Registration Decision for the New Active Ingredient Methyl Mercaptan

PC Code: 100702

Approved by:

RICHARD KEIGWIN

Digitally signed by RICHARD KEIGWIN
Date: 2020.06.03 05:10:24 -04'00'

Richard P. Keigwin, Jr., Director
Office of Pesticide Programs
U.S. Environmental Protection Agency

1. Introduction

This document announces that the U.S. Environmental Protection Agency (EPA) completed its initial evaluation of the new biochemical active ingredient methyl mercaptan, a gopher repellent, and concluded that it meets the regulatory and safety standards under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act.

Methyl mercaptan is a naturally occurring compound that presents as colorless gas in its ambient state and has an odor reminiscent of rotten cabbage. At lower temperatures or when captured in contained systems, methyl mercaptan can also be expressed as a liquid. Methyl mercaptan is naturally found in the blood and brain of humans and other animals, as well as in plant tissues. It is excreted from the human and animal body through feces. It also occurs naturally in certain foods, such as vegetables and some nuts and cheeses, and, as such, is often consumed by humans.

Methyl mercaptan has several commercial uses. Due to its strong odor, it is commonly employed as a leak detector in natural gas lines. Methyl mercaptan is also used in the production of plastics to moderate the growth of free radical polymers. Most notably, methyl mercaptan is used as a Food and Drug Administration (FDA)-approved food additive to impart an umami flavor and to act as an adjuvant (21 CFR 172.515).

As a pesticide, methyl mercaptan is being registered as a new biochemical active ingredient with a food use. It is to be used as a gopher repellent in irrigation/chemigation lines (subterranean, surface drip, and micro irrigation systems). Although no direct application to food is expected, it is possible that some trace amounts of the active ingredient may be taken up into the plant. The repellent mode of action is due to its noxious, putrid odor. The applicant is registering a single end-use product (EP) containing 0.01% methyl mercaptan in a liquid formulation. The pesticide is to be applied in closed irrigation systems by applicators with special familiarity with closed irrigation systems. Handler personal protective equipment (PPE) will include a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and goggles or a face shield. There will be a 24-hour restricted-entry interval (REI) associated with the application.

Overall, methyl mercaptan is considered to be of low toxicity relative to its pesticidal use pattern. Based on the available information and the fact that humans have been exposed to methyl mercaptan in food and nonfood products, the compound is considered to have a history of safe natural exposure. With specific regard to human oral toxicity, EPA notes that the human digestive system is designed to accommodate methyl mercaptan in its digestive processes. Notably, significant levels of methyl mercaptan (in excess of 1000 parts per million) are naturally produced by microflora within the human intestine. Even so, only trivial amounts are absorbed into the body because methyl mercaptan is readily oxidized in the human colon.

Based on its pesticidal use pattern, EPA determined that exposures to the active ingredient methyl mercaptan will be negligible and that, as a result, pesticides containing methyl mercaptan will pose no significant dietary risk to consumers. One, methyl mercaptan, which presents as a gas at ambient temperatures, is highly volatile (vapor pressure = 1650 hPa @ 20°C) and dissipates rapidly in the atmosphere. It has a half-life of 4-46 minutes. Two, methyl mercaptan is readily biodegradable in the soil, where it is applied. And three, any exposures to methyl mercaptan are expected to be indistinguishable from any natural exposures to food. In short, no significant exposure to methyl mercaptan is anticipated, dietary or otherwise.

EPA also considered methyl mercaptan's potential effects on nontarget organisms, including federally listed endangered or threatened species. EPA determined that there would be negligible exposure of nontarget organisms to methyl mercaptan due to its high volatility, rapid degradation and the low application rates at which it will be applied. EPA further noted that the active ingredient has a nontoxic mode of action, is ubiquitous in the environment and has a history of exposure with no adverse effects to nontarget organisms. In sum, EPA does not anticipate any significant risks to nontarget organisms relative to the pesticidal use of methyl mercaptan.

After reviewing all submitted and publicly available data and information, EPA concluded that there is reasonable certainty of no harm from residues of this new active ingredient when it is used as a gopher repellent in irrigation lines and that its use will not cause unreasonable adverse effects to human health or the environment. Therefore, EPA is registering an EP, Protec-T (EPA File Symbol 87809-R) containing the new active ingredient methyl mercaptan, under FIFRA section 3(c)(5). Furthermore, EPA is establishing a tolerance exemption for residues of methyl mercaptan in or on all food commodities when methyl mercaptan is used as a gopher repellent in irrigation lines in accordance with label directions and good agricultural practices.

2. Background

Methyl mercaptan was classified as a biochemical pesticide by the Biochemical Classification Committee on December 12, 2016, due to its natural occurrence, history of safe exposure to humans and the environment, and nontoxic mode of action to the target pest.

On October 9, 2018, EPA received an application from Acqua Concepts, Inc. (d/b/a Ag Water Chemical) (AWC) for the registration of a pesticide product (an EP) containing the new biochemical active ingredient methyl mercaptan. AWC provided a combination of data and waiver rationales to satisfy the data requirements. In addition, AWC submitted a petition (Pesticide Petition 8F8713) to establish an exemption from the requirement of a tolerance for residues of the gopher repellent methyl mercaptan in or on all food commodities that use irrigation lines treated with methyl mercaptan.

In the Federal Register of August 6, 2019 (84 FR 38253), EPA published a Notice of Receipt (NOR) that announced receipt of a pesticide product application containing the new active ingredient methyl mercaptan. In the Federal Register of August 2, 2019 (84 FR 37818), EPA published a Notice of Filing (NOF) for the petition requesting an exemption from the requirement of a tolerance for residues of methyl mercaptan. EPA is revising 40 CFR Part 180 to establish a tolerance exemption for residues of methyl mercaptan in or on all food commodities when methyl mercaptan is used as a gopher repellent in irrigation lines in accordance with label directions and good agricultural practices.

3. Evaluation

In evaluating a pesticide registration application, EPA assesses a variety of studies to determine the likelihood of adverse effects (i.e., risk) from exposures associated with the use of the pesticide product. Risk assessments are developed to evaluate how the active ingredient might affect a range of nontarget organisms, including humans and terrestrial and aquatic wildlife (plants and animals). Based on these assessments, EPA evaluates and approves language for each pesticide label to ensure the directions for use and safety measures are appropriate to mitigate potential risk. In this way, the pesticide label communicates essential limitations and mitigations that are necessary for

public and environmental safety. In fact, FIFRA section 12(a)(2)(G) states that it is unlawful for any person to use a registered pesticide in a way that conflicts with the label.

3.1 Assessment of Human Health Exposure and Risk

To assess risks to human health from use of biochemical pesticides, EPA typically requires a range of Tier I data: acute toxicity data (acute oral, acute inhalation, and acute dermal), primary irritation data (primary eye and primary dermal), dermal sensitization data, subchronic toxicity data (90-day oral, 90-day dermal, and 90-day inhalation), genetic toxicity data (bacterial reverse mutation test and *in vitro* mammalian cell assay), and prenatal developmental toxicity data. Tier II and III testing is triggered only when there is indication, usually through lower tier testing, that a biochemical pesticide has unusual characteristics, such as exhibiting subchronic toxicity or being suspected or known to be a carcinogen.

In the case of the assessment for methyl mercaptan, data requirements were satisfied by a combination of data and waiver rationales.

3.1.1 Toxicological Data/Information

The toxicology database is complete for biopesticide risk assessment for the use of methyl mercaptan. Tier II and III studies have not been triggered at this time. To satisfy the human health assessment data requirements for concentrated methyl mercaptan, the applicant submitted the following: (1) waiver requests to address all acute toxicology data requirements, with the exception of the acute inhalation toxicity data requirement for which the applicant cited information from publicly available scientific literature; (2) information from publicly available scientific literature to satisfy the 90-day inhalation toxicity data requirement; and (3) waiver requests for the 90-day oral toxicity, 90-day dermal toxicity, prenatal developmental toxicity, and genetic toxicity data requirements.

All of the acute toxicology data requirements for concentrated methyl mercaptan were waived, except acute inhalation toxicity, due to the active ingredient's chemical and physical properties as a gas. A guideline study generated on the active ingredient methyl mercaptan resulted in a classification of Toxicity Category II for acute inhalation toxicity. It was determined that the acute toxicity for methyl mercaptan relative to the other routes of exposure was best assessed through guideline studies performed using the liquid EP as the test substance so that oral, dermal, and ocular exposures could be effectively addressed. The EP classified into Toxicity Category III for primary eye irritation, and Toxicity Category IV for acute oral toxicity, acute dermal toxicity, and primary dermal irritation. The Signal Word for the EP is "Warning" due to the acute inhalation toxicity.

A guideline subchronic inhalation toxicity study was done on the concentrated methyl mercaptan gas. The no-observed-adverse-effect-concentration is 17 ppm (0.033 mg/L) and the lowest-observed-adverse-effect-concentration is 57 ppm (0.118 mg/L) based on reduced body weight as determined by the study authors. It is noted, however, that negligible inhalation exposure is anticipated relative to the pesticidal use of methyl mercaptan.

EPA granted waiver requests for the subchronic oral toxicity, subchronic dermal toxicity, prenatal developmental toxicity, and genetic toxicity data requirements based on a weight of the evidence approach that took into account several of the following considerations: (1) negligible exposure

due to methyl mercaptan being highly volatile with a vapor pressure of 1650 hPa @ 20˚C, being readily biodegradable in the soil, and having a short half-life of 4-46 minutes in the air as a result of indirect photo-oxidation; (2) required PPE; (3) closed system for application; (4) methyl mercaptan is naturally occurring and has long been part of the normal human diet; (5) data from the open literature indicate that methyl mercaptan is rapidly metabolized in the colon so only negligible levels are absorbed after ingestion; (6) the methyl mercaptan used in the EP is food-grade; and (7) FDA has approved methyl mercaptan's use as a direct food additive under 21 CFR 172.515 (uses include as a synthetic flavoring substance and adjuvant).

3.1.2 Aggregate and Occupational Exposure and Risk Characterization

Food Exposure and Risk Characterization: A quantitative dietary exposure and risk assessment has not been conducted because dietary exposure to residues of the active ingredient in food is expected to be negligible. This finding is based on the following: (1) negligible exposure due to methyl mercaptan being highly volatile with a vapor pressure of 1650 hPa @ 20˚C, being readily biodegradable in the soil, and having a short half-life of 4-46 minutes in the air as a result of indirect photo-oxidation; (2) methyl mercaptan is naturally occurring and has long been part of the normal human diet; (3) data from the open literature indicate that methyl mercaptan is rapidly metabolized in the colon so only negligible levels are absorbed after ingestion; (4) the methyl mercaptan used in the EP is food-grade; and (5) FDA has approved methyl mercaptan's use as a direct food additive under 21 CFR 172.515 (uses include as a synthetic flavoring substance and adjuvant). As a result of the negligible food exposure expected relative to the use of methyl mercaptan as a gopher repellent in irrigation/chemigation lines, dietary risks through food are not anticipated.

Drinking Water Exposure and Risk Characterization: A quantitative dietary exposure and risk assessment has not been conducted because dietary exposure to residues of the active ingredient in drinking water is expected to be negligible. The pesticide is applied only in a closed system directly into irrigation lines at very low application rates, and the resulting residues are expected to be negligible as the compound will volatilize rapidly as methyl mercaptan returns to its gaseous state. Specifically, the methyl mercaptan captured in the liquid pesticide is expected to break down rapidly in the environment into its nontoxic gaseous degradates (methane, carbon dioxide, and hydrogen sulfide) before it can accumulate in water. As a result of the negligible drinking water exposure expected relative to the use of methyl mercaptan as a gopher repellent in irrigation/chemigation lines, dietary risks through drinking water are not anticipated.

Residential (Non-occupational) Exposure and Risk Characterization: Methyl mercaptan is only intended for commercial agricultural use. As there are no direct residential uses for methyl mercaptan, there are no significant residential exposure contributions to aggregate exposure. The EP is applied at very low application rates and solely in a closed system into irrigation/chemigation lines, and any residues are expected to volatilize or biodegrade rapidly. As a result of the lack of significant residential exposure expected relative to the use of methyl mercaptan as a gopher repellent in irrigation/chemigation lines, non-occupational risks are not anticipated.

Occupational Exposure and Risk Characterization: A qualitative risk assessment was conducted in lieu of a quantitative assessment, given the expected negligible occupational exposure to methyl mercaptan. The qualitative assessment concluded that occupational handler exposure and occupational post-application exposure to methyl mercaptan would be negligible based on very low application rates, the physical and chemical properties of methyl mercaptan, the closed

system for application, the PPE requirements (i.e., a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and goggles or a face shield), and/or a 24-hour REI. As a result of the negligible occupational exposure expected relative to the use of methyl mercaptan as a gopher repellent in irrigation/chemigation lines, occupational risks are not anticipated.

3.1.3 Cumulative Risk

Data have not been identified to suggest that methyl mercaptan has a common mechanism of toxicity with other substances or that methyl mercaptan produces a toxic metabolite produced by other substances. Therefore, EPA has not assumed that methyl mercaptan has a common mechanism of toxicity with other substances.

3.1.4 Human Health Conclusions

EPA concludes that use of methyl mercaptan as a gopher repellent in irrigation/chemigation lines will not result in unreasonable adverse effects to humans and that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of methyl mercaptan. EPA does not expect dietary (food and drinking water) or other non-occupational risks from use of methyl mercaptan as an active ingredient in the pesticide product. Data demonstrated that there will be negligible exposure to methyl mercaptan through all routes of exposure, primarily due to its rapid volatilization and degradation. While methyl mercaptan can be toxic to inhale in a concentrated gaseous state, the use of methyl mercaptan as a liquid EP is not expected to result in significant gaseous concentrations. Moreover, all data indicate that the liquid EP containing methyl mercaptan is not acutely toxic through any route of exposure when used as directed. The human health assessment for methyl mercaptan further found no adverse effects requiring toxicological endpoints for any subchronic or developmental exposures. Any potential occupational risks resulting from exposure to individuals handling methyl mercaptan or re-entering treated areas are expected to be minimized by use of the required PPE, a closed system for application, and/or a 24-hour REI.

The database of studies required to support the assessment of risk to human health is complete. For more information on the human health risk assessment of methyl mercaptan, please see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2019-0368" at www.regulations.gov).

3.2 Assessment of Ecological Exposure and Risk

To assess risks to the environment from the use of biochemical pesticides, EPA initially requires a wide range of studies, including Tier I testing done on the following nontarget organisms: birds (oral and dietary), freshwater fish and aquatic invertebrates, plants, and insects. Testing is organized in a tiered structure, where Tier I studies test worst-case exposure scenarios and higher tiers (Tiers II and III) generally encompass definitive risk determinations and longer-term greenhouse or field testing. Higher tier testing is implemented only when unacceptable effects are seen at the Tier I screening level. All data requirements may be addressed with guideline studies or scientific rationales. In the case of methyl mercaptan, all the nontarget organism data requirements have been satisfied through scientific rationales.

A quantitative risk assessment was not conducted for nontarget organisms, including federally listed endangered or threatened species, due to methyl mercaptan's very low application rates,

volatility, and rapid degradation. In short, exposure is expected to be negligible, and the active ingredient has a nontoxic mode of action. Therefore, risk is not expected from the negligible exposure of nontarget organisms to methyl mercaptan. EPA also considered methyl mercaptan's natural presence in the environment, ubiquity in the environment, and history of exposure with no adverse effects when assessing anticipated risk to nontarget organisms.

3.2.1 Terrestrial Animals and Plants

Wild mammals, birds, terrestrial plants, and nontarget insects may be exposed to methyl mercaptan during and after soil irrigation applications. Many rodents live or burrow in the soil, some nontarget insects dwell below ground, and plants grow from the soil; thus, these terrestrial organisms could be directly exposed during application. Additionally, birds and wild mammals may be exposed when consuming or coming into contact with soil, plants, seeds, insects, and drainage water where methyl mercaptan is present after applications. All potential exposure scenarios, however, are expected to be at roughly background levels of 4 parts per billion (ppb) as detected in ambient air, due to the rapid volatilization of methyl mercaptan. Because of this minimal exposure, EPA does not anticipate any adverse effects to terrestrial animals or plants as a result of the labeled applications of methyl mercaptan.

3.2.2 Aquatic Animals and Plants

Freshwater and estuarine/marine fish and invertebrates and aquatic plants may be minimally exposed to methyl mercaptan. Methyl mercaptan degrades rapidly and is readily volatilized from water surfaces. Estimated volatilization half-lives for a model river and model lake are 0.8 hours and 2.8 days, respectively. Given the very low application rates, rapid volatilization, and further rapid degradation in water bodies, exposure of aquatic organisms to methyl mercaptan is not likely to be different from natural background levels of 4 ppb as detected in ambient air. Because of this minimal exposure, EPA does not anticipate any adverse effects to aquatic animals or plants as a result of the labeled applications of methyl mercaptan.

3.2.3 Endangered Species Conclusion

Based on submitted information regarding methyl mercaptan's minimal toxicity, very low application rates, and rapid dissipation from the environment, EPA does not anticipate any adverse effects as a result of its labeled applications. Therefore, EPA makes a "No Effect" determination for the direct and indirect effects of methyl mercaptan to listed species and their Designated Critical Habitats.

The database of studies required to support the assessment of risk to the environment is complete. For more information on the environmental risk assessment of methyl mercaptan, please see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2019-0368" at www.regulations.gov).

4. Benefits

By definition, biochemical pesticides are favorable when compared to currently registered conventional pesticide alternatives because biochemicals are naturally occurring substances (or substances structurally similar and functionally identical to naturally occurring substances) with a history of exposure to humans and the environment demonstrating minimal toxicity and a nontoxic

mode of action to the target pest(s). Benefits of biochemical pesticides as compared to conventional pesticides typically include lower toxicity profiles for humans and nontarget organisms and faster degradation in the environment.

When used as a gopher repellent, methyl mercaptan has the potential to reduce the amount of more toxic or dangerous pesticides intended to mitigate gopher damage to irrigation lines and crops. While there are no other gopher repellents intended specifically for irrigation lines, most farmers use conventional rodenticides to control gopher populations in agricultural settings. These conventional rodenticides have either a toxic or physically lethal mode of action. Many conventional rodenticides act as poisons, such as strychnine; other conventional rodenticides, such as sodium nitrate, work through an explosive mode of action. In any case, it is expected that the use of methyl mercaptan can reduce the hazards to both users and wildlife associated with the use of conventional rodenticides.

5. Public Comments

EPA provided the public two opportunities to comment on the methyl mercaptan pesticide product and the associated tolerance exemption petition through information presented in the Federal Register (FR). Between these two comment periods opened with FR publications (i.e., NOR and NOF), EPA received only one comment that it did not consider to be substantive.

Because the pesticide product contains methyl mercaptan, which is a new active ingredient, and involves this active ingredient's first food and outdoor uses, EPA opened a 15-day public comment period. EPA took this action in accordance with a policy, first implemented in October 2009, designed to provide a more meaningful opportunity for the public to participate in major registration actions. There were no comments received as part of that process.

6. Registration Decision

The methyl mercaptan database is considered to be complete and supports a pesticidal food use. In considering the assessed risk to human health and the environment, EPA concludes that methyl mercaptan meets the regulatory standard under FIFRA. Therefore, EPA is granting the registration of a pesticide product containing methyl mercaptan, a new active ingredient with a food use, under FIFRA section 3(c)(5).

One product is being registered – an EP, Protec-T (EPA File Symbol 87809-R), containing the new active ingredient methyl mercaptan. The EP is intended for use as a gopher repellent in certain types of irrigation lines (subterranean, surface drip, and micro irrigation systems). The repellency of methyl mercaptan is attributed to the putrid odor of the compound, which deters gophers from chewing or otherwise damaging irrigation lines through burrowing.

The risk assessments and label supporting this decision can be found in the associated regulatory docket (search for "EPA-HQ-OPP-2019-0368" at www.regulations.gov).