DEPARTMENT OF PESTICIDE REGULATION

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Environmental Protection

M E M O R A N D U M

TO: Nan Singhasemanon **HSM-21002**
Assistant Director
Pesticide Programs Division

FROM: Kevin Solari *(original signed by K. Solari)*
Environmental Program Manager I
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(916) 323-7614

DATE: March 2, 2021

SUBJECT: COMPLETION OF THIABENDAZOLE MITIGATION

The thiabendazole mitigation completion memorandum (Wroblicky 2021) describes the findings of the Worker Health and Safety (WHS) Branch with regard to the need for mitigation of thiabendazole.

In 2001, Department of Pesticide Regulation (DPR) completed a Risk Characterization Document (RCD) for thiabendazole (Cochran et al., 2001), which determined that the margins of exposure (MOEs) were at levels considered protective of human health for daily and annual worker exposures, as well as for exposure via dietary consumption for the general public. Given this determination, DPR concluded that no further mitigation measures were needed for pesticide products containing thiabendazole (DPR 2002).

In 2002, the United States Environmental Protection Agency (U.S. EPA) issued a Reregistration Eligibility Decision (RED) for thiabendazole (U.S. EPA 2002), concluding that the uses of thiabendazole registered at that time, when labeled and used as specified in the RED, would not cause unreasonable risk to humans or the environment.

U.S. EPA's 2019 draft human health risk assessment for thiabendazole identified potential occupational dermal and inhalation exposures associated with certain seed treatment activities, and certain mixing, loading, and application activities (U.S. EPA 2019). In September 2020, U.S. EPA published its interim registration review decision for thiabendazole (U.S. EPA 2020). To mitigate occupational exposures of concern identified in its draft human health risk assessment, U.S. EPA proposed formal label revisions that included requirements for additional PPE, such as respirators; engineering controls, such as water-soluble packaging; and reduction of application rates for certain uses. According to U.S. EPA, registrants have agreed to implement these requirements.

Provided registrants implement label revisions specified in U.S. EPA's interim registration review decision to address identified exposures of concern, WHS finds that no further mitigation is needed for thiabendazole. Thiabendazole's relatively low historic usage, lack of exposure

incidents reported, and low severity of associated health impacts when applied according to label requirements further supports this conclusion. Your approval of this conclusion is requested.

Attachment

cc: Shelley DuTeaux, Chief, Human Health Assessment Branch
Eric Kwok, Senior Toxicologist, Human Health Assessment Branch
Svetlana Koshlukova, Senior Toxicologist, Human Health Assessment Branch
Kevin Solari, Environmental Program Manager I, WHS Branch

APPROVAL: *(original signed by N. Singhasemanon* *March 29, 2021*
Nan Singhasemanon, Assistant Director Date

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Department of Pesticide Regulation

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MEMORANDUM

TO: Susan McCarthy
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VIA: Ann Schaffner *(original signed by A. Schaffner)*
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FROM: Greg Wroblicky *(original signed by G. Wroblicky)*
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DATE: February 26, 2021

SUBJECT: COMPLETION OF THIABENDAZOLE MITIGATION

Summary

The Department of Pesticide Regulation (DPR) has determined that no additional mitigation measures are necessary for the use of the active ingredient (AI), thiabendazole, provided that mitigation measures proposed by the United States Environmental Protection Agency (U.S. EPA) as part of its thiabendazole registration review process are adopted by registrants. Low historic agricultural usage of thiabendazole, both in California and nationwide, the lack of reported human health incidents, and the moderate to low severity of health impacts associated with thiabendazole lend additional support to this conclusion. Additional mitigation efforts may be required if U.S. EPA finds any new endocrine effects of concern when making an Endocrine Disruptor Screening Program (EDSP) determination as part of its final decision on the registration review case for thiabendazole.

Classification and Usage

Thiabendazole [2-(4-thiazolyl) benzimidazole] is a systemic fungicide first registered for use in the U.S. in 1963 by Merck and Company, Inc. It also occurs as a salt: [2-(4-thiazolyl) benzimidazole] hypophosphite salt (hereafter, thiabendazole will be used to refer to both thiabendazole and its salt, except when specifically referring to thiabendazole salt). Thiabendazole controls a variety of fruit and vegetable diseases such as mold, blight, rot, and stains caused by various fungi. It is currently registered with U.S. EPA and DPR. It is used as a preplant dust treatment on potato seed pieces, sweet potato seed pieces, soybeans, and wheat, and as a seed treatment via a ready-mix or slurry-mix on corn, soybeans, dry peas, chickpeas, lentils, and wheat. It is also used to control fungal diseases via chemigation in mushroom cultures, and in postharvest applications on a variety of crops such as citrus, apples, pears, bananas, mangos, papayas, plantains, carrots, avocados, peas, and potatoes, as well as some non-food crops, by dipping, spraying, or application during the waxing procedure. Thiabendazole salt uses include a

ready-to-use formulation for ornamental bulbs, and tree injection treatment of elm, sycamore, London plane, and oak trees. It is also used as a preservative, fungicide, and antimicrobial ready-to-use formulation in the manufacture of adhesives (non-food), carpets, ceiling tiles, paper products (non-food), paints and stains (indoor and outdoor), plastics and rubber, clothing textiles, and wallboard (Cochran et al. 2001; U.S. EPA 2002a, 2002b, 2013a, 2019, 2020).

Currently in California, there are 27 registered products containing thiabendazole (DPR 2019a). Thiabendazole is the sole AI in 20 product formulations, while the remaining 7 product formulations contain thiabendazole in combination with one or more of the following AIs: azoxystrobin, fludioxonil, octhilinone, mefenoxam, and zinc 2-pyridinethiol-1-oxide. Product formulations containing thiabendazole include aqueous, flowable and emulsifiable concentrates, regular or wettable dusts/powders, suspensions, and ready-to-use liquid solutions (DPR 2021a). Thiabendazole is designated Toxicity Category III for oral and dermal toxicity, inhalation, and eye and dermal irritation, and is not a dermal sensitizer. Thiabendazole is non-genotoxic and non-mutagenic (U.S. EPA 2014a).

Regulatory History

In August 2001, DPR completed a Risk Characterization Document (RCD) for thiabendazole (Cochran et al., 2001). The RCD determined that the margins of exposure (MOEs) were at levels considered protective of human health for daily and annual exposures to workers associated with handling pesticide products containing thiabendazole, as well as the general public exposed via dietary consumption. Given this determination, DPR concluded in May 2002, that no further mitigation measures were needed for pesticide products containing thiabendazole (DPR 2002).

In October 2002, U.S. EPA issued a Reregistration Eligibility Decision (RED) for thiabendazole (U.S. EPA 2002a). The RED concluded that the uses of thiabendazole registered at that time, when labeled and used as specified in the RED, would not cause unreasonable risk to humans or the environment and were eligible for reregistration. U.S. EPA's Worker Protection Standard and the RED specified the following minimum personal protective equipment (PPE) for mixers, loaders, applicators, and other handlers applying thiabendazole: long-sleeved shirt and long pants, and shoes plus socks. Chemical-resistant gloves were specifically required for handlers making applications to mushroom houses, using hand-held sprayers; post-application reentry workers were required to observe a 12-hour re-entry interval (U.S. EPA 2002a); and manual seed treatments were prohibited. (U.S. EPA 2002a).

More recently, U.S. EPA initiated a registration review for thiabendazole (U.S. EPA 2014a). U.S. EPA evaluated its human health risk assessment for thiabendazole to determine the scope of work necessary to support the registration review, issuing a human health risk scoping document in March 2014 (U.S. EPA 2014b). U.S. EPA identified potential risks to pregnant women, infants, and children based on thyroid toxicity in adult animals. U.S. EPA concluded that re-

evaluation of toxicity endpoints and uncertainty factors would be necessary for registration review, thus necessitating an update to the human health risk assessment (U.S. EPA 2014b). The draft updated human health assessment for registration review was published in March, 2019 (U.S. EPA 2019).

U.S. EPA's draft human health risk assessment evaluated potential occupational dermal and inhalation exposures associated with mixing/loading, application, and post-application activities. Occupational exposure scenarios included agricultural applications made using seed treatment equipment, hand-held sprayers, dip vats, and fixed mechanical sprayers; commercial incorporation of material preservatives by handlers involving mixing/loading of both liquid (open pour) and solid (solid pour) antimicrobial formulations; and applications of preserved paints using a paint brush/roller or airless sprayer. U.S. EPA conducted risk assessments for inhalation exposures assuming baseline PPE. However, dermal risks were not assessed because no toxicological hazards were identified (U.S. EPA 2014b, 2019).

Occupational handler exposure associated with agricultural mixing/loading scenarios did not pose inhalation risks above U.S. EPA's level of concern (i.e., MOEs ≥1000), except for the following scenarios: workers performing multiple activities for cucurbit vegetable seed treatments (MOE = 420), workers mixing and loading wettable powders for use in automated systems for commodity postharvest treatments (MOE = 280), and workers mixing, loading, and applying liquids for drench applications during normal watering operations for mushroom growing beds at casing or between breaks via mechanically-pressurized handgun equipment (MOE = 650). The addition of a respirator rated at a protection factor (PF) of 10 resulted in MOEs that were no longer of concern for these scenarios (U.S. EPA 2014b, 2019).

U.S. EPA's interim registration review decision for thiabendazole was published in September, 2020 (U.S. EPA 2020). To mitigate potential inhalation risk to occupational handlers, U.S. EPA will require that a half-face NIOSH-approved, PF10 respirator and the associated requirements for fit testing, training, and medical evaluation be added to the label. In addition, although handgun sprayers are not typically used in mushroom production, a PF10 respirator must be included for this use, unless mechanically pressurized handgun use is expressly prohibited on the label. According to U.S. EPA, technical registrants have agreed to the respirator requirement and label language (U.S. EPA 2020).

Occupational handler exposure during the open pouring of thiabendazole for use as a material preservative (paints, adhesives, carpets) did not pose inhalation risks above levels of concern for open pouring of liquids (liquid pour) during paint preservation; however, the MOE for open pouring of powder (solid pour) without a respirator (MOE = 45) was found to be of concern (MOE ≤ 1000). Addition of a PF10 respirator requirement (currently not required on product labels) did not mitigate the inhalation risk (MOE = 450, U.S. EPA 2019); however, addition of a PF25 respirator (MOE = 1125) did mitigate the inhalation risk. Thus, U.S. EPA will require the

either the addition of PF25 powered air-purifying respirator to labels, or engineering controls such as water-soluble packaging, to mitigate this potential inhalation risk. According to U.S. EPA, registrants have agreed to implement these requirements (U.S. EPA 2020).

Occupational handler inhalation exposure during the application of thiabendazole-preserved paints was assessed for brush/roller and airless sprayer applications. The inhalation risk for brush/roller application of preserved paint (MOE = 510,000) was not of concern (MOEs ≤ 1000), however it was found to be of concern for airless sprayer paint applications (MOE = 710). This risk cannot be mitigated with respiratory protection because preserved paints are not U.S. EPA registered pesticide products and thus do not have labels that could include PPE requirements (U.S. EPA 2019). The risks for airless sprayer application can be mitigated by reducing the maximum application rate from 0.4% to 0.28% AI, which would increase the MOE from 710 to 1,000. Therefore, U.S. EPA will require that the maximum application rate cannot exceed 0.28% AI; registrants have agreed to implement this requirement (U.S. EPA 2020).

Occupational post-application inhalation exposure scenarios associated with post-harvest uses of thiabendazole, such as sorting/packing/culling activities, when minimum PPE was worn, did not pose risks above the level of concern (i.e., MOEs ≥ 1000) (U.S. EPA 2019).

Thiabendazole is not registered for residential use, but is registered for incorporation as a preservative or antimicrobial into products used by homeowners, such as paints, carpets, and textiles used for clothing or other household items such as towels. Residential handler inhalation exposure scenarios include painter applications involving brush/roller and airless sprayer, neither of which were found to pose risks above levels of concern. Post-application bystander inhalation exposures associated with residential thiabendazole applications are expected to be negligible due to thiabendazole's low vapor pressure, therefore a quantitative residential post-application inhalation exposure assessment was not performed (U.S. EPA 2014b, 2019). The use of thiabendazole as a material preservative to treat textiles could result in human contact with treated clothing and/or carpeting. There is the potential for residential post application incidental oral exposure when children 1 to <2 years old mouth preserved textiles. This exposure is anticipated to be short-term in duration and U.S. EPA did not find risk associated with such incidental oral exposures above levels of concern (U.S. EPA 2019).

Other label changes issued as part of U.S. EPA's interim registration review decision for thiabendazole, which potentially affect human exposure to thiabendazole in California, include removing sugar beets as a registered use and prohibiting application of thiabendazole-treated spent mushroom compost to land used to grow food and feed crops (U.S. EPA 2020).

Although label changes and other changes listed above have been issued as part of U.S. EPA's interim registration review decision for thiabendazole, the Agency did not make human health findings associated with EDSP. A final decision on the registration review case for thiabendazole

will not occur until U.S. EPA makes its EDSP determination. Additional mitigation measures may be required in the event that thiabendazole is found to produce endocrine effects of concern.

Use in California

According to DPR's Pesticide Use Reporting database, from 2009 to 2018, the average total annual use of thiabendazole in California was 25,030 pounds; ranging from 13,369 to 32,034 pounds annually. Thiabendazole salt (hypophosphite) use accounted for less than one percent of total annual use (DPR 2021b).

Principle use sites are citrus (77%) and mushrooms (18%), together accounting for over 95% of total thiabendazole use. Remaining reported use sites include commodity fumigation, structural pest control and landscape maintenance, and a variety of other agricultural crops (DPR 2021b).

Total annual sale of products containing thiabendazole reported in California for this time period ranged between 30,756 and 885,400 pounds, with an average of 265,459 pounds sold annually. The highest sales figure of 885,400 pounds of AI occurred in 2015, however sales data for 2017 and 2018 were much lower, at 30,756 and 37,929 pounds of AI, respectively (DPR 2021c).

Illness Incident Review

A query of DPR's Pesticide Illness Surveillance Program database from 2006 to 2018 found only one illness incident flagged as possibly associated with thiabendazole use. The incident was fatal, reportedly the result of ingestion of lacquer thinner, but the subject also ingested an unknown product containing thiabendazole (DPR 2021d). U.S. EPA reviewed thiabendazole incidents as part of its registration review and concluded that based on the low frequency and severity of incident cases reported for thiabendazole, there is no concern at this time that would warrant further investigation (U.S. EPA 2013b, 2019, 2020).

Conclusion

Generally, the relatively low historic usage of thiabendazole, both in California and nationwide, the lack of exposure incidents reported, and the low severity of health impacts associated with thiabendazole when applied according to label requirements, indicate few exposures of concern for thiabendazole. As part of its registration review, U.S. EPA identified several occupational handler exposure scenarios of concern for thiabendazole. In its interim registration review decision, U.S. EPA proposed mitigation measures including requirements for additional PPE, such as respirators; engineering controls, such as water-soluble packaging; and reduction of application rates to mitigate identified exposures of concern for thiabendazole. U.S. EPA has proposed formal label revisions as part of its interim decision, and reports that registrants have agreed to implement these requirements.

DPR finds that no further mitigation is warranted for the use of thiabendazole in California, provided that registrants comply with label amendments specified in U.S. EPA's interim registration review decision and that no endocrine effects of concern are identified by U.S. EPA's EDSP determination. DPR will continue to monitor U.S. EPA's registration review of thiabendazole and any additional actions taken to mitigate exposure scenarios of concern.

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