● HERBICIDE FACTSHEET

GLYPHOSATE

Glyphosate herbicides (one common brand name is Roundup) are the mostly commonly used herbicides in the U.S. and the world. In agriculture they are widely used with genetically-modified glyphosate-tolerant crops, but they are also widely used in yards, gardens, and other nonagricultural areas.

Symptoms of exposure to glyphosate include eye irritation, burning eyes, blurred vision, skin rashes, burning or itchy skin, nausea, sore throat, asthma and difficulty breathing, headache, lethargy, nose bleeds, and dizziness.

Glyphosate and glyphosate-containing herbicides caused genetic damage in laboratory tests with human cells, as well as in tests with laboratory animals.

Studies of farmers and other people exposed to glyphosate herbicides have shown that this exposure is linked with increased risks of the cancer non-Hodgkin's lymphoma, miscarriages, and attention deficit disorder. For each of the hazards identified in these studies there are also laboratory studies with results that are consistent with the studies of exposed people.

There is also laboratory evidence that glyphosate herbicides can reduce production of sex hormones.

Studies of glyphosate contamination of water are limited, but new results indicate that it can commonly contaminate streams in both agricultural and urban areas.

Problems with drift of glyphosate herbicides occur frequently. Only one other herbicide causes more drift incidents.

Glyphosate herbicides caused genetic damage and damage to the immune system in fish. In frogs, glyphosate herbicides caused genetic damage and abnormal development.

Application of glyphosate herbicides increases the severity of a variety of plant diseases.

BY CAROLINE COX

Glyphosate (see Figure 1) herbicides are "among the world's most widely used herbicides."[1] and glyphosate is "the world's leading agrochemical."[2]

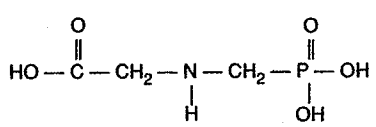
Although glyphosate herbicides have been popular since they were first marketed in 1974, their use in agriculture has expanded recently with the increased use of crops that have been genetically modified to tolerate glyphosate treatment.[3]

Roundup is a popular brand name for glyphosate herbicides,[1] although many other brand names are used.[4]

Glyphosate is marketed in more than 100 countries by a variety of manufacturers, but Monsanto Company has been and continues to be the major commercial supplier worldwide.[3]

Caroline Cox is NCAP's staff scientist.

Figure 1
Glyphosate



N-*(phosphonomethyl)glycine*

Use Estimates

The U.S. Environmental Protection Agency (EPA) recently estimated that annual use of glyphosate in the U.S. is between 103 and 113 million pounds.[5]

Glyphosate is used more than any other pesticide. It is the most commonly used agricultural pesticide, and the second most commonly used pesticide around and in homes and gardens. Home and garden use totals over 5 million pounds per year.[5]

According to Monsanto Company, there are more approved uses for glyphosate than for any other herbicide.[1]

How Does Glyphosate Kill Plants?

Glyphosate blocks the activity of an enzyme used by plants to make certain important amino acids. Without these amino acids, the plant cannot make proteins required for various life processes, resulting in the death of the plant.[1,6]

Glyphosate is a broad spectrum herbicide, so it kills most types of plants.[6]

Overview

It is often said that "there is no indication of any human health concern"[4] for glyphosate and that glyphosate "is virtually nontoxic to mammals, birds, fish, insects, and most

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bacteria."[7] However, this herbicide can actually pose significant hazards to human and environmental health. This article summarizes the research documenting those hazards, with a focus on research published since 2000.

Inert Ingredients

Like most pesticides, commercial glyphosate herbicides contain ingredients other than glyphosate which, according to U.S. pesticide law, are called "inert."[8] Publicly available information about the identity of these ingredients in glyphosate products is incomplete.

For information about the hazards of some of the inert ingredients in commercial glyphosate products, see "Inert Ingredients," at right.

Research studies about glyphosate sometimes use commercial glyphosate herbicide products, and other times use glyphosate alone. In this article we identify as accurately as possible which was used in each study discussed.

Symptoms of Exposure

According to reports made to the California Pesticide Illness Surveillance Program, symptoms of exposure to glyphosate herbicides include eye irritation and inflammation, burning eyes, blurred vision, skin rashes, burning or itchy skin, nausea, sore throat, asthma and difficulty breathing, headache, lethargy, nose bleed, and dizziness.[9]

"Irritation" can seem like a less serious symptom than those caused by other pesticides. However, it can be significant. For example, Italian dermatologists in 2004 reported treating a patient who knelt on the ground where her son had just sprayed a glyphosate-containing herbicide. She then put on clothing that had been on the ground where he had sprayed and napped. Within hours her skin was burning and she developed a blistering rash on her back, legs, and feet that lasted for a month.[10,11]

Ability to Cause Genetic Damage (Mutagenicity)

Four laboratory studies published in the late 1990s demonstrated the ability of glyphosate and glyphosate-containing herbicide products to cause

"Inert" Ingredients in Glyphosate Herbicides

Inert ingredients in commercial glyphosate herbicide products, with examples of their hazards, include the following:

- **5-Chloro-2-methyl 3(2H)-isothiazolone**[1] caused genetic damage and allergic reactions in laboratory tests.[2]
- **FD&C Blue No. 1**[1] caused genetic damage and skin tumors in laboratory tests.[3]
- **Glycerine**[1] caused genetic damage in tests with human cells and laboratory animals. It also reduced fertility in laboratory tests.[4]
- **3-Iodo-2-propynyl butyl carbamate**[1] caused thyroid damage and decreased growth in laboratory tests.[5]
- **Light aromatic petroleum distillate (Chemical Abstract Services No. 64742-95-6)**[1] reduced fertility and growth of newborns in laboratory tests.[6]
- **Methyl p-hydroxybenzoate**[1] caused genetic damage in laboratory tests.[7]
- **Polyoxyethylene alkylamine**[1] is an eye irritant.[8] It is also toxic to fish.[9]
- **Propylene glycol**[1] caused genetic damage, reduced fertility, and anemia in laboratory tests.[10]
- **Sodium sulfite**[1] caused genetic damage in tests with both laboratory animals and human cells.[11]
- **Sodium benzoate**[1] caused genetic damage in tests with human cells and laboratory animals. It also caused developmental problems and reduced newborn survival in laboratory tests.[12]
- **Sodium salt of o-phenylphenol**[1] is a skin irritant. It also caused genetic damage and cancer in laboratory tests.[13]
- **Sorbic acid**[1] is a severe skin irritant and caused genetic damage in laboratory tests.[14]

1. U.S. EPA. Office of Prevention, Pesticides, and Toxic Substances. 2004. Response to Freedom of Information Act request of October 19, 2004. Washington, D.C. Response dated November 17.
2. National Institute for Occupational Safety and Health. 2003. RTECS: 4-Isothiazolin-3-one, 5-chloro-2-methyl-. www.cdc.gov/niosh/rtecs/nx7c76b2.html.
3. National Institute for Occupational Safety and Health. 2000. RTECS: Ammonium, ethyl (4-(p-(ethyl(m-sulfobenzyl)amino)-alpha-(o-sulfophenyl)benzylidene)-2,5-cyclohexadien-1-ylidene)(m-sulfobenzyl)-, hydroxide, inner salt, disodium salt. www.cdc.gov/niosh/rtecs/bq481908.html.
4. National Institute for Occupational Safety and Health. 2003. RTECS: Glycerol. www.cdc.gov/niosh/rtecs/ma7ad550.html.
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6. National Institute for Occupational Safety and Health. 1998. RTECS: Solvent naphtha (petroleum), light aromatic. www.cdc.gov/niosh/rtecs/wf33e140.html.
7. National Institute for Occupational Safety and Health. 2003. RTECS: Benzoic acid, p-hydroxy-, methyl ester. www.cdc.gov/niosh/rtecs/dh256250.html.
8. National Institute for Occupational Safety and Health. 1997. RTECS: Ethomeen T/15. www.cdc.gov/niosh/rtecs/ko92dda8.html.
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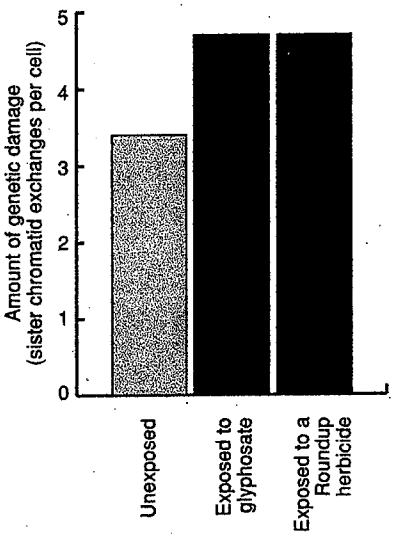
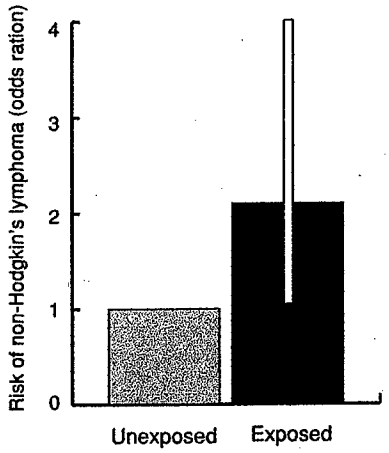
11. National Institute for Occupational Safety and Health. 2003. RTECS: Sodium sulfite. www.cdc.gov/niosh.rtecs/we20ce70.html.
12. National Institute for Occupational Safety and Health. 2003. RTECS: Benzoic acid, sodium salt. www.cdc.gov/niosh/rtecs/dh657890.html.
13. National Institute for Occupational Safety and Health. 2003. RTECS: 2-Biphenylol, sodium salt. www.cdc.gov/niosh/rtecs/dv757e20.html.
14. National Institute for Occupational Safety and Health. 1998. RTECS: Sorbic acid. www.cdc.gov/niosh/rtecs/wg200b20.html.

Figure 2
Ability to Cause Genetic Damage in Human Blood Cells



Source:
Bolognesi, C. et al. 1997. Genotoxic activity of glyphosate and its technical formulation Roundup. *J. Agric. Food Chem.* 45:1957-1962.

Figure 3
Ability to Cause Cancer



Note: Line on and above bar is a 95% confidence interval.

Source:
De Roos, A.J. et al. 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occup. Environ. Med.* 60(9):E11.

Exposure to glyphosate herbicides has caused genetic damage in laboratory tests, and use of glyphosate by farmers is associated with an increased incidence of lymphoma.

genetic damage.[12-15]

Two of the studies, both done by scientists at Italy's Instituto Nazionale per la Ricerca sul Cancro exposed mice to glyphosate and a Roundup herbicide by injection.[12,13] One study also exposed human blood cells to the same chemicals.[12] The first study showed that in mice both glyphosate and the Roundup herbicide damaged DNA (the genetic material in cells) in the liver and kidney and caused a different kind of genetic damage in bone marrow cells. Both substances also caused a third type of genetic damage in human blood cells. (See Figure 2.) In general, the Roundup used in these experiments was more potent than glyphosate.[12] The second study showed that a Roundup herbicide damaged DNA in the liver and kidney of mice.[13]

The other two studies were done at the Universita della Basilicata (Italy). Both used blood cells, one from cows and the other from humans. Both showed that glyphosate caused a significant increase in the number of abnormal chromosomes.[14,15]

A more recent (2004) study from the Institute of Biology and Environmental Sciences (Germany) showed that DNA damage occurred in human connective tissue cells[11] when they were exposed to glyphosate and hydrogen peroxide, a molecule that is commonly found in living things.[16]

The National Institute for Occupational Safety and Health describes glyphosate as a "mutagen."[17]

Ability to Cause Cancer (Carcinogenicity)

Three recent studies have demonstrated a link between glyphosate exposure and non-Hodgkin's lymphoma, a type of cancer:[18-20]

- A 2001 study of Canadian men showed that the risk of non-Hodgkin's lymphoma for men exposed to glyphosate more than two days per year was two times greater than the risk for men who were either unexposed or exposed for less than two days per year. The study was conducted at the University of Saskatchewan (Canada).[18]
- A 2002 study of Swedish men showed that glyphosate exposure was significantly associated with an increased risk of non-Hodgkin's lymphoma. The study was conducted by oncologists at Örebro University (Sweden).[19]
- A 2003 review of three earlier studies of Midwestern farmers showed that exposure to glyphosate was associated with an increased incidence of non-Hodgkin's lymphoma. The studies were conducted by the National Cancer Institute.[20] (See Figure 3.)

A fourth study, an analysis of results from the Agricultural Health Study, did not find an association between non-Hodgkin's lymphoma and glyphosate exposure. However, the incidence of another cancer, multiple myeloma, showed a "suggestive association" with glyphosate exposure. The Agricultural Health Study is sponsored by the National Institutes of Health and EPA.[21]

Several mechanisms by which glyphosate herbicide exposure could cause cancer have recently been identified. Researchers at the University of Minnesota found that both glyphosate and Roundup caused a rapid increase in cell division[11] in human breast cancer cells.[22] In addition, scientists at the Centre National de la Recherche Scientifique (France) showed that five glyphosate-containing herbicide products disrupted cell division in sea urchin embryos, which are commonly used as a model system for studying cell division. The type of disruption found in this study is "a hallmark of tumor cells and human cancers."[23]

EPA classifies glyphosate as a Group E pesticide. This classification means that the agency has found "evidence of non-carcinogenicity for humans."[24]

Effects on Pregnancy

Glyphosate exposure has been linked to increased risks of miscarriages

(spontaneous abortions).[11] In a study of Ontario, Canada farm families, glyphosate use in the three months prior to conception was associated with an increased risk of late (between the 12th and 19th weeks of pregnancy) miscarriages. (See Figure 4.) The study was conducted by researchers from Health Canada and Carleton University (Canada).[25]

Glyphosate-containing herbicides have also caused pregnancy problems in laboratory tests. In a 2003 study conducted by scientists from two Brazilian universities, a Roundup herbicide fed to pregnant rats during the middle part of their pregnancy caused an increase in the number of offspring with abnormal skeletons. The increase in abnormalities was significant at all dose levels tested in this experiment.[26]

Effects on Hormones

Hormones are chemical messengers that regulate all biological processes, including the reproductive system.[27]

Scientists at Texas Tech University studied the effect of a glyphosate-containing herbicide on hormone production. They looked at hormone production by Leydig cells, located in the testes, because these cells "play a crucial role in male reproductive function." The scientists showed that exposure to a Roundup herbicide reduced sex hormone production in these cells by 94 percent.[28] (See Figure 5.)

Association with Attention Deficit Disorder

Exposure of parents to glyphosate has been linked with an increased incidence of attention deficit disorder in children. A 2002 study conducted by researchers at the University of Minnesota found "a tentative association between ADD/ADHD [attention deficit disorder] and use of this herbicide"[29] by Minnesota farm families.[29]

The results of two laboratory studies are consistent with the results of the University of Minnesota study in that they show glyphosate and glyphosate herbicides cause brain and nerve damage. One study, conducted at the Universidad Nacional de San Luis (Argentina) showed that feeding pregnant rats glyphosate-contaminated water caused changes in the activity of several enzymes in the brains of their fetuses.[30] A second study, from the University of Liverpool (United Kingdom) showed that Roundup exposure inhibited the growth and development of nerve cells.[31]

Soil Persistence

Glyphosate's persistence in soil varies widely. According to data compiled by the USDA's Agricultural Research Service, glyphosate's half-life varies from 2 to 174 days.[32] (The half-life is the amount of time required for half of the applied glyphosate to break down or move away from the treatment area.)

Contamination of Water

Glyphosate is not included among the pesticides being studied by the U.S. Geological Survey's (USGS's) National Water-Quality Assessment Program,[33] so there are no comprehensive national statistics about contamination of rivers and streams by glyphosate.

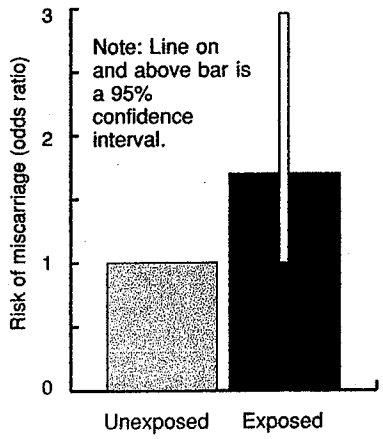
A regional study, however, indicates that glyphosate can be a common contaminant. In a USGS Toxic Substances Hydrology Program survey of Midwest streams in 2002, glyphosate was found in over a third of the samples collected. The primary breakdown product of glyphosate was found in over two-thirds of the samples. The study also showed that glyphosate contaminated water from spring through fall and described glyphosate in samples taken at harvest time as "unexpected"[34] because researchers had "presumed that glyphosate would degrade by this late in the growing season."[34]

USGS has also found glyphosate contamination in a study of urban streams in King County, Washington. Glyphosate was found in all six streams that were tested in this study.[35]

Drift

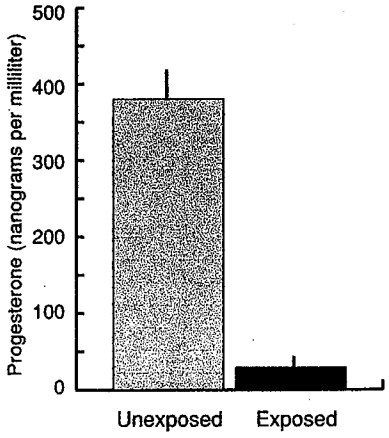
Drift incidents involving glyphosate are common. In 1999, the American Association of Pesticide Control Officials surveyed state pesticide regulatory

Figure 4
Ability to Cause Miscarriages



Source:
Arbuckle, T.E., L.Lin, and L.S. Mary. 2001. An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population. *Environ. Health Persp.* 109:851-857..

Figure 5
Ability to Disrupt Sex Hormone Production



Source:
Walsh, L.P. 2000. Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression. *Environ. Health Persp.* 108:769-776.

Exposure to glyphosate herbicides is linked with an increase in the risk of miscarriage. In addition, a glyphosate herbicide reduced sex hormone production in a laboratory test.

agencies and asked which pesticides were most commonly involved in pesticide drift complaints. Glyphosate was the second most common pesticide; only the herbicide 2,4-D caused more complaints.[36]

Even the labels on glyphosate herbicides acknowledge drift problems. For example, the Roundup Pro label states "Avoid contact of herbicide with foliage, green stems, exposed non-woody roots or fruit of crops, desirable plants and trees, because severe injury or destruction may result. Avoid drift. Extreme care must be used when applying this product to prevent injury to desirable plants and crops."[37]

Researchers at Carleton University (Canada) and Environment Canada who studied glyphosate drift describe its potential effects as "severe ecological changes."[38]

Effects on Birds

Glyphosate use can impact birds when the plants killed by the treatment are plants that birds use for food or shelter. Glyphosate treatment of forests after logging reduced the nesting success of songbirds, according to a study conducted by biologists at the University of British Columbia and the Canadian Wildlife Service.[39] According to reviews by the U.S. Geological Survey, treatment of cattail marshes with Rodeo (a glyphosate herbicide used in wet areas) has reduced populations of the marsh wren[40] and the sora.[41]

Effects on Fish

Glyphosate-containing herbicides can cause genetic damage in fish, and also disrupt their immune systems.

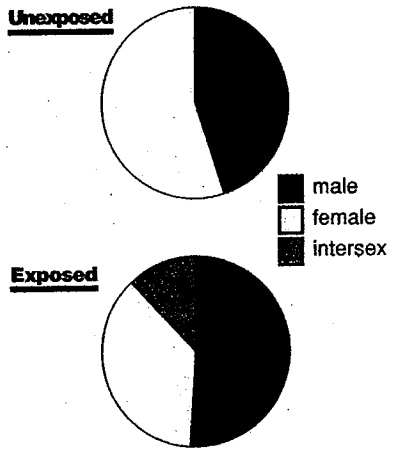
A study conducted at the Universidade de Brasília (Brazil) showed that injection of a Roundup herbicide in Tilapia increased damaged chromosomes in red blood cells.[42,43]

A study conducted at the University of Alexandria (Egypt) showed that exposure to Roundup reduced two measures of immune system function in spleen cells from Tilapia. The reduction occurred at all dose levels tested in this experiment.[44]

Effects on Insects

Glyphosate can cause genetic damage in insects. In a study of fruit flies, significant increases in mutations occurred when larvae were exposed to glyphosate during development. The experiment was conducted by researchers from Akdeniz University (Turkey) and the Universitat Autonoma de Barcelona (Spain).[45]

Figure 6
Effects on Sexual Development of Frogs



Source:
Howe, C.M. et al. 2004. Toxicity of glyphosate-based pesticides to four North American frog species. *Environ. Toxicol. Chem.* 23:1928-1938.

Exposure to glyphosate herbicides caused tadpoles to develop with abnormal sex organs.

Effects on Spiders

Spider populations can be reduced by herbicide treatment when the herbicide kills the vegetation they use for shelter. An experiment conducted by zoologists from Oxford University and the Royal Agricultural College (United Kingdom) looked for this kind of effect in the edges of agricultural fields. These margins "play an important agricultural role in providing a refuge for beneficial invertebrate predators"[46] which prey on pest insects in the fields. The zoologists found that treatment with a Roundup herbicide reduced spider numbers by over 50 percent.[46]

Effects on Frogs

Glyphosate herbicides can harm amphibians in a variety of ways, including causing genetic damage and disrupting their development.[47-49]

A 1997 study showed that a Roundup herbicide caused damage to DNA (genetic material) in bullfrog tadpoles. The University of Windsor (Canada) biologists who conducted the study concluded that its "genotoxicity at relatively low concentrations" was of concern.[47]

A 2003 study showed that a glyphosate-containing herbicide caused both mortality and malformations of a common neotropical tadpole. The study was conducted by scientists at three research institutes in Argentina.[48]

A 2004 study showed that "environmentally relevant" concentrations of several Roundup herbicides caused a common North American tadpole not to grow to its normal size and to take longer than normal to develop. In addition, between 10 and 25 percent of the Roundup-exposed tadpoles were intersex (having abnormal sex organs). The study was conducted by biologists at Trent University, Carleton University, and the University of Victoria (Canada).[49] (See Figure 6.)

Plant Diseases

Use of glyphosate herbicides has been linked to increased problems with a variety of plant diseases.

For example, glyphosate herbicides increased the severity of fusarium head blight in cereal crops,[50] the severity and frequency of sudden death syndrome in soybeans,[51] the severity of Pythium root rot in sugarcane,[52] and the severity of white mold in soybeans.[53]

These studies were conducted by scientists at Agriculture and Agri-Food Canada, Iowa State University, Louisiana State University, and Michigan State University.[50-53]

Resistance

Resistance is the "inherited ability of a plant to survive and reproduce following exposure to a normally lethal dose of herbicide."[54] The development of herbicide resistance is an increasing problem worldwide.[55]

The first glyphosate-resistant weeds were reported in 1996 in Australia. There are now 6 glyphosate-resistant weeds reported from 7 countries.[56]

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