



Is Glyphosate a Carcinogen?

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What Is Cancer?

- o “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



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

How IARC Reviews Chemicals

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

Hazard vs. Risk

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

A Guide to Pesticide Regulation in California,
2011 Edition

- o Risk relates hazard to exposure
 - o Regulatory agencies like DPR and U.S. EPA calculate risk of cancer and other potential health effects

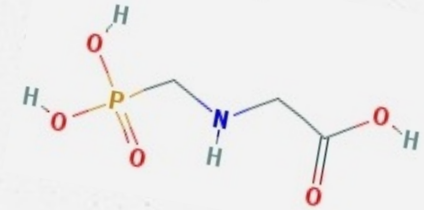
How U.S. EPA and DPR Review Chemicals for Cancer

- 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

U.S. EPA Cancer Risk Assessment Guidance (2005)

- o Guidance covers these questions:
 - o “For hazard—Can the identified agent present a carcinogenic hazard to humans **and, if so, under what circumstances?**”
 - o “For dose response—At what levels of exposure might effects occur?”
 - o “For exposure—What are the conditions of human exposure?”
 - o “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?”

Glyphosate



- 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

- o **World Health Organization International Programme on Chemical Safety (1994)**
 - o Environmental Health Criteria 159: “Available studies do not indicate” it is carcinogenic
- o **World Health Organization (2003)**
 - o Glyphosate in drinking water is not hazardous to human health
- o **Joint FAO/WHO Meeting on Pesticide Residues in Food (2004)**
 - o “No evidence of carcinogenicity”

IARC Classification of Glyphosate

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

IARC: Limited Evidence in Humans

- o 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**)
 - o Individuals were exposed to other pesticides as well
 - o Some of the studies used statistical methods to try to factor out other exposures

IARC: Sufficient Evidence in Animals

- o **Mice (Reviewed 2 feeding studies)**
 - o Rare type of kidney tumor tended to occur in treated males in one study (1983, U.S.)
 - o Rapidly-growing tumors in the lining of blood vessels tended to occur in treated males in the second study (1993, Scotland)
- o **Rats (Reviewed 5 feeding studies)**
 - o 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)

o Humans

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

o Animals

- o DNA strand breaks and other damage seen in multiple studies

U.S. EPA Review



- o In a 1996 pesticide tolerance decision, U.S. EPA gave a history of U.S. EPA's cancer risk assessment of glyphosate
- o In 1985, first carcinogenic review by a committee, consensus decision as "Possible Human Carcinogen"
 - o Available rat study identified as inadequate
- o In 1986, U.S. EPA presented information to Scientific Advisory Panel (SAP)
 - o "Inadequate animal evidence of carcinogenic potential"

U.S. EPA Review (Continued)

- o In 1991, review of a 2nd rat cancer risk study resulted in classification as “evidence of noncarcinogenicity for humans”
 - o “Lack of convincing carcinogenicity evidence in adequate studies in two animal species”
- o Most recent human health risk assessment published in 2012 – relied on 1991 review
 - o “No evidence of carcinogenicity was found in mice or rats.”

U.S. EPA Review of Human Data

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

U.S. EPA (1991) Review of Animal Data

- o **Mice (Reviewed 1 feeding study)**
 - o Rare type of kidney tumor in 1983 U.S. study were not related to glyphosate treatment
 - o Did not review the 1993 study conducted in Scotland
- o **Rats (Reviewed 2 feeding studies)**
 - o Both studies reported increased pancreatic and liver tumors in males, and thyroid tumors in females, but not related to glyphosate
- o **Conclusion: “Lack of convincing evidence”**

U.S. EPA (1991) Review of Genotoxicity (DNA Damage)

- o Human studies reviewed by IARC were not available in 1991
- o Animals
 - o No effects on bone marrow cells in dosed rats or on DNA mutations in dosed mice
- o Animal cells
 - o No effects on DNA repair were seen in a study with rat liver cells
 - o No effects on chromosomes were seen in a study with Chinese hamster ovary cells

Next Steps

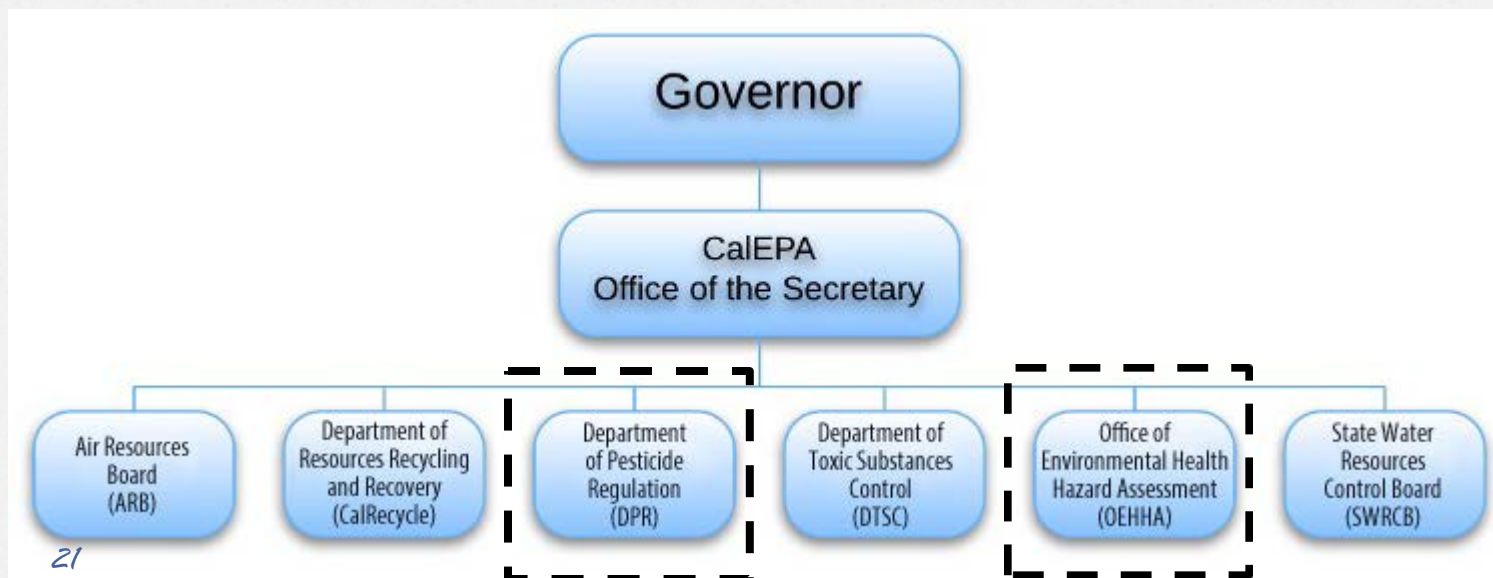
- U.S. EPA plans to release a preliminary risk assessment of glyphosate later this year
- DPR will review this risk assessment and determine whether additional action is needed



(USDA Photo)

California EPA

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



Proposition 65

WARNING

This Product Contains Chemicals
Known To The State Of California
To Cause Cancer And Birth Defects
Or Other Reproductive Harm.

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

Prop 65 List

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

Prop 65 List: http://oehha.ca.gov/prop65/prop65_list/files/P65single082515.pdf

Pesticides listed under Prop 65:

http://www.cdpr.ca.gov/docs/dept/factshts/prop_65_list.pdf

Safe Harbor Levels

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

Glyphosate Proposed Listing

- o On September 4, 2015 OEHHA published a notice of intent to list glyphosate and 3 other pesticides as **known to cause cancer**
 - o Tetrachlorvinphos, Parathion, Malathion
 - o Comment period ended October 20, 2015
- o Listing in response to IARC classification
 - o 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?

