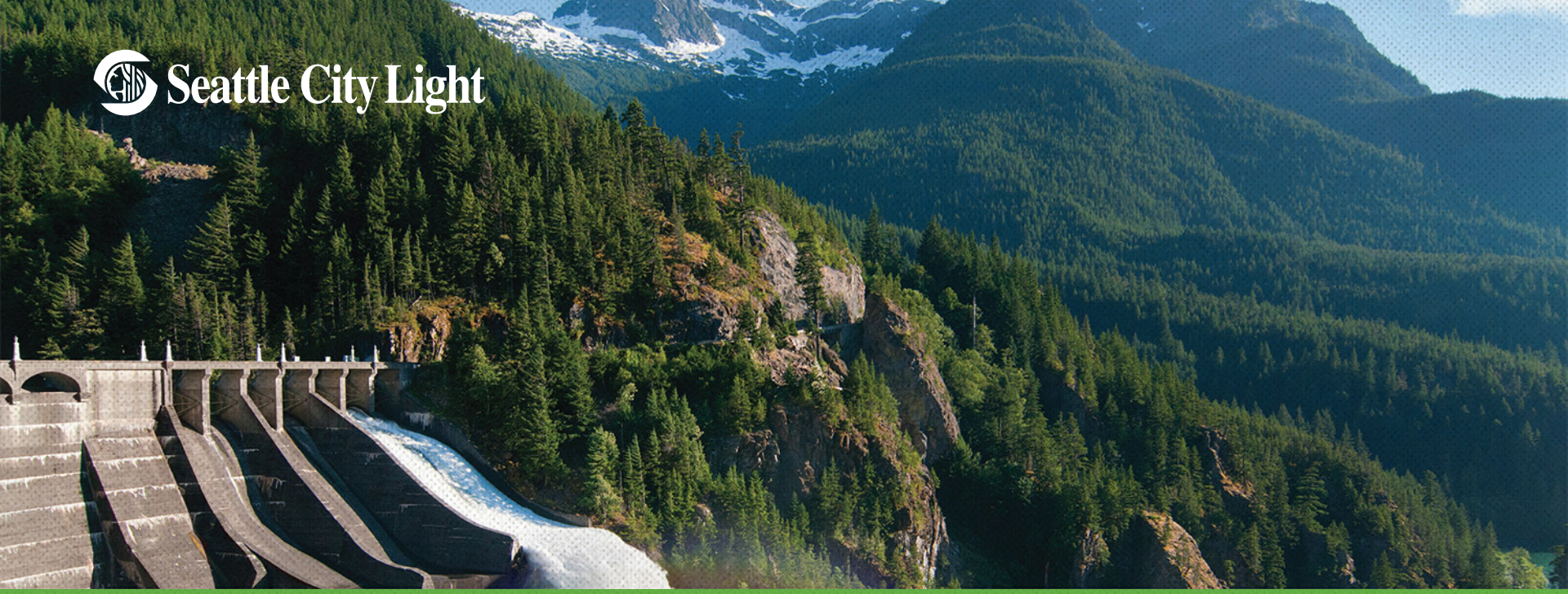


GLYPHOSATE

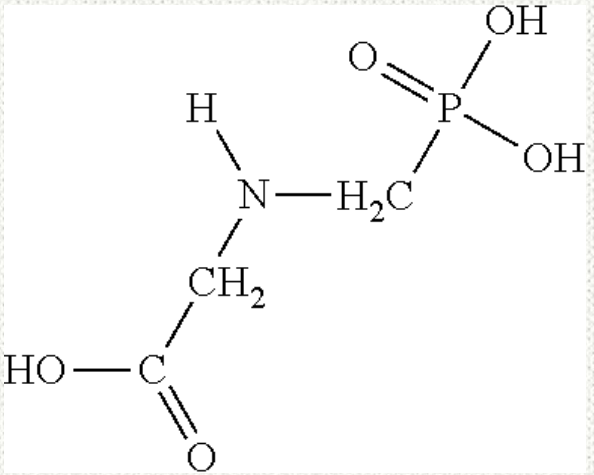
Larry Garcia

Sr. Environmental Analyst

THE NATION'S GREENEST UTILITY
SINCE 1905
SEATTLE CITY LIGHT

OVERVIEW

- Review of the issues
- Industry response to IARC listing
- European response to IARC listing
- EPA Scientific Advisory Panel (SAP)
- Relevant Exposure Data



Glyphosate

GLYPHOSATE

- Legal
  - Monsanto verdict
- Social
  - March against Monsanto
- Political
  - Santa Rosa banning use
- Scientific
  - Our focus today

MODE OF ACTION

- Inhibits production of 3 amino acids
  - Tyrosine
  - Phenylalanine
  - tryptophan
- Blocks enolpyruvylshikimate-3-phosphate synthase
- Shikimate pathway is present in plants, bacteria, fungi and algae, not animals.

BASIC FACTS

- Over 1.7 million tons have been used in the U.S. since 1974
- In a 20 year UCSD study published in 2017, 70% of the study participants exhibited glyphosate exposure (in 2016)
- A 2018 study by the EWG found glyphosate in 43 of 45 conventional oat food products and 5 of 16 organic oat food products

BASIC FACTS

- Half life in soil – ~47 days
  - Explains the presence in food
  - No long term cleanup issues
  - 10 half lives = 0.1% of initial remaining
- Extremely low mobility (high soil sorption – Soil Koc ~24000)
- Low acute toxicity

RECENT HISTORY

- $289 million jury verdict against Monsanto
  - $78 million after appeal
- Groundskeeper in Benicia – non-Hodgkins lymphoma

FARMERS LYMPHOMA

- Meta-analysis 2014
- Positive association with
  - Phenoxy herbicides
  - Organophosphates
  - Carbamate insectides
  - Lindane

RECENT HISTORY

- **March 2015:** The International Agency for Research on Cancer (IARC) reviews literature on glyphosate and ranks it Group 2A

  Group 1: Carcinogenic to humans
  Group 2A: Probably carcinogenic to humans
  Group 2B: Possibly carcinogenic to humans
  Group 3: Unclassifiable as to carcinogenicity to humans
  Group 4: Probably not carcinogenic to humans

- **August 2015:** IARC publishes the comprehensive monograph

- **November 2015:** European Food Safety Authority peer reviews glyphosate risk assessment (over 700 studies reviewed): **Unlikely to be carcinogenic to humans**.

IARC classification of some organophosphate pesticides

	Activity (current status)	Evidence in humans (cancer sites)	Evidence in animals	Mechanistic evidence	Classification
Parathion	Insecticide	Inadequate	Sufficient	..	2B
Malathion	Insecticide	Limited (non-Hodgkin lymphoma, prostate)	Sufficient	Genotoxicity, oxidative stress, inflammation, receptor-mediated effects, and cell proliferation or death	2A
Diazinon	Insecticide	Limited (non-Hodgkin lymphoma, leukaemia, lung)	Limited	Genotoxicity and oxidative stress	2A
Glyphosate	Herbicide	Limited (non-Hodgkin lymphoma)	Sufficient	Genotoxicity and oxidative stress	2A

RECENT HISTORY

- **May 2016:** UN Food and Agriculture Organization (FAO) and World Health Organization conclude glyphosate residue **"Unlikely to pose a carcinogenic risk to humans from exposure through the diet."**
- **September 2016:** *Critical Reviews of Toxicology*, a peer-reviewed journal, publishes a review of the carcinogenic potential of glyphosate. This work was from 4 independent expert panels funded by Monsanto.
- **March 2017:** European Chemicals Agency (ECHA) listed glyphosate as Category 1 for eye damage/irritation and aquatic chronic toxicity Category 2. It was NOT classified as a carcinogen.
- **July 2017:** Glyphosate listed on California Prop 65 list of carcinogens
- **July 2018**: Prop 65 develops Safe Harbor for glyphosate (No Significant Risk Level)

PROP 65 SAFE HARBOR LEVELS

- California Office of Environmental Health Hazard Assessment (OEHHA)
- No Significant Risk Levels (NSRL) for carcinogens
- Maximum Allowable Dose Levels (MADL) for reproductive toxins

EPA HISTORY

- **1985:** Initial review - **Group C Possible Human Carcinogen** based on kidney tumors in male mice
- **1986:** FIFRA Scientific Advisory Panel **Group D Not Classifiable as to Human Carcinogenicity** - increase in kidney tumors not statistically significant
- **1991:** EPA Carcinogenicity Peer Review Committee **Group E Evidence of Non-Carcinogenicity for Humans**
- **September 2016**

EPA HISTORY

- **September 2016:** **"**The available data at this time do no support a carcinogenic process for glyphosate. Overall, animal carcinogenicity and genotoxicity studies were remarkably consistent and did not demonstrate a clear association between glyphosate exposure and outcomes of interest related to carcinogenic potential. In epidemiological studies, there was no evidence of an association between glyphosate exposure and numerous cancer outcomes; however, due to conflicting results and various limitations identified in studies investigating Non-Hodgkin's Lymphoma (NHL), a conclusion regarding the association between glyphosate exposure and risk of NHL cannot be determined based on the available data."
- In the past they used this phrase:

  "Not likely at low doses, but likely at high doses."

IARC BASIS

- Some epidemiologic data links glyphosate exposure in highly exposed populations (farmers and applicators) to NHL and multiple myeloma. Correlations are highest for high-dose individuals. There are multiple confounding exposures.
- Some animal data show kidney, liver and pancreatic tumors at high doses.
- Some cell culture studies show DNA strand breaks, sister chromatid exchange, and chromosomal aberrations.

GLYPHOSATE: GROUP 2A, PROBABLE HUMAN CARCINOGEN

- **Sufficient evidence** of cancer in mice and rats from years of glyphosate ingestion
- **Strong evidence** of carcinogenicity from mechanistic or cellular studies
- **Limited evidence** of cancer in humans from epidemiologic studies of people, particularly pesticide applicators and farmworkers

WHAT DOES THE IARC 2A RATING FOR GLYPHOSATE REALLY MEAN?

- Risk highest for those most exposed and may be quite low for others.
- Applicators are the group of highest concern.
- General public - exposure from food likely higher than incidental exposure from contact with glyphosate-treated vegetation.

SEPTEMBER 2016 ISSUE OF *CRITICAL REVIEWS IN TOXICOLOGY* DEVOTED TO GLYPHOSATE

- Reviewed the weight of the evidence for carcinogenic potential data and compared to IARC conclusions
  - "The Expert Panel concluded that glyphosate, glyphosate formulations, and AMPA do not pose a genotoxic hazard and the data do not support the IARC Monograph genotoxicity evaluation."
- Reviewed the epidemiology data for NHL and multiple myeloma
  - "Overall, our review did not find support in the epidemiologic literature for a causal association between glyphosate and NHL or MM." **(NOTE: Lead author used to work for Amgen)**
- Reviewed the rodent cancer data
  - ". . . given the overall weight-of-evidence (WoE), the expert panel concluded that glyphosate is not a carcinogen in laboratory animals." **(NOTE: Lead author has taken research funding from pesticide manufacturers.)**

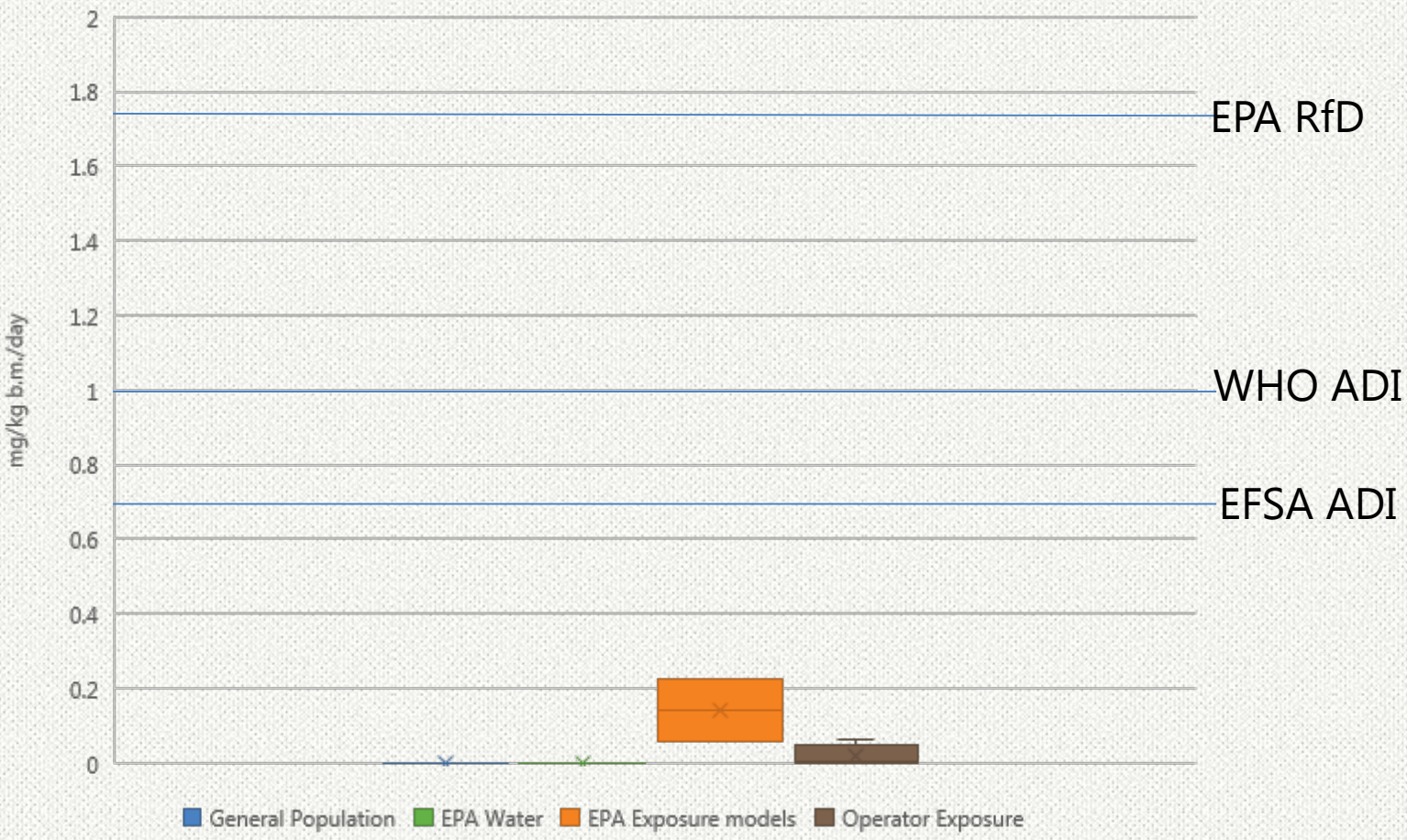
SEPTEMBER 2016 ISSUE OF *CRITICAL REVIEWS IN TOXICOLOGY* DEVOTED TO GLYPHOSATE

- Evaluated the genotoxicity data for glyphosate, AMPA and glyphosate-based formulations
  - "The WoE approach, the inclusion of all relevant regulatory studies, and some differences in interpretation of individual studies led to significantly different conclusions by the Expert Panel compared with the IARC Monograph. The Expert Panel concluded that glyphosate, glyphosate formulations, and AMPA do not pose a genotoxic hazard and the data do not support the IARC Monograph genotoxicity evaluation." **(NOTE: Few academics on this panel. Lead author worked for the biotechnology industry.)**

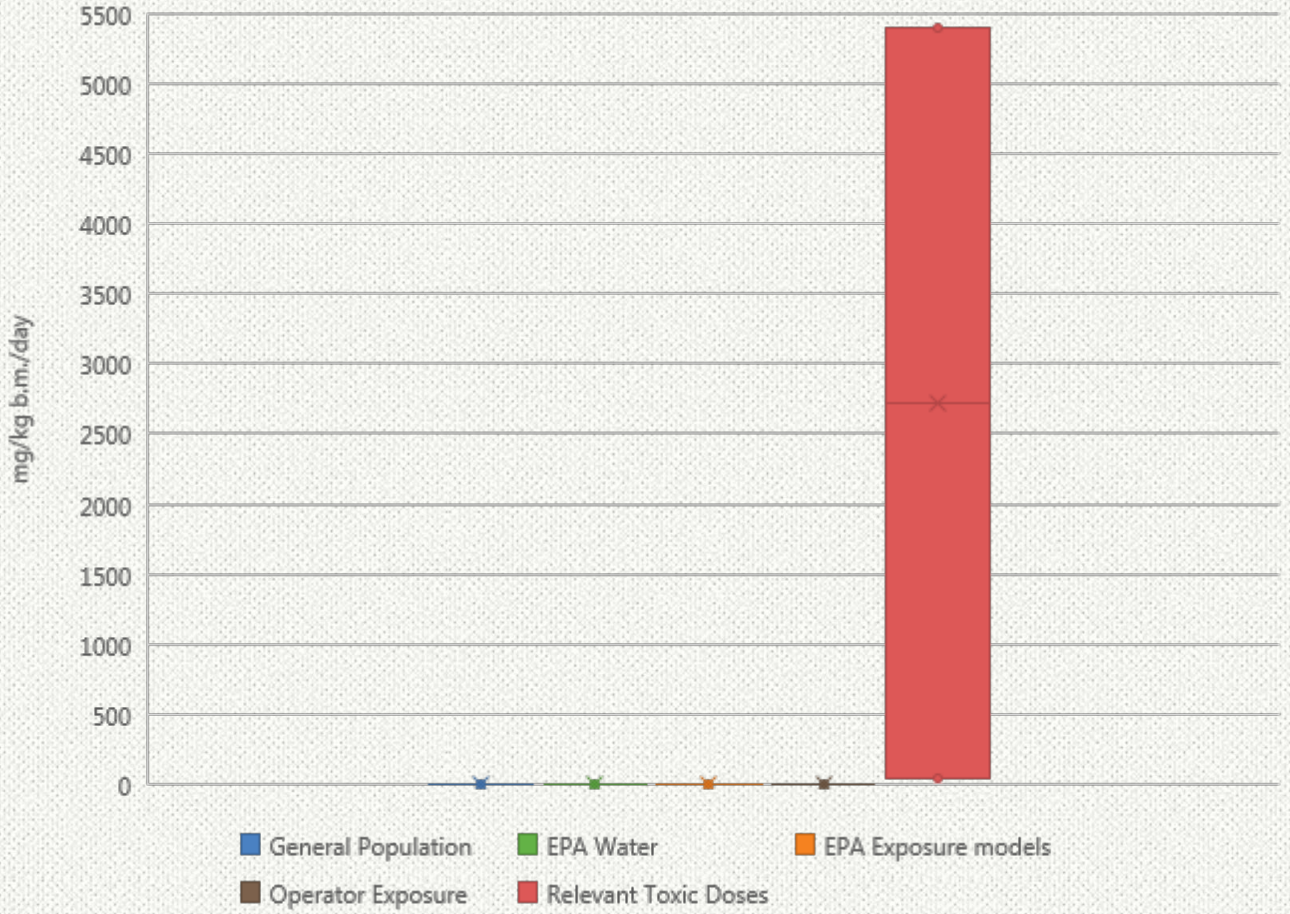
SEPTEMBER 2016 ISSUE OF *CRITICAL REVIEWS IN TOXICOLOGY* DEVOTED TO GLYPHOSATE

- Assessed exposure potential (which IARC did not do)
  - "For applicators, 90th centiles for systemic exposures based on biomonitoring and dosimetry (normalized for penetration through the skin) were 0.0014 and 0.021mg/kg b.m./d, respectively. All of these exposures are less than the reference dose and the acceptable daily intakes proposed by several regulatory agencies, thus supporting a conclusion that even for these highly exposed populations the exposures were within regulatory limits." **(NOTE: Lead author has worked for the chemical industry, but his work is based on monitoring data)**

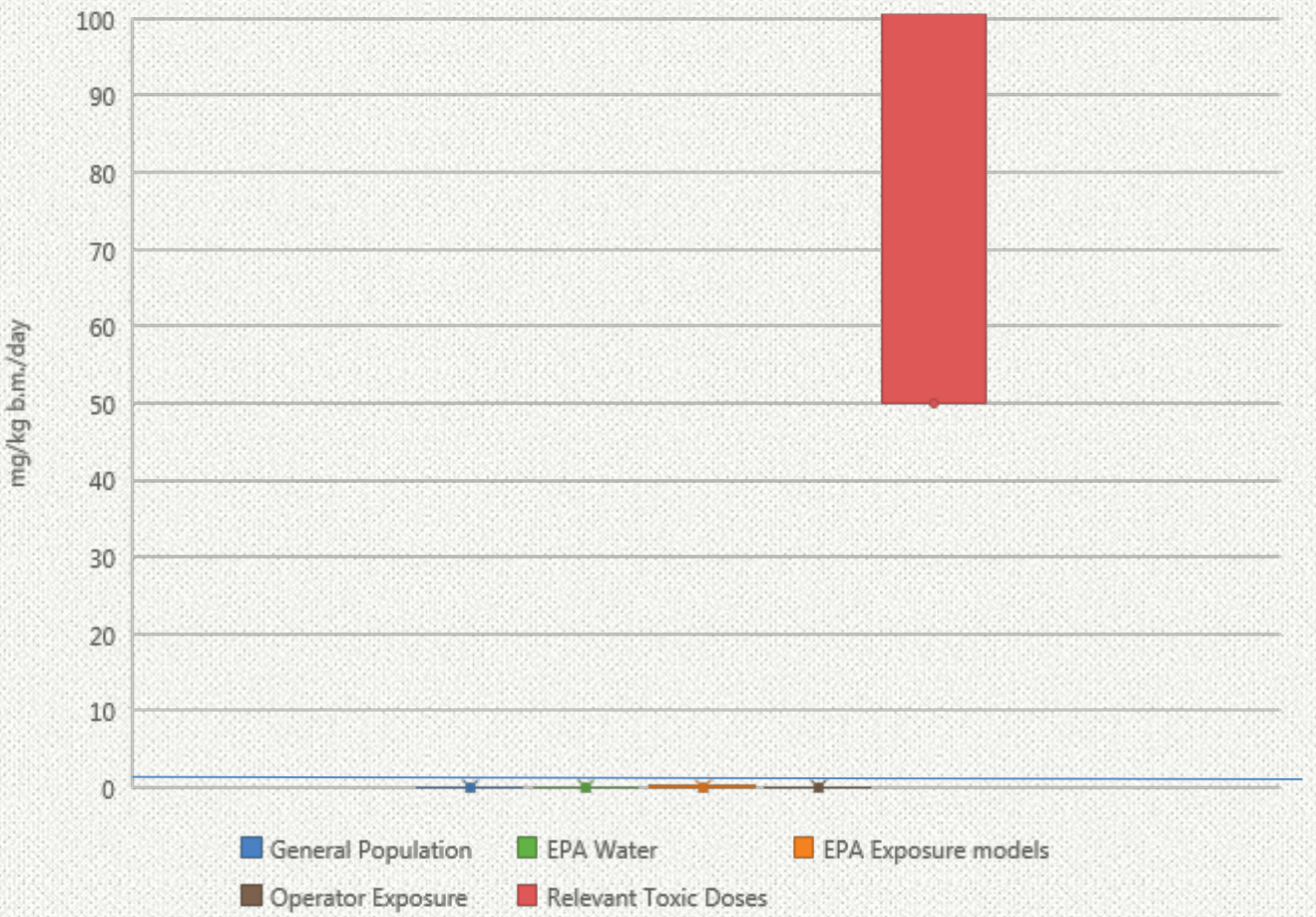
GLYPHOSATE EXPOSURE



EXPOSURES WITH RELEVANT TOXIC DOSES



EXPOSURES WITH RELEVANT TOXIC DOSES



EPA RfD

DIFFERENCE BETWEEN IARC AND EPA

- The differences in outcomes are due to:
  - the information used for the evaluation (industry studies vs independent studies)
  - the rigor and weights applied to the different types of studies
  - the criteria used to incorporate the important issue of human relevance (hazard vs. risk)