

Glyphosate & Glyphosate Formulations

Findings: Evaluation of the herbicide glyphosate, (aminomethyl)phosphonic acid, and glyphosate-based formulations for genotoxic activity using in vitro assays. [Environmental Molecular Mutagenesis. March 7, 2023](#) and [Data Tables](#) are now available.



Research Overview

Status: Ongoing

Substances: [Glyphosate](#)

Nominated: June 2016

BACKGROUND INFORMATION

Glyphosate, a chemical that controls weeds and grasses, is the most widely used herbicide worldwide. The major reason glyphosate is used so broadly is because many crops have been genetically engineered to be resistant to glyphosate, allowing it to target weeds while leaving resistant crops unaffected. When applied as a mixture with other substances, plants can more readily absorb glyphosate, making it more effective. People can be exposed to glyphosate when they use glyphosate-based formulations (GBFs) on their lawns, gardens, or for landscaping around their homes. It can get on a person's skin, get in the eyes, or be brought into the body by breathing it in when using it. Residual amounts of glyphosate can also get into a person's body by ingestion of food or water. Individuals who regularly handle glyphosate products as part of their occupation have higher exposures.

Glyphosate was first nominated to the NTP for testing in 1981, before the development of glyphosate-resistant crops. NTP conducted a series of short-term studies including 13-week toxicity studies of glyphosate in feed, which were [published](#) in 1992. At that time, few toxicological effects were observed and there was no evidence of genetic toxicity for endpoints of chromosomal damage (in vivo) or gene mutations (bacterial reverse mutation assay, a.k.a. Ames assay).

In March 2015, the [International Agency for Research on Cancer \(IARC\)](#) classified glyphosate as "probably carcinogenic to humans" (Group 2A). This was based on "limited" evidence of cancer in humans from epidemiological studies of exposures to GBFs, and "sufficient" evidence of cancer in experimental animals from studies of "pure" glyphosate. IARC also concluded that there was "strong" evidence for genotoxicity, a determination that was based on studies of both glyphosate and GBFs. Additionally, IARC concluded that there was "moderate" evidence for the genotoxicity of (aminomethyl)phosphonic acid (AMPA), a microbial metabolite of glyphosate. Some studies, which are publicly available, suggest that the human intestinal microbiome metabolizes glyphosate to AMPA. The IARC listing was one of the reasons NTP [considered conducting further testing in 2016](#).

Human exposure to glyphosate usually occurs in the form of glyphosate-based formulations (GBFs). Few studies have made side-by-side comparisons of the toxicity of glyphosate and GBFs using the same experimental methods. NTP compared the toxicity of both glyphosate and glyphosate formulations, using the same methods. Specifically, NTP study goals were to:

- Evaluate whether glyphosate causes genotoxicity, or damage to DNA, using the bacterial reverse gene mutation assay (a.k.a. Ames assay), an in vitro micronucleus assay to detect chromosomal damage, and a multiplexed DNA damage assay that distinguishes whether chromosomal damage is due to chromosome breaks or changes in chromosome number. These studies were conducted using human TK6 cells, a cell line that is recommended by the Organization for Economic Cooperation and Development (OECD) for in vitro genetic toxicity assays.
- Evaluate whether glyphosate induces oxidative damage, the harm that cells and tissues experience when overwhelmed with production of free radicals that can damage protein and DNA. These studies were conducted using several high-throughput screening assays with human liver cells and human skin cells.

The genetic toxicity studies and the high-throughput screening studies compare the effects of glyphosate versus glyphosate-based formulations (GBFs) on measures of genotoxicity, oxidative stress, and cell viability.

What did the studies find?

Glyphosate and (aminomethyl)phosphonic acid (AMPA), a microbial metabolite of glyphosate, did not cause permanent changes to DNA, such as gene mutations or chromosomal damage. These kinds of changes to DNA are often associated with increased risk for cancer.

The highest concentration of glyphosate used in NTP's human cell culture studies was comparable to an adult man drinking about 16 ounces of a representative glyphosate-based formulation that contains 41% glyphosate.

In NTP's studies, some glyphosate-based formulations caused DNA damage. Because glyphosate itself did not cause DNA damage in the tests that were used, the DNA damage likely was caused by other components of the formulations. Herbicide product labels list active ingredients, like glyphosate, but other components of formulations are considered "inert" for regulatory purposes and are not reported due to confidential business information (CBI) protection for companies that manufacture herbicides.

Overall, the findings from our genetic toxicity experiments indicate that it is unlikely that glyphosate could cause cancer through a genotoxic mechanism that permanently damages DNA. Our findings do not rule out that exposure to glyphosate might cause cancer through other mechanisms. The results of the high-throughput screening study, which focused on whether glyphosate and GBFs cause oxidative stress, will be submitted for publication consideration later in 2023.

The new findings are similar to results reported in previous NTP studies. [Studies conducted by the NTP in 1992](#) reported that rodents exposed to high levels of glyphosate in feed showed little evidence of toxicity, and there was no evidence of glyphosate causing chromosomal damage to DNA. For these reasons, NTP did not consider conducting a 2-year rodent cancer bioassay of glyphosate.

See the table below for the most up-to-date information on the variety of projects taking place at NTP.

Study	Description	Status	Findings & Supporting Files
In Vitro Screening Tests	Human cell-based tests to study DNA damage, oxidative stress, and cell viability	Ongoing	Supporting files <ul style="list-style-type: none">• Poster (March 2019)
Genetic Toxicity Testing	Human cell-based studies to determine the potential of glyphosate to cause DNA damage (genotoxicity)	Completed	Supporting files <ul style="list-style-type: none">• Poster (September 2019)• Smith-Roe et al. 2023; Data tables

RESEARCH AT OTHER AGENCIES

United States

International

INFORMATIONAL RESOURCES

The informational resources below provide additional details on NTP's research on glyphosate and glyphosate formulations.

FAQs

Presentations

Supporting Documents

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Web page last updated on March 20, 2024

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