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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: **February 23, 2006**

ACTION MEMORANDUM

SUBJECT: Inert Reassessments: 2-(2'-Hydroxy-5'-methylphenyl)benzotriazole and Octyl Epoxytallate

FROM: Pauline Wagner, Chief Pauline Wagner 2/23/06
Inert Ingredient Assessment Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

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

Chemical: 2-(2'-Hydroxy-5'-methylphenyl)benzotriazole and Octyl Epoxytallate
CFR: 40 CFR 180.930 formerly 40 CFR 180.1001(e)
CAS #: 2440-22-4 and 61788-72-5

Table 1. Tolerance Exemptions Expression

40 CFR	Inert Ingredients	Limits	Uses (Pesticidal)	CAS Reg. No. and 9 CI Name
180.930	2-(2'-Hydroxy-5'-methylphenyl)benzotriazole (CAS Reg. No. 2440-22-4)	Not more than 0.5% by weight of pesticide formulation.	Ultraviolet light absorber/stabilizer in animal tag and similar slow-release devices	2440-22-4 Phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-
180.930	Octyl epoxytallate (CAS Reg. No. 61788-72-5)	(none)	Plasticizer, component animal tag	61788-72-5 Fatty acids, tall-oil, epoxidized, octyl esters

Use Summary: 2-(2'-Hydroxy-5'-methylphenyl)benzotriazole is commonly known as Drometrizole and is most commonly used as an UV light absorber helping to stabilize and protect plastics, polyesters, celluloses, acrylates, dyes, rubber, synthetic and natural fibers, waxes, detergent solutions, and orthodontic adhesives against discoloration and deterioration. The U.S. FDA permits its use (with limitations) as an indirect food additive under 21 CFR 178.2010 as an antioxidant and/or stabilizer for polymers. Drometrizole is used as an UV light absorber/stabilizer at not more than 0.5% of the pesticide formulatin in animal tags and similar slow release devices.

Octyl epoxytallate is used as a plasticizer by industry. It is used as a plasticizer, component in animal tags.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the two exemptions from the requirement of a tolerance for the inert ingredients 2-(2'-Hydroxy-5'-methylphenyl)benzotriazole (CAS Reg. No. 2440-22-4) and octyl epoxytallate (CAS Reg. No. 61788-72-5). I consider the two exemptions established in 40 CFR 180.930 [formerly 40 CFR 180.1001(e)] 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

Date: 2/27/06

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 23, 2006

MEMORANDUM

SUBJECT: Reassessment of Two Exemptions from the Requirement of a Tolerance for 2-(2'-Hydroxy-5'-methylphenyl)benzotriazole and Octyl Epoxytallate

FROM: R. Tracy Ward, Biologist R. Tracy Ward
Inert Ingredient Assessment Branch
Registration Division (7505C)

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

Background

Attached is the science assessment for 2-(2'-hydroxy-5'methylphenyl) benzotriazole (CAS Reg. No. 2440-22-4) and octyl epoxytallate (CAS Reg. No. 61788-72-5). For ease of reading, 2-(2'-hydroxy-5'methylphenyl) benzotriazole will be referred to as Drometrizole throughout this document. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, and environmental fate and ecotoxicity of these chemical compounds. Drometrizole has one exemption from the requirement of a tolerance under 40 CFR 180.930 when used as an inert ingredient (ultraviolet light absorber/stabilizer in animal tag and similar slow-release devices) applied to animals only. Octyl epoxytallate has one exemption from the requirement of a tolerance under 40 CFR 180.930 when used as an inert ingredient (plasticizer, component animal tag) applied to animals only. Drometrizole and octyl epoxytallate are being evaluated together based on their similar use pattern. The purpose of this document is to reassess the exemptions from the requirement of a tolerance for residues of Drometrizole and octyl epoxytallate as required under the Food Quality Protection Act (FQPA).

Executive Summary

This report evaluates Drometrizole (ultraviolet light absorber/stabilizer in animal tag and similar slow-release devices) and octyl epoxytallate (plasticizer, component animal tag), inert ingredients which each have one exemption from the requirement of a

tolerance for their residues when used in pesticide formulations applied to animals only under 40 CFR 180.930.

Drometrizole is an inert ingredient incorporated as an ultraviolet (UV) light absorber/stabilizer in animal tag and similar slow-release devices. This chemical has low acute oral and inhalation toxicity. It has mixed results in eye irritation studies, but appears to be a moderate eye irritant. Drometrizole is not irritating to the skin, but has mixed results in dermal sensitization studies. It has a chronic oral of NOAEL of 1000 ppm (47-58 mg/kg bw/day) and a LOAEL of 3000 ppm (142-169 mg/kg bw/day). The chemical is neither a teratogen (with a NOAEL of 1000 mg/kg bw/day in rats and mice) or a carcinogen, but has mixed results in genotoxicity tests. In any case, exposure levels of concern (food, drinking water, inhalation or dermal) are not expected from the use of this substance as an inert ingredient, because it is limited to no more than 0.5% by weight of the pesticide formulation of insecticidal animal ear tags. Additionally, Drometrizole is incorporated into animal ear tags and, therefore, it is not expected to be available to the environment at levels of concern or to present ecological risk concerns.

Octyl epoxytallate is an inert ingredient used as a plasticizer in animal ear tags. It has low acute oral toxicity and is poorly absorbed by all routes of exposure. Exposure levels of concern (food, drinking water, inhalation or dermal) are not expected for octyl epoxytallate because it is incorporated into animal ear tags and is, therefore, not expected to be available to the environment at levels of concern or to present any ecological risk concerns.

Taking into consideration all available information on Drometrizole and octyl epoxytallate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to these chemicals when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the Drometrizole and octyl epoxytallate, which each have one exemption from the requirement of a tolerance established for residues of under 40 CFR 180.930, can be considered reassessed as safe under section 408(q) of the Federal Food, Drug and Cosmetic Act (FFDCA).

I. Introduction

This report evaluates Drometrizole and octyl epoxytallate, pesticide inert ingredients which each have one exemption from the requirement of a tolerance for their residues when applied to animals only under 40 CFR 180.930. Based on their similar use pattern, these chemicals are being reassessed together in this document.

The Phenolic Substrates Association (PSA 2001) sponsored Drometrizole under EPA's High Production Volume (HPV) Challenge Program (http://www.epa.gov/chemrtk/volchall.htm). The goal of the HPV Challenge Program is to collect and make publicly available a complete set of baseline health and environmental effects data on those chemicals that are manufactured in, or imported into, the United States in amounts equal to or exceeding 1 million pounds per year. Industry sponsors volunteer to

evaluate the adequacy of existing data and to conduct tests where needed to fill the gaps in the data, and EPA (and the public) has an opportunity to review and comment on the sponsors' robust summary report. A robust summary has been submitted for phenolic benzotriazoles, which includes Drometrizole and the relevant information has been used in this assessment.

In addition to the HPV summary report (2001), a Cosmetic Ingredient Review report (CIR 1986), a Toxic Substances Control Act Section (TSCA) 8(e) submission (1992), TSCA 8(e) Compliance Audit Program (CP) submissions (1992a-d), and other publicly available literature were reviewed to assess Drometrizole.

Drometrizole is also known as Tinuvin P and Benazol P. Drometrizole is most commonly used as an UV light absorber helping to stabilize and protect plastics, polyesters, celluloses, acrylates, dyes, rubber, synthetic and natural fibers, waxes, detergent solutions, and orthodontic adhesives against discoloration and deterioration (Arisu et al 1992). Drometrizole has been approved by the US Food and Drug Administration (FDA) for various indirect food contact polymers and adhesives (21 CFR 178.2010). As an inert ingredient in pesticide formulations, Drometrizole is used as an UV light absorber and stabilizer in animal tags.

A Structure Activity Team (SAT 2005) report was the primary source of information used to reassess octyl epoxytallate. Octyl epoxytallate is also called Monoplex 573, Plastolein 9214 and epoxidized octyl tallate. It is used as a plasticizer in industry. As an inert ingredient in pesticide formulations, octyl epoxytallate is a plasticizer and animal tag component.

II. Use Information

A. Pesticide Uses

Table 1. Tolerance Exemptions Being Reassessed in this Document

40 CFR [1/]	Inert Ingredients	Limits	Uses (Pesticidal)	CAS Reg. No. and 9 CI Name
180.930	2-(2'-Hydroxy-5'-methylphenyl)benzotriazole (CAS Reg. No. 2440-22-4)	Not more than 0.5% by weight of pesticide formulation.	Ultraviolet light absorber/stabilizer in animal tag and similar slow-release devices	2440-22-4 Phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-
180.930	Octyl epoxytallate (CAS Reg. No. 61788-72-5)	(none)	Plasticizer, component animal tag	61788-72-5 Fatty acids, tall-oil, epoxidized, octyl esters

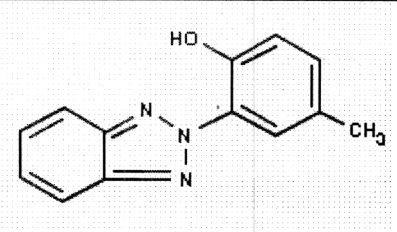
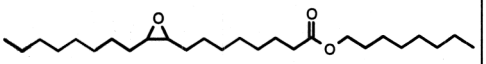
1. Residues listed in 40 CFR 180.930 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

B. Other Uses

Drometrizole is most commonly used as an UV light absorber helping to stabilize and protect plastics, polyesters, celluloses, acrylates, dyes, rubber, synthetic and natural fibers, waxes, detergent solutions, and orthodontic adhesives against discoloration and deterioration (Arisu et al 1992). The U.S. FDA permits its use (with limitations) as an indirect food additive under 21 CFR 178.2010 as an antioxidant and/or stabilizer for polymers. Octyl epoxytallate is used as a plasticizer by industry.

III. Physical and Chemical Properties

Table 2. Physical/Chemical Properties of Drometrizole and Octyl epoxytallate * (Estimated=E, Measured=M)

Parameter	Drometrizole	Octyl epoxytallate
Structure		
Chemical/Common Names	2-(2'-Hydroxy-5'-methylphenyl) benzotriazole, Benazol P, Tinuvin P, 2(2H-Benzotriazol-2-yl)-p-cresol, Drometrizole	Monoplex 573, Plastolein 9214, (Tall oil fatty acids, epoxidized, octyl esters), Epoxidized octyl tallate
CAS Reg. No.	2440-22-4	61788-72-5
Empirical Formula	$C_{13}H_{11}N_3$	$C_{26}H_{50}O_3$
Physical State	Odorless, off-white to yellow, crystalline powder	(not available)
Molecular Weight	225.25 (M)	411 (E)
Water Solubility	25.6 mg/L (E); low solubility	< 0.001 mg/L @ 20ºC or negligible and not dispersible.
Melting Point	131-133 ºC (M)	160 ºC (E)
Henry's Law Constant	6.12×10^{-14} atm-m^3/mole @ 25ºC (E)	1.6×10^{-4} atm-m^3/mole @ 25ºC (E)
Vapor Pressure	7.95×10^{-8} mmHg @ 25°C (E)	< 1.0×10^{-6} mmHg @ 25°C (E)
Octanol/Water Partition Coefficient (Log P)	4.31 (M)	10 (E)

*The physical/chemical properties of Drometrizole were obtained from ChemIDplus (2004) and the CIR (1986); the physical/chemical properties of octyl epoxytallate were obtained from the SAT (2005) report.

IV. Hazard Assessment

A. Hazard Profile

An HPV summary report (2001), a CIR (1986) report, a TSCA 8(e) submission (1992), several TSCA 8(e) CP submissions, and other publicly available literature were reviewed to assess Drometrizole. This chemical has low acute oral and inhalation toxicity. It has mixed results in eye irritation studies, but appears to be a moderate eye irritant. Drometrizole is not irritating to the skin, but has mixed results in dermal sensitization studies. It has a chronic oral NOAEL of 1000 ppm (47-58 mg/kg bw/day), and a LOAEL of 3000 ppm (142-169 mg/kg bw/day). Available information indicates that Drometrizole is neither a teratogen (with a NOAEL of 1000 mg/kg bw/day in rats and mice) or a carcinogen, but has mixed results in genotoxicity tests.

An SAT report (2005) and one acute toxicity study (as cited in ChemIDPlus 2004) were used to assess octyl epoxytallate. Octyl epoxytallate has low acute oral toxicity and the SAT determined that there is "low concern for toxicity" for this chemical.

B. Toxicity Data

1. Drometrizole

Acute Toxicity:

The results and references for acute toxicity studies on Drometrizole described in this section are summarized in Table 3 below.

Drometrizole is considered a substance of low acute oral toxicity. In one study, the LD_{50} of Drometrizole in mice was reported to be >5.0 g/kg body weight (bw). In another acute toxicity study, 10.0 g/kg bw of Drometrizole in sunflower oil was administered by gavage to rats. The rats were observed for 3 weeks after dosing, but there were no deaths and no visible toxic effects.

Rats in an exposure chamber were exposed to Drometrizole for 4 hours at a concentration of 1420 mg/m^3. There were no deaths or clinical signs of inhalation toxicity at the end of a 14-day post-exposure observation period.

In a dermal irritation study, a 0.5 mL sample of nail polish containing 1% Drometrizole was applied under occlusive patches to rabbits for 24 hours with no signs of skin irritation.

In one eye irritation study, moderate eye irritation was observed in rabbits 24 hours after instillation of 500 mg of Drometrizole. Other eye irritation tests conducted on rabbits involved instillation of nail polish containing various concentrations (0.03 to 1.0%) of Drometrizole into the eyes, and either rinsing or leaving the eyes unrinsed after treatment. Results varied from no irritation to moderate or severe eye irritation.

However, it should be noted that nail polish contains other potentially irritating compounds.

Parameter	Toxicity Value	Comments	Reference
Acute Oral, Mouse	LD_{50} =6.5 g/kg		Labor Hygiene and Occupational Diseases 1966, as cited in CIR 1986
Acute Oral, Mouse	LD_{50} >5.0 g/kg		Epstein et al 1967, as cited in CIR 1986
Acute Oral, Mouse	LD_{50} >10 g/kg		Komarova and Maksimova 1979, as cited in CIR 1986
Acute Oral, Rat	LD_{50} >10 g/kg		Ibid.
Acute Inhalation, Rat	LC_{50} (4 h)>1420 mg/m^3		Industrial Bio-Test Labs 1975, as cited in HPV 2001
Eye Irritation, Rabbit	500 mg	500 mg instilled into one eye; moderately irritating at 24 h	Marhold 1972, as cited in CIR 1986
Eye Irritation, Rabbit	0.1 mL of nail polish with 1%, rinsed	Minimally irritating	CTFA November 27, 1978, as cited in CIR 1986
Eye Irritation, Rabbit	0.1 mL of nail polish with 1%, unrinsed	Moderate to severe irritation	CTFA November 30, 1978, as cited in CIR 1986
Eye Irritation, Rabbit	1% in nail polish, rinsed	Mildly irritating	CTFA January 20, 1980, as cited in CIR 1986
Eye Irritation, Rabbit	1% in nail polish, unrinsed	Mildly irritating	CTFA January 21, 1980, as cited in CIR 1986
Eye Irritation, Rabbit	0.1 mL of nail polish with 0.03%	Nonirritating	CTFA May 31, 1984, as cited in CIR 1986
Skin Irritation, Rabbit	0.5 mL of 1.0% under occlusive patches	Nonirritating at 24 h	CTFA November 6, 1978, as cited in CIR 1986

Drometrizole also had varying results when evaluated for skin sensitization. When tested on guinea pigs using the Magnusson-Kligman maximization test, Drometrizole was found to be a "strong sensitizer" (TSCA 8(e) No. 8EHQ-0392-2937 1992; TSCA 8(e) CP No. 8EHQ-0792-5733 1992). Induction of Drometrizole followed by a challenge application resulted in slight edema and very slight to well-defined (and in one case, moderate to severe) erythema. A 2% solution of Drometrizole in DMSO demonstrated skin sensitization in the mouse ear swelling induction test (Ikarashi et al 1994). However, two studies (CTFA August 18, 1978) on guinea pigs described in the CIR (1986) indicated no discernible potential for allergic skin sensitization when induced with 5% Drometrizole.

Chronic Toxicity:

Rats were fed Drometrizole at dietary concentrations of 100, 300, 1000 or 3000 ppm for a period of 104 weeks (Ciba-Geigy Limited March 20, 1975, as cited in HPV 2001). At the 3000 ppm (142-169 mg/kg bw/day) dose level, body weight gain decreased slightly but significantly ($P<0.05$) for males during the second year of treatment. From week 53 to week 80, females had a slight but significant ($P<0.05$) decrease in food intake at this dose. Survival rates in treated rats were not significantly different from controls, and a histopathologic analysis of the rats revealed no morphological abnormalities. The incidence of tumors in treated rats was not significantly different from controls. The chronic NOAEL was determined to be 1000 ppm (47-58 mg/kg bw/day), with a LOAEL of 3000 ppm (142-169 mg/kg bw/day) based on decreased body weight gain.

Subchronic Toxicity:

In rats fed Drometrizole at 0, 0.2, 1.0 or 5.0% in the diet for 14 weeks, the weights of the kidney, spleen and liver increased with increasing dose (TSCA 8(e) CP No. 8EHQ-0592-4278 1992). Testicular weight decreased with increasing dose levels in males. There were microscopic lesions in the kidneys of males at the 1.0% and 5.0% dose level, and swelling of the spleen and inflammation of the pancreas were noted in both sexes at these levels. For this subchronic rat study, a NOAEL of 0.2% was identified, with a LOAEL of 1.0% based on microscopic kidney lesions.

In a 13-week study, dogs were fed daily 0, 1000, 3000 or 10,000 ppm of Drometrizole mixed with dog food (Ciba-Geigy Limited November 25, 1981, as cited in HPV 2001). There were no mortalities or systemic toxic effects observed, but decreased food consumption and body weight gain were noted in dogs fed the 10,000 ppm dose level. At 3,000 ppm, an increase in the enzyme alanine aminotransferase was observed. A NOAEL was determined to be 1000 ppm (equivalent to 31.75 mg/kg in males and 34.6 mg/kg in females), with a LOAEL of 3000 ppm (about 95.25 mg/kg in males and 103.8 mg/kg in females) based on an increase in alanine aminotransferase.

Developmental Toxicity:

In a developmental toxicity study in rats, females were given 150, 500 or 1000 mg/kg bw/day of Drometrizole in 2% aqueous carboxymethylcellulose (1 mL/100 g bw) by gavage on gestation days (GD) 5 to 15 (Ciba-Geigy Limited June 19, 1975, as cited in HPV 2001). There were no maternal toxic effects observed and the rates of implantation and embryotoxicity were not signicantly affected by the treatment. No teratogenic effects were observed, and for rats, the maternal and fetal NOAEL were both determined to be 1000 mg/kg bw/day.

The developmental study described above was also conducted in mice, with 150, 500 or 1000 mg/kg bw/day of Drometrizole in 2% aqueous carboxymethylcellulose (0.1 mL/10 g bw) administered to females by gavage on GD 6 through 15 (Ciba-Geigy Limited August 28, 1975, as cited in HPV 2001). There were no maternal toxic effects

observed, and the rates of implantation and embryotoxicity were not signicantly affected by the treatment. No teratogenic effects were observed, and for mice, the maternal and fetal NOAEL were both determined to be 1000 mg/kg bw/day.

Carcinogenicity/Genetic Toxicity:

Mice administered 5, 50 or 500 ppm (corresponding to a mean daily intake of 0.8, 6.5 or 64 mg/kg bw in males and 0.8, 6.7 and 62 mg/kg bw in females) of Drometrizole daily over a period of 24 months had no significant increase in tumors (Ciba-Geigy Limited August 17, 1981, as cited in HPV 2001). Similarly, rats administered 100, 300, 1000, or 3000 ppm of Drometrizole daily over 104 weeks (as noted in the Chronic toxicity section) had no significant increase in tumors (Ciba-Geigy Limited March 20, 1975, as cited in HPV 2001).

There were mixed results in genetic toxicity studies for Drometrizole. The chemical was negative for mutagenicity in Ames tests using *Salmonella typhimurium* strains both with and without metabolic activation (Jonsen et al 1980; Hacmiya et al 1982, both as cited in CIR 1986). A mouse bone marrow micronucleus test conducted by Hacmiya et al confirmed the negative results of these Ames tests. However, in *in vitro* assays of rat primary hepatocyte cultures, Drometrizole demonstrated a dose-related increase in unscheduled DNA synthesis (TSCA 8(e) CP No. 8EHQ-0892-8164 1992). Mutagenicity occurred in *in vitro* mouse lymphoma assays for Drometrizole with metabolic activation, but not in assays without metabolic activation (TSCA 8(e) CP No. 8EHQ-0892-8136 1992).

2. Octyl Epoxytallate

Octyl epoxytallate has low acute oral toxicity, with an LD_{50} of 32 g/kg in rats (Raw Material Data Handbook 1975, as cited in ChemIDPlus 2004). In addition, the SAT determined that, for octyl epoxytallate, "absorption is poor all routes." Based on its chemical structure and physical/chemical properties, the SAT report gave octyl epoxytallate a low concern for toxicity.

C. Special Considerations for Infants and Children

As an inert ingredient in pesticide formulations, Drometrizole is only used as an ultraviolet light absorber/stabilizer in animal tag and similar slow-release devices (at not more than 0.5% by weight of the pesticide formulation). Octyl epoxytallate's only inert ingredient use in pesticide products is as a plasticizer component of animal tags. As inert ingredients, both chemicals are incorporated into the matrix of small insecticidal animal ear tags that are firmly attached to the animals. Because these chemicals function to stabilize and preserve the plastic eartag, Drometrizole and octyl epoxytallate are expected to remain incorporated in the eartag and not disperse onto the animal during movement. In addition, based on their low acute oral toxicity and physical characteristics (high lipophilicity and low water solubility), the chemicals are expected to

be poorly absorbed through the animal's skin and mouth (which would be expected from the animal licking the tag).

Based on this information and the expected low exposure potential to these chemicals from the eartag use, there is no concern, at this time, for increased sensitivity to infants and children to Drometrizole or octyl epoxytallate from their use as inert ingredients in pesticide products. For these same reasons, a safety factor analysis has not been used to assess risk, and, therefore, an additional tenfold safety factor for the protection of infants and children is also unnecessary.

V. Environmental Fate Characterization and Drinking Water Considerations

As an inert ingredient at not more than 0.5% by weight of the formulation of animal ear tags and similar slow-release devices, Drometrizole is unlikely to be present in drinking water above a part per billion or leach into ground water because it is a small component of the product formulation, there is a low likelihood of leaching from the product matrix, and it has a high affinity to sorb to soils and sediments should small amounts leach from the devices or they are dislodged from the animal. Drometrizole also has a low vapor pressure (7.95 x 10-8 mmHg @ 25°C); only very small amounts of the substance may volatilize in the air.

As an inert ingredient incorporated into animal ear tags, octyl epoxytallate is not expected to be present in drinking water or leach into ground water. The SAT report indicates that with octyl epoxytallate's vapor pressure (< 1.0 X 10-6 mmHg @ 25°C), it is expected to volatilize from a standard river after 10 hours and from a standard lake after 12 days. The report also indicates that octyl epoxytallate would take weeks to aerobically biodegrade in water treatment plants, and longer in the open environment. However, the chemical sorbs strongly to soils and sediments, with negligible migration to ground water expected. Due to octyl epoxytallates use as a plasticizer component of animal tags it is unlikely to leach from the product and be available to the environment.

VI. Exposure Assessment

The only inert ingredient use of Drometrizole in pesticide formulations is as an ultraviolet light absorber/stabilizer in animal ear tags and similar slow-release devices. Animal ear tags are small in size (9.5 to 15.4 g), and the use of Drometrizole is limited to no more than 0.5% by weight of the pesticide formulation. The inert ingredient octyl epoxytallate is used in pesticide formulations only as a plasticizing component of animal tags. Residential exposures (inhalation and dermal) to Drometrizole and octyl epoxytallate are not expected to occur because the chemicals are incorporated into animal ear tags that are firmly attached to the animal and are not expected to leach from the product onto the animal. For the same reason, dietary exposures of concern (food and drinking water) to these chemicals are unlikely, and there are no other food or feed crop uses for these chemicals. In a worst-case scenario, the Agency estimated that the maximum exposure to Drometrizole would be in micrograms (ppb) per kilogram

of animal, which is well below levels of concern. Exposure to octyl epoxytallate is not expected to be a concern because of its expected poor absorption by all routes.

Aggregate Exposure

In examining aggregate exposure, the 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 Drometrizole and octyl epoxytallate, 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 Drometrizole and octyl epoxy-tallate as inert ingredients in pesticide formulations.

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 of toxicity, EPA has not made a common mechanism of toxicity finding as to Drometrizole or octyl epoxytallate 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 Drometrizole or octyl epoxytallate 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

Residential exposures (inhalation and dermal) and dietary exposures (food and drinking water) to Drometrizole and octyl epoxytallate are not expected to occur because the chemicals are incorporated into animal ear tags that are firmly attached to the animal. The chemicals are expected to be poorly absorbed by the animal because of their lipophilicity and low water solubility. In addition, only a small amount of Drometrizole is incorporated into the animal tags due to its limitation of 0.5% by weight of the pesticide formulation, while octyl epoxytallate is poorly absorbed by all routes of

exposure. In a worst-case scenario, maximum exposure to Drometrizole would be in micrograms (ppb) per kilogram of animal, which is well below levels of concern.

Taking into consideration the available information on Drometrizole and octyl epoxytallate, there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure when considering dietary exposure (including drinking water, crops, meats, and fish) and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the two exemptions from the requirement of a tolerance established for residues of Drometrizole and octyl epoxytallate, when applied to animals under 40 CFR 180.930, can be considered reassessed as safe under section 408(q) of the FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

The HPV submission (2001) reported that Drometrizole had an LC_{50} of >100 ppm in zebra fish (*Brachydanio rerio*) in a 96-hour acute toxicity study, and an EC_{50} of >1000 ppm in the aquatic invertebrate *Daphnia magna*. There were no studies available for octyl epoxytallate, but the SAT reported that releases of the chemical to water are minimal. Considering their use in pesticide products as components of animal ear tags, non-target organisms would not be expected to be exposed to Drometrizole and octyl epoxytallate, and therefore, this chemical is not expected to pose an ecological risk to nontarget terrestrial or aquatic species.

References

Arisu, K., Hayakawa, R. Ogino, Y., Matsunaga, K., Kaniwa, M. 1992. Tinuvin P in a spandex tape as a cause of clothing dermititis. Contact Dermatitis 26: 311-316.

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