Glyphosate and Cancer Risk

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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)
Variation in cancer risk among tissues can be explained by the number of stem cell divisions

C Tomasetti¹ and B Vogelstein² Science 2015;347:78-81

• If hereditary and environmental factors cannot fully explain the differences in organ-specific cancer risk, how else can these differences be explained?

• We consider a third factor: the stochastic effects associated with the lifetime number of stem cell divisions within each tissue.

• The majority is due to “bad luck,” that is, random mutations arising during DNA replication in normal, noncancerous stem cells.

• This is important not only for understanding the disease but also for designing strategies to limit the mortality it causes.

¹Johns Hopkins School of Medicine
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Figure 1. The relationship between the number of stem cell divisions in the lifetime of a given tissue and the lifetime risk of cancer in that tissue\textsuperscript{1}.

\textsuperscript{1} Life-time risk - NCI Surveillance, Epidemiology, and End Results (SEER) database
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 much to cause harm?
2. How is it Harmful?
3. Will I be exposed, how much, how often?
4. What is my risk?

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

Specimen Label

Accord® Concentrate

Hazard Symbol:


glyphosate (N-phosphonomethyl)glycine,
isopropylamine salt

Total Ingredients: 100.0%

Contains 5.4 pounds per gallon glyphosate, isopropylamine salt (4 pounds per gallon glyphosate).

EPA Reg. No. 62719-324

Keep Out of Reach of Children

CAUTION PRECAUTION

Sí usó no entiende la etiqueta, busque a alguien que se le explica a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

Precautionary Statements

Hazard to Humans and Domestic Animals

Harmful if Inhaled

Avoid breathing spray mist. Remove contaminated clothing and wash before reuse. Wash thoroughly with soap and water after handling.

Personal Protective Equipment (PPE)

Applicators and other handlers must wear:

- Long-sleeved shirt and long pants
- Shoes plus socks.

Follow manufacturer's instructions for cleaning/maintaining PPE (Personal Protective Equipment). If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Controls

When handlers use closed systems, enclosures, or aircraft in a manner that meets the requirements listed in Worker Protection Standard (WPS) for agricultural pesticides (29 CFR 1910.148), the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.
- Remove clothing immediately if pesticide gets inside. Wash thoroughly and put on clean clothing.

First Aid

If inhaled: Move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-929-8656 for emergency medical treatment information.

Environmental Hazards

Do not contaminate water when cleaning equipment or disposing of equipment washwater. Treatment of aquatic weeds can result in oxygen depletion of local due to decomposition of dead plants. This oxygen loss can cause fish suffocation.

In case of leak or spill, soak up and remove to a landfill.

Physical or Chemical Hazards

Spray solutions of this product should be mixed, stored and applied using only stainless steel, aluminum, fiberglass, plastic, or plastic-lined steel containers.

Do not mix, store or apply this product or spray solutions of this product in galvanized steel or unlined steel (except stainless steel) containers or spray tanks. This product or spray solutions of this product stored with such containers and tanks to produce hydrogen gas, which may form a highly combustible gas mixture. This gas mixture could flash or explode, causing serious personal injury, if ignited by open flame, spark, welder's torch, lighted cigarette or other ignition source.

Notice: Read the entire label. Use only according to label directions. Before using this product, read Terms and Conditions of Use, Warranty Disclaimer, Inherent Risks of Use, and Limitation of Remedies elsewhere on this label. If terms are unacceptable, return at once unopened.
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
Saturday 21 March 2015 13.12 EDT

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.
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.

- Used Option 1
- Expected to use Option 1 and/or 2
- Grows GM maize

GMO Corn & Glyphosate
Protests and cancer concerns raise doubts for Roundup's future in Europe (2015)

June 17, 2018

Johnson, 46, is the first of hundreds of cancer patients to see his case against Monsanto go to trial.

CNN — On bad days, Dewayne Johnson is too crippled to speak. Lesions often cover as much as 80% of his body.

Doctors have said they didn’t expect him to live to see this day. But Monday marks a milestone: Johnson, 46, is the first of hundreds of cancer patients to see his case against agrochemical giant 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

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 applaud California's Office of Environmental Health Hazard Assessment for taking this extra step to clean 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.
California jury awards $289 million to man who claimed Monsanto's Roundup gave him cancer - LA Times 8/10/2018

• Groundskeeper DeWayne Lee Johnson, 46, awarded $39 million in compensatory damages and $250 million in punitive damages; Monsanto’s Roundup caused his incurable non-Hodgkin’s lymphoma.

• Activists, who have long battled to ban glyphosate, lauded the decision.
  – “Monsanto made Roundup the OxyContin of pesticides, and now the addiction and damage they caused have come home to roost,” said Ken Cook, president of Environmental Working Group. “This won’t cure DeWayne Lee Johnson’s cancer, but it will send a strong message to a renegade company.”
  – The verdict “signals a turning tide,” said Linda Wells, Midwest organizing director for Pesticide Action Network. “It’s time to get carcinogenic pesticides off the market, and fight for the protective regulations we all deserve,” Wells said.

• Monsanto (Bayer) will appeal; “We are sympathetic to Mr. Johnson and his family. Today’s decision does not change the fact that more than 800 scientific studies and reviews — and conclusions by EPA and NIH, and regulatory authorities around the world — support the fact that glyphosate does not cause cancer, and did not cause Mr. Johnson’s cancer.”