
Glyphosate and Human Health

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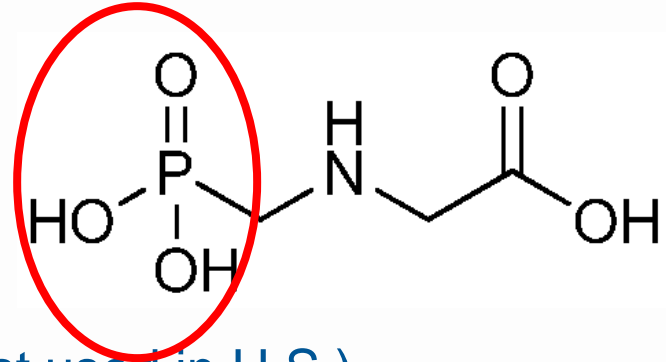
4 County Cooperative Weed Management Area: Herbicide Forum
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What is Glyphosate?



- Broad spectrum herbicide (among most used in U.S.)
- Targets enzyme that plants use to create amino acids (building blocks of protein)
- Target enzyme is only found in plants, not humans (or any other mammals)
- Phosphonomethyl Amino Acid
- Has phosphate group but is not an “organophosphate” (i.e. does not inhibit acetylcholine esterase)

Human Health Effects – Low Acute Toxicity

Chemical	LD50* (mg/kg-body weight)
Glyphosate	5000
Polyoxethyleneamine (POEA)	1200
Microcystin-LR	5
Tetrodotoxin	0.3

*LD50 = dose that is lethal to 50% of test group

Signs and Symptoms of Acute Poisoning

- Most commonly reported: mouth/throat pain, nausea, vomiting, diarrhea, abdominal pain
- High dose (i.e. attempted suicide): targets heart, kidney, and respiratory system
 - Rapid breathing
 - Heart rhythm abnormalities
 - Low blood pressure
 - Pulmonary edema (fluid in lungs)
 - Hypovolemic shock
 - Reduced urine production
 - Respiratory failure
- Death typically caused by low blood pressure and respiratory failure

Chronic Toxicity

Type of Threshold Dose	Mg/kg-day	Basis for Threshold Dose	Year Threshold Dose Established	Agency
Reference Dose	0.1	Kidney damage (rats)	1987	US EPA
Occupational Limit	0.1	Developmental toxicity (rabbits)	2015	EFSA
Acceptable Daily Intake	0.5	Developmental toxicity (rabbits)	2015	EFSA
Acute Reference Dose	0.5	Developmental toxicity (rabbits)	2015	EFSA

Rapidly eliminated (no bioaccumulation)

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Does Glyphosate Cause Cancer?

- International Agency for Research on Cancer (IARC) says “yes” (July 2015)
- European Food Safety Authority (EFSA) says “no” (November 2015)
- US EPA says “We can’t tell” (as of 1989)

Why are they different?

<http://www.efsa.europa.eu/en/press/news/151112>

IARC vs. EFSA

Parameter	IARC	EFSA
Substance evaluated	Commercial formulation	Pure Glyphosate
Tox studies available	Publicly Available	All (including IARC's Assessment)
Statistical approach	Applied their own statistics to data in studies	Accepted statistics used by authors of original studies
Historical laboratory controls	Not considered	Considered

Substance Evaluated

- EFSA identified co-formulants and common contaminants as data gaps in their analysis
 - Polyoxethyleneamine (POEA): surfactant
 - N-acetyl-glyphosate: environmental degradate/metabolite
 - N-acetyl-AMPA: environmental degradate/metabolite
- IARC focused on studies that looked at formulations and lumped them all together even though different formulations may have different health effects

Tox Studies Available

Study Type	IARC	EFSA
Rat	6	9
Mice	2	5
Epidemiological	30	30

Animal Study Conclusions

Rats

- None of the 9 rat studies showed a statistical increase in tumor incidence according to the original authors or EFSA.
- IARC found some statistically significant tumor increases in two of the 9 studies when they applied their own statistics to the raw results.

Mice

- One study found increased tumor incidence at highest dose tested, but the mice were also infected with a virus that increases the incidence of the same type of tumor found in the study.
- IARC found statistically significant increases of tumors in two mouse studies applying their own statistical methods to the raw data. This approach did not take into account the background tumor rates for the specific animals in the specific labs, which the original authors did.

Animal Study Conclusions - Overall

- EFSA concluded that glyphosate is unlikely to cause cancer in humans (especially at environmentally relevant concentrations)
- IARC concluded there is evidence of carcinogenicity based on their own statistical analysis of the published tox data (this approach lacks the context of historical laboratory controls)

Epidemiology Summary

- 10 cohort studies, including the biggest one (Agricultural Health Study), have not found an association between glyphosate and any type of cancer risk
- 9 case-control studies did not indicate cancer risk from glyphosate exposure
- 5 case-control studies and one prospective cohort study had very limited evidence of increased risk to non-Hodgkin lymphoma.
Weaknesses included:
 - Inconsistent classification of cancer type
 - Small numbers of cases
 - Identification and separation of confounders (typically analyzed along with several other pesticides in epi studies).
- EFSA concluded that epi evidence for glyphosate and cancer was very limited and not sufficient to sway overall conclusion

Overall Summary

- EFSA concluded that “glyphosate is unlikely to pose a carcinogenic hazard to humans...”
- IARC concluded that glyphosate is likely to pose a carcinogenic hazard to humans.
- Difference in outcome boils down to substances evaluated (pure vs. formulation), applications of statistics not used by original authors, consideration of historical laboratory-specific background cancer rates, EFSA had access to additional studies and IARC’s review when they developed their conclusions
- EFSA’s conclusion is accompanied by a call for additional research into the other ingredients and impurities in commercial pesticide formulations containing glyphosate