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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: **August 16, 2005**

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3)

FROM: Pauline Wagner, Chief Pauline Wagner 8/17/05
Inert Ingredient Assessment Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of one inert ingredient exemption from the requirement of a tolerance. Current exemption is to be maintained.

Chemical: Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate
CFR: 40 CFR § 180.930 formerly 40 CFR § 180.1001(e)
CAS #: 2082-79-3

Table 1: Tolerance Exemption Expression

40 CFR §	Inert Ingredient	Limits	Uses (Pesticidal)
180.930	Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3)	Not more than 0.5% by weight of pesticide formulation.	Thermal stabilizer/antioxidant in animal tag and similar slow-release devices

Use Summary: Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is predominately used as a thermal stabilizer and antioxidant in plastic materials. It is also used as a thermal stabilizer/antioxidant in animal tags, such as cattle ear tags, and similar slow-release devices at not more than 0.5% by weight of pesticide formulations.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the one exemption from the requirement of a tolerance for the inert ingredient octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3). I consider the one exemption 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: August 19, 2005

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

August 11, 2005

MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate

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

TO: Pauline Wagner, Chief Pauline Wagner 8/17/05
Inert Ingredient Assessment Branch
Registration Division (7505C)

Background

Attached is the science assessment for octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, and environmental fate and ecotoxicity of this chemical compound. The purpose of this document is to reassess the one exemption from the requirement of a tolerance for residues of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate as required under the Food Quality Protection Act (FQPA).

Executive Summary

This report evaluates octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, a pesticide inert ingredient for which one exemption from the requirement of a tolerance exists for its residues when used in pesticide formulations as a thermal stabilizer and/or antioxidant in animal tags and similar slow release devices (at not more than 0.5% by weight of the pesticide formulation) applied to animals only under 40 CFR §180.930.

Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3) is also known as the following: benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester; n-octadecyl β-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-propionate (OBPP);

Antioxidant 1076; Irganox 1076; and TK 10044. The substance is a white crystalline, free-flowing, non-staining, non-volatile, and odorless powder. Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate is an insoluble chemical used as an inert ingredient thermal stabilizer/antioxidant in insecticidal animal ear tags.

In addition to its use as a pesticide inert ingredient, octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is incorporated into a number of plastic materials as a thermal stabilizer and antioxidant. Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is sponsored 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 Irganox 1076 (octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate) and the relevant information has been made part of this assessment.

Octadecyl 3, 5-di-*tert*-butyl-4-hydroxyhydrocinnamate has moderate acute dermal toxicity, low acute oral toxicity and moderate inhalation toxicity, and is not genotoxic. In subchronic studies, the substance appears to target the liver, brain and spleen, and infants and children may be more sensitive to the chemical than adults. However, exceedances of 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 and it is incorporated as a plastic stabilizing agent. For the same reason, ecological risk concerns are not expected to occur from exposure to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate.

Taking into consideration all available information on octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to this chemical 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 one (1) exemption from the requirement of a tolerance established for residues of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate to animals can be considered reassessed as safe under section 408(q) of the FFDCA.

I. Introduction

This report evaluates octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, a pesticide inert ingredient for which one exemption from the requirement of a tolerance exists for its residues when applied to animals only, under 40 CFR §180.930, at not more than 0.5% by weight of pesticide formulation.

II. Use Information

A. Pesticide Uses

The one tolerance exemption for octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate when used as a thermal stabilizer/antioxidant in insecticidal/miticidal animal ear tags is listed below in Table 1.

Table 1. Tolerance Exemption Being Reassessed in this Document

40 CFR §	Tolerance Exemption Expression	Limits	Uses (Pesticidal)
180.930[1/]	Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3)	Not more than 0.5% by weight of pesticide formulation.	Thermal stabilizer/antioxidant in animal tag and similar slow-release devices

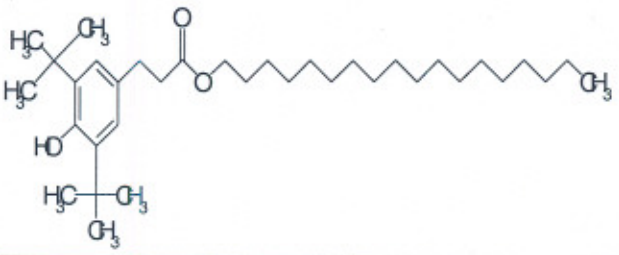
1. Residues listed in 40 CFR §180.930 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

B. Other Uses

Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is also used as a thermal stabilizer and antioxidant in plastic materials.

III. Physical and Chemical Properties

Table 2. Physical and Chemical Properties (Measured (M) or Estimated (E))

Parameter	Value	Source
Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate (CAS Reg. No. 2082-79-3)		
Structure		NIH, 2004; MDL, 2003
Molecular Weight	530.9 (M)	NIH, 2004
Water Solubility	3.978×10^{-8} mg/L at 25° C (M)	Ciba Geigy, 2001
Melting Point	49-54°C (M)	Ciba Geigy, 2001
Henry's Law Constant	1.61×10^{-6} atm-m3/mole @ 25°C (E)	NIH, 2004
Vapor Pressure	4.2×10^{-11} mmHg @ 25°C (E)	Ciba Geigy, 2001
Octanol/Water Partition Coefficient	Log p = 13.4	Ciba Geigy, 2001; NIH, 2004

IV. Hazard Assessment

A. Hazard Profile

The majority of the data and information used in this hazard assessment for octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate are from test plans and robust summaries submitted by Ciba Specialty Chemicals Corporation in 2001 to EPA as part of the HPV Challenge Program. The reader is referred to the HPV submission for more detailed information. A small number of studies that are not part of the HPV submission were also used.

B. Toxicological Data

Unless otherwise noted, the following summarizes data and information available in the HPV submission (Ciba-Geigy, Ltd., 2001). Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is referred to as Irganox 1076 throughout the HPV submission (Irganox 1076 is Ciba-Geigy Limited's trademark name for the chemical) and, for ease of reading, that name will be used in this document for those sections that reference the HPV submission.

Acute Toxicity:

In an oral acute LD_{50} study on rats, five males and five females were given 5000 mg/kg of Irganox 1076 in polyethylene glycol 400 (20 mL/kg bw) by oral gavage. The rats were observed for 14 days for signs of toxicity and mortality. There were no mortalities and adverse effects observed were mild dyspnea, ruffled fur and curved body position. Therefore, Irganox 1076 is considered to be of very low acute toxicity, with an Agency classification of toxicity category IV.

In an acute dermal toxicity study on rats, 2000 mg/kg of the test compound was applied in 0.5% (w/v) carboxymethylcellulose in 0.1% (w/v) aqueous polysorbate. No rats died, but they exhibited piloerection and hunched posture; therefore, Irganox 1076 was determined to have slight toxicity, giving it a toxicity category of III. No negative control was maintained, no details regarding method of application were reported, and the observation period after dosing was not specified in this study.

In a 4-hour acute inhalation toxicity study, male and female rats were exposed nose-only to 0, 500, 1025, or 1811 mg/m^3 (0 to 83,408 ppm) of an aerosol of the test material and observed for 14 days. No exposure-related effects or mortality were observed, giving Irganox 1076 a very low toxicity category of IV for inhalation.

Subchronic Toxicity:

In a subchronic oral toxicity study, young rats (5/sex/dose) were administered Irganox 1076 by oral gavage (10 mL/kg) at doses of 0, 5, 30, 100, or 300 mg/kg/day for 4 weeks. The highest dose level caused centrilobular hepatocytic hypertrophy with an associated increase in liver weight in all rats. These rats also had elevated transaminase activity and high cholesterol.

At 100 mg/kg/day of Irganox 1076, an increase in liver weight was noted, but only in females. A NOAEL of 30 mg/kg/day was determined for Irganox 1076. The results indicate that Irganox 1076 is a weak phenobarbital-like enzyme inducer in male and female rat liver.

Lake et al (1980) administered n-octadecyl β-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-propionate (OBPP) to rats by oral gavage at dose levels of 30, 100, 300, or 1000 mg/kg/day for 14 days. Treatment with the chemical at all dose levels caused dose-related increases in the induction of cytochrome P-450 and in mixed function oxidase enzymes in male rats. At 100 mg/kg/day, OBPP significantly enhanced UDP (uridine diphosphate) glucuronosyl transferase and microsomal protein content in males. Liver weight increased at the 300 mg/kg/day dose level in males, and caused hypertrophy of the centrilobular cells of the liver lobule in both sexes, and induced hepatic xenobiotic metabolism with properties similar to sodium phenobarbital. In addition, the ultra structural studies showed a marked proliferation of smooth endoplasmic reticulum in both sexes. The 1000 mg/kg/day dose of OBPP resulted in significantly reduced body weights in females. Fourteen days after the cessation of treatment, most of these effects were reversed to control levels. However, biphenyl 4-hydroxylase, a hepatic drug-metabolizing enzyme, was still significantly enhanced in both sexes, and male rats still retained liver weights above control levels. NOAELS and LOAELS were not established in this study.

Genotoxicity:

An *in vitro*, reverse mutation test was conducted using *Salmonella typhimurium* strains at 10-250 ug/plate of Irganox 1076. Irganox 1076 was negative for genotoxicity, both with and without metabolic activation. Cytotoxic concentration was not reported, but the precipitation concentration was 100 ug/0.1 mL.

In an *in vivo,* dominant lethal study on mice, 20 males received single gavage doses of 1000 or 3000 mg/kg in carboxymethylcellulose (0.2 mL/kg bw), and then were mated with females for up to 6 weekly periods. No differences in mating ratio, number of implantations, or embryonic deaths were noted between controls and treated groups.

An *in vivo* somatic mutation assay was conducted in Chinese hamsters. Chinese hamsters (6/sex/dose) received single daily doses by gavage of 500, 1000, or 2000 mg/kg in carboxy-methylcellulose (20 mL/kg) for 2 consecutive days. In all groups the percentage of cells displaying anomalies of nuclei did not differ significantly from the negative control.

Reproductive/Developmental Toxicity:

Summary of Studies: A reproduction study concluded that Irganox 1076 targets the liver, brain and spleen in rats. It produces histopathological changes in the liver in adults, and young rats appear to be more sensitive to the chemical. There were also toxic effects in dams related to reduced food intake corresponding with increasing dose-levels of Irganox 1076. The NOAEL was 1500 ppm (75 mg/kg/day) for adults and a LOAEL of < 500 ppm (50 mg/kg/day) was determined in offspring based on changes in brain and spleen weight. In a pair of teratogenicity

studies, rats had maternal toxicity effects from dose-dependent decreases in diet, and a NOAEL of 150 mg/kg/day, while mice had no adverse effects and a NOAEL of 1000 mg/kg/day.

Studies:

For a two-generation reproduction study, Irganox 1076 was administered to rats in dietary concentrations of 0, 500, 1500, or 5000 ppm for 10 months. Statistically significant and dose-dependent increases in liver weights and reductions in brain and spleen weights were observed at all doses in F_1 and F_2 weanlings, but no histopathological changes were seen. Dose-dependent reductions in adult spleen weights were seen at all dose levels in both F_0 and F_1 generations. Increased liver weights and reduced brain weights were observed in adults at 5000 ppm. Centrilobular hepatocellular hypertrophy was also observed in adults at this dose, as well as a slight, but significant, reduction in food consumption, body weight, and body weight gain in adults of both generations. No histopathology was seen in the brain or spleen at any dose in adult rats. Mating performance, pregnancy rate, and the duration of gestation were unaffected by the treatment. At 5000 ppm, the litter size of the F_0 and F_1 generations were significantly reduced (12% and 19%, respectively). Post-partum pup loss significantly increased and pup weight gain was slightly, but significantly, reduced in the F_1 generation at this dose. Increased liver weights and reduced brain and spleen weights in weanlings, but not adults, at 500 ppm suggest young rats have greater sensitivity to Irganox 1076 than adults. The NOAEL for both parental and reproductive toxicity was determined to be 1500 ppm (75 mg/kg/day), with a LOAEL of 5000 ppm (250 mg/kg/day). The NOAEL for offspring toxicity was not determined in this study, but the LOAEL was determined to be < 500 ppm (50 mg/kg/day).

Teratogenicity studies were conducted with Irganox 1076 on rats and mice. In both studies, the test subjects were administered the test material as a 2% aqueous solution in carboxymethylcellulose by gavage from days 6-15 of gestation at doses of 0, 150, 500, or 1000 (limit dose) mg/kg/day. In the rat study, dams were sacrificed on gestation day (GD) 21. At the mid- and high-dose levels, a significant decrease in food consumption was noted in dams. Decreased body weight was evident in pups from dams dosed with Irganox 1076 at the 500 and 1000 mg/kg/day dose levels. Also, an increase in the number of unossified phalangeal nuclei of the hind-limb was observed in pups from dams dosed at 1000 mg/kg/day. Both of these effects may be related to maternal toxicity. The NOAEL for maternal and fetotoxicity (developmental toxicity) was 150 mg/kg/day for the rats. In mice, the dams were sacrificed on GD 18. Unlike the rats, there were no observed treatment-related adverse effects on maternal and fetal parameters. The NOAEL for maternal and developmental toxicity in mice was 1000 mg/kg/day.

C. Conclusions

Results of acute toxicity studies indicate that octadecyl 3,5-di-*tert*-butyl-4-hydroxy-hydrocinnamate displays no acute inhalation toxicity (LC_{50} > 1811 mg/m^3 or 83,408 ppm), low acute oral toxicity (LD_{50} > 5000 mg/kg), and moderate acute dermal toxicity (LD_{50} > 2000 mg/kg). The substance is not considered to be mutagenic or genotoxic.

In subchronic toxicity studies in rats, octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate appears to target the liver, causing centrilobular hepatocytic hypertrophy, liver enlargement

and phenobarbital-like enzyme induction starting at the 100 mg/kg/day dose level (the LOAEL). The NOAEL for adult rats is 30 mg/kg/day. Some of the adverse effects appear to be reversible 14 days post-treatment, with the exception of biphenyl 4-hydroxylase, which retains enhanced function in both sexes, and increased liver weight in males.

The most sensitive endpoints for adult rats were determined in a reproductive study to be a NOAEL of 75 mg/kg/day, and a LOAEL of 250 mg/kg/day, based on significant changes in brain and liver weights and liver effects. The reproductive study also indicates that young rats are more sensitive to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate than adult rats. Though there were no histological effects observed in the young rats, liver weights increased and spleen and brain weights decreased at the 50 mg/kg/day dose level (LOAEL < 50 mg/kg/day) compared to the 250 mg/kg/day dose level in adults. A comparison of the rat and mouse developmental studies indicates that rats are more sensitive to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate than mice. The NOAEL in the rat study for both maternal and fetotoxicity was 150 mg/kg/day, but the NOAEL in the mouse study was 1000 mg/kg/day, the highest dose tested.

D. Special Considerations for Infants and Children

Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate has demonstrated reproductive toxicity, with younger animals showing greater susceptibility to the chemical. However, these effects occurred through repeated oral ingestion of the chemical. Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is used as a thermal stabilizer/antioxidant (at not more than 0.5% by weight of the pesticide formulation) in small insecticidal animal ear tags that are firmly attached to the animals. Because it functions to stabilize and preserve the plastic eartag, the chemical is expected to remain incorporated in the eartag and not disperse onto the animal during movement. Based on its low acute oral and moderate dermal toxicity and physical characteristics (extreme lipophilicity and low water solubility), it is expected to be poorly absorbed through the animal's skin and mouth (which would be expected from the animal licking the tag). In a worst-case scenario, residues from use of the eartags are expected to be in micrograms (ppb) per kilogram of animal weight. Dietary exposure to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate in meats and meat products is expected to be several orders of magnitude less than levels in the animal, due to food processing and cooking, and therefore, far below levels of concern. Based on the expected very low exposure to this chemical, a safety factor analysis has not been used to assess the risks resulting from the inert pesticidal use of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, and therefore, an additional tenfold safety factor for the protection of infants and children is also unnecessary.

V. Environmental Fate Characterization/Drinking Water Considerations

As an inert ingredient at not more than 0.5% of the formulation of animal ear tags, octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate is not expected to be present in drinking water or leach into ground water because of its low likelihood of leaching from the product and high affinity to sorb to soils and sediments. The chemical is a thermal stabilizer and antioxidant that is incorporated into ear tags and is not likely to be available to the environment. Octadecyl

3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate also has an extremely low vapor pressure (4.2 x 10^{-11} mmHg @ 25°C); only very small amounts of the substance may volatilize in the air.

VI. Exposure Assessment

The only pesticide inert ingredient use of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate is as a thermal stabilizer and antioxidant in animal ear tags/slow-release devices. Animal ear tags are small in size (9.5 to 15.4 g), and the amount of the inert ingredient that is used is limited to no more than 0.5% by weight of the pesticide formulation. Residential exposures (inhalation and dermal) to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate are not expected to occur because the chemical is a plastic stabilizing agent incorporated into animal ear tags that are firmly attached to the animal. For the same reason, dietary exposures (food and drinking water) to this chemical are unlikely, and there are no other food or feed crop uses for this chemical. In a worst-case scenario, maximum exposure to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate would be in micrograms (ppb) per kilogram of animal, which is well below levels of concern.

VII. Aggregate Exposures

In examining aggregate exposure, 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). Octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate functions as a thermal stabilizer incorporated into non-pesticidal plastic products used by consumers, where there are no exposure concerns. Similarly, as a thermal stabilizer and antioxidant incorporated into pesticidal animal ear-tags and slow-release devices, food, drinking water and residential exposures are not expected and unlikely with this chemical.

For octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, 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 this chemical when used as an inert ingredient in pesticide formulations.

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."

EPA does not have, at this time, available data to determine whether octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate has a common mechanism of toxicity with other substances. 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 octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate and any other substances, and this substance does not appear to produce toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate 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.

IX. Human Health Risk Characterization

Based on the information from the HPV Challenge Program and open literature, the toxicity data for octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate are sufficient for a qualitative assessment. There are no data or human epidemiology studies that suggest the substance is a carcinogen, despite its widespread use in plastic materials. Studies have indicated that the substance is a slight dermal irritant, and that consumption of moderate doses of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate over time appears to affect the liver, brain and spleen in a phenobarbital-like mode of action. Several studies also indicated that infants and children might be more sensitive to repeated oral ingestion of the chemical than adults.

Although the conclusions of certain laboratory studies have identified toxicity concerns, residential exposures (inhalation and dermal) and dietary exposures (food and drinking water) to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate are not expected to occur because the chemical is incorporated into animal ear tags that are firmly attached to the animal. The chemical is expected to be poorly absorbed by the animal because of its lipophilicity and low water solubility. In addition, only a small amount of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate is incorporated into the animal tags (0.5% by weight of the pesticide formulation). In a worst-case scenario, maximum exposure to octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate would be in micrograms (ppb) per kilogram of animal, which is well below levels of concern.

Taking into consideration the available information on octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate, 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 one exemption from the requirement of a tolerance established for residues of octadecyl 3,5-di-*tert*-butyl-4-hydroxy-hydrocinnamate 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 Challenge Program submission reported the toxicity of octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydrocinnamate on freshwater fish, aquatic invertebrates, and aquatic plants. An

LC_{50} of >100 mg/L was established for both bluegill fish and rainbow trout, and an EC_{50} of >100 mg/L was established for *Daphnia magna*. An EC_{50} of >30 mg/L was established for *Scenedesmus subspicatus*. These enpoint values are 9 to 10 orders of magnitude greater than the water solubility of the chemical (4×10^{-10} mg/L). Based on these studies, octadecyl 3,5-di-*tert*-butyl-4-hydroxyhydro-cinnamate is classified as practically non-toxic to aquatic fish and invertebrates, and moderately toxic to aquatic vegetation. There were no studies conducted on terrestrial plants and animals for this substance. Under the use patterns described in this assessment, non-target organisms would not be expected to be exposed to octadecyl 3,5-di-*tert*-butyl-4-hydroxy-hydrocinnamate, and therefore, this chemical is not expected to pose an ecological risk to terrestrial or aquatic nontarget species.

References:

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