United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508C) | EPA-738-F-02-002 May 2002

R.E.D. FACTS

Thiabendazole and Salts

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. To implement provisions of the Food Quality Protection Act of 1996, EPA considers the special sensitivity of infants and children to pesticides, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with common mechanisms of toxicity. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that meet the safety standard of the FQPA and can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 2760, Thiabendazole and Salts.

Use Profile

Thiabendazole is used to control a variety of fruit and vegetable diseases such as mold, blight, rot and stains caused by various fungi. Thiabendazole is formulated as a ready-to-use, dusts, flowable concentrates, emulsifiable concentrates, wettable powders, granules, and water dispersable granules. It’s registered for use as a pre-planting dust treatment to potato seed-pieces, sweet potato seed pieces, soybean, and wheat. It is also registered for use on mushrooms and is mostly used post-harvest as a dip or spray on citrus fruits, apples, pears, bananas, mangos, papaya, plantain, carrots, avocados, peas, and potatoes. Thiabendazole salt uses include a ready-to-use formulation for ornamental bulbs, elm and sycamore trees. Thiabendazole salt is also used as a preservative in paints, carpets, adhesives and textiles.

Thiabendazole can be applied by dipping, spraying, or application during the waxing procedure for fruits and vegetables. Seed treatments are applied with a ready-mix or slurry-mix. A ready-to-use formulation is added to paints, carpets, textiles and adhesives.

Regulatory History

Thiabendazole was first registered as a pesticide in the U.S. in 1969 by Merck and Company, Inc. Merck and Company, Inc. manufactured the technical product and other companies manufactured end-use products. The primary registrant of end use products has been Syngenta Crop Protection, Inc. Merck and Company, Inc. held the registration of the technical product until 1998. Technical product was later transferred to Syngenta Crop Protection,Inc. and retained it's name as Mertect Fungicide. Currently, 62 Thiabendazole pesticide products are registered. A Data Call-In (DCI) was issued in 1991 for thiabendazole requiring the submission of additional data on product chemistry, toxicity, environmental fate and ecological effects. A subsequent DCI was issued in 1995 requiring data to help estimate post-application exposure. The Reregistration Eligibility Decision (RED) reflects a reassessment of all data which were submitted in response to the DCI's.

Human Health Assessment

Toxicity

Thiabendazole generally has been shown to have low acute dermal toxicity. It is neither irritating to the eyes or skin nor is a dermal sensitizer. Toxicity Categories, which range from 1 (most toxic) to 4 (least toxic), were mostly 4 for thiabendazole. The thyroid and liver are the primary target organs of thiabendazole. In a rat subchronic study, there were increases in liver and thyroid weights. Also, in a chronic dog study, thiabendazole produced a similar effect in increased liver weight.

Thiabendazole generally is of low acute toxicity, however, the Agency has classified thiabendazole as likely to be carcinogenic at doses high enough to cause disturbance of the thyroid hormone balance. It is not likely to be carcinogenic at doses lower than those which could cause a disturbance of this hormonal balance. After consideration of expected exposure authorized under current EPA registered use patterns as well as consideration of allowable dietary exposure from imported crops treated with thiabendazole, the Agency has determined that individuals would be exposed to levels which are far less than those sufficient to cause cancer. The Agency is using the MOE approach for the human cancer risk assessment. Use of Pesticide Data Program (PDP) monitoring data, field trial data, tolerance level residues and calculated livestock residues have resulted in a MOE approach of 13,000 for the general U.S. population which is below the Agency's level of concern. A MOE of 13,000 means that potential exposures to humans is 13,000 times less than the exposure to rats at which no adverse effects were observed. Rats have also demonstrated an increased sensitivity compared to humans to

thyroid induced tumors which adds an even greater comfort level to the significance of the calculated MOE.

Dietary Exposure

People may be exposed to residues of thiabendazole through the diet. Tolerances or maximum residue limits have been established for the following agricultural and livestock commodities in 40 CFR§180.242: apples (post-harvest), avocados, bananas (pre and post-harvest), banana pulp (pre and post-harvest, dry beans, sugar beets pulp (dried/and or dehydrated), sugar beets tops (pre-harvest), sugar beets tops, cantaloupes, carrots (post-harvest), citrus fruits (post-harvest), citrus pulp dried (post-harvest), mangos, mushrooms, papayas (post-harvest), pears (post-harvest), potato processing waste (pre and post-harvest), potatoes (pre and post-harvest), rice hulls, rice rough, rice straw, soybeans, strawberries, sweet potatoes (post-harvest to sweet potatoes only intended for use as seed), Hubbards squash, wheat grain, wheat milled fractions (except flour), wheat straw, cattle fat, meat byproduct, meat; eggs, poultry meat, meat byproduct; goats fat, meat byproduct, meat; hogs fat, meat byproduct, meat; horses fat, meat, meat byproduct; milk, sheep fat, meat byproduct and meat. EPA has assessed the Thiabendazole tolerances and found that some are acceptable, others must be revoked. The Agency is proposing to revoke the tolerances for residues in poultry meat, meat by products and eggs. Based upon the maximum dietary burden for poultry and data, tolerances for residues in poultry meat, meat by products, and eggs should be revoked. In addition, based upon the maximum dietary burden for beef cattle and swine and data, tolerances for residues in fat of cattle, hogs, horses, goats and sheep should be revoked.

The Agency is proposing to revoke the tolerance for thiabendazole residues in banana pulp. The tolerance already established for bananas will include the banana pulp. New tolerances must be established for residues in/on wet apple pomace, citrus oil, pome fruits, wheat forage and hay. Residue data is required before an appropriate tolerance can be determined for residues in/on wheat forage and hay; however, sufficient data is currently available to determine the appropriate tolerance for residues in wet apple pomace and citrus oil.

The registrant is not supporting domestic treatment of thiabendazole on sugar beet raw agricultural commodities (RACs), grapes, rice RACs, processed fractions, and Hubbards squash, and therefore these tolerances should all be revoked. The Agency is proposing to revoke tolerances for residues in dried citrus pulp, potato processing waste, and wheat milled fractions since thiabendazole does not concentrate in potato, wheat processed fractions, and dried citrus pulp in excess of the tolerance on whole citrus fruits.

Risk From Food

For thiabendazole, acute, chronic, and carcinogenic dietary risk from food is not of concern.

Risk From Food +Drinking Water

Model estimates of potential drinking water exposure from ground and surface water sources are not of concern for thiabendazole. Also, acute and chronic dietary risk is below the Agency's level of concern. Therefore, risks from food and drinking water combined are below the Agency's level of concern.

Risk From Non-dietary Exposure

There are no thiabendazole pesticide products registered for use by homeowners. Thiabendazole-treated carpets and paints, can however, be used by homeowners. The Agency does not believe that homeowners exposed to thiabendazole-treated carpets are at a risk since thiabendazole is applied to the backing of carpets during the manufacturing process and estimates are extremely conservative. Also, due to thiabendazole's use profile, the Agency has concluded that there is a low potential for residential exposure. The low concentrations of thiabendazole incorporated in paints, adhesives, paper and carpet greatly reduces the potential for exposure. In all cases, residential exposure is not expected to exceed occupational post-application exposure and therefore would not be expected to exceed the Agency's level of concern.

Aggregate Risk

The short- and intermediate-term aggregate risk assessment includes exposure from nonoccupational settings in addition to the dietary (food and water) exposure. Two short-term (1-7 days) and intermediate term (1-6 months) exposure scenarios were identified for the adult populations: exposure to thiabendazole-treated carpets and paints. These two scenarios were aggregated with the average dietary exposure since they can occur simultaneously. For infants and children, only the carpet exposure was aggregated with average dietary exposure. Estimated average concentrations of thiabendazole in surface and ground water are below the Agency's level of concern.

Occupational Risk

Based on current use patterns, handlers (mixers, loaders, and applicators) may be exposed to thiabendazole applications in agricultural and other settings. However, the Agency has concluded that there is low potential for residential exposure. The low concentrations of thiabendazole incorporated in paints,

adhesives, paper and carpet greatly reduces the potential for exposure. The margin of exposure (MOE) for all residential and occupational scenarios is well below the Agency's level of concern, and therefore risk is minimal.

Exposure and risk to workers will be mitigated by the use of PPE required by the WPS, as required by this RED. Post-application reentry workers will be required to observe a 12 hour Restricted Entry Interval, which is set by the WPS.

FQPA Considerations

EPA has determined that the established tolerances for thiabendazole, with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCA, that there is reasonable certainty of no harm for infants and children. The safety determination for infants and children takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of thiabendazole residues in this population subgroup.

In determining whether infants and children are particularly susceptible to toxic effects from thiabendazole residues, EPA considered the completeness of the database for developmental and reproductive effects, the nature of the effects observed, and other information. for thiabendazole, the FQPA safety factor of 10 was **reduced** to 1 because: (1) the toxicity database includes an acceptable two-generation reproduction study in rats and acceptable prenatal developmental toxicity studies in rats and rabbits. These studies show no increased sensitivity to fetuses as compared to maternal animals following acute *in utero* exposure in the developmental rat and rabbit studies and no increased sensitivity to pups as compared to adults in a multi-generation reproduction study in rats. (2) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies. Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary and residential exposure and to provide a screening level drinking water exposure assessment. (3) The Agency believes that its exposure assessments will not underestimate the potential risk for infants and children from thiabendazole. Therefore, the additional 10X factor as required by FQPA was reduced to 1X.

Environmental Assessment

Ecological Effects

Thiabendzole is highly toxic to freshwater estuarine fish and freshwater/estuarine invertebrates. Thiabendazole is practically non-toxic to birds and mammals. Typically, birds and mammals can be exposed to pesticides applied as foliar sprays or granulars by a variety of routes, including ingestion, dermal contact, and

inhalation. For thiabendazole, which is applied indoor as a seed treatment for wheat, exposure to wildlife is not relevant until treated seeds are planted back in the fields. Applications to and treatment of mushroom houses are also indoor uses, and therefore are of minimal danger to birds and mammals. Exposure of terrestrial wildlife from direct injection of thiabendazole and its salts into trees may occur but is also expected to be a minimal means of exposure. Results of avian reproduction studies on northern bobwhite quail and mallard duck yielded results that show thiabendazole having no adverse effects on avian reproduction.

The ecological risks due to the use of thiabendazole are considered below the Agency's level of concern. Currently registered use patterns for thiabendazole result in low exposures and with the relatively low toxicity of thiabendazole, no environmental mitigation is necessary.

Risk Mitigation

To lessen the risks of dietary exposure posed by thiabendazole, EPA is requiring the following risk mitigation measures:

-**To mitigate acute dietary risk to children 1-6 years of age, Syngenta amended the label to remove the spray application to mushrooms.**

To lessen the risks of occupational exposure posed by thiabendazole, EPA is requiring the following risk mitigation measures:

-**To mitigate risks to agricultural workers (applicators) during spray application to mushroom houses:**

- label language will be changed to specify chemical resistant gloves be worn while applying thiabendazole to mushroom houses during spawning only.

-**To mitigate risks to agricultural workers (mixers/loaders/applicators) during manual seed treatment**:

-since this use was found to be virtually non-existent. The Agency will be changing the label language to prohibit this use.

-**To mitigate risks to agricultural workers during post-harvest sorting/packing/culling of fruit:**

-the Agency recalculated exposure numbers for workers sorting/culling/packing after harvest based on transfer coefficiency information that was not available at the time of the original assessment. The newer data provided an MOE of 1600, well below the Agency's level of concern and therefore no additional risk mitigation is necessary.

Additional Data Required

EPA is requiring the following additional generic studies for thiabendazole to confirm its regulatory assessments and conclusions:

(1) *In vitro* mammalian gene mutation (870.5300)

(2) *In vitro* chromosome aberration assay (870.5375)

(3) UV/visible absorption (830.7050)

(4) Multi-residue method testing (860.1360)

(5) Additional storage stability data for sweet potatoes (860.1380)

(6) Additional residue data for benzimidazole (free and conjugated) in/on cantaloupe and strawberry for foliar application (860.1500)

(7) Residue data on wheat, dry beans, and soybeans (860.1500)

(8) Processing study for the processed fractions of soybeans (860.1520)

The Agency also is requiring product-specific data including product chemistry and acute toxicity studies, revised Confidential Statements of Formula (CSFs), and revised labeling for reregistration.

Product Labeling Changes Required

All thiabendazole end-use products must comply with EPA's current pesticide product labeling requirements. For a comprehensive list of labeling requirements, please see the thiabendazole RED document.

Regulatory Conclusion

The use of currently registered products containing thiabendazole in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

Thiabendazole products will be reregistered once the required product-specific data, revised Confidential Statements of Formula, and revised labeling are received and accepted by EPA.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for thiabendazole during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet are available on the Internet. See http://www.epa.gov/REDs.

Printed copies of the RED and fact sheet can be obtained from EPA's National Service Center for Environmental Publications (EPA/NSCEP), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198; fax 513-489-8695.

Following the comment period, the thiabendazole RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 1-800-553-6847, or 703-605-6000.

For more information about EPA's pesticide reregistration program, the thiabendazole RED, or reregistration of individual products containing thiabendazole please contact the Special Review and Reregistration Division (7508C), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticide Information Center (NPIC). Call toll-free 1-800-858-7378, from 6:30 am to 4:30 pm Pacific Time, or 9:30 am to 7:30 pm Eastern Standard Time, seven days a week. Their internet address is http://npic.orst.edu.