Product Safety Assessment

 Isoxaben

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Names
• CAS No. 82558-50-7 • Isoxaben
• N-[3-(1-ethyl-1-methylpropyl)-5-isoxazolyl]-2,6-dimethoxybenzamide
• N-[3-(1-ethyl-1-methylpropyl)isoxazol-5-yl]-2,6-dimethoxybenzamide

Trade Names
• CENT-7® herbicide • GALLERY® herbicide
• FLEXIDOR® herbicide • TRELLIS® herbicide

Although much of the information in this document supports the registration and sale of isoxaben in the United States of America, a number of other countries around the world, many of which are also member nations of the Organization for Economic Co-operation and Development (OECD) have registered isoxaben products. For further details consult the country-specific Product Label, Safety Data Sheet, or Contact Us.

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Product Overview
• Isoxaben is the common name for a benzamide herbicide registered to Dow AgroSciences LLC, a wholly owned subsidiary of The Dow Chemical Company. The mode of action for isoxaben in plants is a cellulose biosynthesis inhibitor (CBI). This mode of action inhibits cellulose biosynthesis (cell growth) in the cell walls of susceptible weeds, inhibiting the germination and growth of susceptible weeds.¹ For further details, see Product Description.
• Isoxaben is a white to off-white powder that is formulated into water-dispersible powders and granules and liquid concentrates.² For further details, see Product Description.
• Isoxaben offers selective, pre-emergence control of susceptible broadleaf weeds in established turf, ornamentals, nursery stock, non-bearing fruit trees, bearing and non-bearing nut trees, bearing and non-bearing grapevines, Christmas tree plantations, and non-cropland areas. In Western European countries, isoxaben is registered for use in cereals, bearing and non-bearing fruit trees, and vines.³ For further details, see the relevant Product Label and Product Uses.
• Those working in manufacturing, formulation, distribution operations, or field application of these products could be exposed. Workers can minimize the potential for exposure by

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carefully following workplace procedures and label directions and wearing the proper protective equipment.¹⁴ ¹⁵ The potential for exposure resulting from products treated with isoxaben has been estimated to be at an acceptable level for consumers. For further details, see the relevant Product Label and Exposure Potential.

- Prolonged skin contact may cause slight irritation with local redness. Prolonged, excessive inhalation of product dust may cause adverse effects. Isoxaben has very low toxicity if swallowed. For further details, see Health Information or the Safety Data Sheet.
- Isoxaben is highly toxic to aquatic organisms on an acute basis but practically nontoxic to birds and bees. It is not expected to accumulate in the food chain (low bioconcentration potential). It has moderate persistence in soil under field conditions. Isoxaben would be removed by common wastewater-treatment processes.⁶ For further details, see Environmental Information or the Safety Data Sheet.
- Isoxaben formulations are stable under recommended storage and use conditions.⁷ ⁸ Consult the Product Label for specific use and storage information. For further details, see Physical Hazard Information.

**Manufacture of Product**

- **Manufacture** – Dow AgroSciences, a wholly owned subsidiary of The Dow Chemical Company, manufactures Isoxaben in India and the U.K. and formulated products in multiple locations around the world.
- **Process** – Isoxaben is produced using a proprietary complex multistep process. The chemical structure of isoxaben is shown below:

![Chemical Structure of Isoxaben](image)

**Product Description**⁹,¹⁰,¹¹

Ioxaben is the common name for N-[3-(1-ethyl-1-methyl[propyl]-5-isoxazolyl]-2,6-dimethoxybenzamide, a soil-active pre-emergence herbicide manufactured by Dow AgroSciences LLC, a wholly owned subsidiary of The Dow Chemical Company.

Ioxaben is the active ingredient in formulations marketed under the trade names CENT-7® herbicide, FLEXIDOR® herbicide, and GALLERY® herbicide. Isoxaben belongs to the benzamide family of herbicides and inhibits cell wall biosynthesis in germinating susceptible broadleaf weeds. It is applied to the soil before weeds emerge from the soil and controls a wide range of annual broadleaf weeds.

Ioxaben is a white to off-white solid with a musty odor that is formulated into water-dispersible powders and granules or liquid concentrates. Formulated isoxaben products contain 0.25–75% active ingredient, with the balance solvents and stabilizers.

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Product Uses & Regulatory Information\textsuperscript{12,13,14}
Isolexaben formulations control a wide range of broadleaf weeds when applied pre-emergence, prior to germination. Isoxaben is registered by the U.S. Environmental Protection Agency (EPA) for the following applications:
- Established turf
- Landscape, container-grown, and field-grown ornamentals
- Groundcovers/perennials
- Non-bearing fruit and nut trees, non-bearing grape vineyards
- Bearing nut trees and grape vineyards (as of Nov 2010)
- Non-cropland
- Christmas tree/conifer plantations
- Ornamental bulbs

Isoxaben is registered in France and most Western European countries for the following applications:
- Cereals
- Bearing and non-bearing fruit trees
- Vines – blackcurrant, gooseberry, table and wine grapes, blackberry, raspberry, strawberry
- Ornamental plant production and nursery stock

Regulations may exist that govern the manufacture, sale, transportation, use, and/or disposal of isoxaben. These regulations may vary by city, state, country, or geographic region. Information may be found by consulting the relevant Product Label, Safety Data Sheet, or Contact Us.

Exposure Potential\textsuperscript{15,16}
Isolexaben is used in the formulation of commercial herbicides. Based on the uses for isoxaben, the public could be exposed through:
- **Workplace exposure** – Exposure can occur in facilities that manufacture or formulate isoxaben or during field application. It is produced, distributed, and stored in closed systems. Those working with this product in manufacturing and formulation operations could be exposed during maintenance, sampling, testing, or other procedures. Each manufacturing facility should have a thorough training program for employees and appropriate work processes, ventilation, and safety equipment in place to limit exposure. Field applicators should carefully read and follow application instructions on the product label. See Health Information and Product Label.
- **Consumer exposure to products containing isoxaben** – Consumers could be exposed to traces of isoxaben by consuming residues in food and/or drinking water. The U.S. Environmental Protection Agency (EPA) performed a dietary risk assessment for isoxaben residues in grapes, grape juice, and raisins and determined that “chronic dietary risk estimates are well below the level of concern.”\textsuperscript{17} See Health Information.
- **Environmental releases** – This description provides a general overview; please consult the relevant Safety Data Sheet or Product Label for detailed information about protective equipment and procedures. In the event of a spill, the focus is on containing the spill to prevent contamination of soil, ditches, sewers, waterways, or groundwater. Sweep up small spills and place in a suitable container for disposal. Keep product dusts to a minimum. For spills of liquid product, soak up with sand or other noncombustible absorbent material and place in containers for disposal. Isoxaben biodegrades at a moderate rate in soil and will not persist in the environment. It shows a low tendency to bioconcentrate (accumulate in the food chain) and the potential for contaminating ground or surface water is low. Isoxaben is highly toxic to aquatic organisms, but practically nontoxic to mammals and birds. See Environmental, Health, and Physical Hazard Information.
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- **Large release** – Industrial spills or releases are infrequent and generally contained. If a large spill does occur, barricade the area. Keep the material contained and out of waterways. Contact Dow AgroSciences for clean-up assistance. Personnel engaged in clean up of spills must wear appropriate protective equipment. Consult the relevant Safety Data Sheet or Product Label for more detailed information about protective equipment and procedures. See Environmental, Health, and Physical Hazard Information.

- **In case of fire** – Isolate the fire and deny entry. Eliminate all sources of ignition immediately. Use water fog or fine spray, carbon-dioxide or dry-chemical extinguishers, or foam to fight the fire. Foam is preferred. A dust explosion hazard may result from forceful application of fire-extinguishing agents. Pesticide dusts at sufficient concentrations can form explosive mixtures with air. Firefighters should wear positive-pressure, self-contained breathing apparatus (SCBA) and protective firefighting clothing. Stay upwind of the fire. If possible contain the fire water to minimize the potential for environmental damage. Follow emergency procedures carefully. Consult the Product Label and Safety Data Sheet for specific firefighting measures. See Environmental, Health, and Physical Hazard Information.

- **Emergency response information** – In the case of an emergency such as poisoning, product spillage, or fire associated with a Dow AgroSciences product, please use the phone number listed on the Safety Data Sheet for the appropriate country. In some countries, the Emergency Response number is also provided on the artwork of the commercial package.
  - In the United States, call 800-992-5994.
  - In France, call Numero D'appel D'urgence: 03 88 53 36 76 (Drusenheim/Bas Rhin); Centre Anti-Poisons De Paris: 01 40 05 48 48 (Hopital Fernand Widal/Paris).
  - In Europe, the Middle East, and African countries, call 31-115-694-982 (Netherlands).

**Health Information**

**Laboratory Testing** – Isoxaben has been evaluated by comprehensive regulatory schemes used to register products in the US (i.e., Federal Insecticide, Fungicide, and Rodenticide Act of 1972) and EU (Directives for Plant Protection and Biocidal Products). These standards require laboratory testing for potential short-term (acute) and long-term (chronic) health effects. These tests help scientists determine how chemicals might affect humans, domestic animals, or wildlife in cases of overexposure. Pesticide products used according to label directions are unlikely to cause toxic effects. The amount of pesticide to which people and pets may typically be exposed is low compared to that used in laboratory testing.

Health information for isoxaben products is summarized on the relevant Safety Data Sheets. It is important to note that health risks associated with individual products may vary based on their formulation or intended use. The Safety Data Sheet is the preferred source for specific health information. Herbicide formulations may contain components or additives that have additional health risks. An overview of health information for isoxaben technical product appears below.

**Eye contact** – Isoxaben is essentially nonirritating to the eyes.

**Skin contact** – Prolonged contact may cause slight irritation with local redness, but is unlikely to result in absorption of harmful amounts.

**Inhalation** – Prolonged excessive exposure to dust may cause adverse effects.

**Ingestion** – Very low toxicity if swallowed. Harmful effects are not anticipated from swallowing small amounts.

**Repeated exposure** – In animals, effects have been reported on the liver and kidneys.

**Cancer information** – An increase in nonmalignant liver tumors was observed with isoxaben in one of two species tested.
**Birth, developmental, reproductive effects** – Isoxaben has caused birth defects in laboratory animals, but only at doses toxic to the mother. *In vitro* genetic toxicity studies were negative. Animal genetic toxicity studies were predominantly negative.

For more information, see the relevant [Product Label](#) or [Safety Data Sheet](#).

**Environmental Information**

Isoxaben biodegrades at a moderate rate in soil and sediments and will not persist in the environment. It is not expected to migrate to groundwater or volatilize (evaporate) to the atmosphere. Isoxaben does not accumulate in the food chain (low bioconcentration potential).

Isoxaben is highly toxic to aquatic organisms but practically nontoxic to mammals, birds, and honeybees.

For more information, see the relevant [Product Label](#) or [Safety Data Sheet](#).

**Physical Hazard Information**

Isoxaben herbicide formulations are stable at recommended storage and use temperatures. Consult the [Product Label](#) for specific use and storage information.

For more information, see the relevant [Product Label](#) or [Safety Data Sheet](#).

**Additional Information**

- Contact Us ([www.dowagro.com/company/contact/index.htm](http://www.dowagro.com/company/contact/index.htm))
- FLEXIDOR® 125 Herbicide Specimen Label, Dow AgroSciences Limited, Label Code: 9 UKE 1010 FLEXLDR A
- GALLERY® 75 Dry Flowable Specialty Herbicide Specimen Label, Dow AgroSciences LLC, Label Code: D02-081-021, Revised March 2, 2010 ([http://www.cdms.net/idat/id638008.pdf](http://www.cdms.net/idat/id638008.pdf))
- *First Food Registrations of Isoxaben on Bearing Nut Trees and Grape Vineyards*, U.S. Environmental Protection Agency, November 4, 2010

For more business information about isoxaben, visit the [Dow AgroSciences LLC](http://www.dowagro.com/) website at [www.dowagro.com](http://www.dowagro.com/).
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