



R.E.D. FACTS

Pesticide Reregistration

Daminozide

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 daminozide, or butanedioic acid mono (2,2-diemthylhydrazide), also known by the trade name Alar.

Use Profile

Daminozide is a systemic growth regulator registered for use on ornamentals, including potted chrysanthemums and poinsettias, and bedding plants in enclosed structures such as greenhouses, shadehouses and interiorscapes. It is formulated as a soluble concentrate and applied as a pre-plant dip and/or foliar spray.

Regulatory History

Daminozide was initially registered as a pesticide in the United States in 1963 for use on potted chrysanthemums. The first food use, apples, was registered in 1968. EPA issued a Registration Standard for daminozide in June 1984 (NTIS PB87-104782), requiring additional product and residue chemistry, toxicology, worker exposure, ecological effects and environmental fate data.

In July 1984, EPA initiated a Special Review of pesticide products containing daminozide based on findings that daminozide and its degradate and metabolite, unsymmetrical dimethylhydrazine (UDMH), were oncogenic (caused the growth of tumors) at multiple organ sites, in multiple species and strains of test animals. The Agency issued a Data Call-In in 1986 requiring additional toxicology and worker exposure data. As a result of the Special Review, the registrant, Uniroyal Chemical Company, voluntarily cancelled all food use registrations of daminozide on November 14, 1989. EPA revoked the tolerances (maximum residue limits) for these food uses in March 1990.

EPA continued to evaluate the risks to workers (mixers, loaders and applicators) posed by the remaining non-food uses of daminozide, and found that those uses did not pose an unreasonable risk. The Agency allowed the non-food uses to continue in completing the Special Review of daminozide in October 1992.

Currently, four products (two end-use, one technical and one formulation intermediate) containing daminozide are registered in the U.S.

Human Health Assessment

Toxicity

Daminozide is of very low acute and subacute toxicity. It is placed in Toxicity Category IV, indicating the lowest level of acute toxicity, for oral and inhalation effects, and is placed in Toxicity Category III, indicating a slightly greater degree of acute toxicity, for dermal effects. A subchronic feeding study using rats did not produce any discernable toxic effects.

In carcinogenicity studies using mice, daminozide caused some increase in the incidence of malignant and benign tumors. UDMH caused a slight increase in liver tumors in rats, and produced liver vascular tumors and lung tumors in mice. EPA has classified UDMH as a Group B2, "probable human carcinogen." Since UDMH is dependent on the presence of the parent chemical, daminozide also has been classified as a Group B2 carcinogen.

Daminozide produced some maternal toxicity but no developmental toxicity in rats and rabbits. In a reproduction study using rats, daminozide caused systemic toxicity at the highest dose levels, but did not cause reproductive toxicity. Neither daminozide nor UDMH have been shown to cause mutagenic effects. In metabolism studies, daminozide was rapidly excreted by minipigs.

Dietary Exposure

There are no longer any registered food or feed uses of daminozide, and all tolerances have been revoked. Dietary exposure therefore is not anticipated.

Occupational and Residential Exposure

EPA performed a detailed analysis of the cancer risk to workers (mixers, loaders and applicators) from exposure to daminozide and UDMH. The total risk is a sum of the risk from direct exposure to daminozide (which is converted to UDMH when it is absorbed through the skin or lungs), plus the risk from exposure to the UDMH contaminant in commercial products (which increases in the mixing tank, prior to application).

EPA estimated risks from dermal and inhalation exposure to daminozide and UDMH for large greenhouse and small greenhouse uses, assuming application of fine spray (which would result in the greatest exposure). The estimated combined cancer risks range from 1.4 in 1 million (for workers in large greenhouses) to 5.8 in 10 million (for workers in small greenhouses). EPA considers these estimated risks to be reasonable.

In view of the known toxicological properties of daminozide and UDMH, however, as well as the likelihood of foliar residues, EPA is strengthening the current 24 hour Reentry Interval, which allows workers to reenter treated areas during the 24 hours after application if they wear protective clothing. The Agency instead is requiring a 24-hour Restricted Entry Interval, which prohibits reentry to perform hand labor for 24 hours following treatment except under very narrow circumstances, described in the Worker Protection Standard (WPS) for Agricultural Pesticides.

EPA also is requiring personal protective equipment (PPE) for early entry workers, consistent with that required for pesticides classified as Toxicity Category II for acute dermal toxicity. Post-application exposure to daminozide is mostly on the hands from handling treated plants. Therefore, for early entry as allowed by the WPS, level II PPE including chemical-resistant gloves must be used.

Human Risk Assessment

Daminozide does not pose human dietary risks since food-related uses are no longer registered and dietary exposure is not anticipated.

Greenhouse workers may be exposed to daminozide dermally or by inhalation, during or after application of the pesticide to plants. Risks from this exposure should be mitigated by observing the more stringent 24-hour Restricted Entry Interval and, in cases where reentry is necessary, by using the required personal protective equipment including chemical-resistant gloves. Daminozide is not expected to cause an unreasonable cancer risk to workers when used in accordance with these requirements, which will be reflected in product labeling as a result of this RED.

Environmental Assessment

Environmental Fate

Daminozide is stable to hydrolysis (it does not decompose readily by reaction with water); hydrolysis does not contribute significantly to the dissipation of daminozide in the environment. However, daminozide degrades rapidly in soil, leaving only volatile compounds and bound residues, including low levels of the degradate formaldehyde. Thus, its mobility probably is not a concern. Since registered products are labeled only for use in confined greenhouse areas, daminozide is not expected to occur in agricultural runoff or ground water.

Ecological Effects

Since daminozide may be applied only inside greenhouses, eco-toxicity data were used only to evaluate the hazard to non-target organisms that could result from misuse or spillage during transport, and to determine appropriate environmental hazard label statements. Daminozide is practically non-toxic to mammals, birds and freshwater fish, on an acute basis. It is slightly toxic to aquatic invertebrates.

Ecological Effects Risk Assessment

Environmental exposure is expected to be minimal when daminozide is used according to product label directions. Therefore, the ecological risk from use of daminozide also is expected to be very low.

Additional Data Required

The generic data base for daminozide is substantially complete. However, EPA is requiring additional information on a previously submitted aerobic soil metabolism study as confirmatory data. EPA also is requiring product-specific data, including product chemistry and acute toxicity studies, as well as revised Confidential Statements of Formula and revised labeling for reregistration of pesticide products containing daminozide.

Product Labeling Changes Required

All end-use daminozide products must comply with EPA's pesticide product labeling requirements. In addition:

- **Compliance with Worker Protection Standard (WPS)** - Any product whose labeling permits use in the production of an agricultural plant on any agricultural establishment (farm, forest, nursery or greenhouse) must comply with the labeling requirements of:

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- PR Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS)," and
 - PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7."

Unless specifically directed in the RED, all statements required by these two PR Notices must appear on product labeling exactly as instructed in the Notices. Labels must be revised by April 21, 1994, for products distributed or sold by the primary registrant or supplementally registered distributors, and by October 23, 1995, for products distributed or sold by anyone.

- **Exclusionary Statement** - All end-use product labels must carry the following statement on the front panel near the product name or Directions for Use:

"For use only in commercial or research greenhouses or shade houses."

- **Personal Protective Equipment (PPE) Requirements** - All end-use product labeling must carry the following PPE requirements:

"Applicators and other handlers must wear:

- Coveralls over short-sleeved shirt and short pants
- Chemical-resistant or waterproof gloves (*)
- Chemical-resistant footwear plus socks
- Chemical-resistant headgear for overhead exposure
- Chemical-resistant apron when cleaning equipment, mixing, or loading" (**)

* See Supplement Three of PR Notice 93-7.

** "Mixing" or "loading" may be removed if the product is formulated as "ready-to-use."

- **Entry Restrictions** - A 24-hour Restricted Entry Interval (REI) is required for all uses, for all end-use products. The Personal Protective Equipment (PPE) for early entry should be that which is required for applicators of daminozide, except no apron or respirator is required. These REI and PPE instructions should be inserted into the standardized statements required by PR Notice 93-7.

- **Single active ingredient products** - Adopt these entry restrictions and remove any conflicting ones from labeling.
- **Multiple active ingredient products** - Compare these entry restrictions with those on current labeling and retain the more protective restrictions.

**Regulatory
Conclusion**

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

These daminozide products will be reregistered once the 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 daminozide 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 daminozide 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 daminozide RED, or reregistration of individual products containing daminozide, 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.