Glyphosate

Technical Fact Sheet

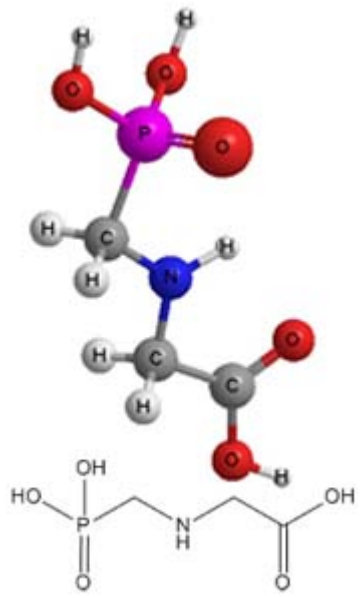
As of 2011, NPIC stopped creating technical pesticide fact sheets. The old collection of technical fact sheets will remain available in this archive, but they may contain out-of-date material. NPIC no longer has the capacity to consistently update them. To visit our general fact sheets, click here. For up-to-date technical fact sheets, please visit the Environmental Protection Agency's webpage.

Chemical Class and Type:

- Glyphosate is a non-selective systemic herbicide that is applied directly to plant foliage.[1] When used in smaller quantities, glyphosate can act as a plant growth regulator.[2] Glyphosate is a glycine derivative.[1] The International Union of Pure and Applied Chemistry (IUPAC) name for glyphosate is N-(phosphonomethyl) glycine[3] and the Chemical Abstracts Service (CAS) registry number is 1071-83-6.[1]
- Glyphosate's potential as an herbicide was reported in 1971.[1,4] Glyphosate was first registered for use by the United States Environmental Protection Agency (U.S. EPA) in 1974[5], and reregistration was completed in 1993.[6] See the text box on **Laboratory Testing**.
- Formulations of glyphosate include an acid, monoammonium salt, diammonium salt, isopropylamine salt, potassium salt, sodium salt, and trimethylsulfonium or trimesium salt.[1,2,4] Unless otherwise stated, all data in this fact sheet refer to the acid form.
- Technical grade glyphosate is used in formulated products, as are the isopropylamine, sodium, and monoammonium salts. Of these, the isopropylamine salt is most commonly used in formulated products.[2,7]

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 given 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.

Molecular Structure - Glyphosate



Physical / Chemical Properties:

Glyphosate and associated forms

Active Ingredient	Form[1,4]	Vapor pressure[1,4,8]	Henry's constant[8]	Molecular weight[1,4,8]	Solubility in water (mg/L)[1,4]	Log K_{ow}[1,4,8]	K_{oc}[3]
Glyphosate acid	odorless, white solids	1.31×10^{-2} mPa (25 °C) 1.84×10^{-7} mmHg (45 °C)	4.08×10^{-19} atm·m^3/mol	169.07 g/mol	pH 1.9: 10,500 mg/L pH 7.0: 157,000 mg/L	Less than -3.2	300 - 20,100
Glyphosate isopropylamine salt	odorless, white solids	2.1×10^{-3} mPa (25 °C) 1.58×10^{-8} mmHg (25 °C)	6.27×10^{-27} atm·m^3/mol	228.19 g/mol	pH 4.06: 786,000 mg/L	-3.87 or -5.4	300 - 20,100
Glyphosate ammonium salt	odorless, white solids	9×10^{-3} mPa (25 °C) 6.75×10^{-8} mmHg (25 °C)	1.5×10^{-13} atm·m^3/mol	186.11 g/mol	pH 3.2: 144,000 mg/L	-3.7 or 5.32	300 - 20,100

Uses:

- Glyphosate is one of the most widely used herbicides with applications in agriculture, forestry, industrial weed control, lawn, garden, and aquatic environments.[1,6] Sites with the largest

glyphosate use include soybeans, field corn, pasture and hay.[2,6]

- Some plants have been genetically engineered to be resistant to glyphosate. Glyphosate-tolerant soybeans, corn, cotton, and canola are examples of such plants.[4,9] This fact sheet does not address glyphosate-tolerant crops.
- Uses for individual products containing glyphosate vary widely. Always read and follow the label when applying pesticide products.
- Signal words for products containing glyphosate may range from Caution to Danger. The signal word reflects the combined toxicity of the active ingredient and other ingredients in the product. See the pesticide label on the product and refer to the NPIC fact sheets on **Signal Words** and **Inert or "Other" Ingredients**.
- To find a list of products containing glyphosate which are registered in your state, visit the website **http://npic.orst.edu/reg/state_agencies.html** select your state then click on the link for "State Products."

Mode of Action:

Target Organisms

- In plants, glyphosate disrupts the shikimic acid pathway through inhibition of the enzyme 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase. The resulting deficiency in EPSP production leads to reductions in aromatic amino acids that are vital for protein synthesis and plant growth.[1,4]
- Glyphosate is absorbed across the leaves and stems of plants and is translocated throughout the plant.[1,3] It concentrates in the meristem tissue.[10]
- Plants exposed to glyphosate display stunted growth, loss of green coloration, leaf wrinkling or malformation, and tissue death. Death of the plant may take from 4 to 20 days to occur.[4,10]
- The sodium salt of glyphosate can act as a plant growth regulator and accelerate ripening of specific crops.[2]

Non-target Organisms

- The shikimic acid pathway is specific to plants and some microorganisms. The absence of this pathway in mammals may explain the low toxicity of glyphosate to non-target organisms.[11,12]
- Studies indicate that the surfactant polyoxyethyleneamine or polyethoxylated tallow amine (both abbreviated POEA), used in some commercial glyphosate-based formulations, may be more toxic by the oral route to animals than glyphosate itself.[13,14]
- The mechanism of toxicity of glyphosate in mammals is unknown, but it may cause uncoupling of oxidative phosphorylation.[15] However, this hypothesis has been disputed.[16]

Acute Toxicity:

Oral

- Glyphosate is low in toxicity to rats when ingested. The acute oral LD_{50} in rats is greater than 4320 mg/kg.[17] See the text boxes on **Toxicity Classification** and **LD_{50}/LC_{50}**.
- The acute oral LD_{50} for rats was also reported to be greater than 5000 mg/kg. The acute oral LD_{50} was greater than 10,000 mg/kg in mice and 3530 mg/kg in goats.[1]

- The isopropylamine salt is of very low toxicity to rats, with an LD_{50} greater than 5000 mg/kg.[1]
- The acute oral LD_{50} for the ammonium salt is 4613 mg/kg in rats.[1]
- The acute oral LD_{50} in three formulated products ranged from 3860 to greater than 5000 mg/kg in rats.[4]

LD_{50}/LC_{50}: A common measure of acute toxicity is the lethal dose (LD_{50}) or lethal concentration (LC_{50}) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD_{50} is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC_{50} 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 LD_{50}/LC_{50} is small and practically non-toxic when the value is large. However, the LD_{50}/LC_{50} 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.

Dermal

- Glyphosate is low in toxicity to rabbits when applied to the skin. The acute dermal LD_{50} in rabbits is greater than 2 g/kg.[17]
- Glyphosate is low in toxicity for eye irritation and very low in toxicity for dermal irritation. In studies with glyphosate manufacturing use products, researchers observed mild eye irritation in rabbits that cleared in seven days.[18,19]
- Glyphosate was not found to be a skin sensitizer.[6]
- The isopropylamine and ammonium salts are also low in toxicity via the dermal route. The LD_{50} in rabbits was greater than 5000 mg/kg for both salts, and these salts are considered slight eye irritants but not skin irritants.[1]
- Of three formulated products tested, skin irritation varied from none to moderate, and eye irritation was rated as none, moderate, and severe. Dermal LD_{50} values in rabbits exposed to these products were greater than 5000 mg/kg.[4]
- The formulated product Roundup®, containing 41% glyphosate, was applied to the skin of 204 male and female volunteers in a modified Draize test. No sensitization was observed. The researchers concluded that exposure would not lead to photoirritation or photosensitization.[20]

Inhalation

- Glyphosate is very low in toxicity to rats when inhaled. The acute inhalation LC_{50} in rats is greater than 4.43 mg/L based on a 4-hour, nose-only inhalation study.[21]
- The 4-hour LC_{50} for rats exposed to the isopropylamine form of glyphosate was greater than 1.3 mg/L air.[1]
- The LC_{50} for rats exposed to the ammonium salt form of glyphosate was greater than 1.9 mg/L in a whole body exposure.[1]
- Inhalation LC_{50} values for two formulated products were greater than 1.3 mg/L and 3.2 mg/L in rats.[4]

TOXICITY CLASSIFICATION - GLYPHOSATE

	High Toxicity	Moderate Toxicity	Low Toxicity	Very Low Toxicity
Acute Oral LD_{50}	Up to and including 50 mg/kg (≤ 50 mg/kg)	Greater than 50 through 500 mg/kg (>50-500 mg/kg)	**Greater than 500 through 5000 mg/kg (>500-5000 mg/kg)**	**Greater than 5000 mg/kg (>5000 mg/kg)**
Inhalation LC_{50}	Up to and including 0.05 mg/L (≤0.05 mg/L)	Greater than 0.05 through 0.5 mg/L	**Greater than 0.5 through 2.0 mg/L**	**Greater than 2.0 mg/L**

		(>0.05-0.5 mg/L)	**(>0.5-2.0 mg/L)**	**(>2.0 mg/L)**
Dermal LD_{50}	Up to and including 200 mg/kg (≤200 mg/kg)	Greater than 200 through 2000 mg/kg (>200-2000 mg/kg)	**Greater than 2000 through 5000 mg/kg (>2000-5000 mg/kg)**	Greater than 5000 mg/kg (>5000 mg/kg)
Primary Eye Irritation	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	Corneal involvement or other eye irritation clearing in 8 - 21 days	**Corneal involvement or other eye irritation clearing in 7 days or less**	**Minimal effects clearing in less than 24 hours**
Primary Skin Irritation	Corrosive (tissue destruction into the dermis and/or scarring)	Severe irritation at 72 hours (severe erythema or edema)	Moderate irritation at 72 hours (moderate erythema)	**Mild or slight irritation at 72 hours (no irritation or erythema)**

The highlighted boxes reflect the values in the "Acute Toxicity" section of this fact sheet. Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7: Precautionary Labeling. http://www.epa.gov/oppfead1/labeling/lrm/chap-07.pdf

Signs of Toxicity - Animals

- Animals exposed to formulated glyphosate herbicides have displayed anorexia, lethargy, hypersalivation, vomiting, and diarrhea. Symptoms persisted for 2 to 24 hours following exposure. The surfactants in formulated products are thought to be responsible for the clinical signs.[22]
- Clinical signs typically appear within 30 minutes to 2 hours following ingestion. Animals may exhibit excitability and tachycardia at first, followed by ataxia, depression, and bradycardia. Severe cases may progress to collapse and convulsions.[15]
- The Veterinary Poisons Information Service in London, England recorded 150 cases over an 8-year period of dogs exposed to glyphosate primarily from eating grass recently treated with formulated products. Of these, roughly 40% of the dogs exhibited no clinical signs, 45% exhibited mild to moderate clinical signs, and roughly 15% were classified as serious.[15]
- The Centre National d'Informations Toxicologiques Veterinaires of France reported 31 certain cases of intoxication of domestic animals by glyposate-containing products in a 3-year period. Most exposures resulted from animals ingesting the product prior to application. Of these cases, 25 were dogs and 4 were cats. Vomiting occurred within 1-2 hours of ingestion in 61% of the cases. Hypersalivation occurred in 26% of cases, and mild diarrhea was reported in 16% of cases. Centre records did not report long-lasting effects or any fatalities.[23]

Signs of Toxicity - Humans

- In a review of 80 intentional ingestion cases, 79 of which were suicide attempts, researchers identified typical symptoms of erosion of the gastrointestinal tract, dysphagia or difficulty swallowing, and gastrointestinal hemorrhage. Seven cases resulted in death.[24] Accidental ingestions are associated with mild gastrointestinal effects.[14]
- Eye and skin irritation have occasionally been reported from dermal exposure to glyphosate formulations.[13,14] However, adverse health effects are typically associated with exposure that occurs while mixing a concentrated product, not the use of dilute spray solutions.[13] Permanent ocular or dermal damage is very rare.[13,14,25]
- Inhalation of spray mist may cause oral or nasal discomfort, as well as tingling and throat irritation.[14]

- Always **follow label instructions** and take steps to **minimize exposure**. If any exposure occurs, be sure to follow the First Aid instructions on the product label carefully. For additional treatment advice, contact the Poison Control Center at 1-800- 222-1222. If you wish to **discuss an incident** with the National Pesticide Information Center, please call 1-800-858-7378.

Chronic Toxicity:

Animals

- Researchers gave beagle dogs capsules containing 0, 20,100, or 500 mg/kg/day of glyphosate for one year. No effects were observed; the NOEL for systemic toxicity is greater than or equal to 500 mg/kg/day.[26] See the text box on **NOAEL, NOEL, LOAEL, and LOEL**.
- Male rats were fed a diet containing glyphosate at 89, 362, or 940 mg/kg/day and females were similarly fed at concentrations of 113, 457, or 1183 mg/kg/day for 2 years. In the high-dose female group, researchers observed decreased body weight gain. In the high-dose male group, researchers observed decreased urinary pH, increased evidence of cataracts and lens abnormalities, and increased liver weight. No effects were observed in the low-dose and mid-dose groups. The LOEL for systemic toxicity was 940 and 1183 mg/kg/day for males and females, respectively. The NOEL for systemic toxicity is 362 mg/kg/day for males and 457 mg/kg/day for females.[27]

NOAEL: No Observable Adverse Effect Level

NOEL: No Observed Effect Level

LOAEL: Lowest Observable Adverse Effect Level

LOEL: Lowest Observed Effect Level

- Laboratory rats were fed diets containing glyphosate at doses of 0, 100, 300, or 1000 mg/kg/day for two years. After 52 weeks, some rats in the two highest dose groups had enlarged salivary glands with cellular changes. The NOEL was determined to be 100 mg/kg/day.[28]
- Based on a battery of tests, glyphosate is not expected to have immunotoxicity or neurotoxicity. Laboratory mice were fed diets containing glyphosate for 28 days. The NOAEL for immunotoxicity was determined to be 1448 mg/kg/day.[29] The NOAEL for subchronic neurotoxicity in rats was determined to be 1546.5 and 1630.6 mg/kg/day for males and females, respectively.[30]
- The Acceptable Daily Intake (ADI) of a combination of glyphosate and certain metabolites (AMPA, N-acetyl glyphosate, and N-acetyl AMPA) for humans is 1.0 mg/kg. In 2011, the International Estimated Daily Intake (IEDI) of glyphosate and major metabolites was estimated to range from 0-2% of the ADI.[31,32]
- The chronic reference dose for glyphosate is 1.75 mg/kg/day.[33] See the text box on **Reference Dose (RfD)**.

Humans

- Researchers collected urine samples over 8 months from workers at two forestry nurseries where glyphosate was used for weed control. No glyphosate was detected in any of the 355 urine samples. The researchers attributed the lack of detected glyphosate in worker urine samples to the poor absorption of glyphosate through the skin.[34] See the text box on **Exposure**.

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.

- Five forestry workers sprayed glyphosate for 6 hours a day over the course of a week. No statistically significant differences were found in medical examinations and laboratory testing performed on the workers following pesticide application.[35]
- Researchers collected urine samples from farm families in South Carolina and Minnesota as part of the Farm Family Exposure Study. On the day of application, 60% of farmers had a detectable level of glyphosate in their urine of at least 1 ppb. The geometric mean of glyphosate detected was 3 ppb, with a maximum value of 233 ppb. Mean urinary concentrations of glyphosate were higher in farmers who did not use rubber gloves during application.[36]

Endocrine Disruption:

- Rats and mice were fed a diet containing 0, 3125, 6250, 12,500, 25,000, or 50,000 ppm of 99% pure glyphosate for 13 weeks. The two highest dose groups of male rats had a significant reduction in sperm concentrations, although concentrations were still within the historical range for that rat strain. The highest dose group of female rats had a slightly longer estrus cycle than the control group.[37]
- Researchers reviewed the scientific literature on glyphosate, its major metabolite AMPA, formulated Roundup® products manufactured by Monsanto, and the surfactant POEA. They found no evidence of endocrine effects in humans or other mammals.[13]
- Using results from the EPA's Endocrine Disruptor Screening Program (EDSP), glyphosate was not considered to be an endocrine disruptor based on a lack of potential interaction with the estrogen, androgen or thyroid pathways.[38]

Carcinogenicity:

Animals

- Researchers fed rats a diet containing glyphosate at 0, 89, 362, or 940 mg/kg/day (males) and 0, 113, 457, or 1183 mg/kg/day (females) for two years. The high dose in this study approaches or exceeds the limit dose recommended for carcinogenicity studies. Slight increases in pancreatic islet cell adenomas, hepatocellular adenomas, and thyroid C-cell adenomas were observed in some cases. None of these findings were statistically significant. The incidence of tumors was within the range of historical controls (historical control data from seven years of laboratory research) for the evaluated tumor types in this study. The U.S. EPA concluded the tumors were not treatment-related.[27,39]
- In a carcinogenicity study, mice were fed a diet containing glyphosate (0, 161/195, 835/968, 4945/6069 mg/kg/day for males and females, respectively) for 24 months. The moderate and high doses in this study exceed or approach the limit dose recommended for carcinogenicity studies. In the high-dose groups researchers observed decreased body weight gain in both male and female mice. In high-dose males, slightly increased incidence of renal tubular adenomas was noted. A later re-evaluation of tissues determined that renal tumors were not related to glyphosate exposure. An independent group of pathologists and biometricians also concluded that the occurrence of adenomas was not caused by glyphosate. Kidney tissue

examinations found chronic interstitial nephritis and tubular epithelial basophilia and hypertrophy in male rats. Overall, there was not an increase in tubular lesions observed in male mice.[39,40,41]

- In a carcinogenicity study, technical grade glyphosate was given to male and female rats in their diet (0, 95, 316.9, and 1229.7 mg/kg/day). In female rats, a slight increase in mammary gland tumors was noted. Tumor incidence was not statistically significant in pairwise comparisons.[39]
- Goldfish (***Carassius auratus***) were exposed to 5, 10, or 15 ppm of the formulated product Roundup® containing the IPA salt of glyphosate and the surfactant POEA for 6 days. Researchers noted increased DNA and micronuclei damage in the peripheral erythrocytes. This may have resulted from decreased DNA repair. Genotoxicity test results are generally mixed, although formulated products appear to be more likely to cause effects than glyphosate alone.[42]
- Glyphosate has been the subject of numerous genotoxicity tests and the results are overwhelmingly negative.[31] Doses that showed positive results ***in vivo*** were too high to be considered relevant for human health risk assessment.[39]

Humans

- The U.S. EPA classified glyphosate as "not likely to be carcinogenic to humans." Human carcinogenic potential was evaluated by reviewing available epidemiological, animal carcinogenicity, and genotoxicity data.[30,39] See the text box on **Cancer**.

> **Cancer: Government agencies in the United States and abroad have developed programs to evaluate the potential for a chemical to cause cancer. Testing guidelines and classification systems vary. To learn more about the meaning of various cancer classification descriptors listed in this fact sheet, please visit the appropriate reference, or call NPIC.**

- Pesticide regulatory authorities in Canada, Japan, Australia, and the European Union have completed independent carcinogenicity assessments that resulted in similar carcinogenicity determinations as the U.S. EPA.[43,44,45,46] The U.S. National Institute of Health's National Toxicology Program has also found "no evidence of glyphosate causing damage to DNA."[47] The Joint Meeting on Pesticide Residues of the Food and Agriculture Organization of the United Nations and the World Health Organization's assessment determined that glyphosate is unlikely to pose a carcinogenic risk from exposure through the diet.[48]
- The International Agency for Research on Cancer (IARC) classified glyphosate as Group 2A, "probably carcinogenic to humans."[49]
- Researchers analyzed the source of variations between IARC and the European Food Safety Authority's (EFSA) cancer classifications. IARC assessments aim to identify carcinogenic hazards while EFSA also incorporated levels of expected exposures into the regulatory determination. The IARC assessment included only research that was available in published literature. Additionally, the EFSA assessment included five animal carcinogenicity studies published after the IARC Monograph.[50] Research used in IARC's determination included studies with both technical grade active ingredient and formulated products containing glyphosate.[49]
- A review of IARC and EFSA carcinogenic evaluations identified differences in the study selection process, including EFSA's use of historical control data and exclusion of non-guideline

research and effects seen at doses higher than the limit dose or the maximum tolerated dose (MTD).[51]

- Researchers reviewed the scientific literature on glyphosate, its major metabolite AMPA, formulated Roundup® products manufactured by Monsanto, and the surfactant POEA. They found that Roundup® and its components did not cause mutations or tumor formation. The researchers concluded that glyphosate is not carcinogenic.[13]
- Researchers assessed the exposure-response relationship between use of products containing glyphosate and cancer in 57, 311 licensed pesticide applicators participating in the Agricultural Health Study. Exposure to glyphosate was not associated with overall cancer incidence or most cancer subtypes. In a small number of cases, there was a "suggested association" between glyphosate exposure and multiple myeloma incidence.[52]
- Additional reviews of AHS data and other epidemiological studies reveal no consistent association between glyphosate and solid tumors, leukemia, Hodgkin's Lymphoma, and multiple myeloma. Available data are insufficient to support conclusions regarding associations between glyphosate and Non-Hodgkin's Lymphoma.[39]

Reproductive or Teratogenic Effects:

Animals

- In a developmental study, pregnant rabbits were given glyphosate by gavage (stomach tube) on gestation days 7-19 at doses of 0, 100, 175, 300 mg/kg/day. Rabbits in the middle and higher doses had diarrhea or few and/or no feces. Rabbits were the most sensitive animal species tested, with a developmental NOAEL of 300 mg/kg/day. Based on this rabbit study, the chronic dietary and incidental exposure NOAEL and LOAEL are 100 and 175 mg/kg/day, respectively.[30]
- Researchers dosed pregnant rats with glyphosate by gavage (stomach tube) on gestation days 6-19 at doses of 0, 300, 1000, or 3500 mg/kg/day. At the highest dose, they detected decreased body weight gains in both the dams and fetuses, increased maternal mortality, and an increased number of fetal skeletal abnormalities. The NOEL for maternal and developmental toxicity was 1000 mg/kg/day and the LOEL was 3500 mg/kg/day.[30,53]
- 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 tested, the animals exhibited diarrhea, nasal discharge, and increased mortality; too many animals died in this group to assess developmental effects at this dose. The NOEL for maternal effects was 175 mg/kg/day.[30,54]
- After reviewing the toxicological database, EPA found no evidence of increased susceptibility of young rats and rabbits to in utero exposures of glyphosate.[30]
- Dietary concentrations of up to 10,000 ppm or 293 mg/kg/day of glyphosate given to rats over two generations had no effect on male or female sexuality and fertility. The NOAEL for parental and offspring toxicity is 3000 ppm, based upon a reduction of body weight at 10,000 ppm.[31,55]
- Researchers reviewed the scientific literature on glyphosate, its major metabolite AMPA, formulated Roundup® products manufactured by Monsanto, and the surfactant POEA. They concluded that neither glyphosate, AMPA, nor POEA caused reproductive effects in various animal studies.[13]

Humans

- Questionnaires filled out by farm operators and eligible couples collected during the Ontario Farm Family Health Study suggested that there was an association between preconception exposure to pesticide products containing glyphosate and elevated risks of late spontaneous abortion.[56]

Fate in the Body:

Absorption

- Animal studies have indicated that 30-36% of glyphosate is absorbed after ingestion.[11,13,57]
- Dermal absorption of glyphosate is poor.[6] An ***in vitro*** experiment with human skin resulted in a maximum of 2.2% of 2.6 µg/cm^2 glyphosate was absorbed across the skin. Absorption peaked 8 hours after administration.[58]
- Researchers applied glyphosate to abdominal skin of monkeys at doses of 5400 µg or 500 µg over 20 cm^2 of skin. Over a 7 day period, 73.5% and 77.1% of the applied dose remained on the skin.[58]
- Glyphosate is non-volatile.[6] Absorption from inhalation exposure is not expected to be significant.[14]

Distribution

- Rats dosed orally with 10 mg/kg glyphosate attained peak concentrations in their tissues 6 hours following dosing. The gastrointestinal tract contents accounted for 50% of the dose, with the tissue of the small intestine accounting for an additional 18%. Approximately 5% of the dose was found in bone and 6% in the carcass, with 1% or less of the dose distributed to abdominal fat, blood, colon, kidney, liver, and stomach.[57]
- Researchers gave rats a single oral dose of 10 mg/kg or 1000 mg/kg of glyphosate. Seven days after administration, the absorbed dose had distributed throughout the body, although it was primarily concentrated in the bone.[59]
- Researchers fed hens and goats glyphosate and found glyphosate and its major metabolite AMPA in eggs, milk, and the animals' body tissues.[13,60,61]

Metabolism

- Glyphosate undergoes little metabolism and is excreted mostly unchanged in the feces and secondarily in the urine.[3,13,62]
- Samples taken from goats and hens fed glyphosate contained the parent compound and AMPA, but there was no evidence of other glyphosate metabolites in body tissues, eggs, or milk.[6]
- High ratios of glyphosate to AMPA were detected in a human patient's blood serum 8 hrs (22.6 µg/mL glyphosate to 0.18 µg/mL AMPA) and 16 hrs (4.4 µg/mL glyphosate to 0.03 µg/mL AMPA) post-ingestion, as well as in the patient's total amount of urine. This indicates that glyphosate metabolism was minimal.[63]

Excretion

- Animal studies indicate that glyphosate is primarily excreted through the urine and feces.[3,13,62]
- A rat given a single oral dose of glyphosate eliminated 0.27% of the administered dose as carbon dioxide, and excreted 97.5% as glyphosate in urine and feces. Researchers detected AMPA in urine (0.2-0.3% of administered dose) and feces (0.2-0.4% of administered dose).[64,65]
- Glyphosate is cleared from the body of rats 168 hours after administration.[11]
- Two human patients who were poisoned with glyphosate had peak plasma glyphosate concentrations within 4 hours of ingestion. After 12 hours, glyphosate was almost undetectable.[66]

Medical Tests and Monitoring:

- Glyphosate exposure can be monitored through measurement of glyphosate and AMPA concentrations in blood or urine.[11,67,68] Detection methods include gas chromatography and high-performance liquid chromatography.[63,68,69] However, the clinical significance of residues in human tissues is unknown.
- Researchers developed a sensitivity enhanced multiplexed fluorescence covalent microbead immunosorbent assay (FCMIA) for the measurement of glyphosate in urine.[70] This method was used to detect glyphosate in a study among farm and non-farm households in Iowa.[71]

Environmental Fate:

Soil

- The median half-life of glyphosate in soil has been widely studied; values between 2 and 197 days have been reported in the literature.[7,62] A typical field half-life of 47 days has been suggested.[4] Soil and climate conditions affect glyphosate's persistence in soil.[1] See the text box on **Half-life**.
- Glyphosate is relatively stable to chemical and photo decomposition.[6] The primary pathway of glyphosate degradation is soil microbial action, which yields AMPA and glyoxylic acid. Both products are further degraded to carbon dioxide.[3]
- Glyphosate adsorbs tightly to soil. Glyphosate and its residues are expected to be immobile in soil.[6]

The "half-life" is the time required for half of the compound to break down in the environment.

1 half-life = 50% remaining
2 half-lives = 25% remaining
3 half-lives = 12% remaining
4 half-lives = 6% remaining
5 half-lives = 3% remaining

Half-lives can vary widely based on environmental factors. The amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied. It should be noted that some chemicals may degrade into compounds of toxicological significance.

Water

- The median half-life of glyphosate in water varies from a few days to 91 days.[1]
- Glyphosate did not undergo hydrolysis in buffered solution with a pH of 3, 6, or 9 at 35 °C. Photodegradation of glyphosate in water was insignificant under natural light in a pH 5, 7, and 9 buffered solution.[72,73]
- Glyphosate in the form of the product Roundup® was applied to aquatic plants in fresh and brackish water. Glyphosate concentrations in both ponds declined rapidly, although the binding

of glyphosate to bottom sediments depended heavily on the metals in the sediments. If chelating cations are present, the sediment half-life of glyphosate may be greatly increased.[74]
- Glyphosate has a low potential to contaminate groundwater due to its strong adsorptive properties. However, there is potential for surface water contamination from aquatic uses of glyphosate and soil erosion.[6]
- Volatilization of glyphosate is not expected to be significant due to its low vapor pressure.[6]

Air

- Glyphosate and all its salts are very low in volatility with vapor pressures ranging from 1.84 x 10^{-7} mmHg to 6.75 x 10^{-8} mmHg at 25 °C.[1,4,8]
- Glyphosate is stable in air.[1]

Plants

- Glyphosate is absorbed by plant foliage and transported throughout the plant through the phloem.[3] Glyphosate absorption across the cuticle is moderate, and transport across the cell membrane is slower than for most herbicides.[4] Because glyphosate binds to the soil, plant uptake of glyphosate from soil is negligible.[3]
- Glyphosate accumulates in meristems, immature leaves, and underground tissues.[4]
- Very little glyphosate is metabolized in plants, with AMPA as the only significant degradation product.[3]
- Lettuce, carrots, and barley contained glyphosate residues up to one year after the soil was treated with 3.71 pounds of glyphosate per acre.[75,76]
- Glyphosate had a median half-life of 8 to 9 days in leaf litter of red alder and salmonberry sprayed with Roundup®.[62]

Indoor

- All surface wipe and dust samples collected from five farm households in Iowa contained detectable levels of glyphosate ranging from 0.0081-2.7 ng/cm^2. In six non-farm households, 28 out of 33 samples collected contained detectable levels of glyphosate ranging from 0.0012-13 ng/cm^2.[77]

Food Residue

- Glyphosate was not included in compounds tested for by the Food and Drug Adminstration's (FDA) Pesticide Residue Monitoring Program (PRMP), nor in the United States Department of Agriculture's Pesticide Data Program (PDP).

Ecotoxicity Studies:

Birds

- An acute oral toxicity study found that a single dose of technical grade glyphosate is practically non-toxic to bobwhite quail, with an LD_{50} of greater than 2000 mg/kg.[78]

- Studies with technical grade glyphosate found an 8-day dietary LC_{50} greater than 4000 ppm for mallard ducks and bobwhite quail, indicating slight toxicity.[78,79]
- Glyphosate is not expected to cause reproductive impairment in birds at dietary levels of up to 1000 ppm.[6]
- An ecological risk assessment concluded that the greatest risk posed by glyphosate and its formulated products to birds and other wildlife results from alteration of habitat.[7]

Fish and Aquatic Life

- Technical grade glyphosate ranges from slightly toxic to practically non-toxic to freshwater fish, with a 48-hour LC_{50} of greater than 24 mg/L to 140 mg/L.[6]
- Formulated glyphosate products range from moderately toxic to practically non-toxic to freshwater fish, with 96-hour LC_{50} values ranging from 1.3 mg/L to greater than 1000 mg/L.[6]
- The preparation of the surfactant POEA known as MON 0818 is used in some glyphosate formulations.[7] POEA is moderately toxic to very highly toxic to freshwater fish. The 96-hour LC_{50} values ranged from 0.65 mg/L to 13 mg/L. Products containing MON 0818 state on the label "This pesticide is toxic to fish".[6]
- The LC_{50} of glyphosate for rainbow trout (***Onchorynchus mykiss***) was 140 mg/L, for fathead minnows (***Pimephales promelas***) was 97 mg/L, for channel catfish (***Icalurus punctatus***) was 130 mg/L and for bluegill sunfish (***Lepomis macrochirus***) was 150 mg/L. When they were exposed to Roundup®, the LC_{50}s for these same fish were 8.3, 2.4, 13.0, and 6.4 mg/L, respectively.[80]
- Technical grade glyphosate is slightly toxic to practically non-toxic to freshwater invertebrates, with a 48-hour LC_{50} ranging from 55 ppm to 780 ppm.[6] The 48-hour LC_{50} for Daphnids was 3.0 mg/L and the LC_{50} for midge larvae was 16 mg/L when exposed to the formulated product Roundup®.[80]
- Researchers calculated LC_{50} values for four species of amphibians (the northern leopard frog (***Rana pipiens***), the wood frog (***R. sylvatica***), the green frog (***R. clamitans***), and the American toad (***Bufo americanus***)) exposed to the original Roundup® formulation of glyphosate. The 24-hour LC_{50} values for the different species ranged from 6.6 to 18.1 mg/L.[81]
- Green frogs (***R. clamitans***) were exposed to technical glyphosate in the form of the isopropylamine salt, the surfactant POEA, and six formulated products containing glyphosate. The surfactant was most toxic to R. clamitans with a 24 and 96- hour LC_{50} of 1.1 mg/L (95% CI 1.1-1.2) and 1.1 mg/L (95% CI 1.0-1.1), respectively. Technical glyphosate was least toxic, with 24 and 96-hour LC_{50} of >38.9 g/L. The toxicity of the formulated products fell between these values.[81]
- A chronic toxicity study with technical grade glyphosate reported reduced reproductive capacity in Daphnia magna with a maximum acceptable toxicant concentration of 50 to 96 ppm.[82]
- Technical grade glyphosate is practically non-toxic to slightly toxic to estuarine and marine organisms. The 96-hour LC_{50} is 281 ppm for grass shrimp (***Palaemonetas vulgaris***) and 934 ppm for fiddler crab (***Uca pagilator***).[83] The 48-hour median lethal time (TL_{50}) is greater than 10 mg/L for Atlantic oyster (***Crassostrea virginica***).[84]

Terrestrial Invertebrates

- Studies indicate that both technical and formulated glyphosate are practically non-toxic to honeybees, with acute oral and acute contact LD_{50} values greater than 100 µg/bee.[85]
- An ecological risk assessment of Roundup® concluded that the greatest risks to arthropods were from altered habitat structure and food availability.[7]
- The earthworm LC_{50} in soil is greater than 5000 ppm for Monsanto's formulated product Roundup®.[4]

Regulatory Guidelines:

- The U.S. EPA classified glyphosate as "not likely to be carcinogenic to humans."[30,39]
- The reference dose (RfD) for glyphosate is 1.75 mg/kg/day.[33] See the text box on **Reference Dose (RfD)**.
- The Acceptable Daily Intake (ADI) of a combination of glyphosate and certain metabolites (AMPA, N-acetyl glyphosate, and N-acetyl AMPA) for humans is 1.0 mg/kg.[31,32]
- The U.S. EPA has set a One-Day Health Advisory of 20 mg/L.[86]
- The U.S. EPA has set a Ten-day Health Advisory of 20 mg/L.[86]
- The maximum contaminant level (MCL) is 0.7 mg/L.[86] See the text box on **Maximum Contaminant Level (MCL)**.

Reference Dose (RfD): The RfD is an estimate of the quantity of chemical that a person could be exposed to every day for the rest of their life with no appreciable risk of adverse health effects. The reference dose is typically measured in milligrams (mg) of chemical per kilogram (kg) of body weight per day.

U.S. Environmental Protection Agency, Health Effects Notebook Glossary, 2019. **https://www.epa.gov/haps/health-effects-notebook-glossary**

Maximum Contaminant Level (MCL): The MCL is the highest level of contaminant that is legally allowed in drinking water. The MCL is enforceable. The MCL is typically measured in milligrams (mg) of contaminant per liter (L) of water.

U.S. Environmental Protection Agency, National Primary Drinking Water Regulations, 2019. **https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations#one**

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