

US EPA ARCHIVE DOCUMENT



R.E.D. FACTS

Pesticide Reregistration

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

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

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document and the *Amendment to the 2003 Imazalil RED* for reregistration case 2325, imazalil.

Use Profile

Imazalil is a systemic fungicide for post harvest use on bananas, citrus, and preplanting seed treatments of barley and wheat. Its only nonfood use is for chicken hatchery treatments. There are no residential or public health uses. Approximately 6000 lbs. a.i. of imazalil are used annually. It can be applied by seed treatment equipment, drenches, waxing and foaming equipment, handwand sprayers and smoke canisters. There are 15 registered products including two technical grade products. Formulations include Magnate technical (98.50-98.94% active ingredient), one impregnated material (14.9% a.i.), four liquids (up to 31% a.i.), seven emulsifiable concentrates (up to 68.25% a.i.), and a flowable concentrate (10% a.i.). Impregnated material is used in smoke generators.

Regulatory History

Imazalil was first registered by Janssen Pharmaceutica (FIFRA Section 3) in 1983. Since then, imazalil has continuously had one or more FIFRA Section 3 registrations for postharvest use on citrus fruits against various fungi. In 1984, the Agency first registered imazalil for use as a seed treatment, and in 1990 for use in chicken hatcheries.

EPA completed the tolerance reassessment for imazalil on July 12, 2002. The Agency concluded that there is a reasonable certainty of no harm to any population subgroup from aggregate exposure to imazalil from dietary (food and water) exposure and all other non-occupational sources for which there is reliable information.

Human Health Assessment

Toxicity

Imazalil is classified as “Likely to be carcinogenic in humans,” according to EPA’s July 1999 Draft Guidelines for Carcinogenic Assessment. Carcinogenicity studies in rodents indicate imazalil is carcinogenic to male Swiss albino mice and Wistar rats based on a significant increase in liver adenomas and combined adenomas/carcinomas. Based on current science policy and absent information supporting a mode of action in test animals, EPA quantified the human cancer risk by a linear low-dose (Q_1^*) extrapolation. The most potent unit risk, $Q_1^*(\text{mg/kg/day})^{-1}$ for imazalil based on male mouse liver adenoma and/or carcinoma combined tumor rates is $6.1 \times 10^{-2} (\text{mg/kg/day})^{-1}$ in human equivalents. In rats, there was also an increased incidence of combined thyroid follicular cell adenomas/carcinomas. In addition, imazalil is placed in Category II, II, and IV for oral, dermal and inhalation toxicity respectively. It is highly irritating to the eye (Category I), but is not a skin irritant (Category IV) or a dermal sensitizer.

Dietary Risks

EPA determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to imazalil when considering dietary (food and water) exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Both acute and chronic dietary exposure were below the Agency’s level of concern.

For acute dietary exposure, the most sensitive group, females 13-50 years of age, was 15% of the acute Population Adjusted Dose (aPAD) at the 99.9th percentile. For chronic dietary exposure, the most highly exposed group was children 1-6 years old at 3% of the chronic Population Adjusted Dose (cPAD). Imazalil was not expected to reach drinking water sources at high concentrations due to its immobility. Drinking water models showed that the estimated environmental concentration (EEC) for groundwater was negligible. The acute surface water EEC of 0.072 ppb is less than the acute drinking water level of comparison (aDWLOC) of 500 ppb, while the

chronic surface water EEC of 0.037 ppb is less than the chronic drinking water level of comparison (cDWLOC) of 25 ppb, thus drinking water exposure is below the Agency's level of concern. The lifetime cancer risk estimate, largely associated with the use of imazalil on citrus, was 2.0×10^{-6} , and thus presents no concern to the Agency. This estimate did not include water because water was well below the Agency's level of concern and is not expected to contribute significantly to exposure.

Residential and Other Nonoccupational Risks

There are no registered residential uses of imazalil and thus residential exposure is not expected.

FQPA Considerations

EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to imazalil when considering dietary (food and water) exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information.

EPA did not perform a cumulative risk assessment as part of this reassessment of imazalil because the Agency has not determined that there are any other chemical substances that have a similar mechanism of toxicity.

Worker Risks

Occupational workers can be exposed to a pesticide through mixing, loading, and/or applying a pesticide, or re-entering treated sites. Occupational handlers of imazalil include the following: individual farmers or growers who mix, load, and/or apply pesticides and professional or custom agricultural applicators. Non-cancer risk for all of these potentially exposed populations is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to a No Observed Adverse Effect Level (NOAEL) taken from an animal study. For imazalil, MOEs greater than 100 do not exceed the Agency's level of concern. With additional personal protective equipment (PPE) and label changes, all worker exposure scenarios have MOEs greater than 100. Cancer risk estimates ranged from 2.0×10^{-3} to 1.0×10^{-7} using conservative exposure assumptions. The following scenarios have cancer risk estimates that exceed the Agency's level of concern.

- **Handlers lighting smoke generators.** Cancer risk was calculated at 2.0×10^{-3} based on the assumption that exposure lasted one minute and the entire contents of the canister were released immediately. The Agency believes this over estimates exposure because it is industry practice to leave the area after lighting the canister and the smoke is released over a couple of minutes. Nonetheless, the Agency is requiring that labels instruct handlers to vacate the area immediately after lighting the canister and prohibiting re-entry until ventilation has occurred.

- **Citrus handlers.** Cancer risk was calculated at 7.0×10^{-4} based on fruit packers wearing no PPE. The Agency believes this over estimates exposure because calculations were based on an assumption of 100% dermal exposure but recently submitted data show the potential transfer of pesticide from citrus to handler is less than 2%. Therefore, exposure would be reduced 50-fold.
- **Loading/applying on-farm seed treatment.** Cancer risk was calculated at 2.0×10^{-4} based on handlers wearing gloves using a dust formulation. The Agency believes this over estimates exposure because imazalil is an emulsifiable concentrate which is shown to have significantly lower dermal exposures. Nonetheless, the Agency is requiring chemical resistant gloves and aprons during on-farm seed treatment.

Environmental Assessment

Ecological Fate

Imazalil is moderately water soluble, very stable to hydrolysis, photo degrades relatively rapidly, degrades very slowly in soil under aerobic conditions, is immobile in soils, is not expected to volatilize, and has a high octanol water partition coefficient.

Ecological Risks

Based on the above environmental fate properties, and with consideration of the product formulations, the application methods, and the application rates, EPA believes that the immobile parent compound is not likely to be found in significant concentrations in the environment. Although persistent in aerobic soil, the seed treatment with a low application rate (0.01 lbs. a.i./A) is the only use that comes in contact with soil.

Risks to Terrestrial and Aquatic Organisms

Imazalil does not exceed acute or chronic levels of concern (LOCs) for freshwater fish, invertebrate, avian, and mammalian species due to extremely low exposure, which is attributable to the low application rate (0.01 lbs. a.i./A) and the seed treatment end-use (only 1% residue was left on soil surfaces). Imazalil is practically non-toxic to seed eating avian and mammalian species. In addition to the seed treatment, all other uses occur within contained areas or structures and no exposure is expected.

Imazalil does not exceed levels of concern for endangered species. The acute risk quotients (RQs) for freshwater fish (0.00005), invertebrate (0.00002), avian (0.00003), and mammal species (0.0002) are all below the endangered species LOC. Because of the extremely low exposure and relatively low toxicity to freshwater organisms, all acute and chronic toxicity testing has been waived.

**Risk
Mitigation****Dietary Risk**

Although EPA determined that there is reasonable certainty that no harm to any population subgroup will result from aggregate exposure to imazalil when considering dietary (food and water) exposure for which there is reliable information, the following risk mitigation measures and label changes are required in order to be eligible for registration.

- This product may not be used when egg or poultry is present.

Occupational Risk

For the potential occupational risks associated with use of imazalil, the use of chemical resistant gloves is necessary for the following scenarios:

- Mixing/loading liquid for on-farm seed treatment.
- Mixing/loading liquid for drenched application.
- Mixing/loading liquid for waxing equipment.
- Mixing/loading liquid for foaming equipment.
- Handling for commercial seed treatment.
- Mixing/loading and applying liquid with commercial seed treatment equipment.
- Mixing/loading/applying seed treatment for on-farm seed treatment.
- Handling used smoke canisters for disposal.

To further address occupational risk concerns for imazalil use in chicken hatcheries in which smoke canisters are used. The following label changes must be made:

- All workers must immediately leave the treatment area after lighting the smoke canister.
- All workers must be prohibited from reentering the treated area while smoke is still visible.
- Workers must be prohibited from reentering unventilated areas for 12 hours following application. For mechanically ventilated areas, workers may reenter two hours after application.

In order to assure that workers are not exposed when imazalil is applied to citrus in truck-beds, the following label statements must be added:

- Stay outside the treatment area until citrus is treated and drained.
- The windows and doors of the transport vehicle must be closed prior to treatment.

Ecological Risk

Based on the Agency's risk assessment, none of the RQ values exceed the Agency's level of concern for either terrestrial or aquatic non-target organisms, and minimal risk to the environment is expected. No environmental risk mitigation is necessary at this time.

Additional Data Required The confirmatory data required to complete the generic data base and/or refine the dietary, occupational and ecological risk assessments from the RED are listed below. These studies include data requirements listed in the July 12, 2002 TRED.

- OPPTS GLN 870.6300 Developmental Neurotoxicity in Rats
- OPPTS GLN 870.6200 Acute Neurotoxicity Study in Rats
- OPPTS GLN 870.6200 Subchronic Neurotoxicity Study in Rats
- OPPTS GLN 860.1200 Direction for Use
- OPPTS GLN 860.1340 Residue analytical method-Animal Commodities
- OPPTS GLN 850.4400 Tier I aquatic plant growth studies with two species of aquatic plants (*Lema gibba* and *Selenastrum capricornutum*).
- OPPTS GLN 830.7050 UV/Visible Light Absorption

Regulatory Conclusion The use of currently registered products containing imazalil in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment if the risk mitigation measures and label changes outlined in the RED and the *Amendment to the Imazalil 2003 RED* are implemented. Therefore, all uses of these products are eligible for reregistration. These products will be reregistered once the required product specific data, confidential statements of formula (CSFs), and revised labeling are received and accepted by EPA. Products which contain ingredients in addition to imazalil will be reregistered when all of their other active ingredients also are reregistered.

For More Information To obtain a copy of the imazalil RED document, please contact the OPP Public Docket (7502C), US EPA, Ariel Rios Building, 1200 Pennsylvania Avenue, NW, Washington, DC 20460-0001, telephone: (703) 305-5805. Electronic copies of the imazalil RED and all supporting documents are also available on the Agency's website at <http://www.epa.gov/oppsrrd1/reregistration/status.htm>.

For more information about EPA's pesticide reregistration program or the imazalil RED, please contact the U.S. EPA, OPP, Special Review and Reregistration Division (7508C), Washington, DC 20460-0001, telephone: (703) 308-8000.

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