Glyphosate and Cancer Risk

Jeffrey Jenkins, Ph.D.
Department of Environmental and Molecular Toxicology
Oregon State University

OSU Extension Service  npic
National Pesticide Information Center
Environmental and Molecular Toxicology
Oregon State University Agricultural Experiment Station
Cancer and Human Health

• Cancer is considered the most severe health condition for the following reasons:
  
  – As a result of the aging of the human population, cancer is today the **most common cause of death in the world**. (WHO, 2014)
  
  – There are many forms of cancer.
  
  – Cancer occurs in **one of every 2 men and 3 women**.
  
• Causes of cancer: genes, lifestyle, diet, chemicals.
The role of genes and environment in the development of cancer

Familial risk ratios = risk to a relative of an affected individual divided by the population prevalence

Percentages = the attributable-fraction of cancer deaths due to the specified environmental risk factor

Anand et. al., Cancer is a Preventable Disease that Requires Major Lifestyle Changes. Pharm Res (2008)
Cancer “Prevention”

• EPA cancer risk assessment goal:
  
  prevent excess cancers due to chemical exposure

• Often assumes daily exposure over a lifetime (~70 years)

• Cancer odds (all causes) – 1 in 2 (men); 1 in 3 (women)

• Acceptable excess cancer risk – 1 in 1 million (10^{-6})

• For each chemical, cancer odds – 1 in 2.000001 (men)
How Does the US Environmental Protection Agency (EPA) Assess Risk?

National Academy of Sciences (NAS) 4-step risk assessment Paradigm*:

1. **How is it Harmful?**
2. **Will I be exposed, how much, how often?**
3. **What is my risk?**
4. **How much to cause harm?**

EPA Office of Chemical Safety and Pollution Prevention harmonized test guidelines:

- 810 - Product Performance
- 830 - Product Properties
- 835 - Fate, Transport and Transformation
- 840 - Spray Drift
- 850 - Ecological Effects
- 860 - Residue Chemistry
- 870 - **Health Effects**
- 875 - Occupational and Residential Exposure
- 880 - Biochemicals
- 885 - Microbial Pesticide
- 890 - Endocrine Disruptor Screening Program
Pesticide Registration process

- Register or reregister a pesticide if it can be used "without unreasonable adverse effects on human health or the environment."

- Pesticide registration in the U.S. is a dynamic process.

- As new science and information becomes available a pesticide product’s registration status may be changed.

- This is accomplished through the EPA Office of Pesticide Programs registration review process.

- Current goal – reevaluate each registered pesticide at least every 15 years.
Long-term Animal Study
Assumptions

Animal models will predict cancer in humans.

High dose, short term, exposure of animals will predict adverse effects of low dose, long term, exposure in humans.
Does a chemical cause cancer?

Weight-of-the-evidence approach

• Summarize human and animal data: sufficient, limited, inadequate, no data, no evidence

• Look at other evidence: short-term tests, pharmacokinetics, structure-activity relationships…

• Classify overall weight-of-the-evidence
EPA 2005 Guidelines
Weight-of-evidence narrative

• EPA weight of evidence descriptors:
  – Carcinogenic to humans
  – Likely to be carcinogenic to humans
  – Suggestive evidence of carcinogenic potential
  – Inadequate information to assess carcinogenic potential
  – Not likely to be carcinogenic to humans
Roundup weedkiller 'probably' causes cancer, says WHO study

The Monsanto product - the world's most widely used herbicide - contains glyphosate, which may also be carcinogenic for non-Hodgkin's lymphoma

Staff and agencies
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Roundup, the world's most widely used weedkiller, "probably" causes cancer, the World Health Organisation (WHO) has said.

The International Agency for Research on Cancer (IARC) - WHO's cancer agency - said that glyphosate, the active ingredient in the herbicide made by agriculture company Monsanto, was "classified as probably carcinogenic to humans".

It also said there was "limited evidence" that glyphosate was carcinogenic in humans for non-Hodgkin's lymphoma.
GMO Corn & Glyphosate

A fractured continent
As Science went to press, 10 governments had asked seed manufacturers to keep GM crops out. Others were considering the same, or Option 2, a national ban.

Who IARC
Protests and cancer concerns raise doubts for Roundup's future in Europe (2015)


Credit: Reuters
Johnson, 46, is the first of hundreds of cancer patients to see his case against Monsanto go to trial.
Does Glyphosate Cause Cancer?

- US National Institute of Health, National Toxicology Program (NTP) – No evidence of carcinogenic activity
- US Environmental Protection Agency (EPA) – Not likely to be carcinogenic to humans
- European Union, Canada, Australia, Japan – No evidence of carcinogenicity
- Joint FAO/WHO Meeting on Pesticide Residues (JMPR) – glyphosate unlikely to pose a carcinogenic risk to humans from exposure through the diet
- WHO International Agency for Research on Cancer (IARC) – Probable human carcinogen
WHO IARC Monographs Programme

Appointed expert working group meets for 7 to 8 days, determines likelihood that an agent can cause cancer in humans.


- Red meat 1
- Ethanol in alcoholic beverages 1
- Solar radiation 1
- Wood dust 1
- Hairdresser or Barber 2A
- Glyphosate 2A
- Coffee 2B
- Gasoline 2B
- Radiofrequency electromagnetic fields (cell phones) 2B

Group 1: Carcinogenic to humans (118)
Group 2A: Probably carcinogenic to humans (75)
Group 2B: Possibly carcinogenic to humans (288)
Group 3: Not classifiable as to its carcinogenicity to humans (503)
Group 4: Probably not carcinogenic to humans (1)
Coffee drinkers, don't fret over California cancer warning

Storm clouds are brewing in California's coffee cups. Companies across the state will have to add a cancer-warning label to coffee, a judge ruled last week, because the drink contains a chemical called acrylamide.

Los Angeles County Superior Court Judge Elihu M. Berle sided with a nonprofit organization in a case against Starbucks, Peets and dozens of other coffee chains, saying that businesses that sold coffee were in violation of a state regulation called Proposition 65. Prop 65 requires businesses with at least 10 employees to disclose any carcinogens and toxic chemicals in their products.

Los Angeles Superior Court Judge Elihu M. Berle ruled in March that coffee should carry the warning labels mandated by California's Proposition 65 because the brew contains acrylamide, a chemical that some studies found increases the incidence of cancer in rats. It was an unfortunate outcome of a ridiculous lawsuit by an opportunistic attorney.

Acrylamide is a naturally occurring chemical formed when coffee is roasted (and when starchy foods such as potatoes are cooked at high heat). But the World Health Organization's International Agency for Research on Cancer, which reviewed 1,000 studies, reported last week that there is just no proof that coffee causes cancer. Furthermore, there's a wealth of scientific data indicating that coffee consumption has health benefits and may even ward off premature death, perhaps because of the other chemicals present in the average cup of joe.

Berle's Chicken Little ruling was made possible by Proposition 65, the well-meaning but clumsy Safe Drinking Water and Toxic Enforcement Act of 1986. It requires all but the smallest businesses to warn people when knowingly exposing them to any of the approximately 850 chemicals that are confirmed or suspected carcinogens.

This seems perfectly reasonable. Who wants to be exposed unknowingly to something that might cause cancer? But warnings are required for chemicals listed in Proposition 65 unless it is shown that exposure isn't dangerous. Because the world is filled with chemicals that may in some instances and concentrations be dangerous but are difficult to avoid, California is littered with unhelpful and vague Proposition 65 warnings tacked up at office buildings, hospitals, parking lots and retailers, even online ones.

Fortunately for coffee drinkers, state regulators took the unprecedented — and most welcome — step Friday of announcing plans to exempt coffee from the warnings in light of the new WHO report. We lift a figurative cold brew to California's Office of Environmental Health Hazard Assessment for taking this extra step to clear up the confusion. We also appreciate the new warning signs the agency designed that identify at least one of the chemicals present by name and include an online link to more information about the exposure. The public badly needs more information about what it is being warned about and why.

But the fact that the agency had to make a rule just for coffee exposes a fundamental flaw in Proposition 65. The measure is so broad, its warnings may actually make it harder for Californians to assess the real dangers they encounter.
Hazard vs Risk

- EPA, EU and other governments evaluate cancer risk; an estimate of the carcinogenic effects expected from exposure to a cancer hazard.

- WHO’s IARC Monographs Programme evaluates cancer hazard; is an agent capable of causing cancer under some circumstances.

- WHO glyphosate cancer hazard determination based largely on epidemiology, did not consider most scientific studies evaluated for registration by US, Canada, EU, Australia, Japan.
When IARC assessed glyphosate, significant changes were made between a draft of its report and the published version.

Multiple scientists' conclusions that their studies had found no link between glyphosate and cancer in laboratory animals was removed.

The agency won't say who made the changes or why.