



R.E.D. FACTS

Pesticide Reregistration

Isofenphos

All pesticides sold or distributed in the United States must be registered by EPA. Registration decisions are based on scientific studies showing that the pesticide 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 studies from pesticide producers that are conducted to elucidate the human health and environmental effects of each pesticide. To implement provisions of the Food Quality Protection Act of 1996 (FQPA), EPA considers issues specific to infants and children, the aggregate exposure of the public to residues of the pesticide from all sources, and the cumulative effects of the pesticide and other compounds with a common mechanism of toxicity. The Agency develops mitigation measures or regulatory controls needed to reduce each pesticide's risks. EPA reregisters pesticides that meet the safety standard of FQPA and can be used without posing unreasonable risks to human health or the environment.

Isofenphos, an organophosphate (OP) pesticide (known in chemical nomenclature as 1-methylethyl 2-((ethoxy((1-methylethyl)amino)phosphinoyl)oxy)benzoate and designated as EPA case number 0105), was scheduled for a reregistration decision in 1999. Accordingly, EPA reviewed the existing database and developed preliminary human health and ecological risk assessments. In 1998, a public docket was opened and initial steps were taken to review Isofenphos along with the other organophosphate pesticides. Before EPA could complete the reregistration process, however, the basic producer of the pesticide gave official notification that they would no longer support Isofenphos through reregistration. EPA then took the necessary administrative steps to process a request to voluntarily cancel a pesticide, as discussed below in the History section.

The following information is based on an abbreviated review of the existing information on Isofenphos. As a result of the voluntary cancellation of the technical grade product, a final review for reregistration was not completed. The preliminary risk assessments were not revised, for example, as has been the case for the other organophosphate pesticides undergoing reregistration and tolerance reassessment.

Use Profile

Isofenphos, marketed under the basic producer's trade name Oftanol, is currently used in the United States on turf and ornamental trees and shrubs to control white grubs, mole crickets, and other insects (mostly subterranean species). According to recent usage data, about 60% of the Isofenphos active ingredient produced annually is used on golf courses; the remainder is used on residential and public turf sites.

History

Isofenphos, the common name for this phenyl derivative, organophosphorus insecticide, was first registered in the United States in 1980 by Bayer Corporation for use on corn for control of the corn rootworm. In recent years, all of the food uses and the various residential indoor uses (including the termiticide use) were dropped by the basic producer. As mentioned above, the remaining turf and ornamental uses of the pesticide are now no longer supported. The Agency was informed that the availability of pesticide alternatives persuaded the basic producer to discontinue manufacturing the technical material.

As required under the pesticide law, EPA announced in the Federal Register on January 15, 1999 (64 FR 2642), that the registrant who supports Isofenphos had requested voluntary cancellation. A second notice published in the Federal Register on May 26, 1999 (64 FR 28471), finalized that action and approved the registrant's phase out plan. The public, given 60 days to comment on the request for voluntary cancellation and the proposed phase out plan, provided no objection. The registrant has been granted various existing stocks provisions, as detailed in the final Federal Register cancellation notice. All food tolerances for Isofenphos have been revoked (effective January 1999).

Human Health Assessment

Toxicity

Although the human health assessment was not completed for Isofenphos, some preliminary conclusions were reached during the toxicology review. The toxicological database is otherwise adequate to support the reregistration of Isofenphos. Acute oral toxicity studies in male and female rats indicate that, like other organophosphate pesticides, oral exposure to Isofenphos induces cholinesterase inhibition. Acute toxicity categories, which are classified as I (most toxic) through IV (least toxic), included Category I for acute oral and dermal toxicity; Category II for inhalation toxicity; Category III for acute eye irritation; and Category IV for acute dermal irritation. Isofenphos is classified as a Group E carcinogen (that is, there was no evidence of carcinogenic potential in long-term studies in rats and mice).

Dietary Exposure

In the preliminary human health risk assessment, acute and chronic dietary (food source) evaluations were not conducted because at that time

there were no Isofenphos products registered for food or feed uses. Although there are no food or feed residue concerns, EPA was concerned about the potential for exposure to humans through the consumption of drinking water containing Isofenphos residues. The Agency evaluated the acute and chronic exposure possibilities. Using cholinesterase inhibition in the rat as the toxicological endpoint, EPA initially established the acute reference dose (RfD) (also commonly referred to as the population adjusted dose (PAD)) at 2 mg per kilogram of body weight per day (mg/kg/day). The purpose of the endpoint was to assess the acute dietary risk resulting from exposure to potentially contaminated drinking water. This value was based on the lowest observed effect level (LOEL) of 2.0 mg/kg/day from an acute neurotoxicity study in the rat. The study had not determined the conventional no observed effect level (NOEL). Additionally, in the absence of a developmental neurotoxicity study the Agency initially decided to retain the 10X FQPA safety factor, resulting in a total uncertainty factor of 3000.

EPA also established the chronic dietary RfD using the NOEL of 0.08 mg/kg/day from a 2-generation reproductive toxicity study in the rat. As before, the toxic effect observed in test animals was cholinesterase inhibition and the preliminary risk assessment described the use of an uncertainty factor of 1000, resulting in a chronic dietary RfD (or chronic PAD) of 0.00008 mg/kg/day.

Subsequent to the public release of the preliminary risk assessments, EPA reevaluated the selection of the 10X safety factor required by FQPA for Isofenphos in a comprehensive report for all organophosphates. While the preliminary human health risk assessment chapter retained the 10X factor, the comprehensive report recommended retaining only a 3X factor. This would have resulted in an adjustment to the RfDs or PADs discussed above.

In the drinking water risk assessment, modeling data were used for estimating surface and ground-water exposure. The modeled values from the preliminary assessment suggest that Isofenphos could pose a drinking water concern. However, the Agency concluded that the limited use associated with Isofenphos was not expected to impact water resources through labeled uses. Thus, EPA does not expect Isofenphos exposure to humans through drinking water.

Occupational and Residential Exposure

In the preliminary human health risk assessment, the Agency used the same acute oral neurotoxicity study as was used for the acute dietary assessment for assessing the short-term or residential dermal exposure risk (1-7 days)(see the previous discussion). For the intermediate term occupational or residential risk (one week to several months), a NOEL of 0.06 mg/kg/day (males) was obtained using a subchronic neurotoxicity screening study in the rat. These assessments assumed that 100% of Isofenphos would be dermally absorbed. The inhalation component of exposure was also added to derive a

total or aggregate exposure value for short and intermediate term exposure situations. No long-term/chronic exposures were expected from the use of Isofenphos. EPA used surrogate exposure data to estimate occupational and residential exposure to Isofenphos.

In general, EPA found that most occupational and residential exposure scenarios were of concern. The preliminary risk assessment provided exposure estimates to mixer/loaders, applicators and residents of such a magnitude that EPA would have pursued extensive exposure mitigation had the registrant not voluntarily canceled the pesticide. Post-application exposure scenarios were also of concern.

Environmental Assessment

The preliminary ecological risk assessment found that Isofenphos is toxic to birds, mammals, beneficial insects, freshwater and estuarine/marine fish, and aquatic invertebrates. When considering the pesticide's toxicity and exposure potential to non-target organisms, EPA found that acute and chronic levels of concern were exceeded for terrestrial animals and aquatic invertebrates. Chronic levels of concern were also exceeded for freshwater and estuarine/marine fish.

The environmental fate of Isofenphos is understood relatively well, but the Agency's knowledge of some aspects is still incomplete. While sufficiently persistent (with soil half-lives up to one year and field dissipation half-lives ranging from weeks to months), Isofenphos is not likely to move appreciably through the soil to ground water (unless ground water is particularly shallow). On the other hand, EPA believes that Isofenphos can be expected to move to surface water via runoff. As mentioned earlier, however, EPA does not believe that the limited use of the pesticide would lead to residues in drinking water.

Isofenphos' major degradate, Isofenphos oxon, is likely to be as toxic as the parent chemical. However, the persistence and fate of Isofenphos oxon is not known.

Additional Data Required

There are a number of outstanding data requirements for Isofenphos. At a minimum, a developmental neurotoxicity study, a 21-day dermal toxicity study in the rat (or dermal absorption study), an aerobic soil metabolism study (on a range of soil types), an aerobic aquatic metabolism study, additional environmental fate studies on the degradate Isofenphos oxon, and an estuarine/marine invertebrate chronic toxicity study would have been required if this chemical were to have continued with reregistration.

Conclusion

Voluntary cancellation is being accomplished in 3 steps:

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- Certain product registrations were canceled effective May 26, 1999. Sale and use of existing stocks is permitted until stocks are exhausted.
 - One product registration (Oftanol 2 insecticide) was canceled effective September 30, 1999. The registrant may sell and distribute existing stocks for one year after that date. Existing stocks already in the hands of dealers and users can be distributed, sold, and used until these stocks are exhausted.
 - Oftanol Technical will be canceled effective December 31, 1999. The registrant (Bayer) will discontinue any further sales or distribution of the technical product after that date. Sales in 1999 are limited to the level of 1998 sales.

For More Information

For more information about EPA's pesticide reregistration program or the pesticide Isofenphos, please contact Dean Monos at the Special Review and Reregistration Division (7508C), OPPTS, U.S. EPA, Washington, DC 20460; telephone 703-308-8074.

Electronic copies of this fact sheet and other REDs are available on the Internet. Please see <http://www.epa.gov/REDs>. The Isofenphos preliminary human health and ecological risk assessments are available at <http://www.epa.gov/pesticides/op/isofenphos.htm>.

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, between 9:30 am and 7:30 pm Eastern Standard Time, seven days a week. The NPTN website is <http://www.ace.orst.edu/info/nptn>.