

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 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 document for reregistration case 0266, hexazinone.

## Use Profile

Hexazinone is a herbicide used to control a broad spectrum of weeds including undesirable woody plants in alfalfa, rangeland and pasture, woodland, pineapples, sugarcane and blueberries. It is also used on ornamental plants, forest trees and other non-crop areas. Hexazinone is registered for pre-emergent, post-emergence, layby, directed spray and basal soil applications. It is used as a non-selective herbicide in non-cropland areas and as a selective herbicide in reforestation practices.

Hexazinone products are formulated as granulars, pellets/tablets, emulsifiable concentrates, ready-to-use liquids, soluble concentrates/solids and a technical grade active ingredient. Products are applied using aerial or ground equipment or by hand, or using a hand-held, boom, knapsack or power sprayer.

Use practice limitations prohibit application of hexazinone through any type of irrigation system. The pesticide also cannot be applied within 30 to 60 days before grazing, harvest or feeding.

## Regulatory History

Hexazinone is the common name for 3-cyclohexyl-6-(dimethylamino)-1-methyl-1,3,5 triazine-2,4(1H,3H)-dione. Hexazinone was first registered as a pesticide in the U.S. in 1975 for general weed control in non-cropland

areas. Use in the culture of Christmas and forest trees was added in 1977, and uses on sugarcane and alfalfa were conditionally registered in 1980 and 1981, respectively.

EPA issued one Registration Standard for hexazinone in February 1982 (NTIS #PB87-110292), and a second in September 1988 (NTIS #PB89-126080). These documents summarized available data supporting the registration of hexazinone products, and required additional product chemistry, residue chemistry, toxicology, ecological effects and environmental fate data.

EPA's Office of Drinking Water issued a drinking water Health Advisory (HA) for hexazinone in August 1988. A lifetime HA was established at 200 ppb for an adult consuming 2 liters of water per day. For a 10 kg child, a one- and ten-day HA was determined to be 2 mg/L.

Currently, 20 end-use pesticide products and one technical grade, manufacturing use product containing hexazinone are registered.

## Human Health Assessment

### Toxicity

Hexazinone is classified as a Group D carcinogen--a chemical that is not classifiable as to human carcinogenicity. Animal data presented to EPA is equivocal--it is not entirely negative, but not convincingly positive. The Agency has concluded that the evidence cannot be interpreted as showing either the presence or absence of a carcinogenic effect. Since hexazinone has not been found to induce cancer, food and feed additive regulations are not prohibited by the Delaney Clause of the Federal Food, Drug, and Cosmetic Act (FFDCA). The Reference Dose (RfD) approach was used to assess human risk from exposure to hexazinone.

In acute toxicity studies using laboratory animals, hexazinone has been shown to be a severe eye irritant and has been placed in Toxicity Category I (the highest of four levels) for primary eye irritation. It is slightly toxic through the acute oral route (Toxicity Category III) and very mildly toxic through the acute dermal and acute inhalation routes (Toxicity Category IV). Hexazinone is only mildly toxic for skin irritation potential (Toxicity Category IV) and is not a skin sensitizer.

Some treatment-related effects were found in developmental toxicity studies using rats and rabbits, at the high dose levels. Similarly, some effects were noted in a reproductive toxicity study at the mid- and high dose levels. Hexazinone was positive in one mutagenicity study but negative in the remaining studies. There are no other acute or chronic toxicological endpoints of concern.

### Dietary Exposure

People may be exposed to residues of hexazinone through their diet. EPA reassessed existing tolerances or maximum residue limits (please see 40 CFR 180.396) for blueberries, pineapple and sugarcane at the time of this RED. Tolerances for meat, meat byproducts and milk cannot be

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reassessed until a cattle feeding study is completed. However, sufficient data were available to conduct a risk assessment, and the Agency believes that the existing tolerances are protective until data are available for reassessment.

The Reference Dose (RfD) or amount believed not to cause adverse effects if consumed daily over a 70-year lifetime is 0.05 mg/kg/day based upon a No Observable Effect Level (NOEL) of 5 mg/kg/day in a one-year feeding study in dogs. EPA calculated that the Anticipated Residue Contribution (ARC) for the overall U.S. population from all hexazinone tolerances equals 7% of the RfD. The ARC for the subgroup most highly exposed, non-nursing infants age less than 1 year, represents 40% of the RfD, while the ARC for children age 1 to 6 years is 20% of the RfD. EPA's calculations overestimate exposure, however, by assuming 100% of crop treated for all commodities. Actual dietary risk from hexazinone is believed to be minimal. When current residue chemistry data gaps are filled, however, dietary exposure estimates for hexazinone could change.

Hexazinone concentrates in certain processed fractions of alfalfa, pineapple and sugarcane. EPA has determined that establishing food and feed additive tolerances for these commodities is appropriate and consistent with the Delaney Clause of the FFDCA, and that such tolerances must be established for alfalfa meal, pineapple processing residue and sugarcane molasses.

EPA's Office of Water has issued a lifetime Health Advisory (HA) which sets a maximum level of 0.21 mg/L, or 200 ppb allowable in drinking water. No international CODEX Maximum Residue Limits are established for hexazinone so compatibility with U.S. tolerances is not an issue.

### **Occupational and Residential Exposure**

Based on current use patterns, workers may be exposed to hexazinone during and after applications in agricultural and other settings. In assessing handler and post-application exposure, Agency concerns are predominantly related to skin contact. Hexazinone is poorly absorbed through the skin, so little or no absorption is anticipated. Therefore, no changes in personal protective equipment (PPE) required by the Worker Protection Standard (WPS) are being imposed at this time. However, the Restricted Entry Interval (REI) is being changed from 24 to 48 hours because hexazinone is in Toxicity Category I for primary eye irritation.

There are no residential uses of hexazinone, so residential exposure is not expected.

### **Human Risk Assessment**

Hexazinone generally is of relatively low acute toxicity but is a severe eye irritant (Toxicity Category I). It is not classifiable as to human carcinogenicity (Group D carcinogen) and does not cause other toxic effects of concern.

The dietary risk posed by hexazinone is expected to be minimal. Most tolerances were reassessed and other existing tolerances are considered protective until confirmatory data are available for reassessment. A lifetime Health Advisory sets a maximum level of exposure to hexazinone from drinking water.

Exposure to workers and other applicators generally is not expected to pose undue risks, due to hexazinone's overall low acute toxicity. However, based on toxicity concerns regarding primary eye irritation, a 48-hour rather than a 24-hour REI is required.

## **Environmental Assessment**

### **Environmental Fate**

Based on laboratory data and confirmed by field and forestry data, hexazinone appears to be persistent and mobile in soil and aquatic environments. The degradates of hexazinone also are believed to be persistent and mobile. Hexazinone was reported in runoff water up to 6 months post-treatment in a forestry dissipation study. Therefore, field and laboratory data indicate that hexazinone may be of concern for both groundwater and surface water contamination.

Hexazinone has been detected in ground water (at levels well below the Health Advisory) in Hawaii, Florida, Maine and North Carolina. Hexazinone also can contaminate surface water by spray drift at application, and for several months post-application via runoff. It is not expected to accumulate in fish but does accumulate in crops grown on treated soil.

### **Ecological Effects**

Hexazinone is practically non-toxic to birds on an acute oral and subacute dietary basis. It is practically non-toxic to freshwater fish and freshwater invertebrates in acute exposures. Hexazinone is practically nontoxic to mollusks, slightly toxic to crustaceans, and relatively non-toxic to honey bees.

### **Ecological Effects Risk Assessment**

Exposure of non-target organisms to hexazinone can result from direct application, spray drift from treated areas, and runoff from treated areas. Such exposure would be chronic as well as acute.

Hexazinone exceeds the levels of concern (LOC) for terrestrial and aquatic plants, at all application rates, using aerial and ground equipment. Contamination of aquatic sites adjacent to treated areas could be of great ecological significance and may be exacerbated by the persistence and mobility of hexazinone.

Aquatic plants are an important component of the ecosystem. Algae are the link between solar radiation, aquatic animals and humans, which are dependent on the oxygen produced by algae during photosynthesis. Algae are responsible for maintaining the quality of the aquatic habitat for fish, while at the same time providing food for fish either directly or indirectly. Effects to aquatic plants expected from the use of hexazinone may alter

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aquatic ecosystems, the severity of which is dependent on the frequency of application and the nature of the receiving body of water.

Hexazinone also exceeds the LOC for small mammals at several of the higher application rates.

### **Risk to Endangered Species**

Hexazinone exceeds the endangered species LOCs for grass- and insect-eating mammals at use rates of 3.6 pounds active ingredient per acre (lb ai/acre) or greater. It also exceeds the LOCs for both aquatic and terrestrial plants at all use rates.

### **Risk Mitigation Measures**

Hexazinone exceeds the levels of concern for both aquatic and terrestrial plants, and exceeds levels of concern for small mammals at several of the higher application rates. Hexazinone also is likely to have a significant impact on ground water quality. In areas where irrigation water is contaminated with hexazinone or where ground water discharges to surface water, hexazinone residues in water could pose a threat to plants. Therefore, the following risk mitigation measures are required:

- All hexazinone product labels must carry a ground water advisory;
- Registrants must report any domestic hexazinone ground water detections at any levels to EPA;
- The registrant must prepare a report summarizing ongoing research regarding ground water detections in the State of Maine;
- The registrant also must submit to EPA the educational materials under development regarding product stewardship and addressing the potential for ground water contamination from use of hexazinone;
- A prospective ground water monitoring study must be conducted to determine the potential for hexazinone to leach to ground water;
- To address surface water concerns, precautionary label language will be required;
- To address the risk to nontarget plants and small mammals, the maximum application rate must be reduced from 13.5 lb ai/acre to 8 lb ai/acre.
- To inform the user of best management practices to minimize spray drift, EPA is preparing labeling statements that may be required in the future for all aerially-applied hexazinone products;
- To address endangered aquatic and terrestrial plant species as well as endangered small mammal concerns, endangered species precautionary labeling will be required in the future;



- Hexazinone may be classified as a Restricted Use Pesticide for ground water concerns once the Agency's Ground Water Restricted Use Rule is finalized.

### Additional Data Required

The Agency is requiring additional generic data on hexazinone's residue chemistry, ecological effects and environmental fate. The following confirmatory generic studies are required: residue analytical methods (ruminant only), magnitude of the residue grass hay and alfalfa seed screenings, magnitude of the residue in meat/milk, storage stability (alfalfa and Metabolite C for grass), rotational crops (sorghum and leafy vegetable), seed germination/seedling emergence (cucumber, onion, pea), vegetative vigor (cucumber), batch equilibrium, aquatic sediment dissipation, spray drift, and a prospective groundwater monitoring study.

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

### Product Labeling Changes Required

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

**Worker Protection Standard (WPS)** - EPA has evaluated the 24-hour interim REI established by the WPS and concluded that it should be changed to 48 hours because hexazinone is in Toxicity Category I for primary eye irritation. The new 48-hour REI must be inserted into the standardized REI statement required by PR Notice 93-7.

The PPE for early entry under the 48-hour REI for hexazinone is coveralls, chemical resistant gloves, shoes plus socks, and protective eyewear. These PPE must be inserted into the early entry PPE statement required by PR Notice 93-7.

**Ground Water Labeling Advisory** - All products must carry the following advisory:

"This chemical is known to leach through soil into ground water under certain conditions as a result of agricultural use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in ground water contamination."

**Surface Water Labeling** - The technical manufacturer of hexazinone is in the process of consolidating label language relating to surface and ground water for all of their hexazinone products. After the Agency has reviewed and approved these label amendments, all hexazinone labels must carry this labeling.

#### Other Ground Water Requirements

- Registrants must report any domestic hexazinone ground water detections at any levels to the Agency.
- The registrant must prepare and submit a report summarizing the ongoing research in Maine regarding ground water

detections in blueberry use areas. This report must be submitted within one year from receipt of the RED document. The registrant also must prepare a one year follow-up to the original report.

- The registrant also must submit an analytical method or immuno assay for detection of hexazinone in ground water, within one year after receipt of the RED document.
- The registrant is required to submit educational materials that are currently being developed to the Agency. These materials should be in specific regard to product stewardship and should address the potential for ground water contamination from use of hexazinone.

**Risk to Non-Target Plants and Small Mammals** - To mitigate the risk to non-target plants and small mammals, registrants must reduce the maximum application rate from 13.5 lb ai/acre to 8 lb ai/acre.

**Spray Drift Label Advisory** - The Agency is preparing spray drift labeling statements to inform users of management practices that would minimize spray drift from the target site. This future labeling may be required for all hexazinone products that may be applied aerially to agricultural crops.

**Endangered Species Statement** - EPA is working with the Fish and Wildlife Service and other Federal and State agencies to develop a program to avoid jeopardizing the continued existence of identified species by the use of pesticides. When this program goes into effect, endangered species precautionary labeling will be required.

## Regulatory Conclusion

The use of currently registered products containing hexazinone in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

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

## For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for hexazinone 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.

Electronic copies of the RED and this fact sheet can be downloaded from the Pesticide Special Review and Reregistration Information System at 703-308-7224, and also can be reached on the Internet via *FEDWORLD.GOV* and EPA's gopher server, *EARTH1.EPA.GOV*.



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Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-0419, telephone 513-489-8190, fax 513-489-8695.

Following the comment period, the hexazinone 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 hexazinone RED, or reregistration of individual products containing hexazinone, 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, between 8:00 am and 6:00 pm Central Time, Monday through Friday.