

PESTICIDE TYPE	Herbicide
CHEMICAL CLASS	Isoxazole
COMMON TRADE NAMES	Balance Flexx, Corvus
MAJOR DEGRADATE	RPA 202248 (DKN), RPA 203328
APPLICATION RATE (lbs a.i./A)	Max Annual: 0.094
REGISTRATION STATUS	EPA: 1998 (conditional on corn), 2005 (unconditional on corn), (anticipated on soybean) Minnesota: May 2015
TOXICITY PROFILE FOR APPLICATORS	Signal word: Caution Toxicity III
BASIC MANUFACTURER	Bayer CropScience
MDA LABORATORY CAPABILITIES	Methods developed for pesticides and degradates

HUMAN HEALTH

NON-CANCER Acute PAD= 0.02 mg/kg/day
Chronic PAD= 0.02 mg/kg/day

CANCER Probable human carcinogen (Group B2)

Acute and chronic PADs are doses that include all relevant uncertainty and safety factors

ENVIRONMENTAL AQUATIC TOXICITY

FISH Acute: >850 ppb
Chronic: Not determined

INVERTEBRATE Acute: >750 ppb
Chronic: Not determined

AQUATIC PLANTS Vascular: 4.9 ppb
Non-vascular: 110 ppb

POLLINATOR TOXICITY

HONEY BEE Acute Contact: Practically non-toxic (LD₅₀ not determined)
Acute Oral: Practically non-toxic (LD₅₀ not determined)

Level of Concern (LOC) has been applied to all values.

Introduction

Isoxaflutole is a selective herbicide approved for control of certain broadleaf and grass weeds in field corn and soybean. Isoxaflutole is the first member of a new structural class of herbicides called the isoxazoles. Isoxaflutole works by preventing the biosynthesis of carotenoid pigments in both broadleaf and grass weeds. Without carotenoid pigments, chlorophyll pigments are damaged by the sun, and the plant eventually dies. Isoxaflutole is effective against weeds resistant to other herbicide classes such as glyphosate and atrazine. Isoxaflutole was registered conditionally from 1998 to 2004 for weed control in field corn. Registration is in progress for recently-approved isoxaflutole and glyphosate resistant soybean cultivars (approved by APHIS in 2013). Isoxaflutole is registered in Minnesota under stipulations of a Commissioner's Order, primarily to address groundwater and surface water concerns. Minnesota Department of Agriculture (MDA) extensive review of U.S. Environmental Protection Agency (EPA) isoxaflutole labels and risk assessments for issues relevant to Minnesota is summarized below.

Projected Use in Minnesota

The EPA approved isoxaflutol for controlling broadleaf and grass weeds in field corn and soybean. Isoxaflutol is expected to control weeds that have become resistant to commonly used herbicides. Isoxaflutole is found in two end-use products.

- **Balance Flexx™ WG (EPA Reg. No. 264-1067)**– a SC formulation registered for weed control in field corn. The product carries 20% isoxaflutole and a safener cyprosulfamide.
- **Corvus™ (EPA Reg. No. 264-1066)**– a SC formulation registered for weed control in field corn. The product carries 19% isoxaflutole and 7.6% thien carbazone-methyl.

Label Environmental Hazards

Minnesota-specific Use Restrictions:

- Use is prohibited in Dakota, Dodge, Fillmore, Goodhue, Houston, Mower, Olmsted, Rice, Wabasha and Winona counties and north of Interstate 94.
- Use is prohibited on soils where the depth of the water table (i.e., the level of saturation) is unknown or is less than 25 feet below the ground surface on course-textured surface soils or subsoils (sandy loam, loamy sand or sand) with low organic matter.
- Use is prohibited within 200 feet of natural or impounded lakes and reservoirs, and within 66 feet of tile surface inlets and perennial or intermittent streams or rivers.
- A list of restricted soils and other MN-specific use requirements are found on Product Bulletin that accompanies each unit of product sold.

Water Quality:

- Label for applications carry restrictions for groundwater and surface water impacts.

Other:

- Do not use on restricted soils if water table <25 ft below the ground surface.
- Do not apply this product through any type of irrigation system.
- Do not apply product using aerial application equipment.
- Plant corn at least 1.5 inches deep and seed must be completely covered with soil and furrow firmed.
- Pesticide is toxic to some plants at very low concentrations. Do not apply when weather conditions favor drift.
- Also there are rotational crop restrictions because of phytotoxicity issues.



Toxicology and Exposure

EPA's screening models generate high-end, conservative exposure estimates for active ingredients and toxicologically significant degradates. Model inputs include annual usage at maximum use rates, maximum treated acres, maximum food residues, peak runoff and drift scenarios, etc. Some proposed products, application rates and use scenarios are not relevant to Minnesota. EPA's estimates, therefore, may not reflect future use and impacts in Minnesota.

Human Health

- **Carcinogenic Effects**- Classified as "Probable human carcinogen." The EPA estimate that aggregate cancer risk from isoxaflutole and degradates in food and water to the general population will be negligible ($<1 \times 10^{-6}$).
- **Drinking Water Guidance**- Model estimates suggest that parent compound isoxaflutole and degradate RPA 202248 are expected to persist and accumulate in groundwater because of high mobility. Based on First Index Reservoir Screening Tool (FIRST) models, the estimated drinking water concentrations for isoxaflutole and degradate RPA 202248 are as follows: Non-cancer chronic exposures: surface water= 1.26ppb; groundwater= 0.255 ppb. Cancer assessments: surface water= 0.53ppb; groundwater= 0.255ppb. These estimates are below the Minnesota Department of Health drinking water guidance values of 7 ppb for chronic non-cancer risk and 9 ppb for cancer risk.
- **Occupational Exposure**- Exposure and risk estimates suggest that occupational risks are not of concern for the proposed use.

Environment- Non-target Species

- **Stressor of concern**- Parent isoxaflutole and its degradate RPA 202248 is phytotoxic to non-target aquatic and terrestrial plants.
- **Aquatic Life Exposure**- Isoxaflutole is highly toxic to aquatic plants and moderately toxic to freshwater fish. Estimates suggest that surface water concentrations could exceed 90% of the acute aquatic vascular plant toxicity benchmark.

Environmental Fate

Isoxaflutole degrades rapidly and sequentially in the environment. The degradates are likely to reach surface and shallow water where they are expected to persist and accumulate. Environmental fate characteristics are listed for isoxaflutole and all relevant degradates where appropriate.

Soil

- **Half-life**- Aerobic: Isoxaflutole = 2.4 days; RPA 202248= 61 days.
Anaerobic: Isoxaflutole= < 2 hours; RPA 202248= Not available.
- **Adsorption** (mL/g) - Parent/degradates are very mobile. Sorption and desorption of isoxaflutole and degradate RPA 202248 is dependent on soil organic carbon content. Isoxaflutole $K_{OC}=101 \text{ ml g}^{-1}$ in sand with 0.5% organic carbon. ; RPA 2002248= $K_{OC} 117$ in sand with 0.38% organic carbon.
- **Photolysis**: Isoxaflutole= 23 hours.
- **Persistence**- Isoxaflutole and degradate RPA 202248 are considered to be highly persistent in soil. Mobility is dependent on soil types with potentially mobile in sand, sandy loam and loam soils and immobile in clay soil and loam sediment.

Aquatic

- Aerobic environments: Isoxaflutole= stable; RPA 202248= stable.
- Anaerobic environments (half-life): Isoxaflutole < 2hrs; RPA 202248= 316 days.
- Loam sediment: Isoxaflutole= immobile; RPA 202248= immobile.

Water

- **Surface water**- Isoxaflutole and degradate RPA 200248 are mobile and expected to persist and accumulate in surface water.
- **Groundwater**- Isoxaflutole and degradate RPA 200248 are mobile and expected to persist and accumulate in groundwater.
- **Half-life via hydrolysis**: Isoxaflutole= 20.1 hours at pH 7; RPA 202248= stable.
- **Photolysis in water**: Isoxaflutole= 6.7 days; RPA 202248= stable.

Air

- **Volatilization**- Not a major route of dissipation. Vapor pressure= 7.5×10^{-9} mmHg; Henry's Law= 1.8×10^{-10} tor $\text{m}^3 \text{mole}^{-1}$.

Degradates

Isoxaflutole has two important degradates; RPA 202248 (DKN) and RPA 203328. Available evidence indicates that 202248 is as toxic as the parent compound and is expected to be detected in groundwater and surface water.