Glyphosate Scientific Briefing

Glyphosate in our bread

Peter Melchett - Soil Association Policy Director
Glyphosate in our bread

Glyphosate spraying of UK cereals has risen 400% in the last 20 years

• 2013, the last year for which there is data, was a record for both the total amount of glyphosate used on cereals and the highest area of cereals sprayed.

• This stood at just over 1 million hectares – nearly a third of UK cereals being sprayed.

• The total amount applied came to around 800,000 kg of glyphosate
Total area of glyphosate applied to cereals in Great Britain between 1990-2013
Total weight of glyphosate applied to cereal crops in Great Britain between 1990 - 2013
Percentage of cereals treated with glyphosate and the number of times treated
Glyphosate in our bread

- According to Government data, the rise in glyphosate use is matched by a rise in the amount of glyphosate found in sampled bread.

- 2013 had the highest numbers of bread samples contaminated with glyphosate on record – nearly a third of bread tested contained the weed-killer.

- The average amount found for 2014 and 2013 was around 0.2mg of glyphosate, per kg of bread, respectively.

- The officially allowed ‘Maximum Residue Level’ (MRL) in wheat is 10 mg per kg, set before the WHO’s IARC found glyphosate is a probable carcinogen to humans.
Percentage of samples of UK bread found to contain glyphosate
Glyphosate is also turning up in our urine and breast milk

- GM Freeze and Friends of the Earth Europe tested the urine of 182 city-dwelling volunteers from 18 European countries in 2013. 44% had urine containing glyphosate.
- Of the 10 volunteers from the UK, 7 out of 10 had traces of the weed-killer.
- Glyphosate has been found in the breast milk of German women.
Glyphosate in our bread – Tesco’s response

• The Food Policy Advisor covering chemical contaminants in food at the British Retail Consortium will be monitoring any new evidence on possible consumer risk from residues in bread products on behalf of the industry.

• This includes any evidence which is published as part of the IARC report and any evidence that comes to light during the glyphosate re-registration process, which will take place later this year.
Glyphosate in our bread – Tesco’s response

• Unfortunately neither ourselves nor the BRC are able to attend the meeting on the 15th, but we are keen to take a look at the outputs.

• If you could please share any outputs with us that would be very helpful. In the meantime, we will continue to be guided by EU legislation on pesticide use.
Glyphosate in our bread
Glyphosate Scientific Briefing
IARC Monograph Review Process and Glyphosate

Christopher J. Portier, Ph.D.

Glyphosate Scientific Briefing
Westminster, London
July 15, 2015
The IARC Monographs Program

- IARC Monographs Evaluate
  - Chemicals
  - Complex substances and mixtures
  - Occupational exposures
  - Physical and biological agents
  - Personal habits
The IARC Monographs Program

• 980 Agents have been reviewed
  – 116 **known** human carcinogens
    • Group 1
  – 73 **probable** human carcinogens
    • Group 2A
  – 287 **possible** human carcinogens
    • Group 2B
  – 503 **not classifiable**
    • Group 3
  – 1 **probably not** carcinogenic
IARC Monographs Process

- Written Guidelines
  - Public Document
  - Who? What? How?
  - Roles
  - Responsibilities
  - Instructions
    - Review
    - Summary of Evidence
IARC Monograph 112 Process

• Working Group Members
  – No real or apparent conflicts of interest
    • Formal process, written declarations of interest
  – Membership
    • Working Group members – review, evaluate
    • Invited Specialist – review only
    • Representatives – government, observe only
    • Observers – interested party, observe only
    • Secretariat – support the Working Group
IARC Monograph Timeline

• 1 year before Monograph Meeting
  – Meeting announced
  – Call for experts
  – Call for data

• 8 months before Monograph Meeting
  – Working Group membership selected
  – Request for observer status opened
  – Draft sections of Monograph developed by Working Group Members
IARC Monograph Timeline

• 1 month before Monograph Meeting
  – Call for data closed
  – Draft sections distributed to Working Group members for review and comment

• At Monograph Meeting
  – Finalize review of all literature
  – Evaluate the evidence in each category
  – Complete the overall evaluation
IARC Monograph Timeline

• 1-2 weeks after Monograph Meeting
  – Publish summary in Lancet Oncology

• 4-12 months after Monograph Meeting
  – Finalize Monograph and publish
The IARC Monograph

Preamble

General Remarks

Several *Monographs* in one volume:

1. Exposure data
2. Cancer in humans
3. Cancer in animals
4. Mechanistic and other relevant data
5. Summary
6. Evaluation and rationale

References
What is reviewed?

- Systematic review of human, experimental and mechanistic data
- All pertinent epidemiological studies and cancer bioassays
- Representative mechanistic data
- Studies must be publicly available
  - Sufficient detail to review
  - Reviewers cannot have been associated with the study
Evidence Review

- **Human Studies**
  - Extract Data
  - Assess Individual Study Quality
  - Rate Confidence in Body of Evidence

- **Animal Studies**
  - Extract Data
  - Assess Individual Study Quality
  - Rate Confidence in Body of Evidence

- **Mechanistic Data**
  - Extract Data
  - Assess Individual Study Quality
  - Rate Confidence in Body of Evidence
Glyphosate - Background

- Broad-spectrum, non-selective herbicide
- First synthesized by Cilag (1950) as a possible drug
- Re-synthesized by Monsanto (1970)
- Hundreds of trade names
- Approximately 91 producers in 20 countries
Glyphosate - Background

• Believed to be the most heavily used herbicide in the world
  – 2012 production volume > 700 million kg

• Production has increased sharply in recent years
  – Genetically modified glyphosate-resistant crop varieties

• Exposure pathways
  – Air (during spraying)
  – Water
  – Food
Glyphosate – Human Evidence

• Literature
  – US Agricultural Health Study (AHS)
  – Multiple independent case-control studies
Glyphosate – Human Evidence

- Epidemiological studies of cancer in humans
  - More than 2 studies
    - Non-Hodgkin Lymphoma (NHL)
    - Multiple Myeloma (MM)
  - Two studies
    - Leukemia, breast cancer, prostate cancer
  - One Study
    - Adult brain, oesophageal, stomach, prostate, soft-tissue sarcoma, lung, oral cavity, colorectal, pancreas, kidney, bladder, melanoma
# Glyphosate – Key Epidemiology Studies for Non-Hodgkin Leukemia

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agricultural Health Study</td>
<td>Cohort – pesticide applicators and spouses</td>
<td>52,395 (+32,347 spouses)</td>
</tr>
<tr>
<td>(Alavanja et al., 2003)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US Midwest</td>
<td>Pooled analysis of 3 case-control studies</td>
<td>NHL: 650 cases, 1933 controls</td>
</tr>
<tr>
<td><em>(De Roos et al., 2003)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cross-Canada</td>
<td>Population-based case-control study</td>
<td>517 cases, 1506 controls</td>
</tr>
<tr>
<td><em>(McDuffie et al., 2001)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swedish Case-Control Study</td>
<td>Population-based case-control study</td>
<td>910 cases, 1016 control</td>
</tr>
<tr>
<td><em>(Eriksson et al., 2008)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swedish Case-Control Study</td>
<td>Population-based case-control study</td>
<td>404 cases, 741 control (limited power)</td>
</tr>
<tr>
<td><em>(Hardell et al., 1999)</em></td>
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</tbody>
</table>
Evaluating Human Evidence
Preamble Part B, Section 6(a)

• Sufficient Evidence
  – Causal relationship is established
  – Chance, bias and confounding ruled out with reasonable confidence

• Limited Evidence
  – Causal interpretation is credible
  – Chance, bias and confounding could not be ruled out with reasonable confidence
• Inadequate Evidence
  – Studies permit no conclusion regarding causality

• Evidence suggesting lack of carcinogenicity
  – Several strong studies showing consistent lack of positive association
  – Conclusion limited to cancer sites and conditions studied
• **Limited Evidence** for NHL
  – Causal interpretation is **credible**
  – Chance, bias and confounding could not be ruled out with reasonable confidence

• **Basis**
  – De Roos et al., 2003 (US), McDuffie et al., 2001 (Canada), Eriksson et al., 2008 (Sweden)
    • Positive association
    • Adjustment for other pesticides
  – **Agricultural Health Study**
    • No additional support for association, does not contradict
Evidence in Experimental Animals

• 1 mouse feeding (glyphosate) study showed significant trend in the incidence of *renal tubule adenoma or carcinoma* (combined) in male mice; renal tubule carcinoma is a rare tumor

• 1 mouse feeding (glyphosate) study showed significant trend in the incidence of *haemangiosarcoma* in male mice

• 2 rat feeding (glyphosate) studies showed significant increase in the incidence of *pancreatic islet cell adenoma* (a benign tumor) in male rats

• 1 mouse study (GLY formulation) showed positive effect on *skin cancer* in an initiation-promotion study

• Several other oral feeding (glyphosate) and drinking water (glyphosate and glyphosate formulation) studies in rats showed no significant effects
• **Sufficient Evidence** in experimental animals
  – More than two independent studies showing a significant, biologically relevant cancer finding
## Mechanistic Evidence

<table>
<thead>
<tr>
<th>Key characteristic</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Electrophilic or ability to undergo metabolic activation</td>
<td>Glyphosate is <strong>not</strong> electrophilic</td>
</tr>
<tr>
<td>2. Genotoxic</td>
<td>Strong (G, GF)</td>
</tr>
<tr>
<td>3. Alters DNA repair or causes genomic instability</td>
<td>No data</td>
</tr>
<tr>
<td>4. Epigenetic Alterations</td>
<td>No data</td>
</tr>
<tr>
<td>5. Oxidative Stressor</td>
<td>Strong (G, GF and AMPA)</td>
</tr>
<tr>
<td>6. Induces chronic inflammation</td>
<td>No data</td>
</tr>
<tr>
<td>7. Immunosuppressant</td>
<td>Weak</td>
</tr>
<tr>
<td>8. Modulates receptor-mediated effects</td>
<td>Weak</td>
</tr>
<tr>
<td>9. Immortalization</td>
<td>No data</td>
</tr>
<tr>
<td>10. Alters cell proliferation, cell death, or nutrient supply</td>
<td>Weak</td>
</tr>
</tbody>
</table>
strong evidence in exposed humans … agent acts through relevant mechanism

strong evidence in exposed humans

strong evidence … mechanism does not operate in humans

strong evidence in exposed humans

strong evidence in exposed humans

belongs to a mechanistic class with supporting evidence from mechanistic and other relevant data

consistently and strongly supported by a broad range of mechanistic and other relevant data

Modified from Vincent Cogliano, IARC
**Glyphosate Monograph – Overall Evidence**

<table>
<thead>
<tr>
<th>EVIDENCE IN EXPERIMENTAL ANIMALS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sufficient</strong></td>
</tr>
<tr>
<td>Sufficient</td>
</tr>
<tr>
<td><strong>Limited</strong></td>
</tr>
<tr>
<td>Group 2A (probably carcinogenic)</td>
</tr>
<tr>
<td>Group 2B (possibly carcinogenic)</td>
</tr>
<tr>
<td>(exceptionally, Group 2A)</td>
</tr>
</tbody>
</table>

**EVIDENCE IN HUMANS**

“for [...] glyphosate, the **mechanistic evidence provided independent support of the 2A classification based on evidence of carcinogenicity in humans and experimental animals**”

(The Lancet Oncology; March 20, 2015)
Glyphosate Scientific Briefing
Health effects of glyphosate and its commercial formulations

Robin Mesnage, PhD, King’s College London, UK

The Soil Association, glyphosate scientific briefing
15 July 2015
The herbicide glyphosate was classified as probably carcinogenic to humans (Group 2A)

“There is no validated or significant relationship between exposure to glyphosate and an increased risk of non-Hodgkin lymphoma or other types of cancer”

Why are the conclusions different?
German Federal Institute for Risk Assessment (Bf), 8 June 2015
"It is not possible to fully comprehend the indications for a genotoxic potential of glyphosate based on the short report published by IARC, in particular also due to the fact that the assessment included studies using different glyphosate containing plant protection products that are not specified in any detail."
Roundup is not a single molecule, but a mixture of glyphosate and adjuvants

Adjuvants are added to stabilize and enhance the cell penetration of glyphosate

Farmers never use glyphosate alone but always commercial formulations

... Thus, commercial formulations are more relevant to test glyphosate chronic toxic effects
We asked to the French health agency what data were used to ensure Roundup safety.

Roundup: Only acute tests without blood testing. Commercial formulations of glyphosate have never been tested for chronic effects.
Glyphosate is considered to be the active principle of secondary side effects. All others ingredients, even toxic ones, are considered inerts.

Some adjuvants or contaminants in glyphosate-based herbicides:

- N-Nitrosoglyphosate: Carcinogenic
- 1,4-dioxane
- 3-iodo-2-propynyl butyl carbamate: Thyroid damages
- Alkylamine polyethoxylated: Cytotoxicity, possible genotoxicity
- Methyl p-hydroxybenzoate: Genetic Damages
- 5-Chloro-2-methyl 3(2H)-iso-thiazolone

Really inert?
Most pesticides that are sold and used have never been tested for their chronic effects on mammals.

Because...

The company asking for the pesticide commercialization is free to choose the molecule that they want to declare as an active principle.

- Only this molecule is tested for chronic effects.
- Other molecules even toxic are called “inert”, like if they are like water.
The differential toxicity of Roundup, and to a lesser extent of glyphosate, is generalizable to at least 10 cell types.
Roundup is up to 1000 times more toxic than glyphosate alone

If it is not glyphosate, then what is the cytotoxic agent?

Benachour et al., 2007
We have tested the human cellular toxicity of 9 Roundup formulations, their adjuvants, and glyphosate. The toxicity was proportional to the concentration in adjuvants. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity.
Is it generalizable for pesticides?

We have tested the toxicity of 9 pesticides (insecticides, fungicides, herbicides), comparing active principles and their formulations.

8 pesticides out of 9 were 2-1056 times more toxic than their active principles.

Differential toxicities between active principles and their formulations appear to be a general property of pesticide toxicology.
Adjuvants are absorbed in living-beings and are even evidenced to be involved in the epidemic of sexual disturbances (Jobling et al., 2009).

Some adjuvants are associated to hypospadias among populations exposed to pesticides (Carmichael et al., 2013).

Some highly toxic adjuvants are found in beehive samples and honey, they could be involved in bee colony collapse disorder (Chen and Mullin, 2014).
Chronic toxicity tests performed with glyphosate alone are unreliable to conclude on effects of glyphosate-based herbicide exposures.

Glyphosate has to be tested for chronic effects, as sold and used, as a mixture with adjuvants.

We have performed a study of toxic effects of environmental levels of a Roundup herbicide in adult male and female rats under a daily regimen for 24 consecutive months.

Published first in 2012

Republished in 2014
Séralini et al. 2014: Major findings

- Males died mostly from pathologies in liver and kidneys. *Escalation of signs of toxicity seen in Monsanto 90-day feeding trial*

- Females: died prematurely almost invariably from mammary tumours (*& pituitary dysfunction*). Statistically significant vs controls in lowest Roundup treatment group

- The low dose toxicity from Roundup could be explained by endocrine disruption (*At permitted levels in drinking water and vastly below ADI*)

Waiting for replication...
Glyphosate endocrine disrupting effects were confirmed by other groups.
The more cows are fed GM soybeans containing Roundup residues,

The more they are exposed to glyphosate,

The more their kidney biochemistry is disturbed
What can be done?

1/ More toxicity tests are needed with appropriate study design.

Glyphosate and its commercial formulations have to be tested at an environmental level.

Because glyphosate is a potential endocrine disruptor, future studies should incorporate testing principles from endocrinology (hormone dosages).

Future studies of laboratory animals should use designs that examine the full lifespan of the experimental animal, including a prenatal period.

The lack of data on toxicity is not a proof of safety. Glyphosate-based herbicides cannot be considered as safe without being tested.
Uncontrolled glyphosate residues can conferound the results of toxicity tests

Laboratory Rodent Diets Contain Toxic Levels of Environmental Contaminants: Implications for Regulatory Tests

Out of 262 pesticides measured in 13 rodent laboratory diets, the main pesticide detected was Roundup, with residues of glyphosate and AMPA in 9 of the 13 diets, up to 370 ppb.
3/ More monitoring of human fluids for glyphosate and its metabolites

Glyphosate levels were similar between fathers, mothers and children from farm households compared with those from non-farm households.

Glyphosate concentrations reported as occupational exposures may be at least in part due to the background of environmental exposures.

Uncontrolled glyphosate residues can confound the results of epidemiological studies.
What can be done?

4/ Limiting exposure to Roundup residues

One issue that may contribute to the high levels of glyphosate residues in crops is the use of glyphosate-based herbicides just prior to harvest.

Since their development, glyphosate-based herbicides have been applied to cropland pre-plant and at-plant, but recently, applications have included spraying as a harvest-aid.

These late season applications leave higher residue levels than more typical pre- and at-plant applications.

We recommend a moratorium on the use of glyphosate-based herbicides to desiccate human food crops prior to harvest.
What can be done?

1/ More toxicity tests are needed with appropriate study design

2/ More monitoring of food/feed for glyphosate and its metabolites

3/ More monitoring of human fluids for glyphosate and its metabolites

4/ Limiting exposure to Roundup residues by a moratorium on the use as a crop dessicant

THANK YOU FOR YOUR ATTENTION!
Glyphosate Scientific Briefing
International reaction to IARC findings
Monsanto response to IARC

Monsanto claimed IARC put glyphosate in same cancer category as coffee, cell phones, aloe vera extract, and pickled vegetables.
Why Monsanto’s claim is false

Coffee, pickled veg are in IARC category 2B, “possible carcinogen”
= limited evidence in humans
= less than sufficient evidence in animals.

Glyphosate is in same category as human papillomavirus type 68, inorganic lead compounds, dry cleaning fluid – IARC category 2A, “probable carcinogen”
= limited evidence in humans
= sufficient evidence in animals.
Implications for GMOs of the IARC glyphosate-cancer verdict

• Over 80% of genetically modified (GM) plants worldwide are engineered to tolerate being sprayed with glyphosate

• Over 80% of GM plants contain probable human carcinogen.
Goodbye glyphosate?

• “Probable carcinogen” verdict on glyphosate
• Spread of glyphosate-resistant weeds MEANS
  • Monsanto has to dump glyphosate and get access to new chemistry – take over Syngenta?
  • GMO companies focusing on GM crops tolerant to other herbicides – dicamba, 2,4-D
  • Escalation of chemical arms race, increased chemical residue mixtures in GM crops.
GMO/pesticide lobbyist Patrick Moore told a journalist that glyphosate is safe enough to drink.

Journalist offered him glass of glyphosate herbicide.

Moore refused to drink it, said, “I’m not an idiot”, stormed out of the interview.
Argentine scientists: “What took you so long, WHO?”

“The international scientific community has warned for years, backed up by studies, that glyphosate is carcinogenic. It is good that WHO has recognized this fact.” – Prof Rafael Lajmanovitch

(Researcher at CONICET, the main national research council of Argentina)
Argentina: 30,000 doctors demand ban on glyphosate herbicides

“Where glyphosate falls, only GMOs can grow. Everything else dies... Agribusiness cannot keep growing at the expense of the health of the Argentine people. [We] ask that glyphosate is banned in our country and that a debate on the necessary restructuring of agribusiness is opened, focusing on the application of technologies that do not endanger human life.”

– Argentina’s union of 30,000 doctors and health professionals, FESPROSA
Brazil’s National Cancer Institute INCA

• Condemned GM crops for placing the country in top ranking globally for pesticide use (glyphosate is most used)

• Said effects of pesticide chronic exposure include infertility, miscarriage, malformations, neurotoxicity, hormonal disruption, immune effects, and cancer

• Called for stronger regulation of pesticides and for agroecological alternatives to pesticide-dependent GMO agriculture model.
South America reassesses glyphosate and GM crops

• Brazil's national health agency Anvisa will reassess glyphosate herbicide risk
• Brazil’s Public Prosecutor has asked Justice Dept to ban glyphosate
• Argentine town of Monte Maiz has limited spraying of pesticides and banned agrochemical storage in town due to health effects. Regional crops are GM soy and maize – sprayed with Roundup and other herbicides.
It’s not just cancer

• El Salvador and Sri Lanka have banned glyphosate herbicides over links to chronic kidney disease.
Colombia govt has banned aerial spraying of glyphosate on coca crops
Europe takes Roundup off the shelves

• Switzerland’s two largest retailers, Migros and Coop, are taking glyphosate products off their shelves

• France will ban self-service sales of glyphosate herbicides to the public by 2018

• German retailers REWE, Toom, Kölle, Knauber, Garden Centre Augsburg and Globus Baumarkt are removing glyphosate herbicides from their shelves.
German states call for ban on Roundup

- Germany’s state consumer protection ministers have called for EU-wide ban on glyphosate herbicides.
Danish authority declares glyphosate a carcinogen

• The Danish Working Environment Authority (WEA) has declared glyphosate a carcinogen.

• Philippe Grandjean, professor of environmental medicine, University of Southern Denmark, commented, "Gardeners should dispose of Roundup as hazardous waste. Pesticides have often proved more dangerous than we thought, and I do not think they belong in our homes.”
Doctors demand immediate ban on glyphosate herbicides

• The International Society of Doctors for the Environment (ISDE) has written to officials of the EU Parliament and Commission asking for an immediate ban on glyphosate herbicides and four insecticides judged by IARC to be probable carcinogens.
Regulatory re-assessments

• The EU and US regulatory authorities are re-assessing glyphosate this year
• We do not expect them to ban glyphosate because in practice they consider only industry studies, which fail to assess long-term toxicity of glyphosate formulations
• EU may even increase the ADI (acceptable daily intake)
• People should not rely on regulators to protect them.
Cancer link no surprise: US EPA concerned in 1981

• 1981: Monsanto and US EPA were aware of cancerous and pre-cancerous conditions in test animals in industry’s own studies with glyphosate

• EPA scientists were concerned – but accepted conflicting evidence from Monsanto, involving inappropriate use of irrelevant data

• These data are kept secret.
Lawsuits begin

• Chinese citizens sue China's Ministry of Agriculture to make public a toxicology study supporting approval of Roundup 27 years ago
• Scientists and NGOs sue EU Commission for authorizing glyphosate-tolerant soybean Intacta without proper risk assessment
• US class action lawsuit accuses Monsanto of false advertising for claiming glyphosate is harmless to humans and animals.
• US law firm advertises for clients harmed by Roundup to join class action lawsuits.
Citizens take glyphosate test

Over 2000 citizens have taken a test set up by an NGO in collaboration with scientists, to measure levels of glyphosate in their urine.
No going back

• If JMPR (residues committee) of WHO disagrees with the IARC and decides glyphosate herbicides are non-carcinogenic, this will not save glyphosate

• Evidence linking glyphosate herbicides with cancer and other diseases is strong enough to justify precaution

• Public and retail industry do not like uncertainty: they will choose not to take the risk because they can do without glyphosate.
Thank you for listening!

Claire Robinson
Editor, GMWatch.org
Glyphosate Scientific Briefing