NPIC Technical Fact Sheets provide information that is complex and intended for individuals with a scientific background and/or familiarity with toxicology and risk assessment. This document is intended to promote informed decision-making. Please refer to the General Fact Sheet for less technical information.

## Chemical Class and Type:

- Glyphosate is a non-selective systemic herbicide that is applied directly to plant foliage.<sup>1</sup> When used in smaller quantities, glyphosate can act as a plant growth regulator.<sup>2</sup> Glyphosate is a glycine derivative.<sup>1</sup> The International Union of Pure and Applied Chemistry (IUPAC) name for glyphosate is N-(phosphonomethyl) glycine<sup>3</sup> and the Chemical Abstracts Service (CAS) registry number is 1071-83-6.<sup>1</sup>
- Glyphosate's potential as an herbicide was reported in 1971.<sup>1,4</sup> Glyphosate was first registered for use by the United States Environmental Protection Agency (U.S. EPA) in 1974<sup>5</sup>, and reregistration was completed in 1993.<sup>6</sup> 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.<sup>1,2,4</sup> 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.<sup>2,7</sup>

## **Physical / Chemical Properties:**

• See the table on page 2 for glyphosate and associated forms.

## **Uses:**

- Glyphosate is one of the most widely used herbicides with applications in agriculture, forestry, industrial weed control, lawn, garden, and aquatic environments.<sup>1,6</sup> Sites with the largest glyphosate use include soybeans, field corn, pasture and hay.<sup>2,6</sup>
- Some plants have been genetically engineered to be resistant to glyphosate. Glyphosate-tolerant soybeans, corn, cotton, and canola are examples of such plants.<sup>4,9</sup> 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 <u>Signal Words</u> and <u>Inert or "Other" Ingredients</u>.
- To find a list of products containing glyphosate which are registered in your state, visit the website <a href="http://npic.orst.edu/reg/state\_agencies.html">http://npic.orst.edu/reg/state\_agencies.html</a> and search by "active ingredient."

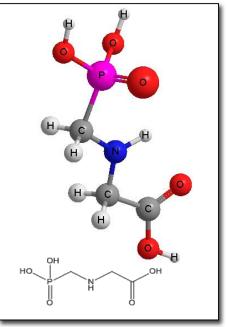
Laboratory animals are purposely given high enough doses to cause toxic effects. These tests help scientists judge how these chemicals might affect humans, domestic animals, and wildlife in cases of overexposure.

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.

## Molecular Structure -Glyphosate





## **Physical / Chemical Properties:**

Active Ingredient	Form <sup>1,4</sup>	Vapor pressure <sup>1,4,8</sup>	Henry's constant <sup>8</sup>	Molecular Weight <sup>1,4,8</sup>	Solubility In water (mg/L) <sup>1,4</sup>	Log K <sub>ow</sub> <sup>1,4,8</sup>	K <sub>oc</sub> <sup>3</sup>
Glyphosate acid	odorless, white solids	1.31 x 10 <sup>-2</sup> mPa (25 °C) 1.84 x 10 <sup>-7</sup> mmHg (45 °C)	4.08 x 10 <sup>-19</sup> atm∙m <sup>3</sup> /mol	169.07 g/ mol	pH 1.9: 10,500 mg/L pH 7: 15,7000 mg/L	Less than -3.2	300 - 20,100
Glyphosate isopropylamine salt	odorless, white solids	2.1 x 10 <sup>-3</sup> mPa (25 °C) 1.58 x 10 <sup>-8</sup> mmHg (25 °C)	6.27 x 10 <sup>-27</sup> atm∙m <sup>3</sup> /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 x 10 <sup>-3</sup> mPa (25 °C) 6.75 x 10 <sup>-8</sup> mmHg (25 °C)	1.5 x 10 <sup>-13</sup> atm∙m <sup>3</sup> /mol	186.11 g/ mol	pH 3.2: 144,000 mg/L	-3.7 or -5.32	300 - 20,100

## **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.<sup>1,4</sup>
- Glyphosate is absorbed across the leaves and stems of plants and is translocated throughout the plant.<sup>1,3</sup> It concentrates in the meristem tissue.<sup>10</sup>
- 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.<sup>4,10</sup>
- The sodium salt of glyphosate can act as a plant growth regulator and accelerate fruit ripening.<sup>2</sup>

### 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.<sup>11,12</sup>
- 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.<sup>13,14</sup>
- The mechanism of toxicity of glyphosate in mammals is unknown, but it may cause uncoupling of oxidative phosphorylation.<sup>15</sup> However, this hypothesis has been disputed.<sup>16</sup>

## **Acute Toxicity:**

## Oral

Glyphosate is low in toxicity to rats when ingested. The acute oral LD<sub>50</sub> in rats is greater than 4320 mg/kg.<sup>17</sup> See the text boxes on **Toxicity Classification** and LD<sub>50</sub>/LC<sub>50</sub>.

 $LD_{s0}/LC_{s0}$ : A common measure of acute toxicity is the lethal dose ( $LD_{s0}$ ) or lethal concentration ( $LC_{s0}$ ) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals.  $LD_{s0}$  is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight.  $LC_{s0}$  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  $LD_{s0}/LC_{s0}$  is small and practically non-toxic when the value is large. However, the  $LD_{s0}/LC_{s0}$  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.

 The acute oral LD<sub>50</sub> for rats was also reported to be greater than 5000 mg/kg. The acute oral LD<sub>50</sub> was greater than 10,000 mg/kg in mice and 3530 mg/kg in goats.<sup>1</sup>



- The isopropylamine salt is of very low toxicity to rats, with an LD<sub>50</sub> greater than 5000 mg/kg.<sup>1</sup>
- The acute oral LD<sub>50</sub> for the ammonium salt is 4613 mg/kg in rats.<sup>1</sup>
- The acute oral LD<sub>50</sub> in three formulated products ranged from 3860 to greater than 5000 mg/kg in rats.<sup>4</sup>

#### Dermal

- Glyphosate is low in toxicity to rabbits when applied to the skin. The acute dermal LD<sub>50</sub> in rabbits is greater than 2 g/kg.<sup>17</sup>
- 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.<sup>18,19</sup>
- Glyphosate was not found to be a skin sensitizer.<sup>6</sup>
- The isopropylamine and ammonium salts are also low in toxicity via the dermal route. The LD<sub>50</sub> in rabbits was greater than 5000 mg/kg for both salts, and these salts are considered slight eye irritants but not skin irritants.<sup>1</sup>
- Of three formulated products tested, skin irritation varied from none to moderate, and eye irritation was rated as none, moderate, and severe. Dermal LD<sub>50</sub> values in rabbits exposed to these products were greater than 5000 mg/kg.<sup>4</sup>
- The formulated product Roundup<sup>®</sup>, 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.<sup>20</sup>

#### Inhalation

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

TOXICITY CLASSIFICATION - GLYPHOSATE								
	High Toxicity	Moderate Toxicity	Low Toxicity	Very Low Toxicity				
Acute Oral LD <sub>50</sub>	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 <sub>50</sub>	Up to and including 0.05 mg/L (≤ 0.05 mg/L) (aerosol)	Greater than 0.05 through 0.5 mg/L (>0.05 – 0.5 mg/L)	Greater than 0.5 through 2.0 mg/L (> 0.5 – 2.0 mg/L)	Greater than 2.0 mg/L (> 2.0 mg/L) (dust)				
Dermal LD <sub>50</sub>	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 relfect 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.<sup>22</sup>
- 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.<sup>15</sup>
- 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.<sup>15</sup>
- 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.<sup>23</sup>

### **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.<sup>24</sup> Accidental ingestions are associated with mild gastrointestinal effects.<sup>14</sup>
- Eye and skin irritation have occasionally been reported from dermal exposure to glyphosate formulations.<sup>13,14</sup> However, adverse health effects are typically associated with exposure that occurs while mixing a concentrated product, not the use of dilute spray solutions.<sup>13</sup> Permanent ocular or dermal damage is very rare.<sup>13,14,25</sup>
- Inhalation of spray mist may cause oral or nasal discomfort, as well as tingling and throat irritation.<sup>14</sup>
- Always follow label instructions and take steps to avoid exposure. If any exposures occur, 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 report an incident, 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 No Observed Effect Level (NOEL) for systemic toxicity is greater than or equal to 500 mg/kg/day.<sup>26</sup> See the text box on NOAEL, NOEL, LOAEL, and LOEL.

NOAEL: No Observable Adverse Effect Level NOEL: No Observed Effect Level LOAEL: Lowest Observable Adverse Effect Level

LOEL: Lowest Observed Effect Level

- 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 Lowest Observed Effect Level (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.<sup>27</sup>
- The chronic reference dose for glyphosate is 1.75 mg/kg/day<sup>28</sup>. See the text box on **Reference Dose (RfD)** on page 10.



### 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.<sup>29</sup> See the text box on **Expo**sure.

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.<sup>30</sup>
- 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.<sup>31</sup>

## **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.<sup>32</sup>
- Researchers reviewed the scientific literature on glyphosate, its major metabolite AMPA, formulated Roundup<sup>®</sup> products manufactured by Monsanto, and the surfactant POEA. They found no evidence of endocrine effects in humans or other mammals.<sup>13</sup>
- Glyphosate is included in the draft list of initial chemicals for screening under the U.S. EPA Endocrine Disruptor Screening Program (EDSP). The draft list of chemicals was generated based on exposure potential, not based on whether the pesticide is a known or likely potential cause of endocrine effects.<sup>33</sup>

## **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 low-dose and high-dose male groups had a slightly increased incidence of pancreatic islet cell adenomas and hepatocellular adenomas. The mid-dose and high-dose male and female groups had a slightly increased incidence of thyroid C-cell adenomas. The EPA concluded the adenomas were not treatment related.<sup>27</sup>
- In a carcinogenicity study, mice were fed a diet containing glyphosate (0, 150, 750, or 4500 mg/kg/day) for 18 months. Researchers observed no effects in the low-dose and mid-dose groups. 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, increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis were noted in the high-dose group. In females, researchers noted increased incidence of proximal tubule epithelial basophilia and hypertrophy at the highest doses. The EPA and an independent group of pathologists and biometricians concluded that the occurrence of adenomas was not caused by glyphosate.<sup>34,35</sup>
- Based on this mouse study, the systemic NOEL and LOEL were determined to be 750 and 4500 mg/kg/day, respectively.<sup>6</sup>



- Goldfish (*Carassius auratus*) were exposed to 5, 10, or 15 ppm of the formulated product Roundup<sup>®</sup> 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.<sup>36</sup>
- Glyphosate has been the subject of numerous genotoxicity tests and the results are overwhelmingly negative.<sup>37</sup>

#### Humans

• The U.S. EPA classified glyphosate as Group E, evidence of non-carcinogenicity in humans. The U.S. EPA does not consider glyphosate to be a human carcinogen based on studies of laboratory animals that did not produce compelling evidence of carcinogenicity.<sup>6</sup> 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.

- 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.<sup>13</sup>
- 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.<sup>38</sup>

## **Reproductive or Teratogenic Effects:**

### Animals

- 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.<sup>39</sup>
- 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.<sup>40</sup>
- 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.<sup>37,41</sup>
- Researchers reviewed the scientific literature on glyphosate, its major metabolite AMPA, formulated Roundup<sup>®</sup> products manufactured by Monsanto, and the surfactant POEA. They concluded that neither glyphosate, AMPA, nor POEA caused reproductive effects in various animal studies.<sup>13</sup>

### 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.<sup>42</sup>



## Fate in the Body:

### Absorption

- Animal studies have indicated that 30-36% of glyphosate is absorbed after ingestion.<sup>11,13,43</sup>
- Dermal absorption of glyphosate is poor.<sup>6</sup> An *in vitro* experiment with human skin resulted in a maximum of 2.2% of 2.6 μg/ cm<sup>2</sup> glyphosate was absorbed across the skin. Absorption peaked 8 hours after administration.<sup>44</sup>
- Researchers applied glyphosate to abdominal skin of monkeys at doses of 5400 µg or 500 µg over 20 cm<sup>2</sup> of skin. Over a 7 day period, 73.5% and 77.1% of the applied dose remained on the skin.<sup>44</sup>
- Glyphosate is non-volatile.<sup>6</sup> Absorption from inhalation exposure is not expected to be significant.<sup>14</sup>

### 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.<sup>43</sup>
- 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.<sup>45</sup>
- Researchers fed hens and goats glyphosate and found glyphosate and its major metabolite AMPA in eggs, milk, and the animals' body tissues.<sup>13,46,47</sup>

### Metabolism

- Glyphosate undergoes little metabolism and is excreted mostly unchanged in the feces and secondarily in the urine.<sup>3,13,48</sup>
- 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.<sup>6</sup>
- 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.<sup>49</sup>

### Excretion

- Animal studies indicate that glyphosate is primarily excreted through the urine and feces.<sup>3,13,48</sup>
- 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).<sup>50,51</sup>
- Glyphosate is cleared from the body of rats 168 hours after administration.<sup>11</sup>
- 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.<sup>52</sup>

## **Medical Tests and Monitoring:**

- Glyphosate exposure can be monitored through measurement of glyphosate and AMPA concentrations in blood or urine.<sup>11,53,54</sup> Detection methods include gas chromatography and high-performance liquid chromatography.<sup>49,54,55</sup> However, the clinical significance of residues in human tissues is unknown.
- Researchers developed a sensitivity enhanced multiplexed fluorescence covalent microbead immunosorbent assay (FC-MIA) for the measurement of glyphosate in urine.<sup>56</sup> This method was used to detect glyphosate in a study among farm and non-farm households in Iowa.<sup>57</sup>



## **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.<sup>7,48</sup> A typical field half-life of 47 days has been suggested.<sup>4</sup> Soil and climate conditions affect glyphosate's persistence in soil.<sup>1</sup> See the text box on Half-life.
- Glyphosate is relatively stable to chemical and photo decomposition.<sup>6</sup> The primary pathway of glyphosate degradation is soil microbial action, which yields AMPA and glyoxylic acid. Both products are further degraded to carbon dioxide.<sup>3</sup>
- Glyphosate adsorbs tightly to soil. Glyphosate and its residues are expected to be immobile in soil.<sup>6</sup>

#### Water

- The median half-life of glyphosate in water varies from a few days to 91 days.<sup>1</sup>
- 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.<sup>58,59</sup>
- Glyphosate in the form of the product Roundup<sup>®</sup> 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.<sup>60</sup>
- 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.<sup>6</sup>
- Volatilization of glyphosate is not expected to be significant due to its low vapor pressure.<sup>6</sup>

#### Air

- Glyphosate and all its salts are very low in volatility with vapor pressures ranging from 1.84 x 10<sup>-7</sup> mmHg to 6.75 x 10<sup>-8</sup> mmHg at 25 °C.<sup>1,4,8</sup>
- Glyphosate is stable in air.<sup>1</sup>

#### Plants

- Glyphosate is absorbed by plant foliage and transported throughout the plant through the phloem.<sup>3</sup> Glyphosate absorption across the cuticle is moderate, and transport across the cell membrane is slower than for most herbicides.<sup>4</sup> Because glyphosate binds to the soil, plant uptake of glyphosate from soil is negligible.<sup>3</sup>
- Glyphosate accumulates in meristems, immature leaves, and underground tissues.<sup>4</sup>
- Very little glyphosate is metabolized in plants, with AMPA as the only significant degradation product.<sup>3</sup>
- Lettuce, carrots, and barley contained glyphosate residues up to one year after the soil was treated with 3.71 pounds of glyphosate per acre.<sup>61,62</sup>
- Glyphosate had a median half-life of 8 to 9 days in leaf litter of red alder and salmonberry sprayed with Roundup<sup>®,48</sup>

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



### 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<sup>2</sup>. In six non-farm households, 28 out of 33 samples collected contained detectable levels of glyphosate ranging from 0.0012-13 ng/cm<sup>2</sup>.<sup>63</sup>

### **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<sub>50</sub> of greater than 2000 mg/kg.<sup>64</sup>
- Studies with technical grade glyphosate found an 8-day dietary LC<sub>50</sub> greater than 4000 ppm for mallard ducks and bobwhite quail, indicating slight toxicity.<sup>64,65</sup>
- Glyphosate is not expected to cause reproductive impairment in birds at dietary levels of up to 1000 ppm.<sup>6</sup>
- 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.<sup>7</sup>

### **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.<sup>6</sup>
- Formulated glyphosate products range from moderately toxic to practically non-toxic to freshwater fish, with 96-hour LC<sub>50</sub> values ranging from 1.3 mg/L to greater than 1000 mg/L.<sup>6</sup>
- The preparation of the surfactant POEA known as MON 0818 is used in some glyphosate formulations.<sup>7</sup> POEA is moderately toxic to very highly toxic to freshwater fish. The 96-hour LC<sub>50</sub> 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."<sup>6</sup>
- The LC<sub>50</sub> 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<sup>®</sup>, the LC<sub>50</sub>s for these same fish were 8.3, 2.4, 13.0, and 6.4 mg/L, respectively.<sup>66</sup>
- Technical grade glyphosate is slightly toxic to practically non-toxic to freshwater invertebrates, with a 48-hour LC<sub>50</sub> ranging from 55 ppm to 780 ppm.<sup>6</sup> The 48-hour LC<sub>50</sub> for Daphnids was 3.0 mg/L and the LC<sub>50</sub> for midge larvae was 16 mg/L when exposed to the formulated product Roundup<sup>®</sup>.<sup>66</sup>
- Researchers calculated LC<sub>50</sub> 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<sup>®</sup> formulation of glyphosate. The 24-hour LC<sub>50</sub> values for the different species ranged from 6.6 to 18.1 mg/L.<sup>67</sup>
- 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<sub>50</sub> of 1.1 mg/L (95% Cl 1.1-1.2) and 1.1 mg/L (95% Cl 1.0-1.1), respectively. Technical glyphosate was least toxic, with 24 and 96-hour LC<sub>50</sub> of >38.9 g/L. The toxicity of the formulated products fell between these values.<sup>67</sup>
- 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.<sup>68</sup>

### **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  $\mu$ g/bee.<sup>71</sup>
- An ecological risk assessment of Roundup<sup>®</sup> concluded that the greatest risks to arthropods were from altered habitat structure and food availability.<sup>7</sup>
- The earthworm LC<sub>50</sub> in soil is greater than 5000 ppm for Monsanto's formulated product Roundup<sup>®</sup>.<sup>4</sup>

## **Regulatory Guidelines:**

- The reference dose (RfD) for glyphosate is 1.75 mg/kg/ day.<sup>28</sup> See the text box on **Reference Dose (RfD)**.
- The U.S. EPA has set a One-Day Health Advisory of 20 mg/L.<sup>28</sup>
- The U.S. EPA has set a Ten-day Health Advisory of 20  $\rm mg/L.^{28}$
- The U.S. EPA classified glyphosate as Group E, evidence of noncarcinogenicity in humans.<sup>6</sup> See the text box on **Cancer** (page 6).
- The maximum contaminant level (MCL) is 0.7 mg/L.<sup>28</sup> See the text box on **Maximum Contaminant Level (MCL)**.

#### **Date Reviewed: September 2010**

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, Technology Transfer Network, Air Toxics Health Effects Glossary, 2009. <u>http://www.epa.gov/ttnatw01/hlthef/hapglossaryrev.html#RfD</u>

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, Region 5, Water, Underground Injection Control Terms, 2011. <u>http://epa.gov/r5water/uic/glossary.htm#mcl</u>

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*Reregistration Eligibility Decision (RED) Glyphosate*; EPA-738-F-93-011; U.S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1993.

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