Overview of USEPA’s Human Health Risk Assessment of Glyphosate

AmericanHort Webinar
June 2019

Christine Olinger
Office of Pesticide Programs/Health Effects Division
Glyphosate Regulatory Timeline

- Glyphosate was first registered in the US in 1974 as a non-selective herbicide registered to control weeds in various agricultural and non-agricultural settings.

- Several human health analyses have been completed, including the reregistration eligibility decision (RED) in 1993.


- EPA released Draft Risk Assessments for Glyphosate, December 18, 2017
  - [https://www.epa.gov/pesticides/epa-releases-draft-risk-assessments-glyphosate](https://www.epa.gov/pesticides/epa-releases-draft-risk-assessments-glyphosate)
  - Received 238,290 comments.

- EPA Preliminary Interim Decision (PID) released April 30, 2019. Interim Decision six-nine months thereafter.
Risk Assessment Paradigm

1. Hazard Assessment
2. Dose Response Assessment
3. Exposure Assessment
4. Risk Characterization

Summary of Glyphosate Hazard Profile

- Rapid excretion from the body (primarily unchanged glyphosate, complete by 24 hours after exposure); absorption is low
- Effects observed in oral toxicity studies were decreases in body weights and minor indicators of toxicity to the eyes, liver, and kidney
- Reproduction and Developmental studies show that infants and children are not more sensitive to the effects of glyphosate
- No evidence that glyphosate is neurotoxic or immunotoxic
- Inhalation toxicity studies - no effects close to the limit dose
- Dermal toxicity studies - no effects up to the limit dose
- Dermal penetration has been shown to be relatively low for human skin (<1%)
- Classified as not likely to be carcinogenic
Dose-Response Assessment

Dietary Exposure (Food & Water)

- No adverse effects found after a single day of exposure, only consider chronic
- Highest no observed adverse effect level (NOAEL) – 100 mg/kg bw/day for repeat-dose studies; diarrhea and other signs of toxicity. Effects were observed at 175 mg/kg/bw
- Applied typical safety factors – 10x interspecies; 10x intraspecies
- Safety factor for infants and children (FQPA safety factor) – 1x. Studies show that infants and children are no more sensitive than adults
- Reference Dose = 1 mg/kg bw/day = NOAEL/safety factors

Occupational and Residential Exposure

- Incidental Oral – Using same study as chronic dietary (NOAEL = 100 mg/kg bw/day)
- Dermal – no adverse effects observed, so no quantitative assessment of exposure and risk
- Inhalation – no adverse effects observed, so no quantitative assessment of exposure and risk

Cancer Classification – Not likely to be Carcinogenic to Humans
Inputs into Occupational and Residential Exposure Assessments

• Residential Exposure Assessments
  • Standard Operating Procedures (SOPs) – define activities and how long activity is typically conducted in a day
  • SOPs include handler and post-application activities

• Occupational Exposure Assessments
  • Potential for handler (applicators and mixer/loaders) and post-application exposures via dermal and inhalation routes, but no hazard via inhalation and dermal routes – did not assess risks to glyphosate quantitatively
Inputs to Dietary Exposure Assessments

• Dietary Exposure = Amount consumed x residue in commodity
• Consumption data from national surveys – USDA What We Eat In America (WWEIA)
• Glyphosate assessment is screening level-assumes that all foods (with registered glyphosate uses and tolerances) have been treated (100% crop treated)
• Glyphosate assessments assume that all foods are at high-end tolerance (Maximum residue limit from legal use of pesticide)
• Assume that everyone in the US consumes water with 75 ppb glyphosate - modeled estimate from direct application to water.
• Use a model to quantify exposure and risk: DEEM™ - Dietary Exposure Evaluation Model. Available at: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#health
Quantitative Results

• Screening Level Dietary Exposure Assessment – Food and Water
  • General population – 9% of the reference dose
  • Children 1-2 – 23% of the reference dose

• Residential Exposure Assessment (based on conservative assumptions) – Incidental Oral Only
  • Highest Potential Exposure – Children – hand-to-mouth activities when playing on turf after application
  • Also assessed ingestion of water while swimming in treated water bodies
  • All high-end exposures estimates are well below level of concern

• Aggregate Exposure Assessment (based on conservative assumptions)
  • Less than 40% of the “aggregate risk cup” is filled when combining high-end dietary exposures with residential exposures.
Cancer Classification

- Convened FIFRA Scientific Advisory Panel (SAP) in December 2016 to comment on OPP’s comprehensive analysis of available data on the carcinogenic potential of the active ingredient glyphosate
  - 2015 OPP Cancer evaluation served as initial analysis
  - Systematic review of open literature and toxicological databases
  - Epidemiological, animal carcinogenicity, and genotoxicity studies
  - Also considered metabolism and potential mechanistic studies
  - Integrated relevant data and analyzed across multiple lines of evidence for weight-of-evidence
- Risk Assessment Conclusion: Glyphosate is not likely to be carcinogenic to humans
Considerations for “Not Likely” Classification

• Epidemiological studies:
  • No evidence of association for solid tumors, leukemia, and Hodgkin lymphoma
  • Agricultural Health Study (AHS)

• Animal carcinogenicity studies:
  • No tumors identified for evaluation in 7 out of 15 studies
  • Tumor findings were not considered treatment-related based on weight-of-evidence
  • Tumors in individual studies not reproduced

• Genotoxicity studies:
  • Negative in all in vitro gene mutation studies
  • In vitro findings not supported by in vivo results
  • No convincing evidence glyphosate is genotoxic in vivo
Human Health Risk Assessment Conclusions

- No meaningful risk to humans when glyphosate is used in accordance with product labels
- Concluded that glyphosate is not likely to be carcinogenic to humans


- Registration Review - Preliminary Ecological Risk Assessment for Glyphosate and its Salts
- Drinking Water Assessment for the Registration Review of Glyphosate
- Updated Statistics Performed on Animal Carcinogenicity Study Data for Glyphosate
- Glyphosate Systematic Review of Open Literature
- Glyphosate Amended Residential and Occupational Exposure Assessment for a Registration Review
- Glyphosate Tier II Incident Report
- Glyphosate Draft Human Health Risk Assessment in Support of Registration Review
- Glyphosate Dietary Exposure Analysis in Support of Registration Review
- Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential
- Summary Review of Recent Analysis of Glyphosate Use and Cancer Incidence in the Agricultural Health Study