The Carcinogenicity of Glyphosate
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Conflict of Interest Statement

I declare no financial interests related to the subject matter of my presentation.
IARC Evaluation of Glyphosate

➢ *Probably carcinogenic to humans (Group 2A)*

IARC evaluations are used as a reference worldwide

- All data in the public domain for independent scientific review
- Reviewed by the world’s leading experts without vested interests

What happens after IARC identifies a carcinogen?

- Risk assessments help regulators and the public understand the extent of potential cancer risk
- Measures to reduce exposures to workers and to the public
How Are the IARC Monograph Evaluations Conducted?

- Procedural guidelines for participant selection, conflict of interest, stakeholder involvement & meeting conduct
- Separate criteria for review of human, animal and mechanistic evidence
- Decision process for overall evaluations

Preamble to the IARC Monographs (2006):
http://monographs.iarc.fr/ENG/Preamble/index.php
Who Does the Evaluation?

IARC Secretariat
Coordinates all aspects of the evaluation

Working Group
Independent scientists without conflict of interest
Review science and develop evaluations

Invited Specialists
Scientists with relevant knowledge but a competing interest

Representatives of governments and health agencies

Observers
Scientists with a competing interest: observe but do not influence outcomes

Preamble to the IARC Monographs (2006):
http://monographs.iarc.fr/ENG/Preamble/index.php
What Evidence is Considered?

- Cancer in humans
- Cancer in animals
- Mechanisms

Overall evaluation

Exposure Data

Preamble to the IARC Monographs (2006):
http://monographs.iarc.fr/ENG/Preamble/index.php
The IARC Monographs Evaluations: A Two-Step Process

**Cancer in humans**
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

**Cancer in experimental animals**
- Sufficient evidence
- Limited evidence
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity

**Mechanistic and other relevant data**
- “Weak,” “moderate,” or “strong” evidence?
- Does this—or can it—occur in humans?

**Overall evaluation**
- **Group 1** Carcinogenic to humans (120)
- **Group 2A** Probably carcinogenic to humans (81)
- **Group 2B** Possibly carcinogenic to humans (294)
- **Group 3** Not classifiable as to its carcinogenicity to humans (505)
- **Group 4** Probably not carcinogenic to humans (1)
IARC Monographs Timeline

**IARC Secretariat:**
- Coordinate all aspects of the Monograph development

**Working Group members:**
- Write the critical reviews and develop evaluations

**Invited Specialists:**
- Have critical knowledge but also a conflicting interest
  - do not draft text or participate in evaluations

**Representatives of national and international health agencies:**
- do not draft text or participate in evaluations

**Observers:**
- Allowed to observe but not to influence outcomes
  - do not draft text or participate in evaluations

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**Meeting announced (1 yr ahead):**
- Preliminary List of Agents
- Call for Data and Experts
- Request for Observer Status
- WHO Col form posted

**Monograph in-person meeting:**
- Sub-group review, revision, summary
- Plenary review and evaluation

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**Participants (and DOI) announced (2 months ahead)**

**The Lancet Oncology Publication (2 weeks later)**

**Monograph Publication (1-2 years later)**

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International Agency for Research on Cancer

World Health Organization
Scientific engagement: Glyphosate _Monograph_

- IARC meetings are open and follow transparent, published methods
- All meeting participants have full access to the data being evaluated
- Fully referenced _Monographs_ published on-line for free download
Glyphosate: Studies

- ~1000 studies identified and screened

- **Laboratory studies**
  - “Pure” glyphosate, glyphosate formulations
    - Cancer in mice, rats
    - DNA damage (genotoxicity)

- **Human studies** (real-world exposures)
  - DNA damage—community residents before and after spraying
  - Cancer in humans—farmers, other workers

- *Published Monograph: >250 references*
# Cancer in Humans

Studies of exposed workers provide “limited” evidence for NHL (Non-Hodgkin lymphoma)

1) **Case-control studies**
   - Canada, Sweden, US
   - **2592 NHL cases**
   - **Increased risks**, not explained by other pesticides

2) **Cohort study (Ag Health Study)**
   - US, 2 states
   - **92 NHL cases**
   - No significant increase in risk

3) **Meta-analysis**
   - Objective method to combine **all studies**
   - **Increased risks** (meta risk-ratio=1.3; 95% CI,1.03–1.65; I²=0%)
Cancers in Mice Fed Glyphosate

Positive results in 2 of 2 feeding studies

- Rare cancers: extremely important in assessing human risk....but challenging to detect signal from background noise
  - High statistical significance
  - Tumours in the absence of toxicity
  - Evaluation fully in line with accepted principles
  - Causal relationship established

➢ Sufficient evidence of cancer in animals
Strong evidence, glyphosate formulations:
- Exposed community residents
  - Experiments using:
    - Human cells
    - Animal cells
    - Mammals and non-mammals
    - Negative in bacteria

Strong evidence, glyphosate:
- No studies in exposed humans
  - Experiments using:
    - Human cells
    - Animal cells
    - Mammals and non-mammals
    - Negative in bacteria
Summary: Glyphosate Hazard Evaluation

Cancer in humans (NHL)

*Limited evidence*
- Studies of real-world exposures (occupational)
- *Glyphosate formulations* in different regions at different times

Cancer in animals

*Sufficient evidence*
- Studies of pure *glyphosate*
- Rare cancers in valid studies

DNA damage & oxidative stress

*Strong evidence*
- Few studies of real-world exposures (communities)
- Experimental studies of pure *glyphosate*
- Experimental studies of *glyphosate formulations*

Overall evaluation of glyphosate:

Group 2A *Probably carcinogenic to humans*
How to prioritize pesticides for cancer hazard evaluation?

• Comprehensive list of pesticides
• Automated text mining of public databases
• Data visualization by chemical class:
  A. Organophosphorus
  B. Organochlorine

http://ehp.niehs.nih.gov/EHP186/

Figure 2, from Guha et al. Environ Health Perspect. 2016 124(12):1823-1829.
## IARC Classifications of Pesticides 1971-2016

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number</th>
<th>Details/Comments</th>
</tr>
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<tbody>
<tr>
<td>Group 1</td>
<td>3</td>
<td>Arsenic and arsenical compounds, including pesticides; <em>Lindane; Pentachlorophenol</em></td>
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<tr>
<td>Group 2A</td>
<td>9</td>
<td>Captafol; *DDT; Diazinon; Dieldrin, Aldrin metabolised to Dieldrin; Dimethylcarbamoyl chloride; Ethylene dibromide; <em>Glyphosate; Malathion; Tetrachloroazobenzene (contaminant)</em></td>
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<tr>
<td>Group 2B</td>
<td>27</td>
<td>Examples evaluated in 2015-2016: <em>Parathion, Tetrachlorvinphos, 2,4,6-Trichlorophenol</em></td>
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<tr>
<td>Group 3</td>
<td>48</td>
<td></td>
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