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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

August 16, 2006

ACTION MEMORANDUM Errata

SUBJECT: Correction to the September 28, 2005, Inert Ingredient Tolerance Reassessment of PEG Fattty Acid Esters

FROM: Pauline Wagner, Chief Pauline Wagner 8/16/06
Inert Ingredient Assessment Branch
Registration Division (7505P)

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

The tolerance reassessment decision document and action memorandum for the PEG fatty acid esters dated September 28, 2005, included two tolerance exemptions (under 40 CFR 180.910 and 40 CFR 180.930, respectively) for "α-Lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600." The inclusion of these tolerance exemptions was in error as this substance is not part of the group of polyethylene glycol (PEG) fatty acid esters, but rather is best characterized as an alcohol ethoxylate. (The two tolerance exemptions for α-lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600 were included among those tolerance exemptions with insufficient data which were proposed for revocation (71 FR 25993; May 3, 2006) and subsequently revoked (71 FR 45415; August 9, 2006)).

Based on this determination, the two tolerance exemptions under 40 CFR 180.910 and 40 CFR 180.930 for "α-Lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600" are **not** reassessed as part of the group of PEG fatty acid esters. The table below correctly lists the eleven (11) tolerance exemptions for the PEG fatty acid esters that were reassessed without changes to the existing exemptions from the requirement of a tolerance (i.e., "as is").

Reassessed Tolerance Exemptions

Tolerance Exemption Expression	CAS Registry Number/ CAS NAME	40 CFR§180.	Use Pattern (Pesticidal)	Limits in the CFR
Alkanoic and alkenoic acids,	Various (see Appendix B of	910	Emulsifiers	--

Tolerance Exemption Expression	CAS Registry Number/ CAS NAME	40 CFR§180.	Use Pattern (Pesticidal)	Limits in the CFR
mono- and diesters of α-hydro-ω-hydroxypoly (oxyethylene) with molecular weight (in amu) range of 200 to 6,000	Decision Document for complete listing)	930	Emulsifiers	--
Oleic acid diester of α-hydro-ω-hydroxypoly (oxyethylene), the poly(oxythylene) having molecular weight (in amu) of 400.	9005-07-6 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	910	Surfactants, related adjuvants of surfactants	--
α-Oleoyl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-96-0 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	910	Emulsifier	--
		930	Emulsifier	
α-Oleoyl-ω - (oleoyloxy) poly(oxyethylene) derived from α-hydro-ω-hydroxypoly (oxyethylene) (molecular weight 600 amu).	9005-07-6 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	920	Component of defoamers	--
		930	Component of defoamers	
α-Stearoyl-ω - hydroxypoly (oxyethylene) average molecular weight (in amu) of 600	9004-99-3 Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-hydroxy-	910	Emulsifier	--
		930	Emulsifier	--
α-Stearoyl-ω - hydroxypoly (oxyethylene), the	9004-99-3	910	Surfactants, related adjuvants of surfactants	--

Tolerance Exemption Expression	CAS Registry Number/ CAS NAME	40 CFR§180.	Use Pattern (Pesticidal)	Limits in the CFR
poly(oxyethylene) content of averages either 8, 9, or 40 moles; if a blend of products is used, the average number of moles ethylene oxide reacted to produce any product that is a component of the blend shall be either 8, 9 or 40	Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-hydroxy-	930	Surfactants, related adjuvants of surfactants	--

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 (RACs) after harvest.

Residues listed in 40 CFR §180.920 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 only.

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.

II. MANAGEMENT CONCURRENCE

I concur with the corrected reassessment of the eleven (11) exemptions from the requirement of a tolerance for the PEG fatty acid esters as listed above. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois A. Rossi

Lois A. Rossi, Director
Registration Division

August 16, 2006

Date:

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

DATE: September 28, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – PEG Fattty Acid Esters

FROM: Pauline Wagner, Chief Pauline Wagner 9/28/05
Inert Ingredient Assessment Branch
Registration Division (7505C)

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

I. FQPA REASSESSMENT ACTION

Action: Reassessment of thirteen (13) inert exemptions from the requirement of a tolerance without changes to the existing exemptions from the requirement of a tolerance (i.e., "as is").

Tolerance Exemptions Being Reassessed

Tolerance Exemption Expression	CAS Registry Number/ CAS NAME	40 CFR§180.	Use Pattern (Pesticidal)	Limits in the CFR
Alkanoic and alkenoic acids, mono- and diesters of α-hydro-ω-hydroxypoly (oxyethylene) with molecular weight (in amu) range of 200 to 6,000	Various (see Appendix B of Decision Document for complete listing)	910	Emulsifiers	--
		930	Emulsifiers	--
α-Lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-81-3 Poly(oxy-1,2-ethanediyl), α-(1-oxododecyl)-ω-hydroxy-	910	Emulsifier	--
		930	Emulsifier	--

Tolerance Exemption Expression	CAS Registry Number/ CAS NAME	40 CFR§180.	Use Pattern (Pesticidal)	**Limits in the CFR**
Oleic acid diester of α-hydro-ω-hydroxypoly (oxyethylene), the poly(oxythylene) having molecular weight (in amu) of 400.	9005-07-6 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	910	Surfactants, related adjuvants of surfactants	--
α-Oleoyl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-96-0 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	910	Emulsifier	--
		930	Emulsifier	
α-Oleoyl-ω - (oleoyloxy) poly(oxyethylene) derived from α-hydro-ω-hydroxypoly (oxyethylene) (molecular weight 600 amu).	9005-07-6 Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-	920	Component of defoamers	--
		930	Component of defoamers	
α-Stearoyl-ω - hydroxypoly (oxyethylene) average molecular weight (in amu) of 600	9004-99-3 Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-hydroxy-	910	Emulsifier	--
		930	Emulsifier	--
α-Stearoyl-ω - hydroxypoly (oxyethylene), the poly(oxyethylene) content of averages either 8, 9, or 40 moles; if a blend of products is used, the average number of moles ethylene oxide reacted to produce any product that is a component of the blend shall be either 8, 9 or 40	9004-99-3 Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-hydroxy-	910	Surfactants, related adjuvants of surfactants	--
		930	Surfactants, related adjuvants of surfactants	--

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 (RACs) after harvest.

Residues listed in 40 CFR §180.920 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 only.

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.

Use Summary: PEG fatty acid esters function as emulsifiers, surfactants, and components of defoamers when used as pesticide product inert ingredients. In addition, PEG fatty acid esters are used as components of cosmetics such as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and sunscreen products, with certain PEG fatty acid esters also approved as indirect food additives under various regulations in 21 CFR Parts 175-178.

List Reclassification Determination: The current List Classification for each of the PEG fatty acid esters listed in the table above is 4B; they will retain their current Classification.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the thirteen (13) exemptions from the requirement of a tolerance for the PEG fatty acid and with the List reclassification determination(s), as listed and described above. I consider the thirteen (13) exemptions from the requirement of a tolerance established in 40 CFR part 180.910, 180.920, and 180.930 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.

/ Donald R Stubbs

Lois A. Rossi, Director
Registration Division

9/28/05

Date:

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

September 28, 2005

MEMORANDUM

SUBJECT: Reassessment of the Thirteen Exemptions from the Requirement of a Tolerance for Polyethylene Glycol Esters of Fatty Acids

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

TO: Pauline Wagner, Chief
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505C)

BACKGROUND

Attached is the science assessment for alkanoic and alkenoic acids, mono- and diesters of α-hydro-ω-hydroxypoly(oxyethylene); α-lauryl-ω-hydroxypoly(oxyethylene); oleic acid diester of α-hydro-ω-hydroxypoly(oxyethylene); α-oleoyl-ω-hydroxypoly (oxyethylene), α-oleoyl-ω-(oleoyloxy) poly(oxyethylene), α-stearoyl-ω-hydroxypoly (oxyethylene), and α-stearoyl-ω-hydroxypoly(oxyethylene). This assessment is primarily based upon an assessment of public domain information on these substances submitted to the Office of Pesticide Programs by the Surfactants Task Force[1] (STF) for the purpose of supporting the Agency's tolerance reassessment of these substances. The STF submission has been reviewed by the Agency for accuracy and completeness; this assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of these substances, each of which are polyethylene glycol esters of fatty acids and, for the purpose of readability, are referred to by the term "PEG fatty acid esters" throughout this document. The purpose of this document is to reassess the thirteen existing exemptions from the requirement of a tolerance for residues of the PEG fatty acid esters as required under the Food Quality Protection Act (FQPA).

EXECUTIVE SUMMARY

[1] The Surfactants Task Force is a consortium of 10 companies that are involved in the production of surfactants formed under the auspices of the Chemical Producers and Distributors Association (CPDA) and Crop Life America (CLA).

This report provides a qualitative assessment for the PEG fatty acid esters, pesticide inert ingredients with a total of thirteen (13) exemptions from the requirement of a tolerance under 40 CFR §180.910, 40 CFR §180.920 and 40 CFR §180.930 and is primarily based on an assessment of public domain information on these substances submitted to the Office of Pesticide Programs by the Surfactants Task Force. Based on the submitted information and other sources of information considered herein, there is sufficient information to conduct this assessment.

PEG fatty acid esters function as emulsifiers, surfactants, and components of defoamers when used as pesticide product inert ingredients. In addition, PEG fatty acid esters are used as components of cosmetics such as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and sunscreen products, with certain PEG fatty acid esters also approved as indirect food additives under various regulations in 21 CFR Parts 175-178.

The principal source of referenced hazard information on PEG fatty acid esters contained in the STF assessment are a number of final reports on various PEG fatty acid esters and related substances published by the Cosmetic Ingredient Review (CIR) Expert Panel. Additionally, the STF assessment references the fact that PEG fatty acid esters are readily hydrolyzed to their respective fatty acid and polyethylene glycol moieties in the gastrointestinal tract; noting that fatty acids have previously been reassessed by the Agency and providing hazard information on polyethylene glycol.

Based upon the referenced hazard information included in the STF assessment and other available data, PEG fatty acid esters, are low toxicity chemicals. In animal studies effects were only seen at limit dose levels which are far greater than exposures resulting from their use as inert ingredients in pesticide products. While some local effects at the site of application were noted in a subchronic rabbit dermal toxicity study, such effects have not been reported in association with the use of PEG fatty acid esters in dermally-applied cosmetics.

PEG fatty acid esters are nonpersistant and readily biodegradable in the environment, and as such would not be expected to be present in drinking water sources at concentrations exceeding the low ppb level, far less than any potential level of concern for these substances. Concentrations of PEG fatty acid esters in surface waters resulting from application of pesticides containing PEG fatty acid esters as inert ingredients to turf and croplands would be expected not to exceed levels of concern for nontarget organisms.

Taking into consideration all available information on PEG fatty acid esters, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to PEG fatty acid esters used as inert ingredients when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended

that the thirteen (13) exemptions from the requirement of a tolerance established for residues of PEG fatty acid esters be considered reassessed as safe under section 408(q) of FFDCA.

I. Introduction

This report provides a qualitative assessment for the PEG fatty acid esters, pesticide inert ingredients with a total of thirteen (13) exemptions from the requirement of a tolerance under 40 CFR §180.910, 40 CFR §180.920 and 40 CFR §180.930 and is primarily based on an assessment of public domain information on these substances submitted to the Office of Pesticide Programs by the Surfactants Task Force. (The STF assessment is included as Appendix A). Based on the submitted information and other sources of information considered herein, there is sufficient information to conduct this assessment.

II. Use Information

A. Pesticide Uses

The specific names and associated tolerance exemptions for the substances included in the PEG fatty acid esters group are provided in Table 1 below.

Table 1. Tolerance Exemptions Being Reassessed in this Document

Tolerance Exemption Expression	CAS Registry Number	40 CFR§180.	Use Pattern (Pesticidal)	Limits in the CFR
Alkanoic and alkenoic acids, mono- and diesters of α-hydro-ω-hydroxypoly (oxyethylene) with molecular weight (in amu) range of 200 to 6,000	Various (see Appendix B for complete listing)	910	Emulsifiers	--
		930	Emulsifiers	--
α-Lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-81-3	910	Emulsifier	--
		930	Emulsifier	--

Tolerance Exemption Expression	CAS Registry Number	40 CFR§180.	Use Pattern (Pesticidal)	**Limits in the CFR**
Oleic acid diester of α-hydro-ω-hydroxypoly (oxyethylene), the poly(oxythylene) having molecular weight (in amu) of 400.	9005-07-6	910	Surfactants, related adjuvants of surfactants	--
α-Oleoyl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-96-0	910	Emulsifier	--
		930	Emulsifier	
α-Oleoyl-ω - (oleoyloxy) poly(oxyethylene) derived from α-hydro-ω-hydroxypoly (oxyethylene) (molecular weight 600 amu).	9005-07-6	920	Component of defoamers	--
		930	Component of defoamers	
α-Stearoyl-ω - hydroxypoly (oxyethylene) average molecular weight (in amu) of 600	9004-99-3	910	Emulsifier	--
		930	Emulsifier	--
α-Stearoyl-ω - hydroxypoly (oxyethylene), the poly(oxyethylene) content of averages either 8, 9, or 40 moles; if a blend of products is used, the average number of moles ethylene oxide reacted to produce any product that is a component of the blend shall be either 8, 9 or 40	9004-99-3	910	Surfactants, related adjuvants of surfactants	--
		930	Surfactants, related adjuvants of surfactants	--

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 (RACs) after harvest.

Residues listed in 40 CFR §180.920 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 only.

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

PEG fatty acid esters are used as components of cosmetics such as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and sunscreen products, with concentrations typically ranging from 0.1% to 10% of the product. PEG dioleate (CAS Reg. No. 9005-07-6) is approved as a secondary direct food additive when used as a component of defoamers for certain foods under 21 CFR 173.340. Certain PEG fatty acid esters are also approved as indirect food additives for use in resinous and other coatings, paper and cardboard products, and textiles under various regulations in 21 CFR Parts 175-178.

III. Physical and Chemical Properties

The chemical structure of polyethylene glycol monostearate, a representative PEG fatty acid ester, is given in Figure 1 below.

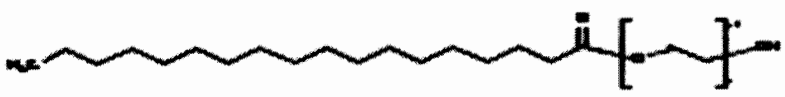

Figure 1

The PEG fatty acid ester structure is that of a mono- or diester of polyethylene glycol with certain monobasic carboxylic acids [typically as derived from animal and vegetable fats and oils (e.g., oleic acid)] with carbon chains that are even-numbered and range from eight to 22 carbons. The physical and chemical characteristics of PEG fatty acid esters are dependent upon the actual chemical structure, with their surfactant properties being based on the hydrophilic polyethylene glycol and the hydrophobic fatty acid ester portions of the molecule. Differences in the degree of esterification, the length of the polyethylene glycol moiety and the carbon chain length of the fatty acid moiety provide for a range of surfactant properties.

The PEG fatty acids are reported to be liquids or low melting point solids that are either soluble or dispersible in water.

IV. Hazard Assessment

A. Hazard Profile

The principal source of referenced hazard information on PEG fatty acid esters contained in the STF assessment are a number of final reports on various PEG fatty acid esters and related substances published by the Cosmetic Ingredient Review (CIR) Expert Panel. The Cosmetic Ingredient Review Expert Panel reviews and assesses the safety of ingredients used in cosmetics and publishes the results in the open, peer-reviewed scientific literature.

Additionally, the STF assessment references the fact that PEG fatty acid esters are readily hydrolyzed to their respective fatty acid and polyethylene glycol moieties in the gastrointestinal tract. A previous OPP tolerance reassessment conducted on fatty acids concluded that "[based on] their low acute toxicity via oral and dermal routes, FDA's designation of certain fatty acids as GRAS, their presence in food products, food additives, and cosmetics, as well as the significant contribution of fatty acids in the diet, the uses of fatty acids as inert and active ingredients in pesticide products are unlikely to pose a significant hazard to the general public or any population subgroup. Exposures from the aforementioned uses are expected to result in human exposure below any dose level that could possibly produce an adverse effect." (EPA 2004) The toxicity of polyethylene glycol is considered in additional references provided in the STF assessment.

B. Toxicological Data

Acute Toxicity

Various referenced acute oral toxicity studies on PEG fatty acid esters in the STF assessment indicate that PEG fatty acid esters are of low acute oral and dermal toxicity and are not eye or skin irritants or dermal sensitizers. The referenced acute oral toxicity studies reported LD_{50} values of greater than 10,000 mg/kg resulting in the PEG fatty acid esters being considered Toxicity Category IV for acute oral effects. Additional information was presented on acute intraperitoneal and intravenous toxicity, but these routes of exposure and resultant endpoints are not relevant to exposures occurring from the use of PEG fatty acid esters as pesticide inert ingredients. No additional acute toxicity data were presented in the STF assessment.

Subchronic Toxicity

The STF assessment referenced a number of subchronic oral toxicity studies in rats and hamsters with PEG fatty acid esters in which effects were seen only at doses exceeding limit dose levels (greater than 5% of the diet). Some local effects at the site of administration were noted in a referenced 20-day rabbit dermal toxicity study at dose levels of 500 mg/kg to 2.0 g/kg of 1.5% PEG stearate. No additional subchronic toxicity data were presented in the STF assessment.

Chronic Toxicity

The STF assessment referenced a number of chronic oral toxicity studies in which no effects were seen at dose levels up to 4% PEG fatty acid esters in the diet. Hepatic cysts and cecal enlargement were observed in a two-year oral rat study only at the two highest dose levels of 10% and 25% in the diet. No additional chronic toxicity data were presented in the STF assessment.

Neurotoxicity

No studies on the neurotoxicity of PEG fatty acid esters were identified or referenced in the STF assessment. A safety assessment of PEGs and their derivatives as used in did not identify any adverse neurotoxicological effects with any PEG fatty acid ester. (Fruijtier-Polloth 2005) A structure activity relationship analysis of PEG fatty acid esters did not identify any concerns for neurotoxicity.

Mutagenicity

No studies on the mutagenicity of PEG fatty acid esters were identified or referenced in the STF assessment. A safety assessment of PEGs and their derivatives as used in did not identify any genotoxic effects with any PEG fatty acid ester. (Fruijtier-Polloth 2005) A structure activity relationship analysis of PEG fatty acid esters did not identify any concerns for genotoxicity.

Carcinogenicity

No studies on the carcinogenicity of PEG fatty acid esters were identified or referenced in the STF assessment. A structure activity relationship analysis of PEG fatty acid esters did not identify any concerns for carcinogenicity.

Developmental and Reproductive Toxicity

The STF assessment referenced one oral rat reproductive toxicity study in which no effects were seen in rats fed a diet of 5% PEG stearate. Dietary levels of 10% to 20% PEG stearate resulted in decreased newborn litter survival time due to maternal neglect, impairment of lactation, lower weaning weight, increased mortality of nurslings, and decreased reproductive performance in the F_3 generation.

C. Metabolism and Pharmacokinetics

References in the STF assessment state that PEG fatty acid esters are hydrolyzed to their respective fatty acids and polyethylene glycol moieties in the gastrointestinal tract. The resultant fatty acids are common components of a wide variety of foods, are readily absorbed, and are primary components of lipid metabolism. The STF assessment also includes references stating that polyethylene glycols are poorly absorbed from the gastrointestinal tract, with absorption decreasing as the molecular weight increases, and the absorbed polyethylene glycols generally being excreted unmetabolized in the urine and feces.

D. Special Considerations for Infants and Children

In the rat oral reproductive study on PEG stearate referenced in the STF assessment, adverse effects were seen only at exposure levels that were maternally toxic and above the limit dose. Based on this information there is no concern, at this time, for increased sensitivity to infants and children to PEG fatty acid esters when used as inert ingredients in pesticide formulations. For the same reason, a safety factor analysis has not been used to assess risk and, therefore, the additional tenfold safety factor for the protection of infants and children is also unnecessary.

V. Environmental Fate Characterization and Drinking Water Considerations

The PEG fatty acid esters range from very slightly soluble to water dispersible, exhibit low to moderate adsorption to soils and sediments and have a low bioconcentration potential. The PEG fatty acid esters are expected move to surface water mainly with the water phase and are unlikely to move into ground water except in very sandy soils low in organic material. On field microbially-mediated degradation is expected to limit transport to surface and ground water from applications or releases to land, with aerobic biodegradation being the major route of environmental degradation. Once in surface waters, degradation will continue via aerobic and anaerobic (in sediments) microbial degradation and ester hydrolysis. Partitioning to air from water or soil surfaces is unlikely due to these substances' low vapor pressure and low Henry's Law Constant (HLC).

Biologically-mediated degradation in both aerobic and anaerobic conditions would result in concentrations of PEG fatty acid esters at levels no greater than the low parts per billion (ppb) range. There are no readily available ambient water monitoring data, ambient water quality criteria or drinking maximum contaminant or health advisory levels for any of the PEG fatty acid esters.

VI. Exposure Assessment

Any exposure to PEG fatty acid esters as a result of their use as pesticide inert ingredients would primarily be via the oral route through the consumption of food to which a PEG fatty acid ester-containing pesticide product has been applied or through sources of drinking water that may contain PEG fatty acid esters as a result of run-off or direct pesticide applications. Any dermal exposures to PEG fatty acid esters resulting from the use of a PEG fatty acid ester-containing pesticide would be far less than the dermal exposures to PEG fatty acid esters resulting from these substances' extensive use in cosmetic products such as shampoos.

The PEG fatty acid esters are of low concern for oral and dermal toxicity, therefore no further oral or dermal exposure assessment is necessary Based on the nonvolatile nature of PEG fatty acid esters, inhalation exposure is unlikely, and an inhalation exposure assessment is not required.

VII. Aggregate Exposures

In examining aggregate exposure, the Federal Food, Drug, and Cosmetic Act (FFDCA) 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 PEG fatty acid esters, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the lack of human health concerns associated with exposure to PEG fatty acid esters as inert ingredients in pesticide formulations.

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 PEG fatty acid esters and any other substances and, these materials do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that PEG fatty acid esters 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

Based upon the referenced hazard information included in the STF assessment and other available data, PEG fatty acid esters, are low toxicity chemicals. In animal studies effects were only seen at limit dose levels which are far greater than exposures resulting from their use as inert ingredients in pesticide products. While some local effects at the site of application were noted in a subchronic rabbit dermal toxicity study, such effects have not been reported in association with the use of PEG fatty acid esters in dermally-applied cosmetics.

PEG fatty acid esters are nonpersistant and readily biodegradable in the environment, and as such would not be expected to be present in drinking water sources at concentrations exceeding the low ppb level, far less than any potential level of concern for these substances.

Taking into consideration all available information on PEG fatty acid esters, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to PEG fatty acid esters used as inert ingredients when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the thirteen (13) exemptions from the requirement of a tolerance established for residues of PEG fatty acid esters be considered reassessed as safe under section 408(q) of FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

The STF assessment for the PEG fatty acid esters did not identify any available acute and chronic aquatic toxicity studies; no studies on acute or chronic toxicity to fish or aquatic invertebrates were found in the EPA ecological toxicity database. Predicted acute and chronic toxicity of representative PEG fatty acid esters utilizing the EPA ECOSAR modeling program resulted in aquatic toxicity classifications ranging from moderate to high for both acute and chronic toxicity to fish and aquatic invertebrates. Concentrations of PEG fatty acid esters in surface waters resulting from application of pesticides containing PEG fatty acid esters as inert ingredients to turf and croplands would be expected not to exceed levels of concern as microbial degradation would result in levels no greater than the parts per billion range. Uses of pesticide products containing PEG fatty acid esters as inert ingredients resulting in exposures to aquatic habitats may result in concentrations in surface water exceeding the level of concern for aquatic species, in which case additional risk mitigation may be needed.

The STF assessment for the PEG fatty acid esters did not identify any available acute and chronic aquatic toxicity studies. A search of the publicly available effects data on the Agency's ECOTOX database identified acute effects data for both freshwater and marine fish α-lauryl-ω-hydroxypoly(oxyethylene) and sediment invertebrate effects data for α-stearoyl-ω-hydroxypoly (oxyethylene) (molecular weight average = 600); no studies on acute or chronic toxicity to fish or aquatic invertebrates were found in the EPA ecological toxicity database for the other compounds Effects data for α-lauryl-ω-hydroxypoly(oxyethylene) included Atlantic salmon, the most sensitive endpoint being mortality at an LC_{50} of 5 ppm and Winter flounder, the most sensitive endpoint being mortality at an LC_{50} of 1 ppm. Effects data for α-stearoyl-ω-hydroxypoly (oxyethylene) was limited to several studies on a vortex worm with the most sensitive endpoint being mortality at >500 ppm. (ECOTOX 2002).

Predicted acute and chronic toxicity of representative PEG fatty acid esters utilizing the EPA ECOSAR modeling program resulted in acute aquatic toxicity classifications ranging from practically non-toxic to slightly toxic according to OPP's classification scheme. (ECOSAR 2000) Concentrations of PEG fatty acid esters in surface waters resulting from application of pesticides containing PEG fatty acid esters as inert ingredients to turf and croplands would be expected not to exceed levels of concern as

on field microbial degradation would result in levels no greater than the low parts per billion range by the time they are transported to surface waters.

REFERENCES:

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U.S Environmental Protection Agency (2004) Glycerol, and Glycerol esters of Fatty Acids: Antimicrobials Division Science Assessment for Tolerance Reassessment

APPENDIX A

VOLUME 2

STUDY TITLE

Science Assessment Document for Tolerance Reassessment:
Polyethylene Glycol Esters of Fatty Acids

DATA REQUIREMENTS

NA

AUTHOR

Richard H. Collier, Ph.D.

STUDY COMPLETION DATE

NA

PERFORMING LABORATORY

NA

LABORATORY PROJECT ID

NA

SUBMITTED BY

SURFACTANTS TASK FORCE
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Valdosta, GA 31603-5126

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).

COMPANY: SURFACTANTS TASK FORCE

COMPANY AGENT: LANDIS INTERNATIONAL, INC.
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SIGNATURE: Richard H. Collier

Richard H. Collier, Ph.D., Agent

DATE: February 10, 2005

GLP COMPLIANCE STATEMENT

This study was not conducted in accordance with the Good Laboratory Practice Standards as published by the U. S. Environmental Protection Agency Good Laboratory Practice Standards (FIFRA), 40 CFR 160 (*Federal Register*, Volume 54, No. 158, August 17, 1989) and differs in the following way(s):

This assessment, which is based upon literature in the public domain, is not a study and is not subject to GLP Standards.

STUDY DIRECTOR: **This information is not subject to GLP Standards.**

SPONSOR/SUBMITTER: **SURFACTANTS TASK FORCE**
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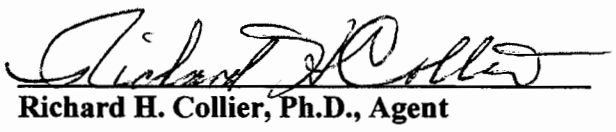
SIGNATURE: 
Richard H. Collier, Ph.D., Agent

DATE: **February 10, 2005**

Background:

The U.S. Environmental Protection Agency (EPA or the Agency) is in the process of reassessing tolerances for inert ingredients used in food-use pesticide products, a requirement of the Food Quality Protection Act (FQPA). The Surfactants Task Force (STF) has prepared this science assessment for tolerance reassessment of polyethylene glycol esters of fatty acids (PEG fatty acids) to assist the Agency in this task.

This science assessment is based upon data in the public domain. It provides a robust assessment of the hazards associated with the use of PEG fatty acids as inert ingredients in pesticide formulations. The scope of this response is limited to the mono- and di-esters of polyethylene glycol with fatty acids. Fatty acid esters of other polyols, such as glycerol, sugars, sugar alcohols (e.g. sorbitan), or polypropylene glycol, and copolymer esters with these or other polyols, as well as polyethylene glycols esters with acids other than fatty acids, are excluded from this assessment.

I. Executive Summary:

The PEG fatty acids considered in this science assessment include the PEG mono- and di-esters of alkanoic and alkenoic acids with a minimum of 8 and a maximum of 22 carbon atoms without limit to the degree of saturation or unsaturation. Branched fatty acids are included in this assessment but cyclic and aromatic fatty acids are not. PEG fatty acids are often identified by several other names, among them are fatty acid esters of polyethylene glycol, ethoxylated fatty acids, and oxirane homopolymer esters of fatty acids.

PEG fatty acids are readily hydrolyzed to their respective fatty acids and polyethylene glycol moieties in the gastrointestinal tract. Fatty acids are common components of a wide variety of foods. They are readily absorbed and are primary components of lipid metabolism. The polyethylene glycol moieties are poorly absorbed and pass through the gastrointestinal tract largely unmetabolized.

The database of toxicological data on PEG fatty acids in the open literature is somewhat limited. The specific data that apply directly to the subject chemical and which we have reviewed are listed in Attachment A. Data on other, related chemicals, which may support the assessment of the subject chemical via structure-activity relationships (SARs) or structure-functionality relationships (SFRs) are listed in Attachment B. Both lists are organized by type of study (endpoint), duration, and species. Reviews and other general resources are listed in the References section of this document. The list of databases and other data sources accessed in this effort are compiled in the Resource List in Attachment C.

In spite of the limited quantity of public domain data, it is clear that PEG fatty acids are of low mammalian toxicity by any route of administration. Over a period that spans several decades, different members of the family of PEG fatty acids have been the subject of mammalian toxicity

studies of various dosing durations. These studies include administration via the oral, dermal, intraperitoneal, and intravenous routes, as well as instillation into the eye.

The public domain database on the environmental fate and effects of PEG fatty acids is also rather limited. However, the EPA has proposed an aquatic level of concern for one member of the family – polyethylene glycol esters of coco-fatty acids – of 0.040 ppm. Given the expectation that PEG fatty acids will bind tightly to soil, it is quite unlikely that environmental concentrations in excess of the Agency's aquatic level of concern will occur.

This science assessment includes analysis of the properties of compounds closely related to PEG fatty acids where necessary for consideration of key aspects of the potential hazards of these compounds. Compounds considered include the polypropylene analogues of these compounds, fatty acids, polyethylene glycol, and polyethylene glycol sorbitan esters of fatty acids. Studies on these additional compounds serve to inform the potential toxicological impacts of structure-activity relationship considerations and add to the range of data under consideration, which is especially important when a limited database exists, as is the case here. For example, certain members of two related chemical families – polypropylene glycol esters of fatty acids and glycerol esters of fatty acids – are "generally recognized as safe" (GRAS) by the US Food And Drug Administration (FDA) and the EPA.

II. Use Information:

This assessment is intended to support the reassessment of the eight (8) tolerance exemptions for PEG fatty acids listed in Table 1. Some of these are listed in multiple subsection sat 40 CFR 180.1001, each of which is listed in the table. The range of surfactant uses of the compounds which are the subject of this assessment are also shown in Table 1. These compounds also have many uses in products other than pesticides. One of the tolerance exemptions is a generic expression which includes a series of compounds for which there are multiple Chemical Abstracts Service (CAS) numbers, indicated in Table 1 as "various." The specific compounds included in that generic expressions and which are evaluated in this science assessment are listed in Table 2, along with their CAS numbers and common descriptors. Some of the tolerance exemptions include compounds that are on different EPA Inerts Lists. In those cases, all the Inerts Lists on which one or more of the compounds are found are listed in the table.

A. Agricultural Uses of PEG Fatty Acids

The uses of PEG fatty acids in pesticide formulations includes defoamers, dispersing agents, emulsifiers, granule coatings, solvents/cosolvents, suspending agents, wetting agents, as well as general surfactants and related functions. The percentage of these surfactants in pesticide formulations varies but the amount in the diluted formulations as applied in the field is typically well below 1%. The application and dilution rates are selected to assure that the treated surface is thoroughly covered.

Table 1. Tolerance Exemptions Being Addressed in this Document

Tolerance Exemption Expression	CAS No.	40 CFR §180.	Use Pattern in Pesticides	Inerts List
Alkanoic and alkenoic acids, mono- and diesters of α-hydro-ω-hydroxypoly (oxyethylene) with molecular weight (in amu) range of 200 to 6,000	Various	1001(c), 1001(e)	Emulsifiers	3, 4B
α-Lauryl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-81-3	1001(c), 1001(e)	Emulsifier	4B
Oleic acid diester of α-hydro-ω-hydroxypoly (oxyethylene) with molecular weight (in amu) of 400	9005-07-6	1001(c)	Surfactants, related adjuvants of surfactants	4B
Oleic acid diester of α-hydro-ω-hydroxypoly (oxyethylene); the poly(oxyethylene) molecular weight (in amu) averages 2,300	9005-07-6	1001(d)	Surfactant	4B
α-Oleoyl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-96-0	1001(c)	Emulsifier	4B
α-Oleoyl-ω-(oleoyloxy) poly(oxyethylene), derived from α-hydro-ω-hydroxypoly (oxyethylene) (molecular weight 600 amu).	9005-07-6	1001(d)	Component of defoamers	4B
α-Stearoyl-ω-hydroxypoly (oxyethylene), average molecular weight (in amu) of 600	9004-99-3	1001(c), 1001(e)	Emulsifier	4B
α-Stearoyl-ω-hydroxypoly (oxyethylene), the poly(oxyethylene) content of averages either 8, 9, or 40 moles; if a blend of products is used, the average number of moles ethylene oxide reacted to produce any product that is a component of the blend shall be either 8, 9 or 40.	9004-99-3	1001(c), 1001(e)	Surfactants, related adjuvants of surfactants	4B

B. FDA Uses of PEG Fatty Acids

Several PEG fatty acids are used as components of cosmetics and pharmaceuticals and have been cleared by the U. S. Food and Drug Administration for use as direct and indirect food additives. These products are used in cosmetics, such as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and suntan/sun block preparations, as surfactants, emulsifiers, and solvents/cosolvents in concentrations typically in the range from 0.1% to 10% but with some products containing up to 25%. [16; based upon 1984 data]

PEG dioleate (CAS 9005-07-6) is approved as a secondary direct food additive when used as a component of defoamers for certain foods (21 CFR 173.340). Certain PEG fatty acids are also

used in resinous and other coatings, paper and cardboard products, and textiles, uses for which these compounds are approved as indirect food additives. [16]

Table 2. PEG Esters of Alkanoic and Alkenoic Acids

FIFRA Description	CAS Number	Common Descriptor
Alkanoic and alkenoic acids, mono- and diesters of alpha-hydro-omega-hydroxypoly (oxyethylene) with molecular weight (in amu) range of 200 to 6,000.	8050-33-7	Rosin PEG
	9004-81-3	Laurate Ethoxylate
	9004-94-8	Palmitate Ethoxylate
	9004-96-0	PEG Monooleate
	9004-97-1	Ricinoleate Ethoxylate
	9004-99-3	PEG Monostearate
	9005-02-1	PEG Dilaurate
	9005-07-6	PEG Dioleate
	9005-08-7	PEG Distearate
	52668-97-0	PEG Dioleate
	56002-14-3	Isostearic Ethoxylate
	61791-00-2	Tall Oil Ethoxylate
	61791-01-3	PEG Ditallate
	61791-07-9	Soy Ethoxylate
	61791-29-5	Coconut Oil Ethoxylate
	65071–95-6	Tall Oil Ethoxylate
	68553-06-0	Soy Ethoxylate

C. Other uses of PEG Fatty Acids

PEG fatty acids find many other uses, including plasticizers for vinyls, liquid nonionic detergents for woolens, dishes, and other household items, antistatic agents in weaving nylon and saran, and as ingredients in paints, penetrating agents for dying fabrics, and as a nonionic wetting agent. [16]

III. Physical/Chemical Properties:

The PEG fatty acids are clear to pale yellow oily liquids and low melting point, oily or waxy solids. Most display a mild, characteristic "fatty" odor. The pH of an aqueous suspension (1% to 5%) of these compounds is typically in the range from 3 to 8. [16] These compounds are either soluble or dispersable in water and are moderately soluble in polar organic solvents, such as acetone, ether, and ethanol. [21, 24]

The surfactant properties of the PEG fatty acids are derived from the hydrophilic polyethylene glycol backbone and the hydrophobic fatty acid ester portion(s) of the molecule. The variations in the degree of esterification (mono- or di-ester), the length of the fatty acid, and the length of the polyethylene glycol backbone combine to generate a range of surfactant properties that accounts for the broad range of uses of this class of surfactants.

IV. Hazard Assessment:

The public domain data used in this assessment were obtained primarily from databases of the National Institutes of Health, the National Institute for Occupational Safety and Health, the Cosmetic Ingredient review, and published literature accessed through the libraries of Florida State University, North Carolina State University, the University of Florida, and Valdosta State University. Other references were obtained through Internet searches utilizing the Google, Scirus, and Yahoo search engines. The list of all resources investigated is provided in Attachment C.

PEG fatty acids are readily hydrolyzed to their respective fatty acids and polyethylene glycol moieties in the gastrointestinal tract. Fatty acids are common components of a wide variety of foods, are readily absorbed, and are primary components of lipid metabolism. These fats are a major source of energy for general metabolism of all species of mammals. As the EPA has recognized in the case of glycerol esters of fatty acids, once fatty acids are released in the gastrointestinal tract, those whose source was polyethylene glycol esters are not distinguishable from those whose source was the food supply. [22] EPA staff have recommended the reassessment of numerous tolerances for fatty acids and their compounds. [22, 38, 39] From these determinations one may conclude that there is no significant hazard from exposure to the fatty acids derived from PEG fatty acids as they are used in pesticide formulations. Therefore, the toxicological properties of fatty acids are not further discussed in this document.

Polyethylene glycols are poorly absorbed from the gastrointestinal tract, absorption decreasing as the molecular weight increases. [17, 18, 19] Further, in oral and intravenous dosing studies, the absorbed polyethylene glycols were excreted unmetabolized in the urine and feces. [21] Only in a study using very high oral doses of PEG fatty acids was significant metabolism noted. [32] In this study in rats, metabolism of polyethylene glycol was evidenced in the form of oxalate bladder stones. Ethylene glycol was detected in the serum of burn victims following dermal exposure, indicating that absorption can occur through damaged skin and that metabolism is possible in this circumstance. [23] Consequently, the potential hazard from acute exposure to the polymeric moiety of polyethylene glycol esters of fatty acids is low for the routes of exposure expected from their use in pesticide formulations.

In the following sections of this document the public domain toxicity data on polyethylene glycol esters of fatty acids are summarized and the hazards associated with each potential route of exposure are assessed.

A. Toxicological Data:

Acute Oral Toxicity

Ten (10) reports on the acute oral toxicity of PEG fatty acids were reviewed. [9, 11, 12, 13, 14, 15, 16, 17, 18, 19] Some of theses references provide substantial details on the underlying studies. Some only provide the results, as an LD_{50} value, without supporting data and with little description of the conditions under which the study was conducted.

Four (4) acute oral toxicity reports on mice were reviewed. In a study on PEG monolaurate, Hopper, et al., found the oral LD_{50} in Harlan albino mice to be >25,000 mg/kg. [9, 16] NIOSH also reports the oral LD_{50} of PEG laurate in mice as >25,000 mg/kg. [12] The European Committee of Veterinary Medicinal Products reports the oral LD_{50} of PEG 12-hydroxystearate [15 mol EtO*] in mice as >20,000 mg/kg. [15] A NIOSH reference to a Russian publication by Israel'son reports the oral LD_{50} of PEG monolaurate in mice as 692 mg/kg. [11] No details on how this study was performed were available, consequently it is considered to be unreliable.

Seven (7) acute oral toxicity reports on rats were reviewed. In a study using PEG stearates, Elder, et al., reported the oral LD_{50} in rats to be >10,000 mg/kg. [16, 17, 18, 19] The specific PEG stearates utilized in that study were those with 2, 8, 12, 20, 40, 50, 100, and 150 moles of EtO. Louisiana State University reports the oral LD_{50} of PEG tall oil in rats to be >5,000 mg/kg in a material safety data sheet (MSDS) for that compound. [13] In a MSDS for a product containing several components, Intercon Enterprises, Inc., reports the oral LD_{50} in rats of PEG ricinoleate and PEG monooleate to be >2,000 mg/kg for each of these compounds. [14] No details about the conditions of the studies are presented in either of the MSDSs. The European

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* This notation is used throughout this document to indicate the average number of moles of monomer in the polyethylene moiety.

Committee of Veterinary Medicinal Products reports the oral LD_{50} of PEG 12-hydroxystearate [8 mol EtO] in rats as 250 mg/kg. [15] This latter report provides no details on the conditions of the study on PEG 12-hydroxystearate [8 mol EtO], consequently its reliability is uncertain. When compared to the acute oral toxicity results of each of the other studies reviewed, the results obtained on this hydroxylated fatty acid compound does not appear to representative of the general class of PEG fatty acids. The studies reviewed indicate that PEG fatty acids present a low hazard level for lethality via the oral route. The PEG fatty acids that are the subject of this assessment may be classified in Toxicity Category IV for oral toxicity effects.

Acute Dermal Toxicity

In a study using PEG stearate [8 mol EtO], Elder, et al., reported a dermal LD_{50} in rabbits of >10 ml/kg. This study indicates that PEG fatty acids present a low hazard level for lethality via the dermal route.

Acute Eye Irritation

Fifteen (15) eye irritation reports on rabbits were reviewed. NIOSH reports a Czechoslovakian publication which reported mild irritation resulting from a 500 mg dose of PEG monolaurate. [10] Elder and Anderson have reported minimal irritation from instillation of PEG stearate. [16, 17, 18, 19] In a series of related publications, K. Chiba, *et al.,* S. Hagino, *et al.,* A. Kurishita, *et al.,* K. Matsukawa, *et al.,* Y. Ohno, *et al.* (primary report), Y. Okamoto, *et al.,* H. Okumura, *et al.,* and T. Uchiyama, *et al.,* report a Draise maximal average total score of 3.3 for PEG monolaurate [10 mol EtO]. [2, 3, 4, 5, 25, 26, 27, 28] This value represents a low potential for acute eye effects. This series of reports also provides data on the effects of PEG monolaurate [10 mol EtO] on several *in vitro* systems that were being investigated as possible replacements for the Draize primary eye irritation test. In a separate study also intended to explore alternatives to the Draize test, M. Watanabe, *et al.*, reported that PEG monooleate [25 mol EtO] was non-irritating. [29] Finally, S. D. Gettings, *et al.*, in a third study intended to explore alternatives to the Draize test, reported minimally irritating Draize scores for a formulated cosmetic product that contained PEG stearate. [30] All of these studies indicate that PEG fatty acids present a low hazard level for acute eye effects.

Acute Skin Irritation

Five (5) skin irritation reports on rabbits were reviewed. Elder and Anderson have reported slight skin irritation from exposure of rabbits to PEG stearate. [16, 17, 18, 19] NIOSH reports a Czechoslovakian publication which reported mild irritation resulting from a 500 mg dermal dose of PEG monolaurate. [10] All of these studies indicate that PEG fatty acids present a low hazard level for acute skin effects.

Dermal Sensitization

Four (4) references reported studies on PEG monostearates [2, 8, 40, 50, and 100 mol EtO], all of which were non-sensitizing. [16, 17, 18, 19] These studies used the procedure of Landsteiner and

Jacobs with guinea pigs. Three (3) of the same references [17, 18, 19] report clinical data that show these compounds to present no sensitizing effects in humans. All of these studies indicate that PEG fatty acids present a low hazard level for skin sensitization.

Acute Intraperitoneal Toxicity

PEG monostearate [8 mol EtO] was the subject of one study using the intraperitoneal exposure route. In this study, the intraperitoneal LD_{50} to be >9 ml/kg in rats given 2 ml injections. NIOSH reports a study on mice which results in a intraperitoneal LD_{50} of 200 mg/kg. No details were available on the latter study. These studies indicate that PEG fatty acids present a low hazard level for lethality by the intraperitoneal route, a route of exposure that is not expected to be applicable to the use of PEG fatty acids in pesticide formulations.

Acute Intravenous Toxicity

Four (4) reports of acute toxicity via the intravenous route in mice were reviewed. Hopper, et al., reported the intravenous LD_{50} in mice for PEG distearate [8 and 20 mol EtO] to be 365 mg/kg and 220 mg/kg, respectively. [9, 16] The same study reported the intravenous LD_{50} in mice for PEG laurate [12 mol EtO] to be 500 mg/kg. A NIOSH report on the same study also lists an intravenous LD_{50} in mice for PEG monostearate of 870 mg/kg. [9/NIOSH] The European Committee of Veterinary Medicinal Products reports the intravenous LD_{50} of PEG 12-hydroxystearate [15 mol EtO] in mice as 3,160 to 5,000 mg/kg. [15] The same study reports the intravenous LD_{50} of PEG 12-hydroxystearate [15 mol EtO] in rabbits and rats as approximately 1,300 mg/kg and in dogs as >3,160 mg/kg. The Cosmetic Ingredient Review reports that an intravenous injection in a dog resulted in a prolonged hypotensive response. [16] Neither the dose that was injected nor the extent or duration of the effect were discussed. Collectively, these data indicate that PEG fatty acids present a low hazard level for lethality by the intravenous route, a route of exposure that is not expected to be applicable to the use of PEG fatty acids in pesticide formulations.

Summary of Acute Toxicity Endpoints

PEG fatty acids have been shown to present low toxicity by all routes of acute exposure. Although the public domain database is small, it is consistent with the results on related compounds, in particular the glyceryl esters of fatty acids and the polypropylene glycol esters of fatty acids. The only studies with endpoints that could point to any but the lowest category of toxic response are suspect because of the lack of information about the manner in which those data were generated.

Short-term and Subchronic Effects

Ringose and Waller reported that male chicks fed PEG laurate [4, 8, & 20 mol EtO] at dietary dosages from 0.1% to 2.0% showed no effects regarding mortality, diarrhea, growth, gross findings, or flavor. [31] Elder reported that calculi were found in the bladders of hamsters fed PEG stearate (dosage and structure unspecified) for up to 260 days and that rabbits whose diet

contained 4% PEG stearate [8 mol EtO] for four (4) months or 5% for 19 weeks showed no treatment-related effects. [18]

Harris, *et al.*, reported a study on rats in which certain PEG Fatty acids at very high dietary dosage rates produced toxic effects. [32] In that study, rats were fed a diet containing 25% PEG laurate [20 mol EtO], PEG stearate [8 mol EtO], or hydrogenate oils (control group) for 59 days. The group of rats fed PEG stearate [8 mol EtO] show a mild decrease in weight gain compared to the control group. The group fed PEG laurate [20 mol EtO] experienced greater decreases in weight gain, diarrhea, anal inflamation, and exhibited various clinical signs of distress. Three rats of this group had oxalate bladder stones at necropsy. Other treatment-related effects seen in both treatment groups included mild degeneration of cortical tubules of the kidneys, increased frequency of giant cells, monocyte/macrophage hyperplasia of the spleen, incomplete maturation of the testes, and increased frequency and prominence of alveolar wall inflammation (pneumonitis). The extreme dietary dosage of PEG fatty acids in this study contributed to the development of toxic symptoms. It is uncertain whether the different fatty acids contributed to the differences in the toxicity between treatment groups or whether those differences are the result of the variations in the amount of the PEG in the test substances. The presence of oxalate bladder stones in the group fed PEG laurate [20 mol EtO] and their absence in the group fed PEG stearate [8 mol EtO] suggests that the latter is the more critical variable.

Elder reported another dietary dosing study, in which hamsters fed a diet of 5% or 15% PEG monostearate for 2-10 weeks developed lesions in the gastrointestinal tract, liver, kidneys, and testes. Yet no signs of toxicity were noted in rats fed a diet of up to 4% PEG stearate [8, 40, 50, 100 mol EtO]. [18]

Anderson reported a 90-day study on free PEG in rats that produced no toxic symptoms of PEG [20 mol EtO] or [6 mol EtO] at doses at or below 4% in the diet or in drinking water. [19]

The dietary exposure studies reviewed present a rather sharp distinction in the presentation of symptoms of toxicity when the dietary dose of PEG fatty acids exceeds approximately 4%.

Anderson reported no toxic symptoms in rabbits treated with topical applications of 2 ml/kg/day of PEG [6 mol EtO] for 18 weeks (5 days per week). [19] Elder further reported a 20-day topical application study in rabbits with 0.5 to 2.0 g/kg doses of 1.5% PEG stearate [6 mol EtO]. Erythema, dryness, wrinkling, desquamation, and hyperkeratosis at the application sites were noted in this study. [18]

Clinical studies in humans with PEG stearates indicate that these compounds are neither irritants nor sensitizers. Elder reported that a 25% aqueous solution of PEG stearate [2 mol EtO] did not induce sensitization or dermal irritation in a repeat insult patch test with 168 subjects. [18] Elder also reported that neither phototoxicity nor photosensitization were seen in tests with PEG stearate [2 mol EtO], PEG stearate [100 mol EtO], or skin conditioners containing 1% to 3% of either of these compounds.

Two (2) reports on the dermal toxicity of free PEG were reviewed. Anderson reported no toxicity in a 30 day study in rabbits in which 0.8 g/kg/day PEG stearate [20 mol EtO] was topically applied daily. [19] Anderson also reported unspecified systemic effects in a seven day study in rabbits using an antimicrobial cream that contained 63% PEG [6 mol EtO], 5%, PEG [20 mol EtO] and 32% PEG [75 mol EtO]. [19]

Clinical studies of free PEG has shown mixed sensitization results. [19] PEG [6 & 8 mol EtO] induced mild sensitization while later production lots of PEG [6 mol EtO] and PEG [75 mol EtO] produced no reactions in the 100 male and 100 female subjects. In another trial, a product containing 3% PEG [8 mol EtO] produced mild irritation in the induction phase and unspecified responses at the challenge phase in an irritation/sensitization test. Nephrotoxicity and contact dermatitis in burn patients was attributed to a topical ointment that contained 63% PEG [6 mol EtO], 5%, PEG [20 mol EtO] and 32% PEG [75 mol EtO].

Chronic Effects

Elder reported a study on rats fed a diet of 4% PEG stearate [8 mol EtO] or 2% PEG stearate [100 mol EtO] for two years had no treatment-related symptoms. [18] In the same review, Elder also reported a study on hamsters fed 5% to 15% PEG monostearate for 28-39 weeks in which numerous symptoms were reported, including increased mortality, chronic diarrhea, atrophic testes, and hemosiderosis. In rats fed a diet of 6% PEG dilaurate [8 mol EtO] for 505 days, Krehl reported no differences in mortality or organ gross or microscopic examinations except that one rat in the treated group had cystic liver spots, one had hemoragic lungs, one had a large fibrosarcoma, and three had focal parenchymal hepatitis. [33]

Fitzhugh reported a two-year study in rats fed 2%, 5%, 10% , or 25% PEG laurate [20 mol EtO]. [34] In this study, no effects were noted on mortality, heart, lungs, spleen, pancreas, small intestine, colon, kidneys, adrenal glands, prostate, urinary bladder, leg bones and muscles, bone marrow, behavior, or appearance at any dose level. Growth reduction was noted at the 25% dietary dose after week 26. A dose-related increase in hepatic cysts and cecal enlargement was observed. Three animals in the highest does group also exhibited gastric mucosal hyperplasia.

As seen in the shorter duration studies, the presentation of symptoms in chronic studies on PEG fatty acids appears only when the dietary does exceeds 4%.

One report on the chronic effects of free PEG was reported by Anderson. [19] In this study, dogs fed PEG [8, 32, or 75 mol EtO] for one year exhibited no observed toxic effects.

Reproductive and Developmental Toxicity

Elder reported that in multi-generational studies, rats fed a diet of 10% to 20% PEG stearate [8 or 20 mol EtO] exhibited decreased newborn litter survival time due to maternal neglect, impairment of lactation, lower weaning weight, increased mortality of nurslings, and decreased reproductive performance in the F3 generation. [18] Rats fed 5% PEG stearate exhibited none of these effects.

Anderson reported a study on free PEG [6, 32, and 75 mol EtO] in which no adverse reproductive effects were exhibited in either a chronic (two-year) at doses up to 0.062 g/kg/day for PEG [6 & 32 mol EtO] and 1.69 g/kg/day for PEG [75 mol EtO] or a subchronic study at doses up to 0.23 g/kg/day for PEG [75 mol EtO]. [19]

It has long been recognized that ethylene glycol and certain of its monoalkyl ethers, for example, ethylene glycol monomethyl ether, exhibit reproductive and developmental toxicity. The toxic effects of these compounds are produced by their alcohol or aldehyde metabolites. [20] However, these substances are not expected to be produced from the surfactant uses of PEG fatty acids. Consequently, no significant reproductive or developmental hazards are expected to derive from the use of these compounds as surfactants in pesticide formulations.

Mutagenicity and Carcinogenicity

No studies on the mutagenicity or carcinogenicity of PEG fatty acids have been found in the public literature. However, Anderson reported that free PEG [8 mol EtO] at a dose of 1% was negative in Chinese hamster ovary cell mutation and sister chromatid exchange tests but that, in the unscheduled DNA synthesis test, a statistically significant increase in thymidine incorporation occurred at the highest does tested (0.1%). [19] In the same review, Anderson also reported that free PEG [150 mol EtO] was not mutagenic up to 150 g/l in the mouse lymphoma forward mutation test.

Anderson also reported that free PEG [8 mol EtO] was negative for carcinogenicity in mice in a 30 week oral dosing study, in rats in a 6 month intraperitoneal dosing study, rats and mice in subcutaneous dosing studies for dosing periods of 20 weeks and one year, respectively, and via injection into the gastric antrum of Guinea pigs for a 6 month dosing period.

Mammalian Metabolism

Polyethylene glycols are poorly absorbed from the gastrointestinal tract, absorption decreasing as the molecular weight increases. [17, 18, 19] Further, in oral and intravenous dosing studies, the absorbed polyethylene glycols were excreted unmetabolized in the urine and feces. [21] Only in a study using very high oral doses of PEG fatty acids was significant metabolism noted. [32] In this study in rats, metabolism of polyethylene glycol was evidenced in the form of oxalate bladder stones. Ethylene glycol was detected in the serum of burn victims following dermal exposure, indicating that absorption can occur through damaged skin and that metabolism is possible in this circumstance. [23] Consequently, the potential hazard from acute exposure to the polymeric moiety of polyethylene glycol esters of fatty acids is low for the routes of exposure expected from their use in pesticide formulations.

Summary of Toxicological Effects

The PEG Fatty acids exhibit low toxicity in all exposure durations tested except at doses far beyond those that could reasonably be expected from their use as adjuvants in pesticide formulations. Based upon the available data in the public domain, the acute toxicity of this class

of compounds is low. The only subchronic and chronic duration studies which show significant systemic effects are those in which the dietary dose was in excess of 5% of the total diet. These results are not surprising. Similar results were noted by the US EPA in its review of the glycerol esters of fatty acids [22] and by the Cosmetic Ingredient Review in its review of polypropylene glycol esters of fatty acids. [17] The Joint FAO/WHO Expert Committee on Food Additives has recognized 5% in the diet (2500 mg/kg/day) as the NOAEL for PEG stearates [8 and 40 mol EtO] and has set an allowable daily intake (ADI) of 25 mg/kg/day using the standard 100X safety factor. [35]

B. Special Considerations for Infants and Children:

The are no data that point to any concern for increased risk to infants or children from exposure to PEG fatty acids. PEG fatty acids are widely used in consumer products used by children and adults, including such products as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and suntan/sun block preparations. [16] These products have a long, safe use history. Further, the fatty acid metabolites of these compounds are biologically indistinguishable from those which are common components of foods for people of all ages. In studies on developmental effects, adverse effects have been seen only at dose levels above those that cause maternal effects. Consequently, no safety factor has been used in this document for special considerations for toxicity to infants and children and such a safety factor is not necessary.

V. Exposure Assessment:

As is the case with the glycerol fatty acid esters, exposure to the PEG fatty acids may be through FDA-approved uses in food, cosmetics, such as bath oils, cleansing preparations, moisturizers, other skin care preparations, shampoos, and suntan/sun block preparations, and household products, such as liquid nonionic detergents for woolens and dishes. [16] Cosmetic products containing PEG fatty acids are approved for daily use, may readily come in contact with both the eyes and nasal mucosae. The fatty acids released form PEG fatty acids, regardless of their source, are indistinguishable from fats in foods of people of all ages.

Human exposure to PEG fatty acids from FDA-approved sources, both from foods and from cosmetics, may be reasonably expected to be much greater than that for the use of these compounds in pesticide formulations. Except in cases of extreme dosages, the PEG fatty acids are of low toxicity to mammals. Consequently, there is no reason to expect that the use of these compounds in pesticide formulations will present any significant hazard, and no quantitative exposure assessment has been performed.

VI. Risk Characterization:

Based upon the hazard aspect only, the PEG fatty acids present little risk in any exposure scenario because of their inherent low toxicity. The exposures expected from the use of these compounds in pesticide formulations are expected to also be low, much lower than those already approved by the FDA for the food additive and cosmetic uses of PEG fatty acids.

The minimal hazard profile of the PEG fatty acids is similar to the hazard profiles of other, related groups of polymeric surfactants for which the US EPA has already reviewed the corresponding data and approved the reassessment of tolerances. [22, 40 CFR 180.960, 40 CFR 180.1001] These documents indicate that the US EPA has already reviewed and approved tolerances for glycerol fatty acid esters, certain PEG sorbitan fatty acid esters, certain 12-hydroxy stearic acid-PEG co-polymers, that have strong structural and functional similarity to the PEG fatty acids. Although these groups are different enough that it is appropriate to separately consider the PEG fatty acids, the data that supported the approval of these similar compounds is consistent with the low toxicity of the PEG fatty acids. Consequently, although the universe of data on the PEG fatty acids is not large, when considered along that of other similar compounds, it is sufficient to conclude that the PEG fatty acids present minimal hazards from their uses in pesticide formulations.

When all the available hazard data are considered, and the exposure to PEG fatty acids from their uses in pesticide formulations are compared to the FDA-approved food additive and cosmetic uses, as EPA concluded in the case of their review of the glycerol fatty acid esters, we conclude that it is unlikely that the uses of PEG fatty acids in pesticide formulations will pose a significant hazard to the general public or any sub-population group. Any exposure from the use of the PEG fatty acids as inert ingredients in pesticide formulations may reasonably be expected to be well below any level that could cause an adverse effect. Consequently, this qualitative assessment has been performed in lieu of a quantitative risk assessment.

VII. Environmental Fate/Ecotoxicity/Drinking Water Considerations:

A. Environmental Fate Characterization:

These compounds are either soluble or dispersable in water and are moderately soluble in polar organic solvents, such as acetone, ether, and ethanol. [21,24]

Few data on the environmental fate of PEG fatty acids were found in the public domain. The surfactant properties of the PEG fatty acids are derived from the hydrophilic polyethylene glycol backbone and the hydrophobic fatty acid ester portion(s) of the molecule. One EPA review document indicated that PEG coco-fatty acids primarily degrade over a period of a few weeks and ultimately degrade over a period of a few months. [7] This EPA review also indicated that the Agency has calculated an aquatic concern level of 0.04 ppm for the PEG coco-fatty acids.

B. Ecotoxicity and Ecological Risk Characterization:

Three (3) studies on the effects of PEG fatty acids were reviewed. Hall reported that PEG caprate [4 mol EtO] produced a LC_{50} of 16.68 µmol/l on the estaurine crustacean, *Mysidopsis bahia*. [1] Wildish reported the EC_{50} of PEG monolaurate [14 mol EtO] for decrease in swimming amplitude of the winter flounder (*Pseudoplueronectes americus*) to lie in the range from 0.1mg/l to 1.0 mg/l. [36] Kaim-Malka reported sublethal effects of 24 hr exposure of the isopod *Idotea balthica basteri* to PEG oleate [14 mol EtO] at 10 mg/l. [37] These results are consistent with the expectation of significant toxicity of PEGs to aquatic organisms in clean water. However, in the environment the actual toxicity hazard is expected to be mitigated, because these compounds bind tightly to soil and sediment.

The hydrolysis of the ester bond results in the destruction of the surfactant properties. The resulting degradation products, free fatty acids and polyethylene glycol, are less toxic that the parent compounds, leading to a relative high aquatic concern concentration of 0.040 ppm. Given the strong binding of PEGs to soil, it seems unlikely that the Agency's level of concern will be exceeded in the environment. [7]

VIII. Aggregate Exposures

Section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) requires the US EPA to consider available information concerning exposure from a chemical in food and all other, non-occupational avenues, including that from drinking water and residential or other indoor uses. In the case of the PEG fatty acids, potential exposure from the FDA-approved uses of these compounds dwarfs that from the pesticidal uses. These compounds are of systemic low toxicity. Consequently, the qualitative assessment provided in this document is appropriate.

As previously discussed, the PEG fatty acids are readily hydrolyzed to fatty acids and polyethylene glycol. Once hydrolyzed the compounds lose the surface active properties that are responsible for both their utility as adjuvants and their limited toxicity. Consequently, no significant hazard is expected from the aggregate exposure to PEG fatty acids from their uses in pesticide formulations.

IX. Cumulative Exposure:

Section 408(B)(2(D)(v) of the FFDCA requires that, when the US EPA makes decision on a tolerance, the Agency will consider "available information" concerning the cumulative effects of a particular compound and "other substances that have a common mechanism of toxicity." As discussed above, the PEG fatty acids are structurally related to other classes of chemicals, all of which are of low-toxicity and which resemble natural products. Consequently, the separate or combined risks are expected to be low.

No information is available that indicates that the PEG fatty acids share a "common mechanism of toxicity" with other classes of chemicals nor has the EPA made a determination that such a relationship exists. Consequently, for the purposes of reassessing the tolerances of the PEG fatty acids, no assumption of a common mechanism of toxicity with any other group of chemicals should be made. Reconsideration of this aspect of this review should occur if new information on a common mechanism of toxicity with some other class of chemicals becomes available.

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ATTACHMENT A

Database of Toxicological Data on PEG Fatty Acids

Polyethylene Glycol Esters of Fatty Acids

Surfactants Task Force

2/7/2005

CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
Acute Oral Toxicity									
9004-81-3	polyethyleneglycol monolaurate	mouse	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	692 mg/kg	lethality (LD_{50})	11
9004-81-3	polyethyleneglycol monolaurate	mouse	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>25,000 mg/kg	lethality (LD_{50})	12
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	mouse	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>20,000 mg/kg	lethality (LD_{50})	15
9004-81-3	polyethyleneglycol monolaurate [12 mol EtO]	mouse	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>25,000 mg/kg	lethality (LD_{50})	9, 16
65071-95-6	ethoxylate tall oil	rat	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>5,000 mg/kg	lethality (LD_{50})	13
9004-97-1	polyethyleneglycol ricinoleate	rat	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>2000 mg/kg	lethality (LD_{50})	14
9004-96-0	polyethyleneglycol monooleate	rat	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>2000 mg/kg	lethality (LD_{50})	14
9004-99-3 and 9004-08-7	polyethyleneglycol monostearate and distearate mixtures [8 mol EtO]	rat	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	250 mg/kg	lethality (LD_{50})	15
9004-99-3	polyethyleneglycol monostearate	rat	oral	870.1100	acute oral toxicity	single dose/ observation period unstated	>10,000 mg/kg	lethality (LD_{50})	16, 17, 18, 19
Acute Dermal Toxicity									
9004-99-3	15% polyethyleneglycol monostearate [8 mol EtO]	rabbit	dermal	870.1200	acute dermal toxicity	single dose/ observation period unstated	>10 ml/kg - slight erythema	lethality (LD_{50})	9, 16

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CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
Acute Eye Irritation									
	polyethyleneglycol monolaurate [10 mol EtO]	rabbit	eye	870.2400	acute eye irritation	single dose/ 10-day observation	3.3	Draize maximal average total score	2, 3, 4, 5
9004-96-0	polyethyleneglycol monooleate	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	mild @ 500mg dose	eye irritation	10
9004-99-3	polyethyleneglycol monostearate	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	minimal	eye irritation	16, 17, 18, 19
	various surfactants	rabbit	eye	870.2400	acute eye irritation - cytotoxicity	24-hr dose/ observation period unstated	varied	maximal average Draize total score	28
	various surfactants	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	varied	maximal average Draize total score	26
	various surfactants	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	varied	maximal average Draize total score	25
	various surfactants	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	varied	maximal average Draize total score	27
9004-96-0	polyethyleneglycol monooleate [25 mol EtO]	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	non-irritating	maximal average Draize total score	29
9004-99-3	polyethyleneglycol monostearate	rabbit	eye	870.2400	acute eye irritation	24-hr dose/ observation period unstated	minimally irritating	maximal average Draize total score	30
Acute Skin Irritation									

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CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
9004-99-3	polyethyleneglycol monostearate [2, 8, 40, 50, and 100 mol EtO]	human	skin	870.2500	acute skin irritation	24-hr dose/ observation period unstated	slight irritation	skin irritation	16, 17, 18, 19
9004-96-0	polyethyleneglycol monooleate	rabbit	skin	870.2500	acute skin irritation	24-hr dose/ observation period unstated	mild @ 500mg dose	skin irritation	10
Acute Dermal Sensitization									
9004-99-3	polyethyleneglycol monostearate [2, 8, 40, 50, and 100 mol EtO]	guinea pig	skin	870.2600	dermal sensitization	24-hr dose/ observation period unstated	not a sensitizer	dermal sensitization	16, 17, 18, 19
9004-99-3	polyethyleneglycol monostearate [2, 8, 40, 50, and 100 mol EtO]	human	skin	870.2600	dermal sensitization	24-hr dose/ observation period unstated	not a sensitizer	dermal sensitization	17, 18, 19
Acute Intraperitoneal Toxicity									
9004-99-3	polyethyleneglycol monostearate	mouse	intraperitoneal	870.xxxx	acute intraperitoneal toxicity	unstated	200 mg/kg	lethality (LD_{50})	8
9004-99-3	polyethyleneglycol monostearate [8 mol EtO]	rat	intraperitoneal	870.xxxx	acute intraperitoneal toxicity	unstated	>9 ml.kg	lethality (LD_{50})	16
Acute Intravenous Toxicity									
9004-99-3	polyethyleneglycol monostearate [40 mol EtO]	dog	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	prolonged hypotensive reponse	systemic effects	16
9004-99-3	polyethyleneglycol monostearate	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	870 mg/kg	lethality (LD_{50})	9
9004-96-0	polyethyleneglycol monooleate	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	500 mg/kg	lethality (LD_{50})	9
9004-81-3	polyethyleneglycol monolaurate	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	500 mg/kg	lethality (LD_{50})	9,16

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CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
9005-08-7	polyethyleneglycol distearate [8 mol EtO]	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	365 mg/kg	lethality (LD_{50})	9, 16
9005-08-7	polyethyleneglycol distearate [20 mol EtO]	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	220 mg/kg	lethality (LD_{50})	9, 16
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	mouse	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	3160 to 5000 mg/kg	lethality (LD_{50})	15
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	rabbit	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	~1300 mg/kg	lethality (LD_{50})	15
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	rat	intravenous	870.xxxx	acute intravenous toxicity	single dose/ observation period unstated	~1300 mg/kg	lethality (LD_{50})	15
Short-Term/Subchronic Intravenous Toxicity									
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	dog	intravenous	870.xxxx	intravenous toxicity	19 daily doses/ observation period unstated	NOEL=25 mg/kg	apathy, transient restlessness, and urticaria	15
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	rat	intravenous	870.xxxx	intravenous toxicity	2-4 weeks dosing/ 4-week recovery period	NOEL=25 mg/kg	lipid deposit	15
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	dog	intravenous	870.xxxx	intravenous toxicity	4 weeks dosing/ observation period unstated	NOEL=25 mg/kg	pseudo-anaphylactic reactions (pruritus and erythema) at 50 and 100 mg/kg doses	15

Polyethylene Glycol Esters of Fatty Acids Surfactants Task Force 2/7/2005									
CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
	polyethyleneglycol 12-hydroxystearate [15 mol EtO]	rat	intravenous	870.xxxx	intravenous toxicity	3-months dosing/ observation period unstated	NOEL<250 mg/kg; LOEL=250 mg/kg	lipid deposit at all doses; lethality at 500 and 750 mg/kg; reversible hematological and biochemical effects	15
Subchronic Toxicity									
9004-81-3	polyethyleneglycol monolaurate [12 mol EtO]	unspecified	oral	870.3050	short term oral toxicity	10 weeks	gastro-intestinal irritation (without necrotic effects)	systemic and organ-specific effects	16
9004-99-3	polyethyeneglycol monostearate	rat	food	870.3550	reproduction screening	>12 weeks	Probability of offspring lethality increased with dose from 5% in feed to 10% and to 20%.	lethality to offspring	6
9004-99-3	polyethyleneglycol monostearate [8 and 40 mol EtO]	unspecified	oral	870.3800	reproduction and fertility		no effect at HDT	reproduction and fertility effects	16, 17, 18, 19
9004-81-3	polyethyleneglycol monolaurate [4, 8, & 20 mol EtO]	chicks	oral	870.xxxx	subchronic toxicity	10 weeks	no effects	mortality, diarrhea, growth, gross findings, & flavor	31
9004-99-3	polyethyleneglycol monostearate [8 mol EtO]	rats	oral	870.xxxx	subchronic toxicity	59 days	slight decrease in weight gain	growth, clinical signs, organ effects	32

Polyethylene Glycol Esters of Fatty Acids

Surfactants Task Force

2/7/2005

CAS Reg. No.	Test Substance Name	Test Organism	Exposure Route	Guideline	Study Name or Type	Duration	Endpoint	Toxic or Environmental Effect	Reference No.
9004-81-3	polyethyleneglycol monolaurate [20 mol EtO]	rats	oral	870.xxxx	subchronic toxicity	59 days	decreased weight gain, diarrhea, anal inflammation, clinical distress	growth, clinical signs, organ effects	32
Chronic Toxicity									
9004-81-3	polyethyleneglycol monolaurate [12 mol EtO]	unspecified	oral	870.4100	chronic toxicity		evidence of liver damage and hyperplasia in several tissues	growth, histopatho-logic observations, and hematological values	16
9004-99-3	polyethyleneglycol monostearate [8, 40, and 100 mol EtO]	unspecified	oral	870.4100	chronic toxicity		no effect at HDT	growth, histopatho-logic observations, and hematological values	16, 17, 18, 19
9004-99-3	polyethyleneglycol monostearate [8 and 40 mol EtO]	unspecified	oral	870.4200	carcinogenicity		no effect at HDT	carcinogeni-city	16, 17, 18, 19
9005-02-1	polyethyleneglycol dilaurate [8 mol EtO]	rats	oral	870.4100	chronic toxicity	505 days	no effects except 3 focal parenchymal hepatitis & 1 each of the following: cystic liver spots, hemoragic lungs, & fibrosarcoma	growth, histopatho-logic observations, and hematological values	33

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9004-81-3	polyethyleneglycol monolaurate [20 mol EtO]	rats	oral	870.4100	chronic toxicity	2 years	Dose related increase in hepatic cysts and cecal enlargement; no other effects at 2%, 5%, or 10%; growth reduction at 25%.	growth, histopatho-logic observations, and hematological values	34
Acute Ecotoxicity Endpoints									
	polyethyleneglycol monocaprate [4 mol EtO]	estaurine crustacean *(Mysidopsis bahia)*	environmental (water)	850.1035	aquatic fauna toxicity	single dose/ observation 48-hr	16.68 µmol/l	lethality (LOEL)	1
	polyethyleneglycol monolaurate [14 mol EtO]	winter flounder (*Pseudoplueronectes americus*)	environmental (water)	850.1035	aquatic fauna toxicity	unstated	0.1 - 1.0 mg/l	EC_{50} swimming	36
	polyethyleneglycol oleate [14 mol EtO]	isopod (*Idotea balthica basteri*)	environmental (water)	850.1035	aquatic fauna toxicity	24 hr	10 mg/l	sublethal effects	37
Degradation/Biodegradation/Environmental fate									
61791-29-5	ethoxylated coco-fatty acids		environmental	835.3100/ 835.3400	aquatic biodegradation	single dose/ observation days-weeks	days (primary)/ weeks (ultimate)	biodegradation	7
61791-29-5	ethoxylated coco-fatty acids		environmental	850.xxxx	risk assessment	unstated	0.040 ppm	aquatic concern level	7

ATTACHMENT B

Database of Toxicological Data on Chemicals Related to PEG Fatty Acids

Polyethylene Glycol Esters of Fatty Acids									
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2/7/2005									
CAS Reg. No.	**Test Substance Name**	**Test Organism**	**Exposure Route**	**Guideline**	**Study Name or Type**	**Duration**	**Endpoint**	**Toxic or Environmental Effect**	**Reference No.**
Acute Toxicity Endpoints									
	penta-ethylene glycol mono *n*-dodecyl ether	human	dermal	870.2500	acute dermal irritation	single and repeated exposure			Bodin
	various surfactants	fish	aquatic	850.1075	acute irritation to fish	96 hour	varied	LC50	Reiff
Metabolism									
	nonylphenol	Atlantic salmon	waterborne and dietary	???	*In vivo* and *in vitro* metabolism	72 h			Arukwe
Peroxidation									
	malondialdehyde (MDA)	*Silurus glanis*	waterborne	???	peroxidation in fish tissues	???			Avci
Adjuvant effect on production of specific IgE antibodies in mice									
	SDBS, SDS, coconut soap, Genapol X-80	mice	intravenous	???	adjuvant effect on production of specific IgE antibodies in mice	24 days	varied	NOEL	Clausen
Environmental analysis									
	various surfactants	N/A	N/A	???	separation and quantitative determination of non-ionic surfactants	N/A	N/A	N/A	Cserhati
Degradation/Biodegradation									
	polyether and polyester based on PEG and (PBT) (PEOT/PBT)	rats	subcutaneous	???	*in vivo* and *in vitro* degradation	24 weeks	???	???	Deschamps
	AEO and ANEO	aquatic and terrestrial environment	varied	???	environmental effects	N/A	N/A	N/A	Krogh
	various surfactants	sludge, swamp and marine	varied	???	anaerobic degradation	varied	varied	varied	Madsen
	various surfactants	various surfactants	N/A	???	anaerobic and aerobic degradation	10 days	varied	chemical oxygen demand (COD)	Mezzanote
	various surfactants	sorbed-phase chlorinated organic contaminants	methanogenesis	???	toxicity and biodegradability of non-ionic surfactants	80 days	varied	methane production	Yeh

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	various surfactants	bacteria in sludge, horticultural waste, biofilm, forest pond sediment	N/A	???	Anaerobic degradability of alcohol ethoxylates and related non-ionic surfactants	~ 1 year	varied	varied	Mosche
	various surfactants	N/A	N/A	???	Environmental relevance of anaerobic degradability of surfactants	N/A	N/A	N/A	ERASM
	Dobanol 45-7 and Dobanol 45-11	rainbow trout	aquatic	850.1400	toxicity of biodegradation products to rainbow trout	7 days	0.63 - 1.11 mg/L	LC50	Turner
Environmental fate									
	sodium dodecyl sulfate and alkyl ethoxylate sulfate	stream mesocosm		???	toxicity assessment by community analysis in a stream mesocosm	8 weeks	various	NOEC	Guckert
	AES, AE and DEEDMAC	sewer	radiolabeled surfactant	???	fate of detergent surfactant in sewers	48 hours for lab and 72 hours for field	varied	µg/L	Matthijs
Long-term consumption of plant sterol esters									
	plant sterol esters	humans	oral	???	Long-term consumption of plant sterol esters	52 weeks	LDL and HDL	effects on cholesterol levels	Hendriks
Developmental toxicity									
	vegetable oil-derived stanol fatty acid esters	rats	oral	870.3700?	developmental toxicity	21 days	not developmentally toxic		Slesinski
Biosynthesis									
	various esters	N/A	N/A	N/A	ester synthesis in lipase-catalyzed reactions	N/A	N/A	N/A	Yahya

ATTACHMENT C

Resource List

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National Toxicology Program	ntp-server.niehs.nih.gov
Eval of Risks to Human Repro	cerhr.niehs.nih.gov
TOXNET	www.toxnet.nlm.nih.gov HSDB IRIS CCRIS GENE-TOX TOXLINE DART/ETIC
GATEWAY	gateway.nlm.nih.gov/gw/Cmd MEDLINE OLDMEDLINE MEDLINEplus DIRLINE
Agency for Tox. Subst. and Disease	www.atsdr.cdc.gov.toxprofiles/
OSHA/NIOSH	www.cdc.gov/niosh/topics/chemical-safety/ www.cdc.gov/niosh/npg/npg.html www.cdc.gov/niosh/ipcsneng/neng0000.html www.cdc.gov/niosh/81-123.html
NTIS	www.ntis.gov
Federal Government orgs.	www.firstgov.gov/ www.science.gov/
TSCA Section 4	www.epa.gov/oppintr/chemtest/sumindex.htm
Internat Agency Res on Cancer	www.iarc.fr
OPPT Fact Sheets	www.epa.gov/opptintr/chemfact/
TSCA Submissions	esc.syrres.com/efdb/TSCATS.htm
High Production Volume Challenge	www.epa.gov/chemrtk/viewsrch.htm
Cosmetic Ingredient Review	www.cir-safety.org/staff_files/publist.pdf
EPA drinking water	www.epa.gov/safewater/mcl.html
INCHEM	www.inchem.org
OECD	cs3-hq.oecd.org/scripts/hpv/
BIBRA	www.bibra.co.uk
EPA Envir Publications	www.epa.gov/ncepihom/
REDs by OPP	www.epa.gov/pesticides/reregistration/status.htm
Google search engine	www.google.com
Yahoo search engine	www.yahoo.com
Florida university library system	http://webluis.fcla.edu/
Georgia university library system	http://gil.valdosta.edu/
Scientific information search engine	http://www.scirus.com/srsapp/
Elsevier electronic journals	http://www.info.sciencedirect.com

APPENDIX B

Chemical Abstract Service (CAS) Registry Numbers associated with the tolerance exemption for "alkanoic and alkenoic acids, mono- and diesters of α-hydro-ω-hydroxypoly(oxyethylene) with molecular weight (in amu) range of 200 to 6,000"

CAS Reg No.	Chemical Name
9004-81-3	Poly(oxy-1,2-ethanediyl), α-(1-oxododecyl)-ω-hydroxy-
9004-94-8	Poly(oxy-1,2-ethanediyl), α-(1-oxohexadecyl)-ω-hydroxy-
9004-96-0	Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-
9004-97-1	Poly(oxy-1,2-ethanediyl), α-[(9Z,12R)-12-hydroxy-1-oxo-9-octadecenyl]-ω-hydroxy-
9004-99-3	Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)- ω-hydroxy-
9005-02-1	Poly(oxy-1,2-ethanediyl), α-(1-oxododecyl)- ω-[(1-oxododecyl)oxy]-
9005-07-6	Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy-
9005-08-7	Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-[(1-oxooctadecyl)oxy]-
52668-97-0	Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecenyl)-ω-[(1-oxooctadecyl)oxy]-
61791-00-2	Poly(oxy-1,2-ethanediyl), α-(1-oxoisooctadecyl)-ω-hydroxy-
61791-01-3	Fatty acids, tall-oil, diesters with polyethylene glycol
61791-07-9	Fatty acids, soya, ethoxylated
61791-29-5	Fatty acids, coco, ethoxylated
65071-95-6	Tall oil, ethoxylated