CFR	Inert Ingredient	Limits	Uses	CAS Reg. No. and 9CI Name

180.910[a]	Alkyl (C_{8-18}) sulfate and its ammonium, calcium, isopropylamine, magnesium, potassium, sodium and zinc salts	None	Surfactants	(See Appendix A)
180.910[a]	Sodium salt of sulfated oleic acid	None	Surfactants; related adjuvants, of surfactants	none
180.930[b]	Alkyl (C_{8-18}) sulfate and its ammonium, calcium, magnesium, potassium, sodium, and zinc salts	None	Surfactant	(See Appendix A)

[a] Residues listed in 40 CFR 180.910 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
[b] Residues listed in 40 CFR 180.930 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

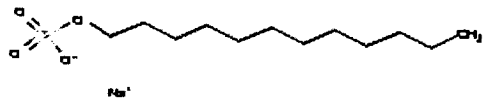
B. Other Uses

The most widely used form of alkyl sulfate is sodium dodecyl sulfate. Alkyl sulfates such as sodium dodecyl sulfate are widely used as detergents in cleaning products and shampoos; emulsifying agents in creams and lotions; and wetting agents. It is estimated that 65,000 tons/year of alkyl sulfates are used in household detergents and cleaning products (HERA, 2002).

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of sodium dodecyl sulfate, the predominant alkyl sulfate, along with a generic structure and nomenclature, are found in Table 2.

Table 2. Physical and Chemical Properties of Sodium Dodecyl Sulfate

Structure		ChemIDplus, 2004
CAS Reg. No.	151-21-3	CAS, 2006
9CI Name	Sulfuric acid, monodecyl ester, sodium salt	CAS, 2006
Physical State	Fine, white or slightly yellow powder	Mallinckrodt Baker, 2004
Molecular Weight	288.38 (M)	EPA,2004
Water Solubility	10,000 mg/L (M)	
Melting Point	205.5 ºC (M)	
Henry's Law Constant	1.11×10^{-15} atm-m^3/mole @ 25ºC (E)	
Vapor Pressure	1.8×10^{-12} mmHg @ 25°C (E)	
Octanol/Water Partition Coefficient (Log P)	1.6 (M)	

(E)=Estimated Value
(M)=Measured Value

IV. Hazard Assessment

A. Hazard Profile

The main sources of hazard information for this reassessment are the human health risk assessment performed as part of the Human & Environmental Risk Assessment on ingredients of household cleaning products (HERA, 2002) as well as other published peer-reviewed references for toxicity data on alkyl sulfates (Palmer *et al* 1975; Walker *et al*, 1967).

The alkyl sulfates are derived from the corresponding aliphatic alcohols. The toxicities of the alcohols are generally well-known with the longer alkyl chain length alcohols (higher molecular weight) being more lipophilic than the shorter alkyl chain length alcohols and thus, more poorly absorbed. The liver appears to be the target organ for most of the alcohols. The longer alkyl chain length alcohols have neurotoxic effects that are generally associated with solvents. These neurotoxic effects are more pronounced with the longer alkyl chain length alcohols, particularly by the inhalation route. Branched alcohols, particularly the branched C_8 ,alcohol can have developmental or reproductive effects at doses ≥45 mg/kg/day (NTP, 1991). The homologous series of linear alkyl alcohols appears to have predictable toxicities based upon chain length and lipophilicity.

The alkyl sulfates elicit similar toxicities to the corresponding alkyl alcohol, and the homologous alkyl sulfate series would generally behave as the corresponding alkyl alcohols. The solvent-type neurotoxicity seen in the alkyl alcohols is not observed with the alkyl sulfates since the alcohol moiety is not present. The inorganic counter ions approved in the above exemptions are not expected to substantively affect the toxicity of the sulfated alcohol. However, for a given alkyl chain length, the toxicity of the isopropylamine salt form of an alkyl sulfate may differ slightly from that of the inorganic salt form of an alkyl sulfate.

The data being considered in this reassessment is primarily data for the sodium dodecyl (C_{12}) sulfate or the sodium $C_{12\text{-}15}$ alkyl sulfates. Because of the predictability of the homologous series, and the fact that these carbon ranges are located in the mid-range of the series, these data will support the reassessment of the alkyl sulfate tolerance exemptions listed in Table 1. The branched-chain alcohol 2-ethylhexanol is a suitable analog for the mono-branched chain alkyl sulfates; the reassessment decision document for 2-ethylhexanol provides the data to support the inclusion of the mono-branched alkyl sulfates within the alkyl sulfate tolerance exemptions being reassessed in this document.

The alkyl sulfates acute oral toxicity ranges from 1.4 to 7.8 g/kg in rats, with the toxicity decreasing with increases in the alkyl chain length of the alkyl sulfates. The main effect of acute oral exposure is irritation to the stomach and GI tract due to their surfactant nature. They all are irritating to the skin and eyes with the longer alkyl chain length compounds having less of an effect than the shorter alkyl chain length compounds. The irritant properties of these chemicals are also concentration dependent (HERA, 2002).

The primary effects of oral repeated dose dietary studies on the sodium $C_{12\text{-}15}$ and the sodium C_{12} alkyl sulfates (28-day and 90-day) are increased liver and kidney weights with some liver hypertrophy in male and female rats and increased testes weight in male rats. The increased organ weights were seen in all repeated dose studies over the entire tested alkyl chain length range. In repeated dose gavage studies the primary effect was irritation to the stomach and GI tract. The no-observed-adverse-

effect levels (NOAELs) and lowest-observed-adverse-effect levels (LOAELs) were in the same range for both routes of exposure (Walker *et al*, 1967; HERA, 2002).

A published oral developmental study of an alkyl sulfate reported slight developmental effects at maternally toxic doses of 600 mg/kg/day. Mice were the most sensitive species in a series of developmental toxicity studies which also included rats and rabbits. There was no increased pre- or postnatal sensitivity in any of the tested species (Palmer *et al,* 1975).

Reliable genotoxicity assays both *in vitro* and *in vivo* were negative for both the sodium C_{12} and $C_{12\text{-}15}$ alkyl sulfates (HERA, 2002).

Several summaries of carcinogenicity studies reported negative results in rats. Two lifetime feeding studies produced no increase in tumors from controls. The non-cancer effects were similar to those seen in the 28-day and 90-day feeding studies (HERA, 2002).

The sodium salt of sulfated oleic acid is derived from the fatty acid, oleic acid. Based on a structure activity relationship analysis, it is expected that the sodium salt of sulfated oleic acid would exhibit similar toxicity to the corresponding aliphatic alcohol derived alkyl sulfate (EPA, 2006).

B. Toxicological Data

Acute Toxicity

Table 3. Summary of Acute Toxicity Data for the Alkyl Sulfates

Parameter	Toxicity Value	Reference
Oral LD_{50}, rat	1.4 – 7.8 g/kg	HERA, 2002
Dermal LD_{50}, rabbit	NA	
Inhalation LC_{50}, rat	NA	
Eye Irritation, rabbit	Moderate to strong	HERA, 2002
Skin Irritation, rabbit	Moderate to strong.	HERA, 2002
Skin Sensitization	NA	

NA = Not Available

Subchronic Toxicity

In a published study (Walker *et al*, 1967) male and female rats were treated for 13 weeks with 0, 40, 200, 1000, or 5000 ppm (approximately 0, 2, 10, 50, or 250 mg/kg/day) of sodium lauryl sulfate or a corresponding synthetic sodium alkyl sulfate made from the $C_{12\text{-}15}$ range of primary alcohols. There were significant decreases in body weight at the highest dose for both chemicals. Increased liver weights were seen in females with both chemicals and increased kidney and spleen weights in females were seen in rats treated with the sodium $C_{12\text{-}15}$ alkyl sulfate at the highest dose. At necropsy there was no evidence of pathological change with either substance. The

NOAEL is 1000 ppm (50 mg/kg/day) based on decreased body weight in males and females at 5000 ppm (250 mg/kg/day) and increased liver, kidney, and spleen weight in females also at 5000 ppm (250 mg/kg/day) for both chemicals. The LOAEL for this study is 5000 ppm (250 mg/kg/day). As supporting evidence, the HERA document reported similar results in its review of several unpublished 13-week studies and noted no increased severity of effects from a few days to 13 weeks of exposure.

Chronic Toxicity

No published chronic studies were identified.

Neurotoxicity

No published neurotoxicity studies were identified, however, no neurotoxic effects were observed from the available data for alkyl sulfates.

Mutagenicity

The HERA document on alkyl sulfates identified both *in vitro* and *in vivo* mutagenicity and genotoxicity studies. The results of the *in vitro* studies were negative and the results of reliable *in vivo* studies were also negative. The studies were performed on various chain lengths of the alkyl sulfate class. Based upon structure, this class of chemicals has not caused any concern for genotoxicity.

Carcinogenicity

No published carcinogenicity studies were identified in the open literature. The HERA document has briefly reviewed two short published summaries of lifetime feeding studies in rats. The summaries did not report any increased incidence of tumors; however, HERA did not find it possible to rate these studies for reliability since only summaries were available. However, based upon structure, this particular class of chemicals does not likely elicit any concerns for carcinogenicity.

Developmental and Reproductive Toxicity

One published developmental study was identified. Female rats, rabbits, and mice were dosed orally with 0, 0.2, 2, 300, or 600 mg/kg/day of an alkyl sulfate from gestation day 6-15 for rats and mice and 6-18 for rabbits. Slight to moderate maternal toxicity was reported at 300 mg/kg/day for rabbits, mice, and rats. At the highest dose mice had a statistically significant reduced number of viable pups, post-implantation loss, and reduced litter weight. These parameters were not affected in rabbits or rats. At the highest dose tested, pups with extra ribs were seen in the rats at an incidence that was statistically significant. Extra ribs were also seen in the 2 mg/kg dose in rabbits, but not at the next two higher doses, therefore no dose-response relationship was established. No developmental effects were observed at statistically significant levels in mice

Overall, the NOAEL for maternal toxicity is 2 mg/kg/day based on the slight maternal toxicity seen at 300 in rats and moderate maternal toxicity seen in rabbits and mice. The developmental NOAEL is 300 mg/kg/day based on the incidence of extra ribs in the rats at 600 mg/kg (Palmer *et al,* 1975). Although the no-adverse-effect level (NOEL) for maternal toxicity is 2 mg/kg/day based on the doses used in the study, the true NOAEL is most likely nearer to 300 mg/kg/day based on the severity of the effects.

B. Mode of Action, Metabolism, and Pharmacokinetics

The proposed metabolic pathway for even-numbered chain length alkyl sulfates is degradation by ω-oxidation, followed by β-oxidation to produce metabolites with chain lengths of C_2 and C_4. Metabolism of odd number alkyl sulfates is thought to follow a similar pathway (Burke *et al,* 1975; Burke *et al,* 1976 as cited in HERA, 2002). The hydrocarbon chain is metabolized through the cytochrome P450 ω-oxidation of aliphatic fatty acids. (Klassen *et al,*1996 as cited in HERA, 2002). A similar metabolic pathway would be observed for the sodium salt of sulfated oleic acid, with the resultant oxidative metabolites of the aliphatic alcohol-derived alkyl sulfates and the sodium salt of sulfated oleic acid being equivalent.

C. Special Considerations for Infants and Children

The database for the alkyl sulfates is sufficient for assessing the potential developmental effects of these chemicals. In a developmental toxicity study in three species, the NOAEL for maternal toxicity is 2 mg/kg/day based on the slight maternal toxicity seen at 300 mg/kg/day in rats and moderate maternal toxicity seen in rabbits and mice. The developmental NOAEL is 600 mg/kg/day based on the incidence of extra ribs in the rats. Therefore, there is no concern at this time for increased sensitivity to infants and children from alkyl sulfates. For the same reason, a safety factor analysis has not been used to assess the risk and, therefore, the additional tenfold safety factor for the protection of infants and children is also unnecessary.

D. Environmental Fate Characterization and Drinking Water Considerations

The alkyl sulfates are readily biodegradable, with a reported half-life in surface water of 0.75 days (HERA, 2002). These compounds are expected to be relatively non-mobile, with a K_{oc} in the 10,000 range, in terrestrial environments. The alkyl sulfates will move off site mainly with the sediment fraction when applied to fields. These compounds are unlikely to undergo abiotic degradation in soils and water. Once in water they are expected to partition to sediment, if not biodegraded. Alkyl sulfates were not detected in U.S. surface water above the individual homologue limit of detection of 5 ppb (Fendinger *et al,* 1992 as cited in HERA, 2002), therefore measurable concentrations of alkyl sulfates in drinking water are not anticipated.

VI. Exposure Assessment

The primary exposure to alkyl sulfates would be as a result of their use in detergents and other household cleaning products, residential exposures (dermal and inhalation) which have been identified as not being of concern under the OECD Screening Information Data Set (SIDS) program (OECD, 1997).

Dietary (food and drinking water) exposures to alkyl sulfates may occur as the result of consuming food following the application of pesticide products containing alkyl sulfates as inert ingredients. However, alkyl sulfates readily biodegrade in the environment, therefore, residues of concern on food and in drinking water are not anticipated.

VII. Aggregate Exposures

In examining aggregate exposure, the Federal Food, Drug, and Cosmetic Act (FFCDA) section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other nonoccupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

For the alkyl sulfates, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the exposure via these pathways is orders of magnitude less than the effects observed in the available repeated dose studies.

VIII. Cumulative Exposure

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

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 these alkyl sulfates and any other substances, and the alkyl sulfates do not appear to produce toxic metabolites produced by other substances. For the purposes of these tolerance actions, therefore, EPA has not assumed that the alkyl sulfates 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 concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

IX. Human Health Risk Characterization

The alkyl sulfates acute oral toxicity ranges from 1.4 to 7.8 g/kg in rats, with the toxicity decreasing with increases in the alkyl chain length of the alkyl sulfates The main effect of oral exposure is irritation to the stomach and GI tract due to the surfactant nature of the alkyl sulfates. All of the alkyl sulfates are irritating to the skin and eyes with the longer alkyl chain length compounds having less of an effect than the shorter alkyl chain alkyl sulfates. The irritant properties of the alkyl sulfates are also concentration dependent.

The primary effects of oral repeated dose dietary studies (28-day and 90-day) are increased liver and kidney weights with some liver hypertrophy in male and female rats and increased testes weight in male rats. The increased organ weights were seen in all repeated dose studies over the entire alkyl chain length range that was tested. In repeated dose gavage studies the primary effect was irritation to the stomach and GI tract. The NOAELs and LOAELs were in the same range for both routes of exposure

A published oral developmental study reported slight developmental effects at maternally toxic doses. Mice were the most sensitive species in a series of experiments which included also rats and rabbits. There was no increased sensitivity demonstrated in any of the tested species.

Reliable genotoxicity assays both *in vitro* and *in vivo* were negative, additionally several summaries of carcinogenicity studies indicate no tumors above background incidence in rats.

Dietary and residential exposures of concern are not anticipated for the alkyl sulfates and their salts considering their ready biodegradation in the environment and their physical-chemical properties. Exposure from the inert ingredient use of the alkyl sulfates and their salts in pesticide products is expected to result in human exposure below any dose level that would produce any adverse effect.

Taking into consideration all available information on the alkyl sulfates identified in Table 1, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to alkyl sulfates when used as an inert ingredient in pesticide products when considering dietary exposure and all non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the three exemptions from the requirement of a tolerance established for residues of the alkyl sulfates and their salts (identified in Table 1) can be considered reassessed as safe under section 408(q) of FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

Sodium dodecyl sulfate is moderately to slightly toxic to fish and aquatic invertebrates, based on numerous studies found in EPA's Ecotox database (http://mountain.epa.gov/ecotox). In toxicity studies with water fleas (*Daphnia magna*),

the lowest reported 48-hr LC_{50} was 7.4mg/L. The lowest reported 96-hr LC_{50} in rainbow trout (*Oncorhynchus mykiss*) was 4.4 mg/L and the lowest reported 96-hr LC_{50} in fathead minnow (*Pimephales promelas*) was 6.6 mg/L.

Based on the results of laboratory toxicity testing, the ready biodegradability of the alkyl sulfates in the environment, and the measured concentrations in surface waters, effects of concern to nontarget aquatic organisms resulting from the use of these substances as inert ingredients in pesticide formulations would occur only at extremely high use rates of alkyl sulfates. Application of approximately 4-5 pounds of alkyl sulfate per acre may exceed the acute level of concern (LOC) for endangered aquatic species and application of 40-50 pounds alkyl sulfates per acre would exceed the non-listed aquatic species acute LOC. Based on the available aquatic toxicity data and ready biodegradation of alkyl sulfates in the environment, chronic effects to aquatic species are less likely to occur. Acute effects to nontarget terrestrial animals, based on the rodent acute toxicity data, are unlikely. However, based on available developmental data, effects to nontarget terrestrial animals cannot be ruled out.

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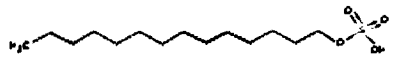
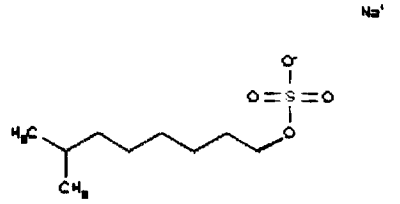
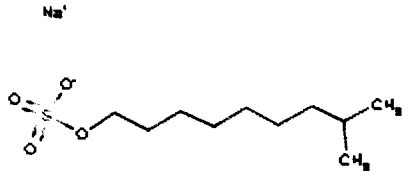
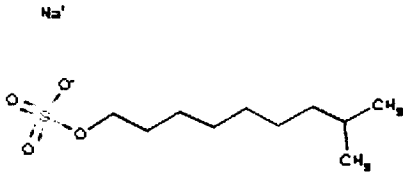
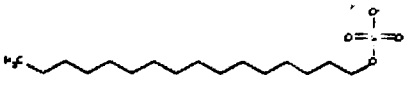
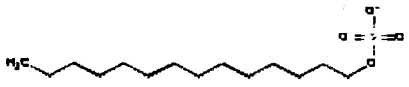
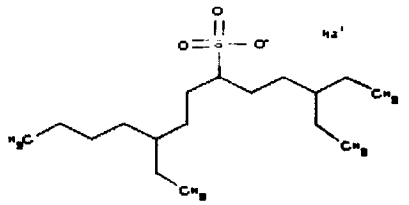
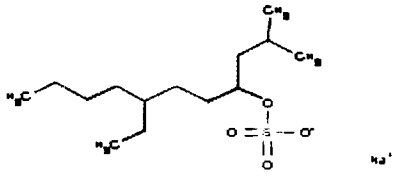
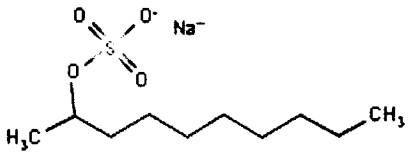
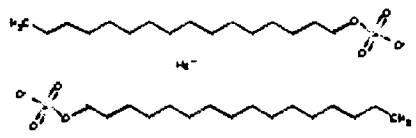
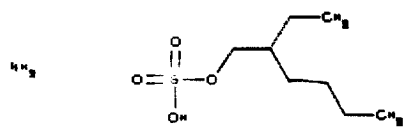
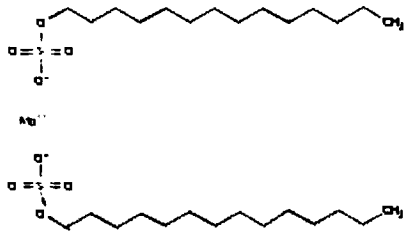
APPENDIX A

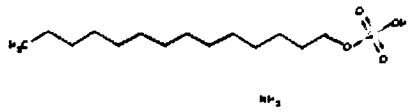
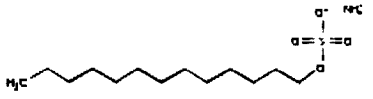
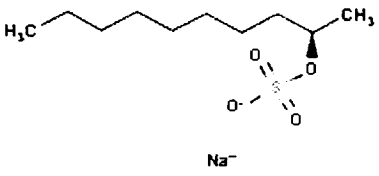
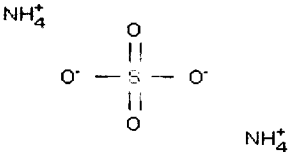
Alkyl (C_{8-18}) sulfate and its ammonium, calcium, isopropylamine, magnesium, potassium, sodium and zinc salts—CAS Reg. Nos, Chemical Names, and Chemical Structures

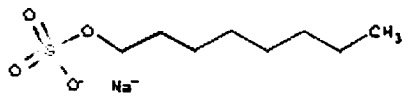
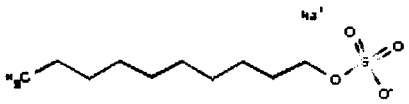
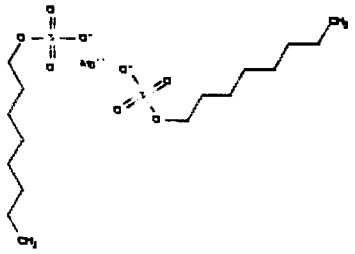
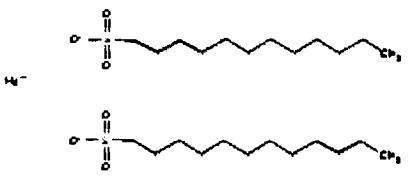
Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, mono-C12-15-alkyl esters, ammonium salts	68815-61-2	No available structure
1-Tetradecanol, hydrogen sulfate (8Cl, 9Cl)	4754-44-3	
Sulfuric acid, monoisononyl ester, sodium salt (9Cl)	26856-96-2	
Sulfuric acid, monoisodecyl ester, sodium salt (9Cl)	68299-17-2	
Sulfuric acid, mono-C12-16-alkyl esters, potassium salts	73296-90-9	No available structure
Sulfuric acid, mono-C12-16-alkyl esters, sodium salts	73296-89-6	No available structure

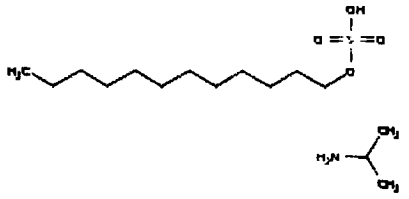
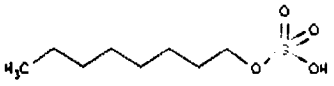
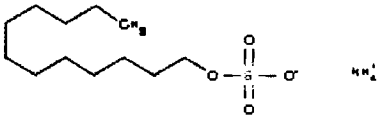
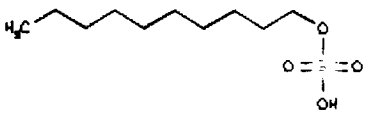
Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, mono-C10-16-alkyl esters, sodium salts	68585-47-7	
Sulfuric acid, mono-C15-18-alkyl esters, sodium salts	68784-79-2	No available structure
Sulfuric acid, mono-C12-15-alkyl esters, sodium salts	68890-70-0	No available structure
Sulfuric acid, mono-C10-16-alkyl esters, potassium salts	68908-46-3	No available structure
Sulfuric acid, mono-C9-13-alkyl esters, sodium salts	72906-11-7	No available structure
Sulfuric acid, mono-C10-16-alkyl esters	68611-55-2	No available structure
Sulfuric acid, monoisodecyl ester, sodium salt (9CI)	68299-17-2	
1-Hexadecanol, hydrogen sulfate, potassium salt (8CI, 9CI)	7065-13-6	

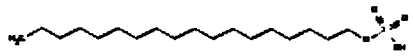
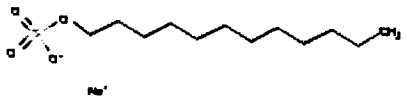
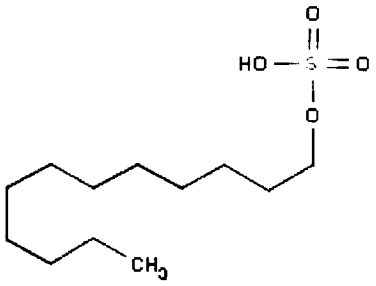
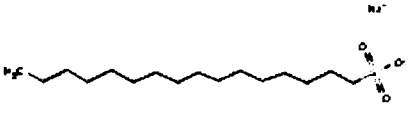
Chemical Name	CAS Reg. No.	Chemical Structure
1-Tetradecanol, hydrogen sulfate, potassium salt (9CI)	13419-37-9	
6-Tridecanol, 3,9-diethyl-, hydrogen sulfate, sodium salt (6CI, 7CI, 8CI, 9CI)	3282-85-7	
4-Undecanol, 7-ethyl-2-methyl-, hydrogen sulfate, sodium salt (6CI, 7CI, 8CI, 9CI)	139-88-8	
2-Decanol, hydrogen sulfate, sodium salt (8CI, 9CI)	32687-84-6	
Sulfuric acid, mono-C>10-alkyl esters, sodium salts	68188-45-4	

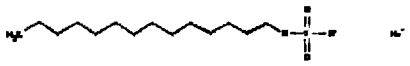
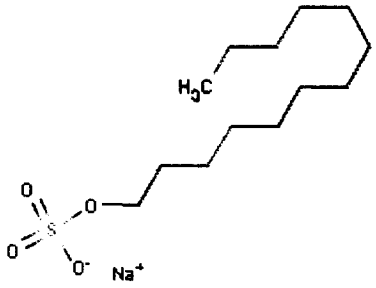
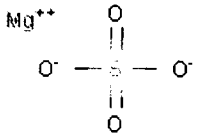
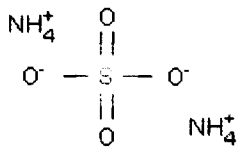
Chemical Name	CAS Reg. No.	Chemical Structure
1-Hexadecanol, hydrogen sulfate, magnesium salt (9CI)	17018-84-7	
4-Hexadecanol, hydrogen sulfate, ammonium salt (9CI)	59862-22-5	
Sulfuric acid, mono(2-ethylhexyl) ester, ammonium salt (9CI)	70495-37-3	
1-Tridecanol, hydrogen sulfate, potassium salt (9CI)	71317-43-6	
1-Tetradecanol, hydrogen sulfate, magnesium salt (9CI)	25446-91-7	
1-Tridecanol, hydrogen sulfate, magnesium salt (9CI)	71317-56-1	

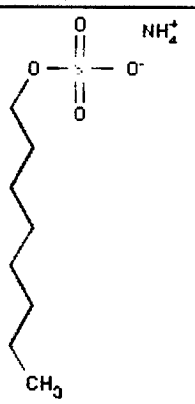
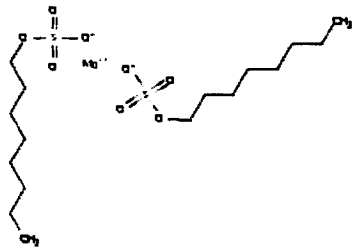
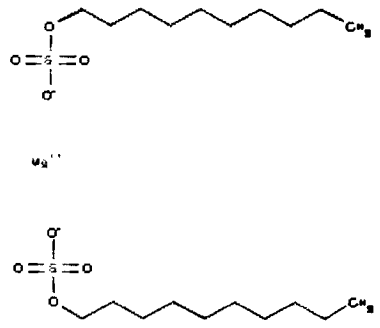
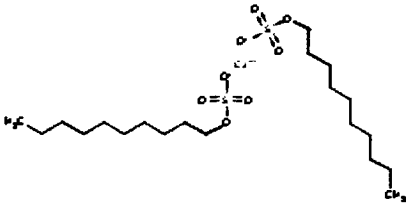
Chemical Name	CAS Reg. No.	Chemical Structure
1-Hexadecanol, hydrogen sulfate, ammonium salt (9CI)	52304-21-9	
1-Tridecanol, hydrogen sulfate, ammonium salt (9CI)	34506-45-1	
Sulfuric acid, mono-C8-18-alkyl esters, sodium salts	68130-43-8	
2-Decanol, hydrogen sulfate, sodium salt, (2R)-(9CI)	57689-21-1	
Sulfuric acid, mono-C6-10-alkyl esters, ammonium salts	68187-17-7	

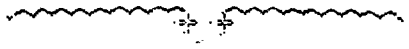
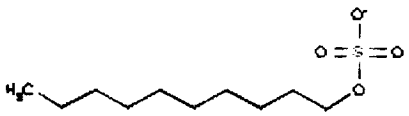
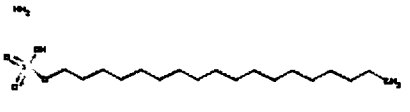
Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monooctyl ester, sodium salt (8Cl, 9Cl)	142-31-4	
Sulfuric acid, monodecyl ester, sodium salt (8Cl, 9Cl)	142-87-0	
Sulfuric acid, monooctyl ester, magnesium salt (9Cl)	67633-86-7	
Sulfuric acid, monododecyl ester, magnesium salt (8Cl, 9Cl)	3097-08-3	

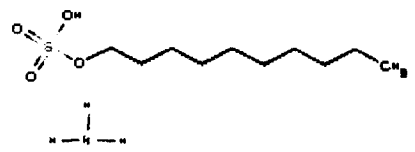
Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monododecyl ester, compd. with 2-propanamine (1:1) (9CI)	3032-58-4	
Sulfuric acid, monooctyl ester (8CI, 9CI)	110-11-2	
Sulfuric acid, monododecyl ester, ammonium salt (8CI, 9CI)	2235-54-3	
Sulfuric acid, monodecyl ester (8CI, 9CI)	142-98-3	

Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monooctadecyl ester (8CI, 9CI)	143-03-3	
Sulfuric acid monododecyl ester sodium salt (8CI, 9CI)	151-21-3	
Sulfuric acid, monododecyl ester (8CI, 9CI)	151-41-7	
1-Hexadecanol, hydrogen sulfate, sodium salt (9CI)	1120-01-0	

Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monooctadecyl ester, sodium salt (8Cl, 9Cl)	1191-50-0	
1-Tridecanol, hydrogen sulfate, sodium salt (9Cl)	30862-33-0	
Sulfuric acid, mono-C8-18-alkyl esters, sodium salts	68130-43-8	
Sulfuric acid, mono-C10-16-alkyl esters, magnesium salts	68081-97-0	
Sulfuric acid, mono-C10-16-alkyl esters, ammonium salts	68081-96-9	

Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monooctyl ester, ammonium salt (9CI)	67633-88-9	
Sulfuric acid, monooctyl ester, magnesium salt (9CI)	67633-86-7	
Sulfuric acid, monodecyl ester, magnesium salt (8CI, 9CI)	25446-93-9	
Sulfuric acid, monodecyl ester, calcium salt (8CI, 9CI)	25446-90-6	

Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monododecyl ester, compd. with 1-amino-2-propanol (1:1) (8CI, 9CI)	21142-28-9	
Sulfuric acid, monooctadecyl ester, magnesium salt (8CI, 9CI)	13006-05-8	
Sulfuric acid, monodecyl ester, potassium salt (8CI, 9CI)	7739-63-1	
Sulfuric acid, monooctadecyl ester, ammonium salt (8CI, 9CI)	4696-46-2	

Chemical Name	CAS Reg. No.	Chemical Structure
Sulfuric acid, monodecyl ester, ammonium salt (9CI)	13177-52-1	
Sulfuric acid, monododecyl ester, potassium salt (8CI, 9CI)	4706-78-9