

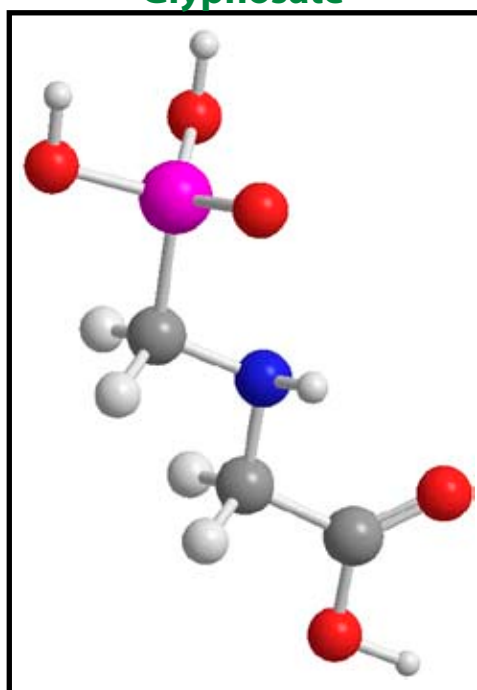
Thank you for visiting the National Pesticide Information Center's fact sheets.

Some of the information in the following fact sheet (scroll down) is out-of-date. NPIC has started a *NEW* set of fact sheets, and glyphosate is high on our list of priorities. If you would like to be notified when NPIC releases new publications, send an email to npicupdates@ace.orst.edu with "subscribe" in the subject line.

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Please call NPIC with any questions you have about pesticides at **1-800-858-PEST (7378)**.

Molecular Structure - Glyphosate



NPTN Technical Fact Sheets are designed to provide information that is technical in nature for individuals with a scientific background or familiarity with the regulation of pesticides by the U.S. Environmental Protection Agency (US EPA). This document is intended to be helpful to professionals and to the general public for making decisions about pesticide use.

National
Pesticide
Telecommunications
Network

Glyphosate

(Technical Fact Sheet)

For less technical information please refer to the **General Fact Sheet**.

The Pesticide Label: Labels provide directions for the proper use of a pesticide product. *Be sure to read the entire label before using any product.* A signal word, on each product label, indicates the product's potential hazard.

CAUTION - low toxicity

WARNING - moderate toxicity

DANGER - high toxicity

What is glyphosate?

- Glyphosate is a post-emergent herbicide registered by the U.S. Environmental Protection Agency (EPA) in 1974 and reregistered in 1993 (1, 2).
- Glyphosate is nonselective. Users apply it directly to foliage to control plants (3). See the **Herbicide Selectivity** box.
- Different formulations of glyphosate (acid and salt) have been used in products. Glyphosate salts include isopropylamine, trimethylsulfonium, monoammonium, and sodium (2, 3). Use of the term “glyphosate” in this fact sheet refers to the acid or salts.
- Glyphosate is water soluble and odorless. It is nonvolatile and has a vapor pressure of 1.84×10^{-7} to 3×10^{-7} mm Hg (3, 4).
- Signal words for products containing glyphosate range from Caution to Danger (2, 5). The signal word reflects the combined toxicity of glyphosate and other ingredients in each product. See the **Pesticide Label** box above.
- Some plants have been genetically engineered to be resistant to glyphosate. Glyphosate-tolerant soybeans are an example of such a plant (6). **This fact sheet does not address glyphosate-tolerant crops.**
- Glyphosate products are used on a variety of sites including food and non-food crops, greenhouses, forests, aquatic environments, right-of-ways, and outdoor residential areas (2). Commercial formulations of the herbicide include granules, powders, pressurized liquids, pellets, emulsions, solutions, flowables, and microencapsulated products (5).

Herbicide Selectivity: Selective herbicides kill some plant species and not others. No plants are known to be naturally resistant to the action of glyphosate. Scientists have genetically altered some crop plants to be resistant to the effects of glyphosate, allowing glyphosate to be used as a selective herbicide in these fields.

How does glyphosate work?

- Glyphosate acts by enzyme inhibition in the shikimic acid pathway. The shikimic acid pathway is found only in plants and microorganisms (7).
- The target of the herbicide is the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSP). Inhibition of EPSP disrupts plant synthesis of aromatic compounds such as vitamin K, ubiquinones, and the amino acids tryptophan, tyrosine, and phenylalanine (7).
- Glyphosate is absorbed across the plant surface and is translocated throughout the plant. The herbicide tends to accumulate in plant regions with actively dividing cells (3, 7).
- Plants exposed to glyphosate display stunted growth, loss of green coloration, leaf wrinkling or malformation, and tissue death. Death of the plant may take several days to weeks (4-20 days) to occur (3, 7).
- The sodium salt of glyphosate can act as a plant growth regulator and hasten the ripening of fruits (2).

What are some products that contain glyphosate?

- Roundup®
- Rodeo®
- Accord®
- Touchdown®

How toxic is glyphosate?

Animals

- Glyphosate is low in toxicity when ingested. The acute oral LD50 in rats is >4320 mg/kg (2). See boxes on **Laboratory Testing**, **LD50/LC50**, and **Toxicity Category**.
- Glyphosate is low in toxicity when inhaled. The acute inhalation LC50 in rats is >0.81 mg/L (4).
- Glyphosate is low in toxicity when applied to the skin. The acute dermal LD50 in rabbits is >2000 mg/kg (2).
- In skin irritation studies, glyphosate caused slight to no skin irritation in rabbits (8).
- Glyphosate caused strong to no eye irritation in rabbits (8). The U.S. EPA categorizes glyphosate as low in toxicity regarding eye irritation. This categorization is based on a study where rabbits ocularly exposed to glyphosate experienced mild eye irritation that cleared in 7 days (2).

Exposure: Effects of glyphosate on human health and the environment depend on how much glyphosate is present and the length and frequency of exposure. Effects also depend on the health of a person and/or certain environmental factors.

Laboratory Testing: Before pesticides are registered by the U.S. EPA, they must undergo laboratory testing for short-term (acute) and long-term (chronic) health effects. Laboratory animals are purposely fed high enough doses to cause toxic effects. These tests help scientists judge how these chemicals might affect humans, domestic animals, and wildlife in cases of overexposure. When pesticide products are used according to the label directions, toxic effects are not likely to occur because the amount of pesticide that people and pets may be exposed to is low compared to the doses fed to laboratory animals.

Toxicity Category (Signal Word) (9)

	High Toxicity (Danger)	Moderate Toxicity (Warning)	Low Toxicity (Caution)	Very Low Toxicity (Caution)
Oral LD50	Less than 50 mg/kg	50 - 500 mg/kg	500 - 5000 mg/kg	Greater than 5000 mg/kg
Dermal LD50	Less than 200 mg/kg	200 - 2000 mg/kg	2000 - 5000 mg/kg	Greater than 5000 mg/kg
Inhalation LC50	Less than 0.05 mg/l	0.05 - 0.5 mg/l	0.5 - 2 mg/l	Greater than 2 mg/l
Eye Effects	Corrosive	Irritation persisting for 7 days	Irritation reversible within 7 days	Minimal effects, gone within 24 hrs
Skin Effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation

LD50/LC50: A common measure of acute toxicity is the lethal dose (LD50) or lethal concentration (LC50) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD50 is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC50 is often expressed as mg of chemical per volume (e.g., liter (L)) of medium (i.e., air or water) the organism is exposed to. Chemicals are considered highly toxic when the LD50/LC50 is small and practically non-toxic when the value is large. However, the LD50/LC50 does not reflect any effects from long-term exposure (i.e., cancer, birth defects, or reproductive toxicity) that may occur at levels below those that cause death.

- In studies with guinea pigs, glyphosate did not cause skin sensitization (8).
- In a 90-day oral study, investigators exposed male and female mice to glyphosate at doses of 0, 250, 500, or 2500 mg/kg/day. At the highest dose (2500 mg/kg/day), body weight gains were lower in both male and female mice. The no observable adverse effect level (NOAEL) was 500 mg/kg/day (2).
- Researchers fed dogs glyphosate for 1 year at doses of 0, 20, 100, or 500 mg/kg/day. The dogs exhibited no adverse effects (2, 8, 10).
- In a 21-day dermal study, laboratory workers exposed both abraded and unabraded skin of male and female rabbits to glyphosate. Workers applied glyphosate at doses of 100, 1000, or 5000 mg/kg/day for 6 hours/day, 5 days/week, for 3 consecutive weeks. Workers noted slight skin swelling and redness at the highest dose (5000 mg/kg), but no systemic toxicity (8, 10).
- Researchers exposed rats to a single oral dose of radiolabeled glyphosate and the animals absorbed 30-36% of the chemical. Elimination of the parent compound in the urine or feces accounted for 97.5% of the administered dose. Amino methyl phosphonic acid (AMPA) was the only glyphosate metabolite detected (2).

Humans

- Clinicians reviewed 93 cases of accidental and intentional exposures to formulated glyphosate products. Accidental dermal exposures were asymptomatic. Ingestion of glyphosate products resulted in mucosal and gastrointestinal irritation, hypotension, and pulmonary dysfunction. Symptoms from accidental ingestion dissipated within 24 hours. Two patients died from intentional ingestion of multiple agricultural pesticides that included glyphosate. Five patients died from intentional ingestion of a sole glyphosate product (11).
- Researchers reported 56 cases of ingestion of glyphosate products. They detected effects to the gastrointestinal, respiratory, cardiovascular, and central nervous systems. Nine of the patients died. The researchers suggested that the clinical findings may be caused by an ingredient other than glyphosate in the formulated products (12).
- No skin irritation occurred on human volunteers exposed dermally to a diluted glyphosate product. Researchers noted skin redness in volunteers treated with an undiluted glyphosate product. The incidence of skin redness increased on abraded skin. No skin sensitization occurred with 204 human volunteers dermally exposed to an undiluted glyphosate product (8). Glyphosate is absorbed poorly through the skin (2).

- Scientists evaluated eye effects from 1513 reported human ocular exposures to glyphosate products. The majority of exposures resulted in no injury (21%) or temporary minor effects (70%). Moderate effects were noted in 2% of the cases and involved symptoms that usually required medical treatment. None of the exposures resulted in permanent eye damage or loss of visual acuity (13).

Does glyphosate cause reproductive or teratogenic effects?

Animals

- Laboratory workers fed rats glyphosate at doses of 0, 3, 10, or 30 mg/kg/day continuously for three generations. Workers noted no fertility effects nor toxicity in adult rats. The male offspring from the third generation mating displayed an increased incidence of kidney effects at the highest dose (30 mg/kg/day) (2, 8, 10, 14). Scientists reevaluated this study and compared it to a two-generation study assessing rats fed glyphosate (see below). They concluded that the kidney effects observed in the three-generation study were not due to glyphosate exposure (2, 10).
- In a two-generation study, laboratory workers fed rats glyphosate at 0, 100, 500, or 1500 mg/kg/day and noted decreased body weight gain in offspring at the highest dose tested (1500 mg/kg/day). Workers detected no reproductive effects. The NOAELs for reproductive and developmental effects are 1500 and 500 mg/kg/day, respectively (2, 8, 10).
- Researchers exposed pregnant rats to glyphosate by gavage (stomach tube feeding) on gestation days 6-19 at doses of 0, 300, 1000, or 3500 mg/kg/day. At the highest dose (3500 mg/kg/day) they detected decreased maternal body weight gains, increased maternal mortality, decreased fetal body weights, and an increased number of fetuses with unossified sternebrae. The NOAEL for maternal and developmental toxicity is 1000 mg/kg/day (2, 8, 10, 14).
- In a developmental study, scientists exposed pregnant rabbits to glyphosate by gavage on gestation days 6-27 at doses of 0, 75, 175, or 350 mg/kg/day. They detected no developmental effects. At the highest dose (350 mg/kg/day) the animals exhibited maternal diarrhea and increased mortality (62.5%). The NOAEL for maternal effects is 175 mg/kg/day (2, 8, 10, 14).

Humans

- Data are not available from occupational exposure, accidental poisonings, or epidemiological studies regarding the reproductive and developmental toxicity of glyphosate.

Is glyphosate a carcinogen?

Animals

- Laboratory workers fed rats diets containing glyphosate for 2 years (males: 0, 89, 362, or 940 mg/kg/day; females: 0, 113, 457, or 1183 mg/kg/day). Workers noted pancreatic, liver, and thyroid adenomas at a variety of doses. The U.S. EPA concludes that the adenomas are not related to glyphosate exposure due to a lack of statistical significance in adenoma occurrence (2, 10).
- In a carcinogenicity study, researchers fed male and female mice glyphosate at doses of 0, 150, 750, or 4500 mg/kg/day for 18 months. At the highest dose (4500 mg/kg/day), they detected decreased body weight gains in both male and female mice, increased size of liver cells (males) and kidney tubules (females), and an increased incidence of kidney adenomas (males). The U.S. EPA concludes that the kidney adenomas are not caused by glyphosate exposure due to a lack of statistical significance in adenoma occurrence at the highest dose (2, 10).
- Researchers often use studies designed to test for mutagenicity to screen chemicals for carcinogenicity. Sufficient evidence exists to determine that glyphosate does not have significant potential for mutagenicity (2, 8, 10, 14).

Humans

- The U.S. EPA currently classifies glyphosate as a group E carcinogen (2, 10, 15). This means that glyphosate is not considered a human carcinogen based on adequate evidence of non-carcinogenicity in laboratory animals. See box on **Cancer**.
- Researchers suggested glyphosate exposure possibly increases the risk for developing some types of cancer, but definitive conclusions could not be attained due to small sample sizes and confounding factors (16, 17).

What is the environmental fate and behavior of glyphosate?

- Glyphosate is stable to hydrolysis and photodegradation (2, 18). Metabolism of glyphosate to amino methyl phosphonic acid (AMPA) by microorganisms is the major route of degradation in the environment, particularly in soil (2, 8, 18).
- The half-life of glyphosate in soils ranges from 3-130 days (8). Researchers evaluated the soil dissipation of formulated glyphosate products in field studies. They noted half-lives of 3-174 days (8). See box on **Half-life**.
- Glyphosate and its metabolite AMPA strongly adsorb to soil and have a low potential to leach to ground water (2, 8).
- Researchers monitored glyphosate applied to a pond and calculated a water-dissipation half-life of 7.5 days (2). Binding to suspended sediment may influence aqueous dissipation of glyphosate (8).
- Glyphosate may adversely affect nontarget plants. Strong soil adsorption limits glyphosate's phytotoxicity in soil (3).

Cancer: The U.S. EPA has strict guidelines that require testing of pesticides for their potential to cause cancer. These studies involve feeding laboratory animals large *daily* doses of the pesticide over most of the lifetime of the animal. Based on these tests, and any other available information, EPA gives the pesticide a rating for its potential to cause cancer in humans. For example, if a pesticide does not cause cancer in animal tests at large doses, then the EPA considers it unlikely the pesticide will cause cancer in humans. Testing for cancer is not done on human subjects.

Half-life is the time required for half of the compound to degrade.

1 half-life = 50% degraded
2 half-lives = 75% degraded
3 half-lives = 88% degraded
4 half-lives = 94% degraded
5 half-lives = 97% degraded

Remember that the amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied.

What effects does glyphosate have on wildlife?

- Glyphosate is slightly to practically nontoxic to fish ($LC_{50} = >24-140$ mg/L) and aquatic invertebrates ($LC_{50} = 780$ mg/L) (2). Some formulated glyphosate products, due to the toxicity of another ingredient, must bear the statement, "This pesticide is toxic to fish." (2). Glyphosate is not likely to bioaccumulate (2, 8).
- Glyphosate is practically nontoxic to birds ($LD_{50} = >2000$ mg/kg) and honeybees ($LD_{50} = >100$ µg/bee) (2).
- Glyphosate has low toxicity to earthworms. In studies using glyphosate products, the 14-day No Observed Effect Concentration (NOEC) ranged from 158-500 mg glyphosate product/kg soil (8).

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For more information contact: NPTN

Oregon State University, 333 Weniger Hall, Corvallis, Oregon 97331-6502.

Phone: 1-800-858-7378 Fax: 1-541-737-0761 Email: nptn@ace.orst.edu

NPTN at <http://nptn.orst.edu/> EXTTOXNET at <http://ace.orst.edu/info/exttoxnet/>

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