UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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**NEW USE REVIEW**

SUBJECT: Review of New Use for Thiabendazole (Mertect 340-F) as a seed treatment on dry peas.

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## I. Executive Summary

### A. Nature of Chemical Stressor

Thiabendazole (CAS No. 148-79-8) is a benzimidazole fungicide currently registered to control diseases in a wide variety of terrestrial food and non-food crops, primarily in post harvest applications. The proposed use is as a seed treatment on dry peas, lentils, and chickpeas. Thiabendazole is applied to seeds indoors; environmental exposure is to treated seeds after planting. It has been previously registered at higher application rates than currently proposed, which can be found in the most recent Reregistration Eligibility Decision (DP Barcode D245780).

Thiabendazole is persistent in aerobic and anaerobic soil environments and has low mobility. One major degradate was found in laboratory soil metabolism laboratory studies but was not detected when thiabendazole was applied in the field. In aquatic environments, thiabendazole is

stable to hydrolysis but degrades by photolysis. Thiabendazole is highly toxic to aquatic fish and invertebrates but is practically nontoxic to birds and mammals. In chronic studies on birds and mammals, no effects were seen at the highest doses tested. No terrestrial or aquatic plant data were submitted.

### B. Potential Risk Conclusions

The only route of aquatic exposure for thiabendazole is transfer of the compound from seeds to soil, followed by transport to water through runoff or movement of entrained sediments. Aquatic exposure is therefore expected to be low. Despite the high toxicity to fish and aquatic invertebrates, no acute or chronic levels of concern (LOCs) were exceeded for aquatic animals at any application rate. Potential transport to drinking water is also expected to be minimal with estimated drinking water concentrations of 2.0 µg/L (acute) and 0.5 µg/L (chronic).

Potential risk to terrestrial animals was estimated by considering exposure from ingestion of treated seeds. Thiabendazole is practically non-toxic to birds and mammals and no acute LOCs were exceeded at any application rate. Chronic risk to mammals is also estimated to be below LOCs.

At the maximum application rate, used on chickpeas, the chronic risk quotient (RQ) for birds exceeds the level of concern for birds. This RQ, however, is based on an avian reproduction study in which no adverse effects were seen at the highest dose tested. Chronic risk to birds is uncertain. The chronic avian LOC is not exceeded at the lower application rates recommended for lentils and dry peas.

### C. Uncertainties and Data Gaps

Specific uncertainties and data gaps for thiabendazole are summarized below. Additional uncertainties include those inherent to the screening level risk assessment process.

- Aquatic modeling for seed treatment uses does not account for the potential for sorption to, or reaction on, the seed coat. Because of model limitations and because EFED has no data to the contrary, EFED assumes that thiabendazole does not sorb to the seed coat, but to soil. In effect, this use is simulated as if the pesticide were applied directly to soil. This assumption provides conservative runoff and leaching scenarios.

- In laboratory studies of reproductive effects to birds and mammals, no adverse effects were observed even at the highest concentrations tested. Estimates of chronic risk to birds and mammals were calculated using the NOAEC from these studies and are likely to overestimate actual risk. For birds, this calculated RQ exceeds the level of concern but there is uncertainty in this value and actual risk is expected to be lower.

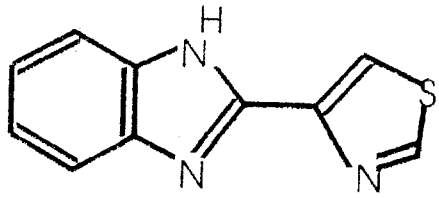
- Risk to terrestrial and aquatic plants could not be assessed because toxicity data were not available.

## II. Problem Formulation

### A. Stressor Source and Distribution

#### 1. Summary of Chemical and Physical Properties of Thiabendazole

Structure:




| | |
|---|---|
| Common Name: | Thiabendazole |
| Chemical Name: | 2-(4'-Thiazolyl)benzimidazole |
| Chemical Abstracts #: | 148-79-8 |
| PC Code | 060101 |
| Chemical Class: | Benzimidazole |
| Molecular formula: | $C_{10}H_7N_3S$ |
| Molecular weight: | 201.1 |
| Physical state: | Colorless powder |
| Water Solubility (25°C): | 10 mg/L @ pH 2; <50 mg/L @ pH 5-12 |
| Vapor Pressure (20°C): | $4 \times 10^{-9}$ mm Hg |

#### 2. Mode of Action

The mode of action of thiabendazole inhibits the mitosis of plant pathogenic fungi species by preventing the polymerization of beta-tubulins. Because dimers of beta-tubulin and alpha-tubulin polymerize to form microtubule structures inside the cells, thiabendazole acts as an inhibitor of microtubuline polymerization and cell division is terminated.

#### 3. Overview of Use

Thiabendazole is a systemic fungicide currently registered for (1) direct injection into trees, (2) post-harvest application to a wide variety of terrestrial food crops and non-food crops and (3) pre-harvest application as a seed treatment or to mushrooms. The end use product examined in this risk assessment is Mertect 340-F (42.3% thiabendazole). The current label for this product includes application as a post-harvest spray or dip for potatoes, pome fruit, carrots, and ornamental bulbs (Reg. No. 100-889). The only pre-harvest uses on the current label are to mushrooms or as a dip for sweet potato seed roots.

The proposed new use is as a seed treatment on dry peas, chickpeas, and lentils to suppress seed borne Ascochyta blight. Thiabendazole is applied to the seed as a water based slurry prior to

planting. The label specifies the volume of product to be applied per 100 pounds of seed. These rates are listed below in Table 1 and converted to lbs a.i./A based on the maximum seeding rate expected. As seed treatments, these uses will be a single application per season. The maximum application rate considered is 0.09 lb a.i./A, which is lower than previously considered rates. The highest application rate considered in previous assessments was 0.2 lb a.i./A as a seed treatment on wheat. Although not on the current label, the wheat use is included in Table 1 for comparison.

**Table 1. Seed Treatment Application Rates of Thiabendazole**

| Use | Label Rate [1] (lb a.i./100 lb seed) | Seeding Rate [2] (lb seed/A) | Application Rate (lb a.i./A) |
|---|---|---|---|
| Chickpea | 0.065 | 140 | 0.09 |
| Lentil | 0.034 | 80 | 0.03 |
| Peas (dry) | 0.033 | 200 | 0.07 |
| Wheat [3] | 0.225 | 90 | 0.20 |

[1] Based on 4.1 lb a.i./gallon product (Reg. No. 100-889)
[2] USDA Crop Profiles (http://cipm.ncsu.edu/CropProfiles/cropprofiles.cfm)
[3] Application rate assessed in most recent RED (DP Barcode D245780).

## B. Ecological Receptors and Assessment Endpoints

Ecological receptors are animals within the ecosystem potentially at risk that may be exposed to the stressor (thiabendazole). The surrogate species used to assess potential risk to all ecological receptors from thiabendazole use are summarized in Table 2 and include two species of birds (mallard duck and bobwhite quail), two mammalian species (laboratory rat and mouse), terrestrial plants (10 species), fish (two freshwater and one saltwater species), aquatic invertebrates (one freshwater and two saltwater species), and two aquatic plant species (duckweed and algae).

Assessment endpoints include survival, growth, and reproductive success of the surrogate ecological receptors. Although the assessment endpoints measure effects at the individual level, they provide insight into potential risks at higher levels (i.e., populations). Toxicity values used to assess survival from short-term (acute) exposures of thiabendazole to wildlife and aquatic plants are levels associated with statistically estimated 50% survival rates. For terrestrial plants, the levels used are those associated with statistically estimated 25% survival rates. Toxicity values used to assess potential reproductive or growth effects for animals are the highest levels tested that did not induce any reproductive or growth effects (NOAEC; No Observable Adverse Effect Concentrations).

Table 2 below summarizes the ecosystems at risk, the assessment endpoints used to assess risk to the ecosystems, and the surrogate species and toxicity values used to assess risk to the surrogate species.

**Table 2. Summary of Ecosystems, Taxa, and Assessment Endpoints Used to Evaluate Potential Ecological Effects from the Currently Labeled Thiabendazole Uses**

| Ecosystem at Risk | Taxonomic group | Assessment Endpoints[a] | Surrogate Species Used in this Assessment | Toxicity Value Used to Evaluate Assessment Endpoints |
|---|---|---|---|---|
| Terrestrial ecosystems: Treated field and run-off onto an adjacent field and runoff onto a low-lying semi-aquatic or wetland area | Bird[b] | Survival, reproduction, and growth | Mallard duck<br>Bobwhite quail | Survival: $LD_{50}$: >2250 - >4640 mg/kg bw<br>Dietary $LC_{50}$: >5620 - >14500 ppm<br>Growth and Reproduction:<br>NOAEC: 400 ppm; LOAEC: >400 ppm |
| | Mammals | Survival, reproduction, and growth | Laboratory rat<br>Laboratory mouse<br>Rabbit | Survival: $LD_{50}$: 3330 - 5070 mg/kg<br>Growth and Reproduction:<br>NOAEC: 90 mg/kg/d; LOAEC: >90 mg/kg/d |
| | Terrestrial plants[c] | Survival and growth | No data | No data |
| | Insects | Survival | Honey bee | No data |
| Aquatic ecosystems: for tier 1 assessments the assessed environment is a standard ecological pond with a volume of 20,000,000 L. | Freshwater fish[d] | Survival, growth, and reproduction of individuals and communities | Rainbow Trout<br>Bluegill Sunfish | Survival: 96-hour $LC_{50}$: 0.56 mg/L<br>Growth and Reproduction:<br>NOAEC: 0.012 mg/L; LOAEC: 0.029 mg/L |
| | Freshwater invertebrates | | Daphnids | Survival: 48-hour $EC_{50}$: 0.31 mg/L<br>Growth and Reproduction:<br>NOAEC: 0.042 mg/L; LOAEC: 0.087 mg/L |
| | Estuaries/ marine fish and amphibians | | Sheepshead Minnow | Survival: 96-hour $LC_{50}$: >10 mg/L<br>Growth and Reproduction: No data |
| | Estuaries/ marine invertebrates | | Mysid Shrimp | Survival: 48-hour $EC_{50}$: 0.34 mg/L<br>Growth and Reproduction: No data |
| | Aquatic plants and algae | Survival and growth of aquatic plants | Duckweed (vascular) | No data |
| | | | Algae (nonvascular) | No data |

[a] The assessment endpoints measure effects at the individual level; however, they provide insight into potential risks at higher levels (i.e., populations).
[b] Birds are used as surrogates for amphibians (terrestrial phase) and reptiles.
[c] Four species of two families of monocots, of which one is corn; six species of at least four dicot families, of which one is soybeans.
[d] Freshwater fish may be surrogates for amphibians (aquatic phase).
$LD_{50}$ = Lethal dose to 50% of the test population.
NOAEC = No-observed-adverse-effect concentration.
LOAEC = Lowest-observed-adverse-effect concentration.
$LC_{50}$ = Lethal concentration to 50% of the test population.
$EC_{50}/EC_{25}$ = Effect concentration to 50/25% of the test population.

## C. Conceptual Model

In order for a chemical to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a contaminant moves in the environment from a source to an ecological receptor. For an ecological exposure pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure. The assessment of ecological exposure pathways includes an examination of the source and potential migration pathways for constituents, and the determination of potential exposure routes (e.g., ingestion, inhalation, dermal absorption).

Ecological receptors that may potentially be exposed to the parent thiabendazole as a seed treatment include terrestrial and semi-aquatic wildlife (i.e., mammals, birds, and reptiles), semi-aquatic plants, and soil invertebrates. In addition to terrestrial ecological receptors, aquatic receptors (e.g., freshwater and estuarine/marine fish and invertebrates, amphibians) may also be exposed to potential migration of pesticides from the site of application to various watersheds and other aquatic environments via runoff and soil erosion.

### 1. Risk Hypotheses

Risk hypotheses are specific assumptions about potential adverse effects (i.e., changes in assessment endpoints) and may be based on theory and logic, empirical data, mathematical models, or probability models. For this assessment, the risk is stressor-linked, where the stressor is the release of thiabendazole to the environment. The following risk hypothesis is presumed for this screening level assessment:

*The use of thiabendazole as a seed treatment on chickpeas, lentils, and dry peas will likely involve situations where terrestrial and aquatic animals and plants will be exposed to the chemical. Based on the environmental fate properties, the mode of action, and the food-web of the target aquatic and terrestrial ecosystems, thiabendazole has the potential to cause reduced survival and reproductive and growth impairment for both aquatic and terrestrial animal and plant species.*

## D. Analysis Plan

The analysis plan describes the three measures used to evaluate the risk hypotheses developed in the conceptual model for thiabendazole usage. First, the measures of exposure are derived as estimated environmental concentrations (EECs) based on model predictions and environmental fate data. Second, the measures of effect characterize the assessment endpoints and are based on toxicity data that describe the effects of thiabendazole on individuals, species, populations, and communities in aquatic and terrestrial ecosystems. Integration of effects and potential exposure provide an estimate of adverse effects (risk) to non-target animals and plants.

All environmental fate, ecotoxicity, and physicochemical property data were taken from previous assessments conducted by EFED. These data were not re-evaluated.

### 1. Measures to Evaluate Risk Hypotheses and Conceptual Model

#### a. Measures of Exposure

For this screening level risk assessment, EECs for aquatic and terrestrial systems are calculated using the maximum application rates. EECs are calculated using Tier I exposure models: T-REX (version 1.2.3) for terrestrial environments, GENEEC2 (version 2.0) for aquatic environments, and FIRST (version 1.0) for drinking water exposure. Tier I aquatic models simulate a generic crop grown in a generic location which have been chosen to represent all crop uses. Estimated EECs are not expected to be exceeded with a return frequency of one in ten years. For the terrestrial assessment, exposure to mammals and birds is estimated using the conceptual approach given in the Tier I model TREX (v 1.2.3), which focuses on uptake through diet as the primary exposure route. In screening-level assessments, the animals are assumed to consume 100% of their diet as seeds, their only food source.

#### b. Measures of Effect

Measures of ecological effects are obtained from a suite of registrant-submitted guideline studies conducted with a limited number of surrogate species. The test species are not intended to be representative of the most sensitive species but rather were selected based on their ability to thrive under laboratory conditions. Consistent with EPA test guidelines, a suite of ecological effects data on technical grade thiabendazole that complies with good laboratory testing requirements has been submitted and is summarized in Section IV.

#### c. Measures of Risk

Integration of effects and potential exposure provide an estimate of adverse effects (risk) to non-target endangered/threatened and non-endangered animals and plants that could potentially affect the registration decision of thiabendazole under the Federal Insecticide, Fungicide, and Rodenticide Act, the Food Quality Protection Act, and the Endangered Species Act. A risk quotient approach (ratio of exposure concentration to effects concentration) is used to determine whether risk of adverse effects to non-target species are above the Agency's levels of concern (LOCs).

## III. Exposure Assessment

### *A. Environmental Fate and Transport Characterization*

Environmental fate studies show that thiabendazole is persistent and immobile with aquatic photolysis as the only significant degradation pathway. Thiabendazole does not metabolize significantly in soil in aerobic or anaerobic conditions; the aerobic soil metabolism half-life was 688 days (MRID 41791201). In aquatic environments, thiabendazole is stable to hydrolysis (MRID 41265301) but degrades by aquatic photolysis with a half life of 2.4 days (MRID 43328305). Thiabendazole binds tightly to soil with a $K_{oc}$ in sand of 1104 mL/g and non-sand $K_{oc}$s ranging from 1813 to 22470 mL/g, so leaching is not expected (MRID 41170102). These

studies are discussed in more detail in the most recent Reregistration Eligibility Decision (DP Barcode D245780).

Four degradates were identified, two major and two minor. Anaerobic soil metabolism led to the major degradate benzimidazole, which was also found as a minor degradate in the aerobic soil metabolism and aquatic photolysis studies. Aquatic photolysis resulted in benzimidazole-2-carboxamide as a major degradate. Minor degradates included 5-hydroxy thiabendazole (from aerobic soil metabolism) and benzimidazole-2-carboxylic acid (from aquatic photolysis).

Terrestrial field dissipation studies confirmed lab results, demonstrating that thiabendazole is persistent in field conditions with no leaching (MRIDs 43187201 and 43187202). In these studies, thiabendazole was applied directly to crops or bare ground, rather than as a seed treatment, and had half-lives ranging from 833 to 1444 days. Thiabendazole was detected at trace levels from 6 to 12 inches and was not detected below 12 inches. The main degradate, benzimidazole, was not found in any of the sites; other degradates were not measured.

B. *Measures of Aquatic Exposure*

The only route of aquatic exposure for thiabendazole is transfer of the compound from seeds to soil, followed by transport to water. Extraction from seed coats will be limited by the compound's high sorption, and any extracted compound will bind strongly to soil. Transport to surface water would then occur primarily through movement of entrained sediments. In surface water, thiabendazole is unlikely to persist, especially in shallow and clear water, because of the rapid aquatic photolysis.

The Tier I simulation GENEEC2 (Version 2.0; August 1, 2001) was used to determine EECs for aquatic exposure resulting from planting of thiabendazole treated seeds. The peak EEC, presented in Table 3, was **0.84 µg/L**. GENEEC2 uses basic environmental fate values and pesticide label information to estimate the EECs in a one-hectare, two-meter deep pond following application to a 10 ha field. The runoff event occurs two days after planting. GENEEC2 takes into account adsorption to the soil or sediment, degradation in soil before runoff, and degradation within the water body. A summary of the model input parameter values used is presented in Table 3. Only the maximum application rate of 0.09 lb/A was modeled, using the conservative assumption that thiabendazole is fully dissociated from the coats of the treated seeds. All other inputs are the same as those used in the most recent RED (DP Barcode D245780). The GENEEC2 output file is provided in Appendix A.

**Table 3. Tier I surface water EECs of thiabendazole used as a seed treatment (µg/L).**

| Use | Peak | Max 21-day avg. | Max 60-day avg. |
|---|---|---|---|
| Chickpea | 0.84 | 0.77 | 0.64 |

C. *Drinking Water Exposure*

The drinking water assessment was conducted for the parent compound only. Considering the limited presence of degradates in laboratory and field studies, degradates are not expected to be present in the field at any concentration which could cause harm to drinking water resources. Tier 1 estimated drinking water concentrations (EDWC) for thiabendazole in surface water were generated using the screening model FIRST (Version 1.0; August 1, 2001). FIRST differs from GENEEC2 in that it simulates the Index Reservoir, a standard water body used by the Office of Pesticide Programs to assess drinking water exposure, rather than the GENEEC2 farm pond. The input parameters used in FIRST were the same as those used for modeling ecological exposure, summarized in Table 4. The output file is provided in Appendix B. Based on modeling results, EFED estimates an acute surface water EDWC of **2.0** $\mu$**g/L** and a chronic EDWC of **0.5** $\mu$**g/L**.

**Table 4. GENEEC and FIRST input parameters for thiabendazole on dry peas.**

| Parameter | Input | Source |
|---|---|---|
| Application Rate (*lb a.i./A*) | 0.09 | Reg. No. 100-889 |
| Number of Applications | 1 | Reg. No. 100-889 |
| Wetted in? | No | Seed treatment |
| Application Method | Granular; no incorporation | Seed treatment |
| Solubility in Water (*mg/L*) | 10 | DP Barcode 245780 |
| Partitioning Coefficient ($K_{oc}$; *mL/g*) | 2903 | MRID 41170102 (median of 4 values) |
| Hydrolysis Half-life at pH 7 *(days)* | 0 | MRID 41265301 |
| Aerobic Soil Metabolism Half-life *(days)* | 688 | MRID 41791201 (DER 2) |
| Aerobic Aquatic Metabolism Half-life *(days)* | 0 | No data |
| Aquatic Photolysis Half-life *(days)* | 2.4 | MRID 43328305 (assuming 12 hr sunlight/day) |
| Percent Cropped Area (used in FIRST only) | 0.87 | Default value for "other" crops |

*Terrestrial Exposure*

*1. Animals*

Thiabendazole is applied indoors as a seed treatment and exposure to wildlife is not relevant until treated seeds are planted outdoors. Birds and mammals in the field may be exposed to seed treated with pesticides by ingesting material directly with the diet. They also may be exposed by other routes, such as incidental ingestion of contaminated soil, dermal contact with treated seed surfaces and soil during activities in the treated areas, preening activities, and ingestion of drinking water contaminated with pesticide. Only the ingestion of treated seed is considered in this assessment. The terrestrial exposure model T-REX (Version 1.2.3; August 8, 2005) is used to estimate exposures and risk quotients for avian and mammalian species and the results are summarized in Table 5. The model calculates estimated exposure in two ways. One method looks at the dietary dose by estimating daily food intake and assuming that an animal has been foraging only on treated seed. The second method estimates the available concentration of pesticide on an areal (per square foot) basis. Details regarding these calculations are provided in Appendix C along with the T-REX input and output tables. For both calculation methods, it is assumed that all seeds are available for ingestion. Deeper planting could lead to lower exposure.

**Table 5. Terrestrial exposure from thiabendazole used as a seed treatment.**

| Use | Application Rate (lb a.i./A) | Max. Seed App. Rate (mg a.i./kg seed) | Avian Nagy Dose (mg a.i./kg-bw/day) | Mammalian Nagy Dose (mg a.i./kg-bw/day) | Available A.I. (mg a.i./ft$^2$) |
|---|---|---|---|---|---|
| Chickpea | 0.09 | 650 | 164.57 | 137.77 | 0.95 |
| Lentil | 0.03 | 330 | 83.50 | 69.90 | 0.69 |
| Peas (dry) | 0.07 | 340 | 85.93 | 71.94 | 0.28 |

*2. Plants*

No terrestrial plant toxicity data were submitted. Therefore, exposure values for terrestrial plants were not determined.

## IV. Ecological Effects Assessment

### A. *Aquatic Animals*

Thiabendazole was found to be highly toxic to freshwater fish and invertebrates and to estuarine/marine invertebrates. Toxicity to estuarine/marine fish could not be determined because the limited solubility of thiabendazole in seawater prevented testing at concentrations greater than 10 mg/L. The most sensitive endpoints were used in calculating risk quotients and are summarized below in Table 6. These are the same endpoints used in the most recent RED (DP Barcode D245780). All of the studies cited were performed using technical grade active ingredient of 98 to 99.6%. Except for the estuarine and marine fish study, classified as supplemental, all were classified as acceptable studies. The results of all aquatic animal toxicity studies are characterized in Appendix D.

**Table 6. Most sensitive aquatic animal toxicity data for thiabendazole.**

| Most sensitive species | Acute Toxicity | | Chronic Toxicity | |
|---|---|---|---|---|
| | $LC_{50}$ or $EC_{50}$ | Category of Toxicity (MRID No.) | NOAEC, LOAEC | Most Sensitive Endpoint (MRID No.) |
| *Freshwater Fish* | | | | |
| Rainbow trout *Oncorhynchus mykiss* | 0.56 mg/L (96-h $LC_{50}$) | highly toxic (41025005) | no data | no data |
| Fathead minnow *Pimephales promelas* | no data | no data | 0.11 mg/L, 0.23 mg/L | wet weight (42508901) |
| *Freshwater Invertebrates* | | | | |
| Water flea *Daphnia magna* | 0.31 mg/L (48-h $EC_{50}$) | highly toxic (ESTBZ-2) | 0.042 mg/L, 0.087 mg/L | survival; offspring production (246711) |
| *Estuarine/Marine Fish* | | | | |
| Sheepshead Minnow *Cyprinodon variegatus* | > 10 mg/L (96-h $LC_{50}$) | not determined (41192003) | no data | no data |
| *Estuarine/Marine Invertebrates* | | | | |
| Mysid Shrimp *Americamysis bahia* | 0.34 mg/L (96-h $EC_{50}$) | highly toxic (41192002) | no data | no data |

*B. Terrestrial Animals*

Thiabendazole was categorized as practically non-toxic to birds in acute oral studies with mallard ducks and bobwhite quail. Additionally, no avian reproductive effects were seen. In studies with rats, mice, and rabbits, thiabendazole was determined to be practically non-toxic to small mammals on an acute oral basis. A 2-generation reproduction study in rats found no adverse reproductive effects in small mammals. The most sensitive endpoints obtained by the Agency's Health Effects Division are listed below (Table 7). These studies, characterized in Appendix D, were conducted with technical grade active ingredient of greater than 98% purity.

**Table 7. Most sensitive avian and mammalian toxicity data for thiabendazole.**

| Most sensitive species | Acute Toxicity | | Chronic Toxicity | |
|---|---|---|---|---|
| | $LD_{50}$ in mg/kg-bw | Category of Toxicity (MRID No.) | NOAEC/ LOAEC | Most Sensitive Endpoint (MRID No.) |
| *Avian* | | | | |
| Northern bobwhite *Colinus virginianus* | >2250 | practically nontoxic (41025002) | NOAEC = 400 ppm LOAEC >400 ppm | no effects (235974) |
| *Mammal* | | | | |
| Laboratory rat *Rattus norvegicus* | 3330 | practically nontoxic (100853) | NOAEC = 90 LOAEC >90 mg/kg/day | no effects (43190301) |

*C. Terrestrial and Aquatic Plants*

Because the only use being considered in this action is a seed treatment, terrestrial and aquatic plant data were not required. Terrestrial plant studies are currently required for all outdoor uses and if Thiabendazole is petitioned in the future for outdoor uses, this may be considered a data gap.

## V. Risk Characterization

*A. Risk Estimation*

A risk quotient (RQ)-based approach is used in this assessment, comparing the ratio of exposure concentrations to effects endpoints with predetermined levels of concern (LOCs). A presumption of risk occurs when an RQ equals or exceeds an LOC. Although risk is often defined as the likelihood and magnitude of adverse ecological effects, the risk quotient-based approach does not provide a quantitative estimate of likelihood and/or magnitude of an adverse effect.

*1. Aquatic Animals*

All aquatic acute RQs are calculated based on the peak EEC from the maximum labeled rate of 0.09 lb ai/A. For freshwater and estuarine/marine fish and invertebrates, acute RQs are all less than 0.01 (Table 8). Compared to the acute endangered species LOC of 0.05, thiabendazole will result in minimal effects to fish and invertebrates. Chronic RQs for freshwater fish and invertebrates are ≤ 0.02, below the chronic LOC of 1 based on 60-day and 21-day average EECs, respectively. Toxicity data were not available to calculate chronic RQs for estuarine/marine fish and invertebrates; in estimating risk, an assumption was made that marine/estuarine fish and invertebrates would be of similar sensitivity as the freshwater fish and invertebrates. On that basis, it is unlikely that thiabendzaole will pose a risk to estuarine/marine fish or invertebrates.

**Table 8. Acute and chronic risk quotients for fish and aquatic invertebrates for thiabendazole as a seed treatment.**

| | Acute | | | Chronic | | |
|---|---|---|---|---|---|---|
| **Group** | **$EC_{50}$ or $LC_{50}$ (µg/L)** | **Peak EEC (µg/L)** | **RQ[1]** | **NOAEC (µg/L)** | **21-D and 60-D EECs (µg/L)** | **RQ[2]** |
| Freshwater Fish | 560 | 0.84 | <0.01 | 110 | 0.64[A] | 0.01 |
| Freshwater Invertebrates | 310 | 0.84 | <0.01 | 42 | 0.77[B] | 0.02 |
| Estuarine/Marine Fish | >10,000 | 0.84 | <0.01 | No data | 0.64 | No data |
| Estuarine/Marine Invertebrates | 340 | 0.84 | <0.01 | No data | 0.77 | No data |

[1] Acute RQ = EEC/$LC_{50}$ (fish) or $EC_{50}$ (invertebrates)
[2] Chronic RQ = EEC/ NOAEC
[A] 60-day EEC
[B] 21-day EEC

*2. Terrestrial Animals*

Risk quotients for avian and mammalian species were calculated using the terrestrial exposure model T-REX (Version 1.2.3; August 8, 2005). Inputs and outputs from the model are included in Appendix C. The acute RQs for birds and mammals, both dose-based and areal, are all < 0.1. The chronic RQs for birds and mammals are 1.63 and < 1, respectively, assuming 100% of the diet is treated seeds. The avian chronic RQ is based on the maximum labeled rate, used on chickpeas. The lower rates, recommended for use on dry peas and lentils, lead to chronic RQs of < 1.

*3. Terrestrial and Aquatic Plants*

Terrestrial and aquatic plant data were not required for a seed treatment use, an estimate of risk quotients to plants is not available.

## B. *Risk Description*

### 1. *Risks to Aquatic Organisms*

Based on a screening-level assessment of fate and toxicity data for thiabendazole as a seed treatment, acute and chronic risk to fish and aquatic invertebrates is expected to be minimal. Although thiabendazole is classified as highly toxic to aquatic organisms, low exposure is expected from the seed treatment use. No acute or chronic LOCs are exceeded for freshwater fish and invertebrates and no acute LOCs are exceeded for estuarine/marine fish or invertebrates. Chronic toxicity tests are not required for estuarine/marine fish and invertebrates. Based on the low potential for exposure, however, it is unlikely that thiabendazole poses a risk to these species.

### 2. *Risks to Terrestrial Animals*

Risk to birds and mammals is unlikely due to thiabendazole's low toxicity and the limited exposure expected for a seed treatment. For mammals, no acute or chronic LOCs are exceeded. For birds, there are no acute exceedances.

For the maximum rate of 0.09 lb a.i./A used on chickpeas, the calculated RQ of 1.63 triggers the Agency's concerns for reproductive risk to birds (LOC >1). However, there is uncertainty regarding the LOC exceedance for reproductive risk to birds: 1) no survival, growth, or reproduction effects were seen at the highest test concentration tested in the laboratory-submitted avian reproduction study (NOAEC = 400); and 2) although the TREX model assumes a default half-life of 35 days for residues on food items, it is possible that thiabendazole decreases faster than that when the seedling starts growing. In addition, since it is assumed there are a variety of untreated seeds on the field prior to planting, it is unlikely that a granivorous bird will consume 100% of its diet directly from treated seeds. Because there were no adverse effects to birds observed in the reproduction studies (including sublethal effects), and because it is unlikely that treated seeds will compose 100% of the diet, chronic risk to birds from foraging treated seeds is likely to be lower than that estimated and exposure may not exceed levels of concern. Use at the lower rates recommended for dry peas and lentils does not lead to any LOC exceedances for terrestrial animals.

### 3. *Risks to Terrestrial and Aquatic Plants*

Risk to terrestrial and aquatic plants was not determined because plant toxicity data were not required for this use.

### 4. *Federally Threatened and Endangered (Listed) Species Concerns*

Risk from the proposed seed treatment use of thiabendazole does not exceed any endangered species levels of concern. No presumption of concern is made for endangered species.

## Appendix B: FIRST Model Outputs

RUN No. 1 FOR thiabendazole ON chickpeas * INPUT VALUES *

| RATE (#/AC) ONE(MULT) | No.APPS & INTERVAL | SOIL Koc | SOLUBIL (PPM ) | APPL TYPE (%DRIFT) | %CROPPED AREA | INCORP (IN) |
|---|---|---|---|---|---|---|
| .090( .090) | 1 1 | 2903.0 | 10.0 | GRANUL( .0) | 87.0 | .0 |

FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)

| METABOLIC (FIELD) | DAYS UNTIL RAIN/RUNOFF | HYDROLYSIS (RESERVOIR) | PHOTOLYSIS (RES.-EFF) | METABOLIC (RESER.) | COMBINED (RESER.) |
|---|---|---|---|---|---|
| 688.00 | 2 | N/A | 2.40- 297.60 | .00 | 297.60 |

UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.0 AUG 1, 2001

| PEAK DAY (ACUTE) CONCENTRATION | ANNUAL AVERAGE (CHRONIC) CONCENTRATION |
|---|---|
| 2.023 | .521 |

## Appendix A: GENEEC Model Outputs

RUN No. 1 FOR thiabendazole ON chickpeas * INPUT VALUES *

| RATE (#/AC) ONE(MULT) | No.APPS & INTERVAL | SOIL Koc | SOLUBIL (PPM) | APPL TYPE (%DRIFT) | NO-SPRAY (FT) | INCORP (IN) |
|---|---|---|---|---|---|---|
| .090( .090) | 1 1 | 2903.0 | 10.0 | GRANUL( .0) | .0 | .0 |

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

| METABOLIC (FIELD) | DAYS UNTIL RAIN/RUNOFF | HYDROLYSIS (POND) | PHOTOLYSIS (POND-EFF) | METABOLIC (POND) | COMBINED (POND) |
|---|---|---|---|---|---|
| 688.00 | 2 | N/A | 2.40- 297.60 | .00 | 297.60 |

GENERIC EECs (IN NANOGRAMS/LITER (PPTr)) Version 2.0 Aug 1, 2001

| PEAK GEEC | MAX 4 DAY AVG GEEC | MAX 21 DAY AVG GEEC | MAX 60 DAY AVG GEEC | MAX 90 DAY AVG GEEC |
|---|---|---|---|---|
| 844.19 | 833.56 | 776.87 | 666.89 | 597.92 |

## Appendix C: T-REX Model Calculations and Outputs

Birds and mammals in the field may be exposed to seed treated with pesticides by ingesting material directly with the diet. They also may be exposed by other routes, such as incidental ingestion of contaminated soil, dermal contact with treated seed surfaces and soil during activities in the treated areas, preening activities, and ingestion of drinking water contaminated with pesticide. Only ingestion of treated seed is considered in this review.

Terrestrial EECs and acute risk quotient values were calculated using the T-REX Model version 1.2.3. This model assesses dietary consumption in two different ways for the purposes of assessing the risk from treated seeds. The first approach estimates a dietary dose assuming that an animal has been eating only treated seed. This approach uses the acute oral toxicity for the toxicity endpoint ($LD_{50}$). The second approach also uses the acute oral dose for toxicity ($LD_{50}$), but compares it to the available concentration of pesticide on the basis of pesticide applied per square foot.

For seed treatment calculations, only acute values ($LD_{50}$s) are adjusted for the size of the animal tested compared with the size of the animal being assessed (e.g. 20-gram bird and 35-gram mammals). These exposure values are presented as mass of pesticide consumed per kg body weight of the animal being assessed (mg/kg-bw). EECs and toxicity values are relative to the animal's body weight (mg residue/kg bw) because consumption of the same mass of pesticide residue results in a higher body burden in smaller animals compared with larger animals.

***Calculating EEC Equivalent Doses based on Estimated Dietary Concentrations on Selected Bird and Mammal Food Items***

Acute Avian Exposure, Method 1(DOSE-BASED)
The first approach of assessing exposure to treated seeds was used to assess risk to the smallest granivorous birds, which weigh about 20 g. Small birds tend to eat more per unit body weight; therefore, they are likely to be the most vulnerable. Exposure is estimated from the concentration of active ingredient on treated seed. The maximum application rate is converted to units of mg a.i./kg of seed. Using daily food intake, as estimated using the allometric equation in EPA (1993), a 20-g bird will consume approximately 5.1 g of food (wet weight) per day:

$$F = \frac{0.648 * BW^{0.651}}{(1 - W)}$$

where F is the food intake in grams of fresh weight per day, BW is the body mass (wet weight, kg) of the animal, and W is the mass fraction of water in the food. W is assumed to be 0.1 for seeds. This results in a dose in units of mg a.i./day. In order to convert the units of exposure to mg/kg bwt-day diet, the dose is divided by the weight of the bird (0.020 kg). The resulting EEC (Nagy Dose) is in units of mg ai/kg bwt-day.

Acute Mammal Exposure, Method 1 (DOSE-BASED)
An approach similar to the one detailed for birds (Method 1) was used for estimation of exposure to mammals. The first approach of assessing exposure to treated seeds was used to assess risk to

the smallest granivorous mammals, which weigh about 35 g. Exposure is estimated from the concentration of active ingredient on treated seed. The maximum application rate is converted to units of mg a.i./kg of seed. Using daily food intake, as estimated using the allometric equation in EPA (1993), a 35-g mammal will consume approximately 5.1g of food (wet weight) per day:

$$F = \frac{0.621 * BW^{0.564}}{(1 - W)}$$

where F is the food intake in grams of fresh weight per day, BW is the body mass (wet weight, kg) of the animal, and W is the mass fraction of water in the food. For this assessment W is assumed to be 0.1 for seeds. This results in a dose in units of mg a.i./day. In order to convert the units of exposure to mg/kg bwt-day diet, the dose is divided by the weight of the mammal (0.035 kg). The resulting EEC (Nagy Dose) is in units of mg ai/kg bwt-day.

The scaling factors result in a percent body weight consumed presented in the following table for each weight class of mammal. These values are used in the same manner described for birds to calculate dose-based EECs (mg/kg-bw). Note the difference in food intake of granivores compared with herbivores and insectivores. This is caused by the difference in the assumed mass fraction of water in their diets.

| Organism and body weight | Food intake ($g\ day^{-1}$)[a] | Percent body weight consumed ($day^{-1}$)[a] |
|---|---|---|
| 15 g | 14.3 / 3.2 | 95 / 21 |
| 35 g | 23 / 5.1 | 66 / 15 |
| 1000 g | 150 / 34 | 15 / 3 |

[a] The first number in this column is specific to herbivores/insectivores. The second number is for granivores. These groups have markedly different consumption requirements.

T-REX calculates food intake based on dry weight and wet weight of food items (wet weight is used for RQ calculations). The dose-based assessment uses the wet weight food consumption values by assuming that dietary items are 80% water by weight (10% for granivores). However, if dietary items of a species being assessed are known, then a refined dose-based EEC can be calculated using appropriate water fractions of the food items.

Acute Avian and Mammal Exposure, Method 2 (AREAL; mg a.i./$ft^2$)

For the second approach of assessing risk due to treated seed, it is assumed that 100% of the bird's diet is treated seed. In order to estimate the amount of thiabenzadole to kill 50% of exposed animals in each square foot of applied area, risk to animals are estimated using the exposure index (mg ai/$ft^2$) divided by the adjusted toxicity value (adjusted $LD_{50}$ x kg body weight) and then compared with the Agency's levels of concern. The amount of available pesticide is calculated by converting the maximum application rate (lbs/acre) to mg ai/$ft^2$ using the following equation:

$$\textbf{Available AI (mg ai/ft}^2\textbf{)} = \frac{\text{maximum application rate (lbs/acre) x } 10^6 \text{ mg/kg)}}{\text{43,560 square feet / 2.2 lb/kg}}$$

### *Calculating Adjusted Toxicity Values*

The dose-based EECs (mg/kg-bw) derived above are compared with $LD_{50}$ or NOAEL (mg/kg-bw) values from acceptable or supplemental toxicity studies that are adjusted for the size of the animal tested compared with the size of the animal being assessed (e.g., 20-gram bird). These exposure values are presented as mass of pesticide consumed per kg body weight of the animal being assessed (mg/kg-bw). EECs and toxicity values are relative to the animal's body weight (mg residue/kg bw) because consumption of the same mass of pesticide residue results in a higher body burden in smaller animals compared with larger animals. For birds, only acute values ($LD_{50}$s) are adjusted because dose-based risk quotients are not calculated for the chronic risk estimation. Adjusted mammalian $LD_{50}$s and reproduction NOAELs (mg/kg-bw) are used to calculate dose-based acute and chronic risk quotients for 15-, 35-, and 1000-gram mammals. The following equations are used for the adjustment (U.S. EPA 1993):

Adjusted avian $LD_{50}$:

$$Adj.LD_{50} = LD_{50}\left(\frac{AW}{TW}\right)^{(x-1)}$$

where:

*Adj. $LD_{50}$* = adjusted $LD_{50}$ (mg/kg-bw) calculated by the equation
*$LD_{50}$* = endpoint reported from bird study (mg/kg-bw)
*TW* = body weight of tested animal (178g bobwhite; 1580g mallard)
*AW* = body weight of assessed animal (*avian*: 20g)
x = Mineau scaling factor for birds; EFED default 1.15

Adjusted mammalian $LD_{50}$s:

$$Adj.\ LD_{50} = LD_{50}\,(TW/AW)^{(0.25)}$$

where:

*Adj. $LD_{50}$* = adjusted $LD_{50}$ (mg/kg-bw)
*$LD_{50}$* = endpoint reported from mammal study (mg/kg-bw)
*TW* = body weight of tested animal (350g rat)
*AW* = body weight of assessed animal (35g)

### *Calculating Risk Quotients*

Acute RQ approach #1 = (avian or mammal) Nagy Dose / (adjusted $LD_{50}$)

Acute RQ approach #2 = Available AI / (adjusted $LD_{50}$ x kg body weight)

Chronic Avian and Mammalian Exposure (SEED APPLICATION RATE)

Chronic exposure to treated seed is estimated from the concentration of active ingredient on treated seed. The maximum application rate (lbs ai/A) is converted to the maximum seed application rate (mg ai/kg seed) using a series of equations:

**1) Application rate (fl oz./cwt):** These data are obtained from the product label. In this case, the application rate obtained from the thiabenzadole label is 2.03 fl oz/cwt.

**2) Application Rate (Lbs AI/cwt) =** (Application rate (fl oz/cwt) × decimal % of AI in formulation) / 128 fl oz/gallon) × density of product (lbs/gallon) = (2.03 fl oz/cwt x 100% / 128 fl oz/gallon) x 4.1 lbs/gallon = 0.0650 lbs ai/cwt

**3) Maximum Seed Application Rate (mg ai/kg seed) =** (Application rate × $2.2 \times 10^6$) / (100 × 2.2) = (Application rate × 10,000) = 0.0650 lbs a.i./cwt x 10,000 = 650 mg a.i./kg seed.

Then

The chronic risk quotient is calculated using this equation:

$$\text{Chronic RQ} = \frac{\text{mg ai/kg seed}}{\text{NOAEC}} = \frac{\text{650 mg ai/kg seed}}{400} = 1.63$$

Chronic RQs are not adjusted to allow for an assessment of risk to different weight class of birds or mammals.

Inputs and results from TREX calculations for birds foraging seeds treated with thiabenzadole can be seen below.

Data inputs are in blue

| Endpoints | Reported | Tested Body Weight (g) | Adjusted LD50 | |
|---|---|---|---|---|
| | | | | 4.1 |
| | | | | 0.0650 |
| | | | | 0.0330 |
| | | | | 0.0340 |

| | | | | |
|---|---|---|---|---|
| 0.09 | 650.23 | 184.57 | 137.77 | 0.95 |
| 0.07 | 329.92 | 83.50 | 69.90 | 0.69 |
| 0.03 | 339.53 | 85.93 | 71.94 | 0.28 |

| Acute (# 1) | Acute (# 2) | Chronic | Acute (# 1) | Acute (# 2) | Chronic |
|---|---|---|---|---|---|
| 0.10 | 0.03 | 1.63 | 0.02 | 0.01 | 0.36 |
| 0.05 | 0.02 | 0.82 | 0.01 | 0.01 | 0.18 |
| 0.05 | 0.01 | 0.85 | 0.01 | 0.00 | 0.19 |

† Acute RQ #1 = (mg ai /kg-bw/day) / LD50
Acute RQ #2 = mg ai ft-2 /(LD50*bw)
Chronic RQ = mg kg-1 seed / NOEC

## APPENDIX D. ECOLOGICAL EFFECTS CHARACTERIZATION

Toxicity test values (*i.e.*, measures of effects) for terrestrial biota used in the screening risk assessment were derived from the results of registrant-required animal toxicity studies. Toxicity results that were consistent with risk assessment practices and toxicity testing guidelines (FIFRA 40 CFR-Part 158 and Part 160) were used. After a critical review, a data evaluation record is created and the study is identified as "acceptable" (meets guideline requirements), "supplemental" (scientifically sound but does not meet guideline requirements) or "invalid" (scientifically unsound). In characterizing a chemical's toxic potential, acute oral toxicity results (14-day [except as noted] $LD_{50}$) for birds and mammals are classified, based on the magnitude of the chemical required to illicit a response, as practically nontoxic (>2000 mg/kg), slightly toxic (501 - 2000) mg/kg), moderately toxic (51 - 500 mg/kg), highly toxic (10 - 50 mg/kg), and very highly toxic (<10 mg/kg) and subacute dietary toxicity results (8-day $LC_{50}$) for birds are classified as practically nontoxic (>5000 ppm), slightly toxic (1001 - 5000 ppm), moderately toxic (501 - 1000 ppm), highly toxic (50 - 500 ppm), and very highly toxic (<50 ppm). This classification scheme for birds and mammals excluding plants is used in the sections below when discussing the results of toxicity studies using thiabendazole.

### 1. TOXICITY TO TERRESTRIAL ANIMALS

#### i. Birds, Acute and Subacute

An acute oral toxicity study (Table 1) using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of thiabendazole to birds. The preferred test species is either the mallard or northern bobwhite. Results of this test are tabulated below.

**Table 1. Avian Acute Oral Toxicity**

| *Species* | *% ai* | *$LD_{50}$ (mg/kg)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|
| Northern bobwhite *(Colinus virginianus)* | 99.6 | >2250 | practically nontoxic | 410250-02 (Grimes and Jaber 1988) | acceptable |
| Northern bobwhite | 98 | >4640 | practically nontoxic | 232421 (1977) | supplemental |
| Northern bobwhite | 26 | >4640 | practically nontoxic | 232421 (1977) | supplemental |
| Mallard *(Anas platyrhynchos)* | 98 | >4640 | practically nontoxic | 232421 (1977) | supplemental |

The $LD_{50}$s exceed 2000 mg/kg, which categorizes thiabendazole as practically nontoxic to birds on an acute oral basis. The guideline (71-1) is fulfilled (MRIDs 41025002 and 232421).

Two subacute dietary studies (Table 2) using the TGAI are required to establish the toxicity of thiabendazole to birds. The preferred test species are mallard and northern bobwhite. Results of these tests are tabulated below.

**Table 2. Avian Subacute Dietary Toxicity**

| *Species* | *% ai* | *$LC_{50}$ (ppm)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|
| Northern bobwhite *(Colinus virginianus)* | 99.6 | >5620 | practically nontoxic | 410250-03 (Grimes and Jaber, 1989) | acceptable |
| Northern bobwhite | 98 | >10,000 | practically nontoxic | 232421 (1977) | acceptable |
| Northern bobwhite | tech. | >14,500 | practically nontoxic | ESVII (1968) | supplemental |
| Northern bobwhite | 26 | 6849 | practically nontoxic | 232421 (1977) | supplemental |
| Mallard *(Anas platyrhynchos)* | 99.6 | >5620 | practically nontoxic | 410250-04 (Grimes and Jaber, 1989) | acceptable |

Because the $LC_{50}$ values exceed 5000 ppm, thiabendazole is categorized as practically nontoxic to birds on a subacute dietary basis. The guideline (71-2) is fulfilled (MRIDs 41025004 and 41025004).

### ii. Birds, Reproduction

Avian reproduction tests (Table 3) are currently being required for all pesticides having outdoor uses. The preferred test species are the northern bobwhite and mallard. Test results for thiabendazole are tabulated below.

**Table 3. Avian Reproduction**

| *Species* | *% ai* | *NOAEC/ LOAEC (ppm)* | *Affected Endpoints* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|
| Northern bobwhite *(Colinus virginianus)* | 98.5 | NOAEC = 400 LOAEC >400 | none | 235974 (Fink 1978) | acceptable |
| Mallard *(Anas platyrhynchos)* | 98.5 | NOAEC = 400 LOAEC >400 | none | 235974 (Fink 1978) | acceptable |

Thiabendazole had no adverse effects on avian reproduction at dietary concentrations up to 400 ppm, the highest concentration tested. The guideline (71-4) is fulfilled (MRID 235974).

### iii. Mammals, Acute

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies (Table 4 (oral) and 5 (reproduction)), intended use patterns, and pertinent environmental fate characteristics of the pesticide. Laboratory rat or mouse toxicity values obtained from the Agency's Health Effects Division usually substitute for wild mammal testing. The available data for thiabendazole are tabulated below.

**Table 4. Mammalian Acute Oral Toxicity**

| *Species* | *% ai* | *$LD_{50}$ (mg/kg)* | *Toxicity Category* | *MRID No.* |
|---|---|---|---|---|
| Laboratory rat *(Rattus norvegicus)* | 98.5 | 5070 (♂)<br>4734 (♀) | practically nontoxic | 412582-01 |
| Laboratory rat | 98.5 | 3330 (♂) | practically nontoxic | 100853 |
| Laboratory mouse *(Mus musculus)* | 98.5 | 3810 (♀) | practically nontoxic | 100853 |
| Rabbit | 98.5 | 3850 (♂) | practically nontoxic | 100853 |

Because the $LD_{50}$ values exceed 2000 mg/kg, thiabendazole is considered practically nontoxic to small mammals on an acute oral basis.

**Table 5. Chronic Toxicity of Thiabendazole to Mammals.**

| **Mammalian Reproduction** | | | | |
|---|---|---|---|---|
| *Species* | *% ai* | *Test type* | *Toxicity value* | *MRID No.* |
| Laboratory rat | >99 | 2-generation | NOAEC = 90 mg/kg/day<br>LOAEC >90 mg/kg/day | 43190301 |

Results from the 2-generation reproduction study indicate no adverse reproductive effects as high as 90 mg/kg/day to small mammals on a chronic exposure basis.

## 2. TOXICITY TO TERRESTRIAL PLANTS

Terrestrial plant testing (seedling emergence and vegetative vigor) is required for fungicides that have terrestrial non-residential outdoor use patterns and that may move off the application site through volatilization (vapor pressure >$1.0 \times 10^{-5}$mm Hg at 25°C) or drift (aerial or irrigation) and/or that may have endangered or threatened plant species associated with the application site. Because the only outdoor use is as a seed treatment and minimal contamination is expected, terrestrial plant data are not required.

## 3. TOXICITY TO AQUATIC ANIMALS

Toxicity test values (*i.e.*, measures of effects) for aquatic biota used in the screening risk assessment were derived from the results of registrant-required aquatic plant and animal toxicity studies. Toxicity results that were consistent with risk assessment practices and toxicity testing guidelines (FIFRA 40 CFR-Part 158 and Part 160) were used. In characterizing a chemical's toxic potential, acute toxicity results (96-hr [except as noted] $LC_{50}$ or $EC_{50}$) for fish and invertebrates excluding plants are classified, based on the magnitude of the chemical required to illicit a response, as practically nontoxic (>100 mg/L), slightly toxic (100 to 10 mg/L), moderately toxic (10 to 1 mg/L), highly toxic (1 to 0.1 mg/L), and very highly toxic (<0.1 mg/L). This classification scheme is used in the sections below when discussing the results of toxicity studies using thiabendazole.

### i. Freshwater Fish, Acute

Two freshwater fish toxicity studies (Table 6) using the TGAI are required to establish the toxicity of thiabendazole to fish. The preferred test species are rainbow trout (coldwater species) and bluegill sunfish (warm water species). Results of these tests are tabulated below.

**Table 6. Freshwater Fish Acute Toxicity**

| *Species* | *% ai* | *Test Conditions* | *96-h $LC_{50}$ (mg/L)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|---|
| Rainbow trout *(Oncorhynchus mykiss)* | 99.6 | flow-through (measured) | 0.56 | highly toxic | 410250-05 (Belinger and O'Boyle 1989) | acceptable |
| Rainbow trout | 98 | static | 1.8 | moderately toxic | 227331 (1978) | acceptable |
| Rainbow trout | tech. | static | 3.5 | moderately toxic | ESVIIGI (1968) | acceptable |
| Rainbow trout | 30 | static | 3.8 | moderately toxic | ESM-LSP-6 (1977) | supplemental |
| Bluegill sunfish *(Lepomis macrochirus)* | 98.5 | static (measured) | 19 | slightly toxic | 424777-01 (Holmes et al. 1992) | acceptable |
| Bluegill sunfish | 99.6 | flow-through (measured) | >6.8 | not determined | 410250-06 (Belinger and O'Boyle 1989) | supplemental |
| Bluegill sunfish | 98 | static | 22 | slightly toxic | 227331 (1978) | acceptable |
| Bluegill sunfish | tech. | static | 14 | slightly toxic | ESVIIGI (1968) | acceptable |
| Bluegill sunfish | 30 | static | 56.3 | slightly toxic | ESVIIGI (1968) | acceptable |

Because the lowest $LC_{50}$ (rainbow trout) is >0.1 but <1 mg/L, thiabendazole is categorized as highly toxic to freshwater fish. The guideline (72-1) is fulfilled (MRIDs 41025005 and ESVIIGI).

### ii. Freshwater Fish, Chronic

A freshwater fish early life-stage test (Table 7) using the TGAI is not required for indoor uses or for the seed treatment use of thiabendazole, but data were previously submitted and reviewed. The preferred test species is the rainbow trout. Results of chronic tests are tabulated below.

**Table 7. Freshwater Fish Early Life-Stage Toxicity**

| *Species* | *% ai* | *Test Conditions* | *NOAEC/ LOAEC (mg/L)* | *MATC (mg/L)*[1] | *Endpoint Affected* | *MRID No. (Author/ Year)* | *Study Classification* |
|---|---|---|---|---|---|---|---|
| Fathead minnow *(Pimephales promelas)* | 98.5 | flow-through (measured) | NOAEC = 0.11 LOAEC = 0.23 | 0.16 | wet weight | 425089-01 (Holmes and Swigert 1992) | acceptable |
| Rainbow trout *(Oncorhynchus mykiss)* | 98.5 | flow-through (measured) | NOAEC = 0.012 LOAEC = 0.029 | 0.018 | embryo viability | Acc. # 247102 (Wilson 1982) | acceptable |

[1] Maximum Allowed Toxic Concentration, defined as geometric mean of the NOAEC and LOAEC

### iii. Freshwater Invertebrates, Acute

A test (Table 8) using the TGAI is required to establish the toxicity of thiabendazole to freshwater aquatic invertebrates. The preferred test species is *Daphnia magna*. The test results are tabulated below.

**Table 8. Freshwater Invertebrate Acute Toxicity**

| *Species* | *% ai* | *Test Conditions* | *48-h $EC_{50}$ (mg/L)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|---|
| Water flea *(Daphnia magna)* | 99.8 | flow-through (measured) | 0.85 | highly toxic | 417094-01 (Holmes et al. 1990) | acceptable |
| Water flea | 98 | static | 0.31 | highly toxic | ESTBZ-2 | acceptable |
| Water flea | 30 | static | 0.49 | highly toxic | ESM-LSP-5 (1977) | supplemental |
| Water flea | 26 | static | 2.6 | moderately toxic | 232421 (1977) | supplemental |

Because the lowest $EC_{50}$ is between 0.1 and 1 mg/L, thiabendazole is categorized as highly toxic to aquatic invertebrates on an acute basis. The guideline (72-2) is fulfilled (MRIDs 41709401 and ESTBZ-2).

### iv. Freshwater Invertebrates, Chronic

A freshwater aquatic invertebrate life-cycle test (Table 9) using the TGAI is not required for the seed treatment use of thiabendazole, but data were previously submitted and reviewed. The preferred test species is *Daphnia magna*. Results of this test are tabulated below.

**Table 9. Freshwater Aquatic Invertebrate Life-Cycle Toxicity**

| *Species* | *% ai* | *Test Condition* | *21-day NOAEC/ LOAEC (mg/L)* | *MATC (mg/L)* [1] | *Endpoint Affected* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|---|---|
| Water flea (*Daphnia magna*) | 98 | flow-through (measured) | NOEC = 0.042<br>LOEC = 0.087 | 0.060 | survival; offspring production | 246711 (Surprenant 1981) | acceptable |

[1] Maximum Allowed Toxic Concentration, defined as geometric mean of the NOAEC and LOAEC

## 4. TOXICITY TO ESTUARINE & MARINE ANIMALS

### i. Estuarine & Marine Fish, Acute

Acute toxicity testing with estuarine/marine fish (Table 10) using the TGAI is not required for thiabendazole, because minimal exposure is expected due to the low aquatic EEC for the seed treatment. However, a study was previously submitted and reviewed to support other uses not being supported for reregistration. Results of that study are tabulated below.

**Table 10. Estuarine/Marine Fish Acute Toxicity**

| *Species* | *% ai.* | *Test Conditions* | *96-h $LC_{50}$ (mg/L)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|---|
| Sheepshead minnow (*Cyprinodon variegatus*) | 99.6 | flow through (measured) | >10 | not determined | 411920-03 (Surprenant 1989) | supplemental |

An $LC_{50}$ could not be determined for the sheepshead minnow, because the limited solubility of thiabendazole in organic solvents and seawater precludes testing at concentrations greater than 10 mg/L. The guideline (72-3a) is fulfilled (MRID 41192003).

### ii. Estuarine & Marine Invertebrates, Acute

Acute toxicity testing with estuarine/marine invertebrates (Table 11) using the TGAI is not required for thiabendazole, because minimal exposure is expected due to the low aquatic EEC for the seed treatment. However, studies were previously submitted and reviewed for uses not being supported for reregistration. Test results are tabulated below.

**Table 11. Estuarine/Marine Invertebrate Acute Toxicity**

| *Species* | *% ai.* | *Test Conditions* | *96-h $EC_{50}$/ $LC_{50}$ (mg/L)* | *Toxicity Category* | *MRID No. (Author/Year)* | *Study Classification* |
|---|---|---|---|---|---|---|
| Mysid shrimp *(Americamysis bahia)* | 99.6 | flow through (measured) | 0.34 | highly toxic | 411920-02 (Surprenant 1989) | acceptable |
| Pacific oyster (larvae) *(Crassostrea gigas)* | 99.6 | flow through (measured) | >10 | not determined | 411920-04 (Surprenant 1989) | supplemental |

Because the $LC_{50}$ for the mysid shrimp, the most sensitive species, is in the range of 0.1 to 1 mg/L, thiabendazole is categorized as highly toxic to estuarine/marine invertebrates on an acute basis. An $EC_{50}$ was not established for the oyster, because the limited solubility of thiabendazole in organic solvents and seawater precludes testing at concentrations greater than 10 mg/L. The guidelines (72-3b and c) are fulfilled (MRIDs 41192002 and 41192004).

## 4. TOXICITY TO AQUATIC PLANTS

Aquatic plant testing is required for any fungicide that has outdoor non-residential terrestrial uses and that may move off-site by runoff (solubility >10 ppm in water) and/or by drift (aerial or irrigation) or that is applied directly to aquatic use sites (except residential). Because the only outdoor use is as a seed treatment and minimal contamination of surface water is expected, aquatic plant data are not required.