Is Glyphosate a Carcinogen?

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What Is Cancer?

“Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body’s cells begin to divide without stopping and spread into surrounding tissues.”

National Cancer Institute
IARC

- International Agency for Research on Cancer
  - Program of the World Health Organization (WHO)
- Goal is to identify causes of cancer so preventive measures can be taken
  - Program focuses on environment and lifestyle
  - Reviews “represent the first step in carcinogen risk assessment,” which is identifying hazard
  - Reviews do not consider levels of exposure
How IARC Reviews Chemicals

- A Working Group is formed:
  - “Members generally have published significant research related to the carcinogenicity of the agents being reviewed”
- Examines all *publicly available* studies
  - Can miss studies from pesticide registrants
- Criteria for carcinogenicity
  - Increased *numbers* or *severity* of tumors
  - Tumors appear *sooner*
Hazard vs. Risk

“Hazard and risk are two distinct but interrelated concepts, the first a reflection of potential effect and the second of likelihood it will occur.”


- Risk relates hazard to exposure
  - Regulatory agencies like DPR and U.S. EPA calculate risk of cancer and other potential health effects
How U.S. EPA and DPR Review Chemicals for Cancer

- Reviews are conducted by scientific staff
- Review all available scientific data
  - Pesticide registrants are required to submit cancer studies in two species (often rats & mice)
  - Registrants must submit several laboratory studies to determine possible effects on DNA
  - Any published studies also reviewed
- U.S. EPA guidance for assessing cancer risk used by both agencies
Guidance covers these questions:

- “For hazard—Can the identified agent present a carcinogenic hazard to humans and, if so, under what circumstances?"
- “For dose response—At what levels of exposure might effects occur?"
- “For exposure—What are the conditions of human exposure?"
- “For risk—What is the character of the risk? How well do data support conclusions about the nature and extent of the risk from various exposures?”
Widely used herbicide, used in many products including Roundup and Rodeo

In California in 2013, potassium salt and isopropylamine salt were two of the state’s top 10 ag-use chemicals, for a total use of:

- More than 10 million pounds
- On more than 5.5 million acres
- More than 20 million pounds sold
- Sales include ag and non-ag products
Cancer Reviews Before 2015

- U.S. EPA first reviewed cancer studies in 1985
  - Discussed later
- Germany’s Federal Institute for Risk Assessment prepared draft risk assessments in 2013 and 2014 for the European Food Safety Authority (EFSA)
  - Reviewed hundreds of studies, including > 30 human studies
  - Concluded there is “no validated or significant relationship between exposure to glyphosate and an increased risk of non-Hodgkin lymphoma or other types of cancer”
- Three other WHO programs reviewed glyphosate...
Previous Reviews by WHO Programs

  - Environmental Health Criteria 159: “Available studies do not indicate” it is carcinogenic

  - Glyphosate in drinking water is not hazardous to human health

  - “No evidence of carcinogenicity”
IARC Classification of Glyphosate

- Carcinogenic in **Group 2A** (probably carcinogenic to humans) based on:
  - Limited evidence in humans
  - Sufficient evidence in animals
  - Strong evidence for genotoxicity
  - Other effects related to carcinogenic potential (causing oxidative stress, acting on nuclear receptor-mediated pathways, etc.)
IARC: Limited Evidence in Humans

- IARC (2015) found that epidemiological studies in the USA, Canada, and Sweden showed statistically significant associations between occupational exposure to glyphosate and cancer (non-Hodgkins Lymphoma)
  - Individuals were exposed to other pesticides as well
  - Some of the studies used statistical methods to try to factor out other exposures
IARC: Sufficient Evidence in Animals

- Mice (Reviewed 2 feeding studies)
  - Rare type of kidney tumor tended to occur in treated males in one study (1983, U.S.)
  - Rapidly-growing tumors in the lining of blood vessels tended to occur in treated males in the second study (1993, Scotland)

- Rats (Reviewed 5 feeding studies)
  - Two studies reported increased pancreatic and liver tumors in males, and thyroid tumors in females; other 3 studies were negative
IARC: Strong Evidence of Genotoxicity (DNA Damage)

- **Humans**
  - People exposed to glyphosate had DNA strand breakage in their white blood cells.
  - DNA strand breaks also seen in laboratory studies with human cells and tissues; chromosome changes seen in one study.

- **Animals**
  - DNA strand breaks and other damage seen in multiple studies.

In 1985, first carcinogenic review by a committee, consensus decision as “Possible Human Carcinogen”

Available rat study identified as inadequate.

In 1986, U.S. EPA presented information to Scientific Advisory Panel (SAP)

“Inadequate animal evidence of carcinogenic potential”
In 1991, review of a 2nd rat cancer risk study resulted in classification as “evidence of noncarcinogenicity for humans”

- “Lack of convincing carcinogenicity evidence in adequate studies in two animal species”

Most recent human health risk assessment published in 2012 – relied on 1991 review

- “No evidence of carcinogenicity was found in mice or rats.”
U.S. EPA Review of Human Data

- U.S. EPA’s 2005 cancer risk assessment guidance state that human data are “extremely valuable in risk assessment”
  - High quality and adequate statistical power
  - Exposures under relevant conditions
- Most of the studies reviewed by IARC (2015) were published after U.S. EPA’s 1991 review of cancer risk of glyphosate
  - Were not considered in U.S. EPA’s review

- **Mice (Reviewed 1 feeding study)**
  - Rare type of kidney tumor in 1983 U.S. study were not related to glyphosate treatment
  - Did not review the 1993 study conducted in Scotland

- **Rats (Reviewed 2 feeding studies)**
  - Both studies reported increased pancreatic and liver tumors in males, and thyroid tumors in females, but not related to glyphosate

- **Conclusion: “Lack of convincing evidence”**

- Human studies reviewed by IARC were not available in 1991

- Animals
  - No effects on bone marrow cells in dosed rats or on DNA mutations in dosed mice

- Animal cells
  - No effects on DNA repair were seen in a study with rat liver cells
  - No effects on chromosomes were seen in a study with Chinese hamster ovary cells
Next Steps

- U.S. EPA plans to release a preliminary risk assessment of glyphosate later this year.
- DPR will review this risk assessment and determine whether additional action is needed.
California EPA

- DPR is one of the 6 boards, departments, and offices of CalEPA
Proposition 65

- Requires state to publish list of chemicals and update annually
  - Administered by OEHHA
- Businesses (> 10 employees) must notify people about significant amounts of listed chemicals:
  - In products being purchased, used in home or workplace, or released into the environment
- Businesses cannot knowingly discharge significant amounts of listed chemicals into sources of drinking water

Prop 65 Fact Sheet: [http://oehha.ca.gov/prop65/p65faq.html](http://oehha.ca.gov/prop65/p65faq.html)
Prop 65 List

- List contains several hundred chemicals
  - More than **90 pesticides** are on the list
    - More than **50** are listed as causing **cancer**
    - More than **40** are listed as causing **birth defects or reproductive harm**
- DPR may work with OEHHA in evaluating pesticides (e.g., methyl bromide)
  - DPR does not have a role in enforcing the law

Pesticides listed under Prop 65: [http://www.cdpr.ca.gov/docs/dept/factshts/prop_65_list.pdf](http://www.cdpr.ca.gov/docs/dept/factshts/prop_65_list.pdf)
Safe Harbor Levels

- “Exposure levels and discharges to drinking water sources that are below the safe harbor levels are exempt from the requirements of Proposition 65.”
  - Developed for some of the listed chemicals
  - No Significant Risk Levels (NSRLs) for Carcinogens
  - Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity

On September 4, 2015 OEHHA published a notice of intent to list glyphosate and 3 other pesticides as known to cause cancer
- Tetrachlorvinphos, Parathion, Malathion
- Comment period ended October 20, 2015
- Listing in response to IARC classification
- Because IARC is an “authoritative body,” OEHHA “cannot consider scientific arguments concerning the weight or quality of the evidence considered by IARC when it identified these chemicals.”
Questions?

(DPR Photo)