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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: May 20, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – Members of the Sorbitan Fatty Acid Esters and the Polysorbates (see table below)

FROM: Dan Rosenblatt, Chief
Minor Use, Inerts, and Emergency Response Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

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

Chemicals:

Number of exemptions	CFR Reference			
	40 CFR **	**Tolerance Exemption Expression**	**Limits**	**Uses**
1	180.920	Poly(oxyethylene)(5) sorbitan monooleate	(none)	Surfactants, related adjuvants of surfactants
1	180.910	Polyoxyethylene (20) sorbitan monostearate	(none)	Surfactants, related adjuvants of surfactants
1	180.920	Polysorbate 60, conforming to 21 CFR 172.836	(none)	Surfactant
1	180.910	Polysorbate 65, conforming to 21 CFR 172.838,	(none)	Emulsifier

Number of exemptions	CFR Reference			
	40 CFR **	Tolerance Exemption Expression	Limits	Uses
1	180.910	Sorbitan fatty acid esters (fatty acids limited to C12, C14, C16, and C18 containing minor amounts of associated fatty acids) and their derivatives; the poly(oxyethylene) content averages 5-20 moles.	(none)	Surfactants, related adjuvants of surfactants
1	180.930	Sorbitan fatty acid esters (fatty acids limited to C12, C14, C16, and C18 containing minor amounts of associated fatty acids) and their poly(oxyethylene) derivatives of sorbitan fatty acid esters; the poly(oxyethylene) content averages 16-20 moles.	(none)	Buffering agent, corrosion inhibition

**Residues listed in 40 CFR 180.910 (formerly 180.1001(c)) are exempt from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.

Residues listed in 40 CFR 180.920 (formerly 180.1001(d)) are exempt 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 (formerly 180.1001(e)) are exempt 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: The sorbitan fatty acid esters and polysorbates are inert ingredients used as surfactants, related adjuvants of surfactants, emulsifiers, buffering agents, and corrosion inhibitors in a variety of pesticide products. They also have extensive FDA approved uses as emulsifiers, defoaming agents, synthetic flavorings, stabilizers and thickeners in food, and are used in a wide variety of cosmetics, medical products, lubricants and other applications applied up to several times a day to all areas of the skin, hair, nails, and mucous membranes with daily and/or occasional use extending over many years.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the six exemptions from the requirement of a tolerance for the inert ingredients listed in the table above, I consider the six exemptions established in the applicable 40 CFR parts 180.910, 180.920, and 180.930 [formerly 40 CFR180.1001 (c), (d), and (e)] reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois A. Rossi

Sorbitan Fatty Acid Esters

Lois A. Rossi, Director
Registration Division

Date:

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 20, 2005

MEMORANDUM

SUBJECT: Reassessment of the Six Exemptions from the Requirement of a Tolerance for the Sorbitan Fatty Acid Esters and the Polysorbates

FROM: Keri Grinstead, Inerts Team
Minor Use, Inerts, and Emergency Response Branch
Registration Division (7505C)

THROUGH: Pauline Wagner, Special Assistant 5/23/05
Registration Division (7505C)

TO: Dan Rosenblatt, Chief
Minor Use, Inerts, and Emergency Response Branch
Registration Division (7505C)

Background

Attached is the science assessment for the sorbitan fatty acid esters and the polysorbates; there are six exemptions from the requirement of a tolerance for the inert ingredients listed in **Table 1** below. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, and environmental fate and ecotoxicity of the sorbitan fatty acid esters and polysorbates. The purpose of this document is to reassess the existing exemptions from the requirement of a tolerance (as listed in **Table 1**) for residues of the sorbitan fatty acid esters and polysorbates as required under the Food Quality Protection Act (FQPA).

Table 1 (see Appendix A for additional information on nomenclature, CAS Reg. Numbers, and inert list classification)

Number of exemptions	CFR Reference			
	40 CFR **	**Tolerance Exemption Expression**	**Limits**	**Uses**
1	180.920	Poly(oxyethylene)(5) sorbitan monooleate	(none)	Surfactants, related adjuvants of surfactants

Number of exemptions	CFR Reference			
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1	180.920	Polysorbate 60, conforming to 21 CFR 172.836	(none)	Surfactant
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1	180.910	Sorbitan fatty acid esters (fatty acids limited to C12, C14, C16, and C18 containing minor amounts of associated fatty acids) and their derivatives; the poly(oxyethylene) content averages 5-20 moles.	(none)	Surfactants, related adjuvants of surfactants
1	180.930	Sorbitan fatty acid esters (fatty acids limited to C12, C14, C16, and C18 containing minor amounts of associated fatty acids) and their poly(oxyethylene) derivatives of sorbitan fatty acid esters; the poly(oxyethylene) content averages 16-20 moles.	(none)	Buffering agent, corrosion inhibition

**Residues listed in 40 CFR 180.910 (formerly 180.1001(c)) are exempt from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.

Residues listed in 40 CFR 180.920 (formerly 180.1001(d)) are exempt 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 (formerly 180.1001(e)) are exempt 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.

Executive Summary

This report evaluates the sorbitan fatty acid esters and the polysorbates. Members of these two groups of chemicals have six exemptions from the requirement of a tolerance when used as inert ingredients in pesticide formulations.

The substances listed in **Table 1** are collectively referred to as sorbitan fatty acid esters and polysorbates. The sorbitan fatty acid esters are mono-, di-, and triesters of fatty acids (such as lauric, stearic, palmitic and oleic acids) and sorbitan. Sorbitan is a generic name for anhydrides derived from sorbitol, a naturally occurring crystalline hexahydric alcohol found in fruits, seaweed, and algae (CIR 2000). The polyoxyethylene derivatives of sorbitan fatty acid esters are known as polysorbates.

The sorbitan fatty acid esters and polysorbates are inert ingredients used as surfactants, related adjuvants of surfactants, emulsifiers, buffering agents, and corrosion inhibitors in a variety of pesticide products. They also have extensive FDA-approved uses as emulsifiers, defoaming agents, synthetic flavorings, stabilizers and thickeners in food, and are used in a wide variety of cosmetics, medical

products, lubricants and other applications applied up to several times a day to all areas of the skin, hair, nails, and mucous membranes with daily and/or occasional use extending over many years.

This hazard assessment was developed using robust summaries of information and data that are publicly available and most have been peer-reviewed. The individual studies have not been reviewed by the Agency. The major sources of information used in this assessment include four safety assessments published by the Cosmetic Ingredient Review (CIR) Expert Panel[1] (1984, 1985, 2000, 2002), evaluations by the Joint FAO/WHO (Food and Agriculture Organization/World Health Organization)(JECFA), as well as The High Production Volume (HPV) Chemical Challenge Program's Test Plan for the Sorbitan Esters Category of the Aliphatic Esters Chemicals prepared by the American Chemistry Council (ACC) in November, 2003.

Extensive information is available to address the toxicity of sorbitan fatty acid esters and polysorbates. Sorbitan fatty acid esters and polysorbates show low acute toxicity by the oral and dermal routes and, in general, their chronic and subchronic toxicity is also low. They show little potential for reproductive or developmental effects, and are generally not considered mutagenic or carcinogenic via oral exposure. They have shown tumor promotion and cocarcinogenic activity at high concentrations in dermal studies following exposure with other known genotoxic/carcinogenic compounds. There are no inhalation studies for the sorbitan fatty acid esters or the polysorbates, however, due to their solid or viscous liquid state, large molecular weight, and low vapor pressure, they are not volatile and, therefore, inhalation is not expected to be a major route of exposure from the use of these chemicals as inert ingredients in pesticide products. Given the available information, as well as their metabolism and excretion by the body, adverse effects from human exposure to sorbitan fatty acid esters and polysorbates are only expected at concentrations well above those that would be expected from normal use of products containing these chemicals. It is likely that the average dietary and dermal exposure to these chemicals from their extensive use in consumer products and as direct and indirect food additives is far greater than any exposure expected from normal uses of these chemicals as inert ingredients in pesticide formulations. Given the lack of human health concerns associated with exposure to residues of these chemicals used as inert ingredients in pesticide formulations, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate.

Reported aquatic toxicity data for sorbitan monolaurate and sorbitan monooleate indicate the sorbitan esters are not acutely toxic to aquatic organisms. Most sorbitan esters have toxicity above the water solubility of the compound, therefore, are unlikely to be present in the environment at concentrations that would exceed the Agency's levels of concern, including the endangered species level of concern.

Taking into consideration all available information on the sorbitan fatty acid esters and the polysorbates, as well as their long history of use in food, cosmetics, and personal care products, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to the sorbitan fatty acid esters and the polysorbates when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable

[1] The Cosmetic Ingredient Review (CIR) was established in 1976 by the Cosmetic, Toiletry, and Fragrance Association (CTFA) with the support of the Food and Drug Administration and Consumer Federation of America. In order to review and assess the safety of cosmetic ingredients openly and without bias, an Expert Panel was established. Results of the CIR Expert Panel's reviews are published in scientific, peer-reviewed literature.

information. Therefore, it is recommended that the six exemptions from the requirement of a tolerance established for residues of the sorbitan fatty acid esters and the polysorbates as listed in **Table 1** can be considered reassessed as safe under section 408(q) of the FFDCA.

I. Introduction

This report evaluates six exemptions from the requirement of a tolerance for members of the sorbitan fatty acid esters and polysorbates as inert ingredients in pesticide formulations. The exact CFR references are listed in **Table 1** and the associated CAS numbers and chemical names are listed in **Appendix A**.

Sorbitan fatty acid esters are mono-, di-, and tri-esters of fatty acids (such as lauric, stearic, palmitic, and oleic) and sorbitan. Sorbitan is a generic name for anhydrides derived from sorbitol, a crystalline hexahydric alcohol that occurs naturally in fruits, seaweed, and algae. Sorbitan fatty acid esters are solids or viscous liquids that are generally insoluble in water. Water solubility for the compounds decreases with increasing chain length of the fatty acid and increasing degree of esterification. Five of the sorbitan fatty acid esters (sorbitan laurate, sorbitan stearate, sorbitan oleate, sorbitan sesquioleate, and sorbitan trioleate) are sponsored by the American Chemistry Council's Aliphatic Esters Panel under the EPA High Production Volume (HPV) Chemical Challenge Program[2].

Polysorbates are produced by partial esterification of sorbitan with a fatty acid followed by polymerization with ethylene oxide. Polysorbates differ in the number of polymerized oxyethylene subunits and the number and type of fatty acid moieties. Polysorbates are composed of 1 or 3 moles of a fatty acid such as lauric, palmitic, stearic, or oleic and up to 20 moles of ethylene oxide per mole of sorbitol and its anhydrides. They are viscous, oily liquids or waxy solids soluble or dispersable in water and possessing a faint characteristic odor.

II. Use Information

Pesticide Uses

Sorbitan fatty acid esters and polysorbates are used as surfactants, related adjuvants of surfactants, emulsifiers, buffering agents, and corrosion inhibitors in a variety of residential pesticide products including yard, garden, and turf products as well as in agricultural crop products.

Other Uses

Sorbitan fatty acid esters and polysorbates are nonionic surfactants which have extensive use as emulsifiers, stabilizers and thickeners in food, cosmetics, personal care and medical products, and lubricants. They are used in a wide variety of cosmetic products applied to all areas of the skin, hair, scalp, nails, and mucous membranes up to several times per day with daily and/or occasional use extending over many years. The majority of cosmetic product concentrations range between 0.1% and 5% with a maximum of 25% (CIR 1984, 1985). They are also used as indirect food additives approved

[2] HPV chemicals are those that are manufactured or imported into the United States in volumes greater than one million pounds per year. The HPV Challenge Program is a voluntary partnership between industry, environmental groups, and the EPA which asks chemical manufacturers and importers to provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products.

for manufacturing articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

The sorbitan fatty acid esters are used as emulsifiers, stabilizers, rehydration aids, defoaming agents, and synthetic flavors in foods and beverages (CIR 1985), and as lubricants or ingredients in lubricants (CIR 2002).

The polysorbates have numerous uses in industry, research, pharmacy, and food production. They have been approved by the Food and Drug Administration (FDA) as direct and indirect food additives for human and animal consumption. They are used in a wide variety of specific food types as surfactants, emulsifiers, adjuvants, solubilizers, dispersing agents, wetting agents, opacifiers, dough conditioners, defoaming agents at concentrations ranging from 10 ppm to 4.5% of the finished product. They are used in adhesives, components of coatings, adjuvants, production aids, and sanitizers, as food additives for feed and drinking water of animals, and as diluents in color additive mixtures for food and drug use (CIR, 1984).

III. Physical and Chemical Properties

The chemical and structural similarities of the sorbitan fatty acid esters and the polysorbates are being used to justify the assessment of these chemicals as a group. They have close commonalities in their physicochemical properties, chemical characteristics, and biological/toxicological activities. These same principles are used when evaluating data for structurally similar/related chemicals.

See **Appendix B** for details regarding the representative physical and chemical properties for members of the sorbitan fatty acid esters and the polysorbates.

IV. Hazard Assessment

A. Hazard Profile

Extensive information is available defining the low toxicity of sorbitan fatty acid esters and polysorbates. This hazard assessment was developed using robust summaries of information and data that are publicly available and most have been peer reviewed. The individual studies have not been reviewed by the Agency. The major sources of information used in this assessment include four safety assessments published by the Cosmetic Ingredient Review (CIR) Expert Panel[3] (1984, 1985, 2000, 2002), evaluations by the Joint FAO/WHO (Food and Agriculture Organization/World Health Organization)(JECFA), as well as The High Production Volume (HPV) Chemical Challenge Program's Test Plan for the Sorbitan Esters Category of the Aliphatic Esters Chemicals prepared by the American Chemistry Council (ACC) in November, 2003. The HPV test plan has not been reviewed by the Agency, however, its contents, including robust summaries of both publicly available and non-published confidential business information, was used as supporting information for this assessment.

[3] The Cosmetic Ingredient Review (CIR) was established in 1976 by the Cosmetic, Toiletry, and Fragrance Association (CTFA) with the support of the Food and Drug Administration and Consumer Federation of America. In order to review and assess the safety of cosmetic ingredients openly and without bias, an Expert Panel was established. Results of the CIR Expert Panel's reviews are published in scientific, peer-reviewed literature.

B. Metabolism and Pharmacokinetics

Sorbitan fatty acid esters

The parent esters are metabolized back to sorbitan and common fatty acids which both have low orders of toxicity. Oral gavage studies in rats administered radio-labeled sorbitan monostearate indicated that approximately 90% of the sorbitan dose was absorbed and hydrolyzed to sorbitan and stearic acid. These results would suggest that other sorbitan fatty acid esters may undergo similar enzymatic hydrolysis when orally ingested; metabolizing to sorbitan and the corresponding fatty acid. Those resulting metabolites would then be expected to further metabolize via fatty acid beta oxidation or carbohydrate metabolic pathways into either smaller and more polar water-soluble metabolites excretable in the urine or as carbon dioxide exhaled in the lungs (ACC 2003). Dermal absorption on intact skin is not likely based on the large molecular weights of the sorbitan fatty acid esters.

Polysorbates

The metabolism of Polysorbate 20 in rats is detailed in studies using C14 -label tracer techniques. The ester link of the polysorbate molecule undergoes hydrolysis by pancreatic lipase resulting in the fatty acid moiety and the polyoxyethylene moiety. The fatty acid moiety is rapidly absorbed and oxidized followed by the following distribution: 80% as expired CO2, 12% in the carcass, 4% unabsorbed in the gastrointestinal (GI) tract, 2.5% in the urine, and 1.2% in the liver. The remaining polyoxyethylene sorbitan moiety is poorly absorbed in the GI tract with approximate excretions of 90% in the feces and 8% in the urine for Polysorbate 20 and 91% in the feces, 2.1% in the urine, and 1.6% in the carcass for Polysorbate 80 (CIR 1984). Dermal absorption on intact skin is not likely based on the large molecular weights of the Polysorbates.

C. Toxicological Data

Sorbitan Fatty Acid Esters

Oral Toxicity – Results of oral toxicity studies for the sorbitan fatty acid esters indicate they are relatively non-toxic at low doses via ingestion.

Acute - In 20 studies using sorbitan esters, the lowest rat LD_{50} was 31,000 mg/kg for sorbitan stearate. The rat LD_{50} values from acute toxicity studies of sorbitan laurate ranged from 33,600 mg/kg to 41,500 mg/kg (CIR 2000).

Chronic/subchronic - In subchronic feeding studies of sorbitan laurate to several species (chickens, rats, monkeys, and hamsters), no toxic effects were seen when the ester concentration in the diet was <10% (CIR 1985). Chronic feeding studies conducted with sorbitans stearate, laurate, and oleate at 5% dietary concentration had no adverse effects on rats over a 2-year period (CIR 1985). Subchronic feeding of sorbitan oleate to rats produced no abnormalities at levels of less than 10% in the diet. Chronic feeding studies with sorbitans laurate and oleate had no adverse effects on rats at 5% in the diet over a two-year period and dogs fed 5% sorbitan stearate for 20 months had no compound related changes (CIR 1985).

Dermal Irritation/Toxicity – Based on their large molecular weights, dermal absorption to intact skin is expected to be very low.

Acute – In two acute dermal toxicity studies of sorbitan sesquioleate on rabbits dosed with 6.8 g/kg or 10.2 g/kg for 24 hours, no abnormal behavior, adverse body weight changes, or gross alterations were noted during the following 14-day observation period. Erythema was noted at the site of application, however, it subsided by day 7 (CIR 1985). In Draize-type irritation testing, 100%

sorbitan trioleate was mildly irritating, and 50% sorbitan palmitate, 30% sorbitan stearate, and 30% sorbitan tristearate all produced no irritation after being applied to rabbit skin under occlusion for 24 hours. Test sites were scored at 24 and 72 hours. The primary skin irritation potential of 50% sorbitan stearate on rabbit skin under occlusion for 24 hours was minimally irritating when graded at 2 and 24 hours after the dressing was removed (CIR 1985). Sorbitans stearate(60%, 10%, or 1%), laurate(100%, 60%, 10%, or 1%), oleate(100%, 60%, or 10%), and trioleate(100%, 10%, or 1%), when applied daily, were each determined to be irritating to rabbit skin on day 10 of acute skin irritation studies. Sorbitans laurate(100%, 60%, or 10%), oleate(100%), and trioleate(100%, 10%, or 1%) each were irritating on day 3 of the studies and sorbitans stearate(60%, 10%, or 1%), laurate (1%), and oleate(60% or 10%) each were non-irritating on day 3 of the studies (CIR 1985).

Chronic/subchronic – Subchronic dermal toxicity testing of sorbitans stearate, sesquioleate, palmitate, and trioleate on rabbit skin resulted in no systemic toxicity. Two studies of 2% sorbitan stearate applied daily to rabbit skin for 3 months resulted in moderate erythema; slight edema and desquamation. 1% sorbitan sesquioleate applied 5 days per week to rabbit skin for 13 weeks produced minimal to slight skin irritation. 4% sorbitan palmitate applied 5 days per week for 4 weeks to rabbits showed severe erythema and severe dermatitis at the end of the study. 5% sorbitan trioleate applied for 93 days to rabbit skin showed slight erythema (CIR 1985).

Sensitization – When tested in four Magnusson-Kligman guinea pig maximization studies, sorbitan isostearate had very low sensitization potential at 50-100% topical application (CIR 2002).

Ocular Irritation - Results of numerous ocular irritation studies showed no irritation to minimal irritation with concentrations of sorbitan fatty acid esters ranging from 4% to 100%. "The sorbitan fatty acid esters and fatty acids were generally not ocular irritants" (CIR 2002).

Reproductive/Developmental Toxicity – Results from a two-year, four-generation toxicity study in rats administered sorbitan monostearate at dietary dose levels of 0%, 5%, 10%, or 20% showed no observed effects on reproduction, gestation, growth, lactation, and mortality at 5 and 10% in the diet. Slight effects on growth and impairment of lactation were reported at 20% in the diet and there were no reports of developmental effects (ACC 2003). Additionally, subchronic toxicity studies of various sorbitan esters and a structurally analogous surrogate, sorbitan, fatty acid C6-10 tetraester (CAS 228573-47-5), have been shown not to adversely affect the reproductive organs as determined by gross observations and histopathology (ACC 2003). Feeding up to 10% sorbitol to rats had no significant adverse reproductive effects in a 96 week multi-generation study. The safety of hydrogenated starch hydrolysates (HSH), which are mixtures of polyhydric alcohols, did not produce reproductive or developmental effects when investigated in a 2 year ingestion study of rats (CIR, 2002).

Mutagenicity - Sorbitan stearate, at concentrations of 0.01 to 300 μg/ml, did not induce *in vitro* transformation of hamster ovary cells and was not mutagenic in *S. typhimurium* strains with or without metabolic activation. There was an equivocal result of an unspecified sorbitan fatty acid ester (maximum dose 0.3 mg/ml in DMSO) in the chromosomal aberration test using Chinese hamster fibroblasts. The HPV Test Plan data showed no evidence of mutagenic or clastogenic activity, with or without metabolic activation, based on bacterial or mammalian gene mutation assays or *in-vitro* chromosomal aberration assays for the sorbitan esters and surrogate (ACC 2003).

Carcinogenicity – A carcinogenicity study performed by feeding mice sorbitan stearate in dietary levels of 0%, 0.5%, 2.0%, or 4.0% for 80 weeks showed no difference in tumor type or incidence from that of controls. No carcinogenic effects were seen after undiluted sorbitan laurate was applied twice weekly to the clipped skin of male Swiss mice for 73 weeks. In a tumor promotion and cocarcinogen study of sorbitans laurate, oleate, and trioleate, only sorbitan laurate was active as a tumor

promoter after initiation by 150 μg DMBA (7,12-dimethylbenz(a)anthracene)(0.3% in paraffin). Sorbitans oleate and trioleate were inactive as tumor promoters after initiation with DMBA. This same study also investigated their cocarcinogenic activity by dissolving either 0.3%(150 μg), 0.03%(15 μg) , or 0.003%(1.5 μg) DMBA in the various sorbitans and applied three times per week to the shaved backs of mice. The results showed sorbitans laurate and trioleate as active on mouse skin as cocarcinogens when used as the solvent for 0.003% DMBA (CIR 2002).

Polysorbates

Oral Toxicity – The polysorbates had low oral toxicity in both acute and long-term animal studies.

Acute - The LD_{50} values for 33 acute oral toxicity studies in rats ranged between 5000 and 38,900 mg/kg (CIR 2000).

Chronic/subchronic – Numerous feeding studies of polysorbates at diet concentrations of 0.1-25% have been performed on a variety of animal species for periods of 6 weeks to 2 years and over several generations. The results of these studies concluded that effects were seen starting around 5% in the diet, but those effects were primarily related to diarrhea, likely resulting "from having high concentrations of the unabsorbed polyoxyethylene sorbitan moiety within the intestinal lumen" (CIR 1984). The diarrhea itself could have been aggravated by use of a poor basal diet in early studies (CIR 1984). "Evaluations of these substances should be based on the levels causing no adverse effects indicated by the results of more recent studies with considerably improved testing procedures" (JECFA, 1974). JECFA has also determined the estimate of acceptable daily intake for man is 0-25 mg/kg bw and the level causing no toxicological effect in the rat is 2500 mg/kg bw (5% in the diet) with many species tolerating much greater dietary quantities over extended periods of time (CIR, 1984).

Dermal – Based on their large molecular weights, dermal absorption on intact skin is expected to be very low. The polysorbates showed little potential for rabbit and mouse skin irritation in acute studies (CIR 2000).

Acute - Primary rabbit skin irritation studies using the Draize method were performed, with 6 studies showing no signs of irritation, 3 studies showing minimal irritation, and one study showing mild irritation. All of these studies used 100% concentrations of polysorbate, 20, 40, 60, or 80 (CIR 1984).

Chronic/subchronic - Polysorbates tested in subchronic skin irritation tests for up to 60 days produced minimal irritation to necrosis to local skin. These effects were attributable to damage of the epidermal cell membrane by the emulsifying action of the polysorbates.

Sensitization – PEG-20 sorbitan oleate(Polysorbate 80) and PEG-20 sorbitan Tristearate(Polysorbate 65) were non-sensitizers, and PEG-20 sorbitan laurate(Polysorbate 20) was a moderate to strong sensitizer in a Magnusson-Kligman guinea pig maximization test (CIR 2000).

Ocular Toxicity – The polysorbates were non-irritating to mildly irritating in both *in-vivo* and *in-vitro* ocular irritation assays (CIR 2000). Twenty-three Draize rabbit eye irritation studies of the polysorbates showed either no irritation or minimal irritation using concentrations ranging between 30% w/v in distilled water and 100% polysorbate 20, 21, 40, 60, 61, 65, 80, 81, or 85 (CIR, 1984).

Reproductive/Developmental Toxicity – PEG-20 sorbitan laurate was given by gavage in doses of 0, 500, or 5000 mg/kg/day in a volume of 5 ml/kg bw to time-mated Sprague-Dawley-derived rats on gestational days 6 through 15 with termination on gestational day 20. The maternal LOAEL was 5000 mg/kg/day (based upon a 14% decrease in weight gain during treatment) and the maternal NOAEL was 500 mg/kg/day. No adverse effects upon prenatal development were noted, therefore, the developmental NOAEL was > 5000 mg/kg/day. An *in-vivo* teratology screening study of PEG-20

sorbitan oleate did not cause developmental toxicity when administered by gavage (2500 mg/kg/day) to pregnant mice on gestational days 8 to 12. There were no harmful effects on the prenatal development in a teratogenicity study of PEG-20 sorbitan stearate(Polysorbate 60) which was fed to pregnant rats at 99 mg/kg/day(0.1%), 960 mg/kg/day(1.0%), or 7693 mg/kg/day(10%) from gestational days 7 to 14. In subchronic and chronic oral toxicity studies, the PEGs did not cause adverse reproductive effects" (CIR 2000).

Mutagenicity/Genotoxicity – "The polysorbates were nonmutagenic in a number of bacterial and mammalian systems, with the exception of PEG-20 sorbitan stearate which produced both positive and negative results in genotoxicity assays" (CIR 2000).

Carcinogenicity – Generally, the polysorbates were considered weak tumor promoters in numerous oral and dermal initiation-promotion studies, however, they are not generally not considered oral or dermal carcinogens by themselves.

Oral – No increase in the incidence of neoplasms was observed in male or female mice or female rats fed 25,000 ppm or 50,000 ppm Peg-20 sorbitan oleate daily in a 2-year study, however, there was "equivocal evidence of carcinogenicity for the male rat in the high-dose group based upon the increased incidence of pheochromocytomas of the adrenal medulla (equivocal evidence = marginal increase of neoplasms that may be chemical related). PEG-20-sorbitan stearate did not increase the incidence of tumors in a gastric carcinogenesis study in the male rat. Numerous oral studies performed on the Polysorbates showed no evidence of carcinogenicity by this route (CIR 1984). No tumors were seen in 11 studies of various animals (rats, hamsters, dogs, mice, rabbits) at 1-25% in the diet over periods of 59 days – 13 months (CIR 1984).

Skin – While topical application of high concentrations of polysorbates to the skin did produce skin tumors in some studies, most tumors were benign with a tendency to regression, and subsequent review of the studies concluded the polysorbates are not carcinogenic when applied to the skin (CIR 1984).

Extensive information is available to address the toxicity of sorbitan fatty acid esters and polysorbates. Sorbitan fatty acid esters and polysorbates show low acute toxicity by the oral and dermal routes and, in general, their chronic and subchronic toxicity is also low. They show little potential for reproductive or developmental effects, and are generally not considered mutagenic or carcinogenic via oral exposure. They have shown tumor promotion and cocarcinogenic activity at high concentrations in dermal studies following exposure with other known genotoxic/carcinogenic compounds. There are no inhalation studies for the sorbitan fatty acid esters or the polysorbates, however, due to their solid or viscous liquid state, large molecular weight, and low vapor pressure, they are not volatile and, therefore, inhalation is not expected to be a major route of exposure from the use of these chemicals as inert ingredients in pesticide products.

D. Special Consideration for Infants and Children

There is no evidence indicating sorbitan fatty acid esters or polysorbates adversely interfere with reproduction. Sorbitol, the parent compound of sorbitan, showed no adverse effects in a multigeneration reproductive study. A 4-generation reproductive toxicity study of sorbitan monostearate saw increased sensitivity to pups (effects on growth and lactation); however, these effects were only seen at the highest dietary dose of 20%. While polysorbates have shown reproductive and developmental effects in some studies, the effects were also only seen at exposure levels that were maternally toxic and above the limit dose. A 1992 NTP developmental toxicity study of

polyoxyethylene sorbitan monooleate (Polysorbate 80) yielded a maternal LOAEL of 500 mg/kg/day (based upon an increase in maternal relative liver weight) with no definitive developmental adverse effects noted(developmental NOAEL > 5000 mg/kg/day) (CIR 2000). Based on this information there is no concern, at this time, for increased sensitivity to infants and children. For these same reasons 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/Drinking Water Considerations

See **Appendix C for the Summary Table of Physicochemical Properties and Environmental Fate Data for the Sorbitan Esters from the HPV Sorbitan Esters Report

There are limited studies characterizing the environmental fate of the sorbitan fatty acid esters and the polysorbates. Although there is no available fate data on the polysorbates, they are expected to have similar characteristics in the environment. These chemicals appear to be non-volatile and have low vapor pressures. The sorbitan fatty acid esters are insoluble in water. Both the sorbitan fatty acid esters and the polysorbates are unlikely to hydrolyze or photolyze in soil or water in the environment and, as a group, are unlikely to be very mobile, based on their log Kow values.

Biodegradation data have been reported for sorbitan monolaurate, sorbitan monooleate, and a surrogate material sorbitan, fatty acid C6-C10 tetraester (CAS 228573-47-5) (**Table 2**). These chemicals undergo moderate biodegradation in the environment (60-83% in 28-days). "Calculated data for environmental fate endpoints using EPIWIN and EQC (Level III) modeling programs also support the biodegradation conclusions for the sorbitan esters. The resulting high biodegradation of the poorly water-soluble surrogate, sorbitan tetraester, indicates that enzymatic cleavage of the multiple ester linkage must be taking place in order to achieve the observed level of biodegradation. This is consistent with the fact that the fatty acids arising from the enzymatic ester bond cleavage of the sorbitan esters would also be expected to rapidly degrade" (ACC 2003). Although no data were identified in the open literature, by analogy, the polysorbates would be expected to have similar characteristics in the environment. Considering the available data and physical/chemical properties, neither the sorbitan fatty acid esters nor the polysorbates would be likely to be present in the environment at any appreciable levels when used as pesticide inert ingredients.

Table 2. Biodegradation Data from the HPV Sorbitan Esters Report (ACC 2003)

Chemical/CAS/Reference	Biodegradation
Sorbitan Monolaurate 1338-39-2	Not readily Biodeg. 60% in 28 days OECD 301D (BOD)
Sorbitan monooleate 1338-43-8	Not readily Biodeg. 62% in 28 days OECD 301D (BOD)
Sorbitans, fatty acids C6-10, tetraester 228573-47-5	Not readily Biodeg. 70% in 28 days OECD 301D (BOD)

VI. Exposure Assessment

Sorbitan fatty acid esters and polysorbates are used as surfactants, related adjuvants of surfactants, emulsifiers, buffering agents, and corrosion inhibitors in a variety of residential pesticide products including yard, garden, and turf products, as well as in agricultural crop products, applied to growing crops, raw agricultural commodities after harvest, and/or to animals. Additionally, they are used extensively as emulsifiers, stabilizers and thickeners in food, cosmetics, personal care and medical products, and lubricants. The JECFA estimate of acceptable daily intake (ADI[4]) for man for the sorbitan fatty acid esters and the polysorbates is 0-25 mg/kg bw each (JECFA 1974).

For the general population, the majority of exposure to the sorbitan fatty acid esters and the polysorbates occurs from their extensive use in consumer products and as FDA-approved direct and indirect food additives. The dietary exposure to these chemicals as components of pesticide inert ingredients is expected to be much less than that from their use in consumer products, particularly as direct and indirect food additives, and they are easily metabolized and/or excreted by the body, therefore, no further dietary exposure assessment is necessary. The potential for surfactant lung effects resulting from inhalation of respirable particles of either sorbitan fatty acid esters and/or polysorbates would be more commonly associated with exposures to high concentrations of the neat solid material, a scenario that would not be realized in conjunction with the use of sorbitan fatty acid esters or polysorbates as inert ingredients in pesticide products where inhalation exposures would be negligible, therefore no further inhalation exposure assessment is necessary. The most likely exposure to these chemicals in pesticide formulations is by the dermal route; however, a low concern for human health effects is anticipated based on their low potential for irritation and dermal absorption on intact skin.

VII. Aggregate Exposure

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in garden, lawns, or buildings (residential and other indoor uses).

For sorbitan fatty acid esters and polysorbates, 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 sorbitan fatty acid esters and polysorbates.

VIII. Cumulative Exposure

Section 408(b)(2)(D)(v) of the 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 or toxicity, EPA has not made a common mechanism of safety finding as to

[4] ADI (Acceptable Daily Intake): An estimate by JECFA of the amount of a food additive, expressed on a body weight basis that can be ingested daily over a lifetime without appreciable health risk.

sorbitan fatty acid esters, polysorbates, and any other substances, and sorbitan fatty acid esters and polysorbates do not appear to produce toxic metabolites produced by other substances. For the purpose of these tolerance actions, therefore, EPA has not assumed that the sorbitan fatty acid esters and polysorbates 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

Sorbitan fatty acid esters and polysorbates show low acute toxicity by the oral and dermal routes and, in general, their chronic and subchronic toxicity is also low. They show little potential for reproductive or developmental effects, and are generally not considered mutagenic or carcinogenic via oral exposure. They have shown tumor promotion and cocarcinogenic activity at high concentrations in dermal studies following exposure with other known genotoxic/carcinogenic compounds. They are metabolized and excreted by the body. They are unlikely to hydrolyze or photolyze in soil or water in the environment and they are unlikely to be very mobile based on their log Kow resulting in low concern for high exposure to these chemicals in drinking water. Given the available information, adverse effects from human exposure to sorbitan fatty acid esters and polysorbates are only expected at concentrations well above those that would be expected from normal use of products containing these chemicals. It is likely that the average dietary and dermal exposure to these chemicals from their extensive use in consumer products and as direct and indirect food additives is far greater than any exposure expected from normal uses of these chemicals as inert ingredients in pesticide formulations.

Taking into consideration all available information on sorbitan fatty acid esters and polysorbates, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to sorbitan fatty acid esters and polysorbates used as inert ingredients when considering the dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the 6 exemptions from the requirement of a tolerance established for residues of sorbitan fatty acid esters and polysorbates as detailed in **Table 1** be maintained and considered reassessed as safe under section 408(q) of the FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

There are limited measured toxicity data to characterize the effects of the sorbitan fatty acid esters or the polysorbates on aquatic and terrestrial organisms. The available information is shown in the table below. Reported aquatic toxicity data for sorbitan monolaurate and sorbitan monooleate indicate the sorbitan esters are not acutely toxic to aquatic organisms. Most sorbitan esters have toxicity above the water solubility of the compound, therefore, are unlikely to be present in the environment at concentrations that would exceed the Agency's levels of concern, including the endangered species level of concern.

Table 3. Aquatic Toxicity Data

Chemical/CAS/Reference	Acute Fish LC_{50} or LL_{50}	Daphnia LC_{50} or LL_{50}	Algal LC_{50} or LL_{50}
Sorbitan Monolaurate 1338-39-2	75 mg/L		
Sorbitan monooleate 1338-43-8	>1000 mg/L		
Sorbitans, fatty acids C6-10, tetraester 228573-47-5	>1000 mg/L	>1000 mg/L	>1000 mg/L

References:

American Chemistry Council; Test Plan for the Sorbitan Esters Category of the Aliphatic Esters Panel, 201-14869A, 201-14869B, November 26, 2003.

CIR (Cosmetic Ingredient Review); Final Report on the Safety Assessment of Polysorbates 20, 21, 40, 60, 61, 65, 80, 81, and 85; Journal of the American College of Toxicology; 3(5): 1-82, 1984.

CIR; Final Report on the Safety Assessment of Sorbitan Stearate, Sorbitan Laurate, Sorbitan Sesquioleate, Sorbitan Oleate, Sorbitan Tristearate, Sorbitan Palmitate, and Sorbitan Trioleate; Journal of the American College of Toxicology; 4(3): 65-121, 1985.

CIR; Final Report on the Safety Assessment of PEG-20 Sorbitan Cocoate; PEG-40 Sorbitan Diisostearate; etc.; International Journal of Toxicology, 19(Suppl 2): 43-89, 2000.

CIR; Final Report on the Safety Assessment of Sorbitan Caprylate, Sorbitan Cocoate, Sorbitan Diisostearate, etc.; International Journal of Toxicology; 21 (Suppl 1): 93-112, 2002.

JECFA – Joint FAO/WHO (Food and Agriculture Organization/World Health Organization); Sorbitan Monoesters of Palmitic and Stearic Acids and Triesters of Stearic Acid; 17th Report of the Joint FAO/WHO Expert Committee on Food Additives; Wld Hlth Org. techn. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53; 1974a.

JECFA – Joint FAO/WHO (Food and Agriculture Organization/World Health Organization); Polyoxyethylene (20) Sorbitan Monoesters of Lauric, Oleic, Palmitic and Stearic Acids and Triester of Stearic Acid; 17th Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53; 1974b.

JECFA – Joint FAO/WHO (Food and Agriculture Organization/World Health Organization); Sorbitan Monoesters of Palmitic, Stearic, Oleic and Lauric Acids and Triesters of Stearic Acid; 26th Report of

the Joint FAO/WHO Expert Committee on Food Additives, Geneva, Wld Hlth Org. techn. Rep. Ser., 683, 1982.

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APPENDIX A

CAS numbers and chemical names

Polysorbates:

9005-65-6(LIST 4B): Glycol (polysorbate 80), PEG-3 Sorbitan oleate, PEG-6 Sorbitan oleate, Polyethylene glycol (3) sorbitan monooleate, Polyethylene glycol 300 sorbitan monooleate, Polyoxyethylene (20) sorbitan monooleate, Polyoxyethylene (3) sorbitan monooleate, Polyoxyethylene (5) sorbitan monooleate, Polysorbate 80, Polysorbate 80, Polysorbate 81, Sorbimacrogol oleate 300, Sorbitan, mono-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs

9005-67-8: PEG-3 Sorbitan stearate, PEG-40 Sorbitan stearate, PEG-6 Sorbitan stearate, PEG-60 Sorbitan stearate, Polyethylene glycol (3) sorbitan monostearate, Polyethylene glycol 2000 sorbitan stearate, Polyethylene glycol 300 sorbitan monostearate, Polyethylene glycol 3000 sorbitan monostearate, Polyoxyethylene (20) sorbitan monostearate, Polyoxyethylene (3) sorbitan monostearate, Polyoxyethylene (4) sorbitan monostearate, Polyoxyethylene (40) sorbitan stearate, Polyoxyethylene (6) sorbitan monostearate, Polyoxyethylene (60) sorbitan monostearate, Polysorbate 60, Polysorbate 61, Sorbimacrogol stearate 300, Sorbitan, monooctadecanoate, poly(oxy-1,2-ethanediyl) derives

9005-71-4: Polyoxyethylene (20) sorbitan Tristearate, Polysorbate 65, Sorbimacrogol tristearate 300, Sorbitan, trioctadecanoate, poly(oxy-1,2-ethanediyl) derivs.

Sorbitan fatty acid esters (fatty acids limited to C12, C14, C16, and C18 containing minor amounts of associated fatty acids) and their derivatives; the poly(oxyethylene) content averages 5-20 moles:

8007-43-0(LIST 3): sorbitan sesquioleate

9005-64-5(LIST 4B): PEG-10 Sorbitan laurate, PEG-40 Sorbitan laurate, PEG-44 Sorbitan laurate, PEG-75 Sorbitan laurate, PEG-80 Sorbitan laurate, Polyethylene glycol (44) sorbitan Monolaurate, Polyethylene glycol (80), sorbitan Monolaurate, Polyethylene glycol 2000 sorbitan laurate, Polyethylene glycol 4000 sorbitan Monolaurate, Polyethylene glycol 500 sorbitan Monolaurate, Polyoxyethylene (10) sorbitan Monolaurate, Polyoxyethylene (20) sorbitan Monolaurate, Polyoxyethylene (4) sorbitan Monolaurate, Polyoxyethylene (40) sorbitan laurate, Polyoxyethylene (44) sorbitan Monolaurate, Polyoxyethylene (75) sorbitan Monolaurate, Polyoxyethylene (80) sorbitan Monolaurate, Polysorbate 20, Polysorbate 21, Sorbimacrogol laurate 300, Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs.

9005-66-7: Polyethylene glycol (80) sorbitan monopalmitate, Polyoxyethylene (20) sorbitan monopalmitate, Polyoxyethylene (80) sorbitan monopalmitate, Polyoxyethylene sorbitan monopalmitate, Polysorbate 40, Sorbimacrogol palmitate 300, Sorbitan, monohexadecanoate, poly(oxy-1,2-ethanediyl) derivs.

9005-67-8(LIST 4B): see above

9005-70-3: Polyoxyethylene (20) sorbitan trioleate, Polysorbate 85, Sorbimacrogol trioleate 300, Sorbitan, tri-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs

9005-71-4(LIST 4B): see above

1338-39-2(LIST 3): 1,4-Anhydro-D-glucitol, 6-dodecanoate, Anhydrosorbitol monolaurate, Sorbitan laurate, Sorbitan Monolaurate, Sorbitan, monododecanoate

1338-41-6(LIST 4B): 1,4-Anhydro-D-glucitol, 6-octadecanoate, Anhydrosorbitol monostearate, D-Glucitol, 1,4-anhydro-, 6-octadecanoate, Sorbitan monostearate, Sorbitan stearate, Sorbitan, monooctadecanoate

1338-43-8(LIST 3): 1,4-Anhydro-D-glucitol, 6-(9-octadecenoate), Anhydrosorbitol monooleate, D-Glucitol, 1,4-anhydro-, 6-(9-octadecenoate), Sorbitan monooleate, Sorbitan oleate, Sorbitan, mono-9-octadecenoate

9005-65-6: see above

26266-57-9(LIST 4B): 4-Anhydro-D-glucitol, 6-hexadecanoate, D-Glucitol, 1,4-anhydro-, 6-hexadecanoate, Sorbitan monopalmitate, Sorbitan palmitate

26266-58-0(LIST 3): Anhydrosorbitol trioleate, Sorbitan trioleate, Sorbitan, tri-9-octadecenoate

26658-19-5(LIST 3): Anhydrosorbitol Tristearate, Sorbitan tristearate, Sorbitan, trioctadecanoate

29116-98-1(LIST 3): Anhydrosorbitol dioleate, Sorbide dioleate, Sorbitan dioleate, Sorbitan, di-9-octadecenoate

61790-88-3(LIST 3): Fatty acids, tall-oil, triesters with sorbitan, ethoxylated

61790-90-7(LIST 4B): Fatty acids, tall-oil, hexaesters with sorbitol, ethoxylated

61791-48-8(LIST 3): Fatty acids, tall-oil, monoesters with sorbitan

68648-20-4(LIST 4B): Fatty acids, tall-oil, sesquiesters with sorbitol, ethoxylated

APPENDIX B

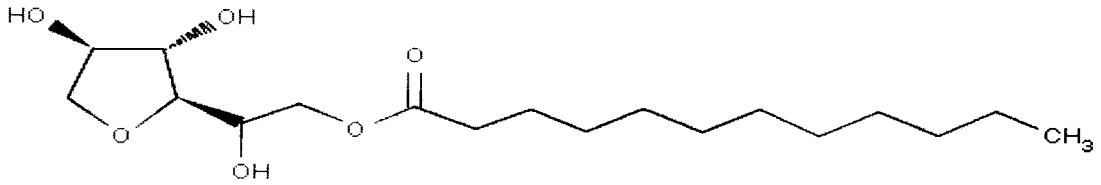
Physical/Chemical Properties

Table 2 Physical/Chemical Properties of Sorbitan Fatty Acid Esters

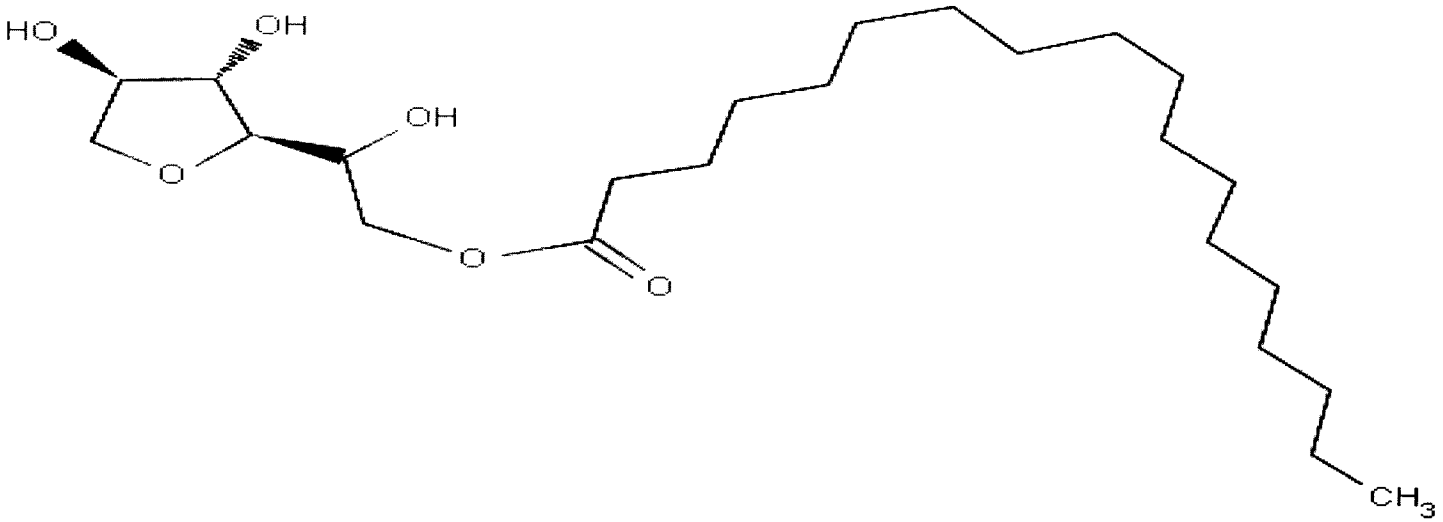
Property	Sorbitan Laurate	Sorbitan Stearate	Sorbitan Oleate	Sorbitan Sesquioleate	Sorbitan Palmitate	Sorbitan Trioleate	Sorbitan Tristearate
CAS No.	1338-39-2	1338-41-6	1338-43-8	8007-43-0	26266-57-9	26266-58-0	26658-19-5
Physical State	Yellow liquid	White to tan waxy solid	Yellow to amber liquid	Yellow liquid	White solid	Yellow liquid	White solid
Molecular Formula	C18H34O6	C24H46O6	C24H44O6	---	C22H42O6	C60H108O8	C60H114O8
Molecular Weight	346	431	430	569	403	958	964
Specific Gravity (at 25 C)	1.0 - 1.06	0.98 - 1.03	~1.0	0.95 - 1.00	1.0 - 1.05	---	~1.0
Melting point (C)	176 (E)	49-65 222 (E)	223 (E)	248 (E)	~54	350 (E)	~54
Boiling point (C)	462 (E)	531 (E)	535 (E)	609 (E)	---	916 (E)	---
Vapor Pressure (Pa at 25 C)	9.34 E-12 (E)	1.38 E-14 (E)	1.03 E-14 (E)	6.83 E-17 (E)	---	1.32 E-19 (E)	---
Log Kow	3.15 (E)	6.10 (E)	5.89 (E)	10.11 (E)	---	21.71 (E)	---
Water solubility (mg/L at 25 C)	13.19 (E) Insoluble in water	0.0122 (E) Insoluble in water	0.0191 (E) Insoluble in water	5.93 E-7 (E) Insoluble in water	Insoluble in water	5.97 E-19 (E) Insoluble in water	Insoluble in water
Photodegradation Half-life (days)	0.20 (E)	0.17 (E)	0.05 (E)	0.04 (E)	---	0.02 (E)	---
Hydrolysis Half-life (yrs)	14.2 (E)	7.7 (E)	2.2 (E)	0.90 (E)	---	0.59 (E)	---

E = Value estimated by EPIWIN as reported in the 2001 Robust Summaries for Aliphatic Esters (American Chemistry Council, 2001).

*See representative structures on the next 2 pages



Sorbitan laurate
1338-39-2
(structure from ChemID)



Sorbitan monostearate
1338-41-6
(structure from ChemID)

POLYSORBATES

Chemical	CAS	Formula	Physical State
Polysorbate 20	9005-64-5	C_{58}-H_{114}-O_{26}	Viscous, oily liquid
Polysorbate 60	9005-67-8	C_{64}-H_{126}-O_{26}	Oily liquid or semigel, wax, Vaseline-like
Polysorbate 65	9005-71-4	C_{100}-H_{194}-O_{28}	Waxy solid
Polysorbate 80	9005-65-6	unspecified	Viscous, oily liquid

APPENDIX C

Summary Table of Physicochemical Properties and Environmental Fate Data for the Sorbitan Esters***

***This table was reproduced from this exact table found in the High Production Volume (HPV) Chemical Challenge Program Test Plan for the Sorbitan Esters Category of the Aliphatic Esters Chemicals prepared by the American Chemistry Council's Aliphatic Esters Panel, November 26, 2003

Total Carbon in Ester	MW	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	Vapor Pressure (mm Hg@25 °C)	Octanol-Water Partition Coefficient (log Pow)	Water Solubility (mg/L@25°C)	Photo-Degradation Half-life (days)	Hydrolysis Half-life (yrs)	Chemical Distribution (Transport) within Environmental Compartments-Fugacity Model			
											Soil% %	Air %	Water %	Sediment %
18	346	1338-39-2	Sorbitan, monolaurate	176c	462 c	9.34E-12c	3.15c	13.19c	0.20c	14.2c	68.2 c	0.04 c	31.4 c	0.3c
18-20	346-374	68154-36-9	Fatty acids, coco, monoesters with sorbitan (main fatty acids are lauric and myristic acids)	176-191c	462-485 c	1.1-9.3E-12c	3.15-4.14c	1.29-13.2c	0.19-0.20c	7.7-14.2c	64.6-68.2 c	0.04-0.3c	31.4-33.4 c	0.3-1.8c
24	429	1338-43-8	Sorbitan, monooleate	223c	535 c	1.03E-14c	5.89c	0.0191c	0.05c	2.2c	37.2 c	0.1c	15.6 c	47.1c
24	431	1338-41-6	Sorbitan, monostearate	222c	531 c	1.38E-14c	6.10c	0.0122c	0.17c	7.7c	36.2 c	0.3c	12.6 c	50.9c
33	569	8007-43-0	Sorbitan, sesquioleate	248c	609 c	6.83E-17c	10.11c	5.93E-07c	0.04c	0.90c	28.6 c	0.1c	7.2c	64.1c
38	669	228573-47-5	Sorbitan, Fatty Acid C6-10 Tetraester	<-25C 266c	>295C 636 c	1.7E-07 Pa at 25C 1.87E-14c	>7.7 11.57c	<0.02 7.37E-09c	0.19c	0.79c	32.1 c	0.5c	10.7 c	56.7c
60	958	26266-58-0	Sorbitan, trioleate	350c	916 c	1.32E-19c	21.71c	5.97E-19c	0.02c	0.59c	27.4 c	0.0c	3.5c	69.1c

Highlighted row denotes substance that was not on the HPV list for the Sorbitan Esters category but that was included in table to facilitate group evaluation or for bridging purposes due to their chemical/structural similarities as sorbitan esters.

C = calculated data using EPIWIN; all other values in table are derived from measurements or data obtained from company reports, documents, MSDS, reference handbooks, secondary literature sources.

* = Note: Mixtures are expected to have melting points below those of pure components. Modeled data may not accurately reflect melting points for these substances.

** = many of the substances have boiling points determined under reduced pressure and some values may have been extrapolated to one atmosphere.