

US EPA ARCHIVE DOCUMENT



R.E.D. FACTS

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 humans 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 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 the safety standard of the FQPA 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 for ethoxyquin (Chemical Code No. 055501; Case No. 0003).

Use Profile

Ethoxyquin is registered for use as an antioxidant to control scald (browning) in pears. It is applied post-harvest by spraying/drenching, paper wrapping, or a combination thereof. Currently only two formulation types are registered for this chemical, which includes an emulsifiable concentrate (1 product) and an impregnated wrap (3 products). Production of ethoxyquin is estimated to be less than 25,000 lbs. active ingredient over the past five years (averaging less than 5,000 lbs. active ingredient per year); hence, ethoxyquin is being considered a minor use chemical. Ethoxyquin is also regulated by the Food and Drug Administration for its use as a preservative in animal feed, dehydrated crops and sorghum, and as an antioxidant for the preservation of color in the production of chili powder, paprika, and ground chili.

Regulatory History

Ethoxyquin was developed by Monsanto in the 1950's. Ethoxyquin was initially registered as a pesticide in 1965 as an antioxidant used as a deterrent of scald in pears through post-harvest indoor application via a drench and/or

impregnated wrap. There are three companies, Decco, Ceraxagri, Inc., and Wrap Pack, Inc., who are ethoxyquin registrants.

Human Health Assessment Toxicity

The ethoxyquin risk assessment was done using a streamlined process for lower risk/ exposure pesticide chemicals. Although the ethoxyquin toxicology database is not complete, the toxicology database provides adequate information for evaluating and characterizing the risks under FIFRA and FQPA for the limited use of this chemical. Ethoxyquin has low to moderate acute toxicity by the oral (Category III), dermal (Category III), and inhalation (Category III) exposure routes. It is not an eye irritant (Category IV), and it produces minimal irritation to the skin (Category IV). Tests in animals show it to have a weak sensitizing potential, and extensive human experience from the use of this chemical showed strong association with contact dermatitis that ceased upon discontinuation of working in an ethoxyquin environment. The primary target organs affected by ethoxyquin in experimental animals are the liver and the kidneys, and studies indicate that ethoxyquin is not a teratogen or a developmental toxicant in rats or rabbits. There is low concern (and no residual uncertainty) for pre- and/or postnatal toxicity resulting from exposure to ethoxyquin.

Ethoxyquin has not been tested for its carcinogenic potential, though a closely related chemical, 1,2-dihydro-2,2,4-trimethylquinoline, showed some evidence of carcinogenic activity in rats. The only suggestion of a potential carcinogenic effect for ethoxyquin came from a Manson et al (1987) study. For more information please see the accompanying RED document.

Dietary Risks

The ethoxyquin dietary assessment included food exposure from EPA registered pesticidal use in pears as well ethoxyquin's FDA approved uses as an antioxidant in feeds (e.g., meat, poultry, eggs) and as a food preservative (e.g., spices). In the assessment, the Agency concluded that the residue of concern remains the parent ethoxyquin (40 CFR § 180.178). The current tolerance for ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) is in pears for pre or post-harvest use. The Agency is proposing the tolerance expression be amended for post-harvest use only. The Codex MRL residue definition and the U.S. tolerance definition will be compatible after amending the ethoxyquin tolerance expression. For the overall U.S. population and all subgroups as measured by the Population Adjusted Dose (PAD), both the acute and chronic endpoint analyses were below the Agency's level of concern.

To ensure safety in the absence of ethoxyquin- specific carcinogenicity studies, a bounding Q^*_1 of $0.04 \text{ (mg/kg/day)}^{-1}$ was created as a possible dietary endpoint for ethoxyquin, and included an assessment of the FIFRA use on pears, the FDA regulated uses on spices as a food preservative and the antioxidant use in feeds from which secondary residues may result in meat, poultry, and eggs. The

conservative assessment produced an estimated cancer risk of less than 2×10^{-6} which does not exceed the Agency's level of concern.

No drinking water scenarios are presented because ethoxyquin is indoor use only and waste water from the drench application onto the fruit is commonly recycled. There is very low likelihood of water contamination from the registered indoor use of ethoxyquin. A residential exposure assessment was not performed because there are no registered products containing ethoxyquin that would result in residential exposure.

Worker Risks

Occupational assessment was based on non- cancer and potential cancer risk for ethoxyquin handlers and post- application workers. Non- cancer risk for potentially exposed populations is measured by a Margin of Exposure (MOE), which determines how close the occupational exposures come to a No Observed Adverse Effect Level (NOAEL). Potential occupational exposure scenarios include mixing/ loading for post-harvest treatments using drench/spray application methods, exposure during post-harvest sorting/packing/culling pears following ethoxyquin treatment, and handling treated pears wrapped in impregnated paper.

For mixing/loading, workers in the baseline assessment are assumed to be wearing long sleeved shirts and long pants. A MOE =100 is sufficient to protect occupational pesticide handlers. The mixer/loader scenario requires gloves be worn in order to achieve a MOE above 100 with gloves; the MOE for the mixer/ loader scenario is 1500 which does not exceed the Agency's LOC. The estimated lifetime cancer risk for a mixer/loader wearing gloves is 2.1×10^{-6} and does not exceed the Agency's LOC.

The Agency does not have data addressing the sorting/ packing/culling of products following ethoxyquin treatment. The estimates of exposure were derived from residue chemistry data, surface areas calculations, and a study found in scientific literature. Though commonly worn, gloves are not required by label for the sorting/packing/culling process. The scenario was assessed assuming no gloves. The MOE for the above scenario is greater than 1800, therefore the risks for sorting/packing/culling do not exceed the Agency's LOC. The estimated lifetime cancer risk for workers handling treated fruit is 1.8×10^{-7} ; this does not exceed the Agency's LOC.

Based on scenarios with true historical exposure data, exposure from impregnated paper would not exceed (i.e. negligible in comparison to drench/spray scenario) the exposure from handling treated pears after drenching/spraying.

FQPA Considerations

An aggregate exposure risk assessment was considered under FQPA, but because residential and water exposures are not anticipated to result from any of the current uses of ethoxyquin, the results are the same as the dietary risks, and below the Agency's level of concern.

In addition, unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to ethoxyquin and any other substances, and ethoxyquin does not appear to produce a toxic metabolite produced by other substances. For the purpose of this reregistration decision, therefore, EPA has not assumed that ethoxyquin has a common mechanism of toxicity with other substances.

Environmental Assessment

Ecological Risks

Because use patterns include only indoor uses, there is low likelihood of outdoor or water exposures, and risks to non-target species are not anticipated. Because the pesticidal use pattern of ethoxyquin includes only the indoor food processing of pears, EPA has concluded that outdoor environmental or water exposure is highly unlikely and any exposure to terrestrial wildlife or aquatic organisms would be negligible. Therefore, EPA has determined that the pesticidal uses of ethoxyquin discussed in the RED will have no effect on federally listed endangered and threatened species.

Summary

This Fact Sheet explains the Agency's decision regarding the reregistration eligibility of the registered uses of ethoxyquin. The Agency has found that the current uses of ethoxyquin are eligible for reregistration, provided the changes specified in the RED are made to the packaging and labels.

Additional Data Required

The generic database currently supports the use of ethoxyquin on pears, and no confirmatory studies are required in the reassessment of the chemical ethoxyquin for this use. Should a registrant petition for the use of ethoxyquin to be expanded, at a minimum, the following data would be required:

- A Teratology study in rabbits
- A 2-generation reproduction study
- A chronic oncogenicity study in rats
- A carcinogenicity study in mice
- A 21/28 dermal toxicity study

Product Labeling Changes Required

All ethoxyquin end-use products must comply with EPA's current pesticide product labeling requirements and with the following. For a comprehensive list of labeling requirements, please see the Ethoxyquin RED document.

Regulatory Conclusion

In order to be eligible for reregistration, all product labels are to be amended to incorporate measure outlined in the attached RED document. Furthermore, many of the existing labels for ethoxyquin need to be revised to provide clear use directions. EPA has determined that all mixer/loaders of ethoxyquin post-harvest application use must wear chemical resistant gloves.

**For More
Information**

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for ethoxyquin during a 60-day time period, as announced in a Notice of Availability published in the *Federal Register*. To obtain a copy of the ethoxyquin 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 ethoxyquin RED and all supporting documents are also available on the Agency's website at <http://www.cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg>.

For more information about EPA's pesticide reregistration program or the ethoxyquin 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>.