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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

DATE: December 21, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessment: Sucrose Octaacetate (CAS Reg. No. 126-14-7).

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

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

FQPA REASSESSMENT ACTION

Action: Reassessment of one inert exemption from the requirement of a tolerance. The reassessment decision is to maintain the inert tolerance exemption "as-is."

Chemical: Sucrose octaacetate

CFR: 40 CFR 180.910

CAS Registry Number and Name: CAS Reg. No. 126-14-7; α-D-Glucopyranoside, 1,3,4,6-tetra-O-acetyl-β-D-fructofuranosyl, tetraacetate

Table 1. Tolerance Exemption Being Reassessed in this Document

40 CFR 180§	Tolerance Exemption Expression	Limits	Use Pattern (Pesticidal)	CAS Registry Number and name
.910[a]	sucrose octaacetate	--	Adhesive	126-14-7 α-D-Glucopyranoside, 1,3,4,6-tetra-O-acetyl-β-D-fructofuranosyl, tetraacetate

Use Summary: Pesticide products containing sucrose octaacetate as an inert ingredient are used as insect repellents, herbicides, flea and tick sprays, and other insecticides. Commercial uses of sucrose octaacetate include use in impregnating and insulating papers, as well as in lacquers and plastics. It has also been approved by the

U.S. Food and Drug Administration as both a direct and indirect food additive, and as a nail-biting and thumb-sucking deterrent in over-the-counter drug products.

List Reclassification Determination: The current List Classification for sucrose octaacetate is three. Because EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to sucrose octaacetate when used as an inert ingredient in pesticide formulations, the List Classification for sucrose octaacetate will change from List 3 to List 4B.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the exemption from the requirement of a tolerance for the inert ingredient sucrose octaacetate (CAS Reg. No. 126-14-7), and with the List reclassification determination, as described above. I consider the exemption established in 40 CFR 180.910 to be reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois A. Rossi

Lois A. Rossi, Director
Registration Division

December 23, 2005
Date:

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

December 21, 2005

MEMORANDUM

SUBJECT: Reassessment of the Exemption from the Requirement of a Tolerance for Sucrose Octaacetate (CAS Reg. No. 126-14-7)

FROM: Christina M. Jarvis
Reregistration Branch 2
Health Effects Division (7509C)

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

BACKGROUND

Attached is the science assessment for sucrose octaacetate. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of sucrose octaacetate. The purpose of this document is to reassess the existing exemption from the requirement of a tolerance for residues of sucrose octaacetate as required under the Food Quality Protection Act (FQPA).

EXECUTIVE SUMMARY

This document evaluates sucrose octaacetate, a pesticide inert ingredient for which one exemption from the requirement for a tolerance exists. An inert ingredient is defined by the U.S. Environmental Protection Agency (USEPA) as any ingredient in a pesticide product that is not intended to affect a target pest.

As an inert pesticide ingredient, sucrose octaacetate is exempt from the requirement for a tolerance when used as an adhesive in pesticide formulations applied to growing crops or to raw agricultural commodities (40 CFR 180.910). Pesticidal products containing sucrose octaacetate as an inert ingredient are used as insect repellents, herbicides, flea and tick sprays, and other insecticides. Commercial uses of sucrose octaacetate include use in impregnating and insulating papers, as well as use in

lacquers and plastics (Merck Index, 2001). Sucrose octaacetate is also approved for use by the U.S. Food and Drug Administration (US FDA) as both a direct and indirect food additive (21 CFR 172.515 and 21 CFR 175.105, respectively), and as a nail-biting and thumb-sucking deterrent in over-the-counter drug products (21 CFR 310.536). Sucrose octaacetate is not considered a high production volume (HPV) chemical.

The data base for sucrose octaacetate is limited. Available data show low acute oral and dermal toxicity in animal studies, and slight skin irritation in rabbit studies. Subchronic oral studies in rats and rabbits show no difference in weight gains between treated animals and control groups, and no abnormalities were observed in liver, stomach, and kidney tissues of treated animals. There are no available data on genotoxicity, carcinogenicity, developmental toxicity, reproductive toxicity, neurotoxicity, or immunotoxicity related to sucrose octaacetate.

Given its likely dissociation in the mammalian body to sucrose and acetic acid, neither of which are compounds of toxicological concern, as well as its long history of use by the US FDA as an approved direct and indirect food additive, exposure and risk to residues of sucrose octaacetate at levels that would be of concern is unlikely. Sucrose octaacetate biodegrades rapidly, often in a matter of hours to days. It is soluble, non-volatile, and poorly mobile. Leaching to ground water is not expected. Based on these properties, exposure via drinking water is expected to be low.

When used as an inert ingredient in pesticide formulations, exposure to sucrose octaacetate would primarily be through the oral route, via consumption of raw agricultural commodities to which pesticide products containing sucrose octaacetate have been applied, and/or through drinking water. Exposure may also occur through the dermal and inhalation routes of exposure, via the use of residential pesticide products containing sucrose octaacetate as an inert ingredient (i.e., insect repellents, flea and tick sprays, and herbicides).

Taking into consideration available toxicity and exposure information on sucrose octaacetate, the Agency has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure (dietary and non-occupational sources of exposure) to sucrose octaacetate used as an inert ingredient in pesticide formulations. Therefore, it is recommended that the exemption from the requirement of a tolerance under 40 CFR 180.910 can be considered reassessed as safe under section 408(q) of the Federal Food, Drug, and Cosmetic Act.

Introduction

This report provides a qualitative assessment for sucrose octaacetate, a pesticide inert ingredient with one tolerance exemptions under: 40 CFR 180.910. There is sufficient information to conduct this assessment.

II. Use Information

A. Pesticidal Uses

The tolerance exemption for sucrose octaacetate, when used as an inert ingredient in pesticide formulations, is provided in Table 1 below.

Table 1. Tolerance Exemption Being Reassessed in this Document

40 CFR 180	Tolerance Exemption Expression	Limits	Use Pattern (Pesticidal)	CAS Registry Number and name
.910[a]	sucrose octaacetate	--	Adhesive	126-14-7 α-D-Glucopyranoside, 1,3,4,6-tetra-O-acetyl-β-D-fructofuranosyl, tetraacetate

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

B. Other Uses

Sucrose octaacetate may be used in commercial products such as impregnating and insulating papers, as well as in lacquers and plastics. Sucrose octaacetate may be directly added to food as a synthetic flavoring substance and adjuvant. It may also be used as an indirect food additive as a component of adhesives used in food packaging materials. Table 2 summarizes the direct and indirect food additive uses (FDA uses) of sucrose octaacetate.

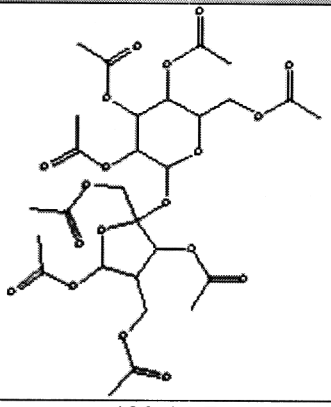
Table 2. FDA Direct / Indirect Food Additive Uses for Sucrose Octaacetate

Name	21 CFR	Use Pattern
Sucrose octaacetate	172.515	Direct food additive: synthetic flavoring substances and adjuvants
Sucrose octaacetate	175.105	Indirect food additive: Adhesive

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of sucrose octaacetate, along with its structure and nomenclature, are found in Table 3.

Table 3. Physical and Chemical Properties of Sucrose Octaacetate

Parameter	Value	Reference
Structure		ChemFinder
CAS Number	126-14-7	Merck Index, 2001
CAS Name	α-D-Glucopyranoside, 1,3,4,6-tetra-O-acetyl-β-D-fructofuranosyl, tetraacetate	TOXNET
Empirical Formula	$C_{28}H_{38}O_{19}$	Merck Index, 2001
Molecular Weight	678.6	Merck Index, 2001
Physical State	Crystalline powder	MSDS
Melting Point	89 C	Merck Index, 2001
Boiling Point	260 C	Merck Index, 2001
Water Solubility	0.09% in water	Merck Index, 2001
Other Solubility	Soluble in acetic acid, acetone, benzene	MSDS
Relative Density (water=1)	1.466 g/cm^3	Merck Index, 2001
Vapor Pressure	~1.6E-12	McCall, Mylan (1998), Mylan (2000)
log Kow	~1.3E-14	McCall, Mylan (1998), Mylan (2000)
Henry's Law Constant	-0.42	McCall, Mylan (1998), Mylan (2000)

IV. Hazard Assessment

Sucrose octaacetate is being evaluated as part of the US EPA's tolerance reassessment process of inert ingredients. The toxicity data base for sucrose octaacetate is limited, and no information was found to indicate that sucrose octaacetate has been the subject of a previous hazard or risk assessment by the USEPA. A literature review was conducted by BIBRA Information Services, Ltd. (1990); sucrose octaacetate was also briefly discussed by Opdyke and Letizia (1982) in Fragrance Raw Material Monographs.

A. Hazard Profile

The available toxicity data base for sucrose octaacetate is limited; however, available data do not identify any major health hazards associated with acute or subchronic exposure to sucrose octaacetate. Sucrose octaacetate has low acute oral and dermal toxicity in rats and rabbits, and is slightly irritating when applied to rabbit skin. Subchronic oral studies in rats and rabbits show no difference in weight gains between treated animals and control groups, and no abnormalities were observed in liver, stomach, and kidney tissues of treated animals.

No data are available on genotoxicity, carcinogenicity, developmental toxicity, reproductive toxicity, neurotoxicity, or immunotoxicity; however, sucrose octaacetate is likely metabolized in the mammalian body to sucrose and acetic acid, in which case additional information on these endpoints may not be needed (BIBRA, 1990).

Available toxicity data are summarized in the following section.

B. Toxicological Data

Acute Toxicity

Table 4. Summary of Acute Toxicity Data for Sucrose Octaacetate

Parameter	Toxicity Value	Reference
Oral LD_{50}	>5 g/kg (rats) >45 g/kg (rabbits)	BIBRA (1990)
Dermal LD_{50}, rabbit	>5 g/kg	BIBRA (1990)
Inhalation LC_{50}, rat	NA	--
Eye Irritation, rabbit	NA	--
Skin Irritation, rabbit	Slight irritant	BIBRA (1990)

NA = Not Available

Subchronic Toxicity

In a limited study, 27 rats were given sucrose octaacetate in their diet for 98 days, at an average daily dose of 4.28 g/kg bw. Twenty rabbits were given sucrose octaacetate at an average daily dose of 6 g/kg bw, by stomach tube, four times a week for 13 weeks. The weight gains of the treated animals were comparable to those of control animals. Tissues examined microscopically included the liver, stomach, and kidneys of approximately one-third of the treated animals. No abnormalities of these tissues were reported (Linegar, 1943 as cited in BIBRA, 1990).

Chronic Toxicity

No relevant data identified.

Neurotoxicity

No relevant data identified.

Mutagenicity

No relevant data identified

Carcinogenicity

No relevant data identified.

Developmental and Reproductive Toxicity

No relevant data identified

C. Metabolism and Pharmacokinetics

No relevant pharmacokinetic data have been identified. In the mammalian body, sucrose octaacetate likely metabolizes to sucrose and acetic acid, neither of which are compounds of toxicological concern (BIBRA 1990).

D. Special Considerations for Infants and Children

The data base for sucrose octaacetate is limited. With regards to special considerations for infants and children, there are no available data on developmental and reproductive effects of sucrose octaacetate. However, in the mammalian body, sucrose octaacetate will likely metabolize to sucrose and acetic acid, neither of which are components of toxicological concern. Sucrose is a naturally occurring sugar that is widely consumed through the diet, and salts of acetic acid (sodium, potassium, and calcium) are identified by the EPA as inert ingredients (under 40 CFR 180.950) of minimal risk with no use restrictions.

Additionally, sucrose octaacetate has a long history of FDA-approved use as a direct and indirect food additive (dating back to 1977), with no reports of human health risks. Its bitter taste will likely limit oral intake.

Based on this information there is no concern, at this time, for increased sensitivity to infants and children to sucrose octaacetate when used as an inert ingredient 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 potential environmental fate of sucrose octaacetate will limit its likelihood of reaching either surface or ground water or bioaccumulating in the environment. There were no environmental transformation and/or occurrence data located in the readily available open literature. Therefore, this assessment is based solely on estimated properties. Sucrose octaacetate is expected to biodegrade in the environment rather rapidly with primary degradation occurring in a matter of hours to days. Mineralization is likely in weeks. Sucrose octaacetate is soluble, non-volatile, and likely to be poorly mobile. Leaching to ground water is not expected because of its high estimated soil partition coefficient and due to biodegradation. Potential to volatilize from surface waters is very low and atmospheric degradation is expected to be rapid.

OPP-modeled estimates for environmental fate indicate that concern for exposures via drinking water is likely to be very low. This conclusion is based on its rather rapid primary degradation (estimated to be to hours to days) and high soil adsorption which will increase removal during flocculation, coagulation and sedimentation should it reach this process without first undergoing biodegradation. Migration to ground water drinking water sources is very unlikely due to its high estimated partition coefficient, greater than 600,000.

VI. Exposure Assessment

Pesticide products containing sucrose octaacetate as an inert ingredient are used as insect repellents, herbicides, flea and tick sprays, and other insecticides. Commercial uses of sucrose octaacetate include use in impregnating and insulating papers, in lacquers and plastics, and as a denaturant for alcohol. The use of sucrose octaacetate as an indirect food additive (adhesives and components of coatings) has been approved by the US FDA since 1977 (21 CFR 175.105).

Based on its use pattern as an inert ingredient in pesticide formulations, human exposure to residues of sucrose octaacetate is possible via the diet (food, drinking water) and/or residential pathways of exposure. For the dietary pathway, exposure to residues of sucrose octaacetate would primarily be through the oral route, via consumption of raw agricultural commodities to which pesticide products containing sucrose octaacetate have been applied, and/or via consumption of drinking water. Its bitter taste will likely limit oral exposure. Based on the environmental fate properties of sucrose octaacetate, it is expected that it will biodegrade rapidly in a matter of hours to days. Therefore, contributions to drinking water are not anticipated from the use of sucrose octaacetate as an inert ingredient in pesticide formulations. In addition, sucrose octaacetate is not expected to bioaccumulate.

Exposure may also occur via the residential pathway (dermal and inhalation routes of exposure) through the use of residential pesticide products containing sucrose octaacetate as an inert ingredient (i.e., insect repellents, flea and tick sprays,

herbicides, etc.). While dermal exposure may occur, inhalation exposure is expected to be minimal because sucrose octaacetate is considered to be non-volatile.

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 sucrose octaacetate, 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 sucrose octaacetate as an inert ingredient in pesticide formulations.

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 sucrose octaacetate and any other substances, and sucrose octaacetate does not appear to produce toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that sucrose octaacetate has 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/.

Human Health Risk Characterization

Sucrose octaacetate is of low toxicity via the acute oral and dermal routes of exposure. It is a slight skin irritant to rabbits. Subchronic oral studies in rats and rabbits show no difference in weight gains between treated animals and control groups, and no abnormalities were observed in liver, stomach, and kidney tissues of treated animals. No relevant chronic, neurotoxicity, mutagenicity, carcinogenicity, developmental, or reproductive toxicity studies have been identified for sucrose octaacetate.

Exposure to sucrose octaacetate as a result of its use as an inert ingredient in pesticidal products may occur via the oral route of exposure (food and drinking water), or via

residential exposure to pesticide products containing sucrose octaacetate. Such products may include insect repellents, flea and tick sprays, and herbicides. Exposure to sucrose octaacetate may also occur as a result of its FDA-approved use as a direct and indirect food additive. The FDA allows sucrose octaacetate to be added to food as a flavoring substance, adjuvant, and/or as a component of adhesives used in food packaging materials. It is noted that FDA regulations stipulate that flavoring substances and adjuvants be used "in the minimum quantity required to produce the intended effect".

Despite the potential for exposure to residues of sucrose octaacetate as identified in the preceding paragraph, physical and environmental fate properties of sucrose octaacetate limit the potential for exposure and risk to human health. In the human body, sucrose octaacetate is likely to metabolize to sucrose and acetic acid, neither of which are compounds of toxicological concern. Sucrose is a naturally occurring sugar that is widely consumed through the diet, and salts of acetic acid (sodium, potassium, and calcium) are identified by the EPA as inert ingredients (under 40 CFR 180.950) of minimal risk with no use restrictions. In the environment, sucrose octaacetate biodegrades rapidly (within hours to days) and does not bioaccumulate; therefore, it is not expected to be present in drinking water. Sucrose octaacetate is soluble, non-volatile, and poorly mobile. Leaching to ground water is not expected. The Agency expects exposure and risk to sucrose octaacetate from food and drinking water to be low.

Some dermal exposure to residues of sucrose octaacetate may occur; however, sucrose octaacetate has low dermal toxicity in animal studies, and is only a slight skin irritant in rabbit studies. Dermal risk is expected to be minimal. Because sucrose octaacetate is non-volatile, inhalation exposure and risk is expected to be minimal.

Taking into consideration all available information on sucrose octaacetate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to sucrose octaacetate when considering exposure through dietary exposure and all other non-occupational sources for which there is reliable information. Therefore, it is recommended that the one exemption from the requirement of a tolerance established for residues of sucrose octaacetate when used as an adhesive in pesticide products can be considered reassessed as safe under section 408(q) of the FFDCA.

X Ecotoxicity and Ecological Risk Characterization

Sucrose octaacetate may be considered practically non-toxic to most aquatic organisms based on the ester and neutral organic SAR (Structure Activity Relationship) estimates. Toxicity values exceeded 100 parts per million (ppm) for fish and aquatic invertebrate on an acute basis. There were no effects data located in the Agency's Ecotox Database (http://www.epa.gov/ecotox).

Predicted acute toxicity values are approximately 150 ppm for green algae 96h EC_{50}'s, much greater than 1000 ppm for aquatic invertebrate 48h EC_{50}'s, and much greater than 1000 ppm for fish 96h LC_{50}'s regardless of structural class. Concentrations at which chronic effects may occur tended to be only slightly lower; however, because of potential for rapid biodegradation, repeated exposures at short intervals would likely be necessary for effects to occur.

Sucrose octaacetate is not expected to bioaccumulate in the environment. Therefore, based on potential exposures and estimated toxicity to aquatic and terrestrial organisms (using available rat, mouse, and rabbit data as surrogate for all terrestrial animals), ecological concerns for listed and non-listed species are not likely from the use of sucrose octaacetate as an inert ingredient in pesticide products, unless application rates exceed hundreds of pounds per acre on a yearly basis.

REFERENCES:

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