United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508W) | EPA-738-F-94-009 June 1994

R.E.D. FACTS

Maleic Hydrazide

Pesticide Reregistration

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

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency imposes any regulatory controls that are needed to effectively manage each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA announces this and explains why in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED for Case 0381, technical maleic hydrazide and maleic hydrazide potassium salt, referred to as maleic hydrazide.

Use Profile

Maleic hydrazide is a plant growth regulator (sprout inhibitor) and herbicide, that acts by inhibiting cell division in plants. It is used to control sprouting of potatoes and onions, suckers in tobacco, and growth of weeds, grasses and trees in/along lawns, turf, ornamental plants, non-bearing citrus, utility and highway rights-of-way, airports and industrial land. Most of the maleic hydrazide used in the U.S. is applied to tobacco (86-88%), followed by potatoes (11-12%).

Formulations include an emulsifiable concentrate and soluble concentrate/liquid and solid. Maleic hydrazide is applied by aircraft or ground spray equipment. Current use practice limitations prohibit treating crops within 7 days of harvest, and grazing or feeding forage or hay from treated areas to livestock.

Regulatory History

Maleic hydrazide was first synthesized in 1895 but its ability to regulate plant growth was not discovered until 1949. It was first registered as a plant growth regulator in 1952. In October 1976, maleic hydrazide went into Special Review (then called Rebuttable Presumption Against Registration or RPAR) because it met the risk criteria for oncogenic, mutagenic and reproductive effects.

A Data Call-In notice issued in August 1980 resulted in suspension of the diethanolamine salt of maleic hydrazide (DEA-MH) when its manufacturers did not submit the required data. All DEA-MH registrations now are cancelled.

Based on other data submitted, EPA determined that the oncogenicity and reproductive effects triggers were not supported, and that only weak evidence supported the mutagenicity trigger. In concluding the RPAR in June 1982, EPA allowed continued use of maleic hydrazide and its potassium salt (K-MH), but established an upper limit of 15 ppm for the contaminant hydrazine (associated with tumor induction) in technical grade maleic hydrazide. At this level, lifetime cancer risks for both dietary and worker exposure are not of concern.

The Registration Standard issued in June 1988 (NTIS #PB88-236849) continued to limit hydrazine in the technical product to 15 ppm. A Data Call-In issued in November 1992 required additional ecological effects and environmental fate data. Currently, 26 maleic hydrazide products remain registered including 4 technical grade/manufacturing-use product(s).

Human Health Assessment

Toxicity

In acute toxicity studies using laboratory animals, maleic hydrazide is practically non-toxic by the oral, dermal and inhalation routes and has been placed in Toxicity Category IV (the lowest of four levels) for these effects. It causes slight irritation to the eyes (Toxicity Category III) and skin (Toxicity Category IV), and is not a skin sensitizer.

Maleic hydrazide does not appear to cause any adverse developmental or reproductive effects of concern. The potassium salt (K-MH) was not found to be carcinogenic and has been classified as a "Group E" carcinogen--a chemical that is not considered to be a human carcinogen.

Maleic hydrazide and its potassium salt appear to be genotoxic (that is, they have the potential to affect DNA repair processes) at high doses in some mutagenicity tests. However, when all the available mutagenicity studies are considered together with the results of all the other toxicological studies on maleic hydrazide and its potassium salt, especially the negative cancer studies, the potential genotoxic hazard is considered negligible.

Dietary Exposure

People may be exposed to residues of maleic hydrazide in the diet when consuming potatoes, potato chips and other potato products made from potato granules; onions; and meat, milk, poultry and eggs.

Tolerances or maximum residue limits are established, and have been reassessed, for residues of maleic hydrazide in or on potatoes, potato chips, potato granules, potato waste (from processing), onions and cranberries (please see 40 CFR 180.175, 185.3900, and 186.3900). The potato and onion tolerances are acceptable, but an increased tolerance is needed for potato chips and new, food/feed additive tolerances are needed for potato granules and potato waste. The cranberry use is not on any currently registered product labels and is not supported for reregistration by its manufacturer. Unless another party decides to support this use, the tolerance should be revoked.

Tolerances are needed but have not yet been established for meat, milk, poultry or eggs. Animal feeding studies are being required in order to set these tolerances. Also, a confined rotational crop study is required to determine whether tolerances are needed for winter wheat planted as a rotational crop in fields treated with maleic hydrazide.

Compatible international Codex Maximum Residue Levels (MRLs) are established for potatoes and onions.

Based on reassessed tolerance levels for cranberries, onions, potatoes, potato chips, potato granules and potato waste, and based on upper bound residue levels for meat, milk, poultry and eggs, EPA estimates that the overall U.S. population is exposed to about 29.5% of the Reference Dose (RfD), or amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. Most of this exposure (27.5% of the RfD) is contributed by potatoes. For children age 1-6 and non-nursing infants, the two most highly exposed subgroups, the TMRC represents about 60% of the RfD. These TMRCs are overestimates, however; and actual chronic dietary risk (of decreased body weight gain) posed by maleic hydrazide is minimal.

Occupational and Residential Exposure

Pesticide handlers (mixers, loaders and applicators) may be exposed to maleic hydrazide via the inhalation and dermal route. However, based on the lack of toxicological concerns with maleic hydrazide, the risk is considered minimal for all workers.

Smokers and others near them may be exposed to maleic hydrazide and the contaminant hydrazine as pyrolysis products from tobacco. However, increased levels of hydrazine are not expected, so the risk is no greater than that already associated with the use of tobacco.

Human Risk Assessment

Maleic hydrazide is of low acute toxicity. It has been shown to cause genotoxic effects in some mutagenicity studies. However, in view of several negative cancer studies, its genotoxic hazard is considered negligible. The contaminant hydrazine has been shown to induce tumors. However, EPA has set an upper limit of $\leq$ 15 ppm hydrazine in technical grade maleic hydrazide products. This level alleviates any concern of lifetime cancer risk to humans considering both dietary and worker exposure.

Environmental Assessment

Environmental Fate

Maleic hydrazide is mobile, especially in sandy soils, but not persistent in the environment. It therefore is not likely to impact groundwater quality. It could contaminate surface waters, however, if it is washed into anaerobic soil zones by rainfall soon after application. EPA is requiring a surface water label advisory to address this concern.

When maleic hydrazide is aerially or air-blast sprayed, drift from use sites could affect non-target crops or endangered plant species.

Ecological Effects

In acute toxicity studies, maleic hydrazide is "practically nontoxic" to birds, fish, invertebrates and honey bees. It is considered to pose minimal risks to birds, mammals, aquatic organisms, non-target insects and aquatic plants.

Maleic hydrazide may pose risks of concern to non-target terrestrial and semi-aquatic plants as a result of runoff from ground application, and runoff and drift from aerial and air-blast applications.

Ecological Effects Risk Assessment

Maleic hydrazide does not pose risks to ground water but it has the potential to contaminate surface water. It also may drift from target use sites when it is aerially or air-blast applied. EPA is requiring that a surface water advisory statement and spray drift management information be added to maleic hydrazide end-use product labels to address these concerns.

Maleic hydrazide poses minimal acute risks to birds, mammals, aquatic species, insects and non-target aquatic plants, but exceeds levels of concern for non-target semi-aquatic and terrestrial plants. To mitigate exposure to non-target plants, EPA is requiring that the number of applications to fallow land, rights-of-way, turf and lawns be limited to one per year.

EPA has concerns about the exposure of endangered plant species to maleic hydrazide. These concerns will be addressed through implementation of the Endangered Species Protection Program.

Additional Data Required

EPA is requiring the following additional generic data for maleic hydrazide to confirm its regulatory assessments and conclusions:

Nature of the residue in animals;

Analytical method for residue in animals;

Magnitude of the residue in animal commodities;

Confined rotational crop;

Droplet size spectrum; and

Drift field evaluation.

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

Product Labeling Changes Required

All maleic hydrazide end-use products must comply with EPA's current pesticide product labeling requirements, and with the following:

Worker Protection Standard (WPS) - All maleic hydrazide products within the scope of the Worker Protection Standard (WPS) for Agricultural Pesticides (see PR Notice 93-7) must, within the timeframes listed in PR Notices 93-7 and 93-11, revise their labeling to be consistent with the WPS, as directed in those notices and the requirements of the RED.

Surface Water Advisory - All end-use labels must be revised to bear the following statement:

> "Under some conditions, maleic hydrazide may have a significant potential for runoff into surface water (primarily via dissolution in runoff water), for several days post-application. Conditions favoring runoff include poorly draining soils or wet soils with readily visible slopes, frequently flooded areas, areas where an intense or sustained rainfall is forecast to occur within 48 hours, areas overlying extremely shallow ground water, and areas overlying tile drainage systems that flow to surface water."

Application Rates - Application rates must be provided for all uses. In instances where labels indicate to spray to "drip-point," labels must clearly state the maximum application rate per acre. For fallow land, lawns, turf and rights of way uses, labels must indicate that the number of applications is limited to one per year.

Regulatory Conclusion

The use of currently registered pesticide products containing maleic hydrazide and the potassium salt of maleic hydrazide in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these currently registered products are eligible for reregistration. (The cranberry use of maleic hydrazide, which is not on any currently registered product labels, is not among the uses eligible for reregistration.)

Eligible maleic hydrazide products will be reregistered once the required confirmatory generic data, product specific data, Confidential Statements of Formula and revised labeling are received and accepted by EPA.

Products which contain active ingredients in addition to maleic hydrazide will be reregistered when all of their other active ingredients also are eligible for reregistration.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for maleic hydrazide during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Following the comment period, the maleic hydrazide RED document will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

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

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, from 8:00 am to 6:00 pm Central Time, Monday through Friday.