UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: June 2, 2008

SUBJECT: Denatonium Saccharide (PC code 129045). **Revised** Human Health Risk Scoping Document in Support of Registration Review. DP Barcode **D352579**.

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Executive Summary

Health Effects Division's (HED) denatonium saccharide scoping team has **revised** the revised human health risk assessment status update issued on May 8, 2008. Denatonium saccharide is registered as a repellent or feeding depressant to reduce chewing and biting damage to outdoor structures and surfaces by tree squirrels, dogs and cats. Currently there is only one active registered product (Ro-Pel). No dietary, residential, or aggregate risk assessment was conducted before. The Agency's most recent documentation on denatonium saccharide was a memo dated May 9, 1996, where it was concluded that acute oral, dermal, and inhalation toxicities for the formulated product are all category IV. Denatonium saccharide is not an eye or skin irritant (Category IV). It is not a skin sensitizer. No subchronic or chronic toxicity studies are available. Denatonium saccharide and denatonium benzoate (Bitrex) both share the same cation: denatonium, which is a quaternary ammonium cation. No subchronic or chronic toxicity studies are available on denatonium benzoate either. Based on acute toxicity studies on the denatonium benzoate salt, the acute oral LD_{50} is category III, the acute inhalation LC_{50} is II, but the acute dermal LD_{50} study is unacceptable.

HED's denatonium saccharide scoping team concludes that since this is a non-food use chemical, it is not subject to FQPA, therefore, no aggregate risk assessment is needed for the Registration Review of denatonium saccharide. However, depending on the outcome of the Agency's drinking water exposure assessment, a dietary assessment (drinking water exposure only) may be needed. An ORE assessment may be needed if denatonium saccharide is shown to be dermally absorbed. As for the data requirements, HED's scoping team concludes that a dermal absorption study on the denatonium saccharide active ingredient is needed to determine if there is potential dermal exposure to residential handlers. A 90-day oral on rodent may be needed to assess chronic dietary (water only) risk to denatonium saccharide.

Introduction

HED has evaluated the status of the human health assessment for denatonium saccharide to determine whether sufficient data are available and whether a new or updated human health risk assessment is needed to support Registration Review. HED has considered the most recent risk assessments for denatonium saccharide, HED databases, the OPPIN database, and a Google online search during the process of this scoping. For a complete listing of the references, see **Reference** Section at the end of this memo.

Denatonium saccharide and denatonium benzoate (Bitrex) both share the same cation: denatonium, which is a quaternary ammonium cation. Denatonium cation is the most bitter substance known to date - dilutions of as little as 10 ppm are unbearably bitter to humans. The salts are often used as aversive agents to prevent accidental ingestion (Google search-Wikipedia). Denatonium saccharide is registered as a repellent or feeding depressant to reduce chewing and biting damage to outdoor structures and surfaces (such as bark of trees, fences, poles, decks, planters, siding, garbage cans, and furniture) by tree squirrels, dogs and cats. Currently there is only one active registered product: Ro-Pel Tree Squirrel, Vole, Dog, and Cat Repellent (EPA Reg. # 81117-1). It is a ready-to-use liquid formulation which contains 0.065% denatonium saccharide and 0.035% thymol. This scoping document is for the denatonium saccharide active ingredient only. All products containing denatonium benzoate as an active ingredient have been cancelled.

Hazard Identification/Toxicology

No subchronic or chronic toxicity studies are available for denatonium saccharide. Acute oral, dermal, and inhalation toxicities are category IV for the product formulation. Denatonium saccharide is not an eye or skin irritant (Category IV). It is not a skin sensitizer (Agency memo of 05/09/1996, C. Glasgow). No subchronic or chronic toxicity studies are available on denatonium benzoate either. Based on acute toxicity studies on the benzoate active ingredient, the acute oral LD_{50} is category III, the acute inhalation LC_{50} is II, but the acute dermal LD_{50} study is unacceptable (HED memo of 10/23/2007, E. Reaves, TXR Nos. 0054508).

A screening search on OPP's incident data system (IDS) indicated that no incident has been reported for denatonium saccharide.

Conclusions: The HED registration review scoping team determined that a dermal absorption study is needed to determine potential dermal exposure to residential handlers. Depending on

the outcome of the Agency's drinking water exposure assessment, a 90-day oral study on rodent may be needed to assess chronic dietary (drinking water only) risk to denatonium saccharide.

Exposures

No dietary or residential exposure assessment was conducted previously.

Conclusions: There are no food uses for denatonium saccharide and contamination of home grown produce from residential use of denatonium saccharide is unlikely, so exposure from consumption of food is not assessed. Dietary exposure from drinking water is not known at this time since the Environmental Fate and Effects Division (EFED) does not have enough environmental fate data to make the determination yet. Depending on the outcome of EFED's drinking water assessment, a chronic dietary assessment for drinking water exposure only may be needed. HED does not believe that there is acute dietary risk of concern, because denatonium saccharide is such a bitter compound that it is unlikely that human will accidentally consume enough to cause any acute toxic effects.

Exposures to residential handlers during application can occur. Denatonium saccharide is a ready-to-use liquid formulation which can be applied using paintbrush or sprayer. Dermal and inhalation exposures can occur during application, especially dermal exposure. A residential handler dermal assessment may be necessary if denatonium saccharide is dermally absorbed. HED does not believe that risk from inhalation exposure will be of concern since this product is to be applied using coarse spray or paint brush, and the % ai in the RTU liquid formulation is very low (0.065%).

Aggregate

No aggregate risk assessment was conducted previously.

Conclusions: HED's scoping team concluded that since this is a non-food use chemical, therefore, it is not subject to FQPA. No aggregate risk assessment is needed.

Occupational Exposure and Risk

No occupational risk assessment was conducted previously.

Conclusions: HED's scoping team concludes that although there are exposure scenarios to workers who apply the pesticide, no occupational handler assessment is needed at this time, based on the low acute toxicity of the formulation, the required personal protective equipment stated on the product label, and the fact that no incidents have been reported so far.

Data Requirements

- A dermal absorption study on the saccharide active ingredient is needed.
- A 90-day oral study on rodent may be needed.

References

1) Bibliography for Denatonium saccharide and Denatonium benzoate (OPPIN database);
2) Agency memo of 05/09/1996, C. Glasgow, "EPA File Symbol/EPA Reg. No.: 45735-2/RoPel Animal, Rodent and Bird Repellant";
3) HED memo of 10/23/2007, E. Reaves, TXR Nos. 0054508, "RED-0350-26839: Denatonium benzoate/**Bitrex**". D340792;
4) Google online search- Denatonium- Wikipedia;
5) Google on line search- Denatonium saccharide- ChemBlink.

DCI Table

Guideline Number: 870.7600 **Study Title:** Dermal Penetration Study
Rationale for Requiring the Data
The use pattern of this product results in potential dermal exposure to handlers.
Practical Utility of the Data
How will the data be used? To determine how much, if any, the saccharide is absorbed through the skin. **How could the data impact the Agency's future decision-making?** The result of this data will affect whether or not EAP needs to do a dermal exposure assessment for residential handlers. If EPA does not have this data, then 100% absorption will needed to be assumed, and a repeated dose dermal study will be required to assess handler dermal exposure.

Guideline Number: 870.3100
Study Title: 90-day Oral Study on Rodent

Rationale for Requiring the Data

This study is required for non-food use pesticides if oral exposure could occur. The 90-day rat oral study is required for hazard characterization (possibly endpoint selection) and dose-setting for the chronic/carcinogenicity study (40 CRF parts 9 and 158, subpart F). In the case of denatonium saccharide, the scoping conclusions indicated that there may be dietary exposure from drinking water; therefore, it is recommended that a 90-day study be conducted to assess chronic dietary risk.

Practical Utility of the Data

How will the data be used?
The results of this study will be used to characterize the hazard of denatonium saccharide and serve as the base for chronic dietary endpoint selection.

How could the data impact the Agency's future decision-making?
The result of this data may affect the Agency's decision to continue to grant the existing use of denatonium saccharide with or without risk mitigations.