

Overview of this case:



Overview of this case:



Overview of this case:



Overview of this case:



Not the first lawsuit:

United States District Court
 DISTRICT OF MONTANA

DAVID W. COUTURE
 v.
 DOW CHEMICAL U.S.A., ET AL.

SUMMONS IN A CIVIL ACTION
 CASE NUMBER: CV-91-87-04-PA

DATE SERVED: 12/27/91
 TIME SERVED: 11:55 AM
 OFFICE: 570

TO: Name and Address of Defendant
 MONSANTO COMPANY
 800 N. Lindbergh Blvd.
 St. Louis, MO

Reg. Agent: C. T. Corporations
 406 Fuller Avenue
 Helena, MT 59601

IN THE COURT OF COMMON PLEAS OF MONTGOMERY COUNTY, PENNSYLVANIA
 CIVIL ACTION - LAW

KEITH DEANGELIS :
 vs. : No. 95-01922
 E. I. DU PONT DE NEMOURS & :
 COMPANY, INC. :
 and :
 MONSANTO COMPANY :
 and :
 DOW CHEMICAL COMPANY :
 and :
 ELANCO PRODUCTS COMPANY :
 DIVISION OF ELI LILLY COMPANY :

COMPLAINT

UNITED STATES DISTRICT COURT
 SOUTHERN DISTRICT OF CALIFORNIA

EMANUEL RICHARD GIGLIO,
 Plaintiff
 v.
 MONSANTO COMPANY and JOHN
 DOES 1-50.

Civil Action No.: '15CV2279 BTM NLS

COMPLAINT
 JURY TRIAL DEMANDED

SUPERIOR COURT OF THE STATE OF CALIFORNIA
 FOR THE COUNTY OF SAN FRANCISCO

STEVEN BIDEGAIN and YVETTE
 BIDEGAIN,
 Plaintiffs,
 v.
) CASE NO. 05445155
)
) COMPLAINT FOR TOXIC INJURIES
) ASSERTING CAUSES OF ACTION
) FOR:

UNITED STATES DISTRICT COURT
 EASTERN DISTRICT OF NEW YORK

JUDI FITZGERALD,
 Plaintiff,
 v.
 MONSANTO COMPANY,
 Defendant.

COMPLAINT
 Civil Action No.
 JURY TRIAL DEMANDED

UNITED STATES DISTRICT COURT
 CENTRAL DISTRICT OF CALIFORNIA

CHRISTINE SHEPPARD
 Plaintiff,
 vs.
 MONSANTO COMPANY,
 Defendants.

Case No.: 2:15-CV-8632
 JURY TRIAL DEMANDED

How the trial works:

1. Opening statements
2. Plaintiff's case
3. Monsanto's case
4. Rebuttal (possible)
5. Closing arguments
6. Deliberations



Current & Former Employees



Current & Former Employees



Dr. Donna Farmer
Product Protection Lead



Dr. Daniel Goldstein
Medical Sciences and Outreach



Dr. William Heydens
Product Safety Assessment
Strategy Lead



Current & Former Employees



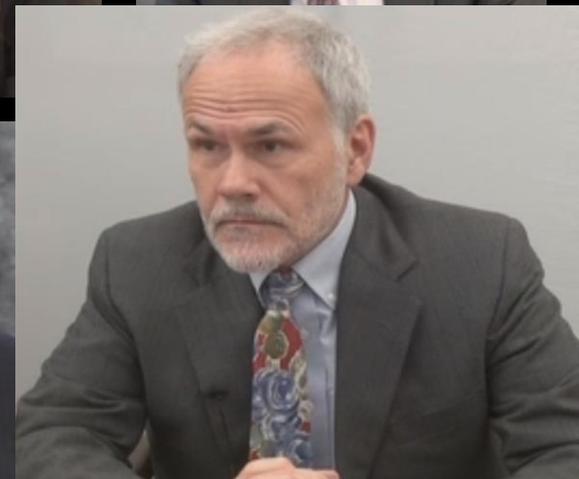
Current & Former Employees



Dr. Mark Martens
Toxicology Director
(former)



Dr. David Saltmiras
Toxicology Manager



Dr. John Acquavella
Epidemiologist (former)



Current & Former Employees



Current & Former Employees



Daniel Jenkins
Manager for Regulatory Affairs



David Heering
Strategy, Compliance, Operations
Lead



Current & Former Employees



Current & Former Employees



Steve Gould
National Accounts Manager
(includes California)

Dr. Kirk Azevedo
Sales Representative (former)



Opening Statement Roadmap:

1. What is Roundup?
2. Can Roundup cause cancer?
3. Did Roundup cause Mr. Johnson's cancer?
4. What are Mr. Johnson's damages?
5. Should Monsanto be punished for its conduct?

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1. What is Roundup?



1. What is Roundup?



ACTIVE INGREDIENT:

*Glyphosate, N-(phosphonomethyl)glycine,
in the form of its potassium salt..... 48.7%

OTHER INGREDIENTS: 51.3%

100.0%



ACTIVE INGREDIENT:

*Glyphosate, N-(phosphonomethyl)glycine,
in the form of its isopropylamine salt..... 41.0%

OTHER INGREDIENTS (including surfactant): 59.0%

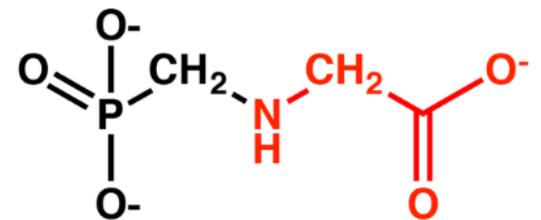
100.0%

1. What is Roundup?

Glyphosate



glyphosate



1. What is Roundup?

Surfactant

ACTIVE INGREDIENT:

*Glyphosate, N-(phosphonomethyl)glycine,
in the form of its isopropylamine salt.....

41.0%

OTHER INGREDIENTS (including surfactant):

59.0%

100.0%

POlyEthoxylated tallow Amine

1. What is Roundup?

Surfactant

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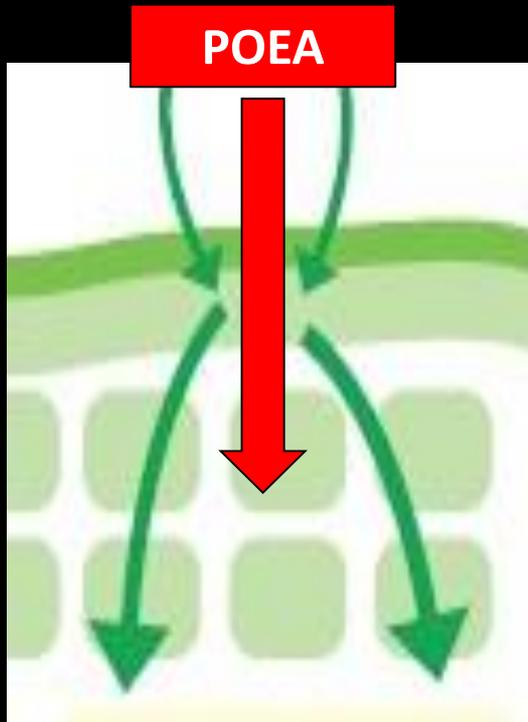
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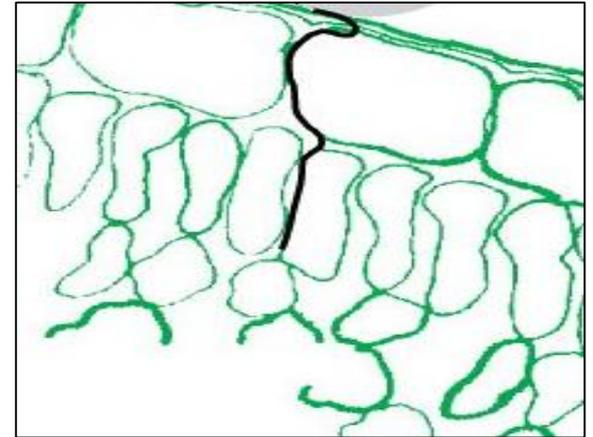
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POEA

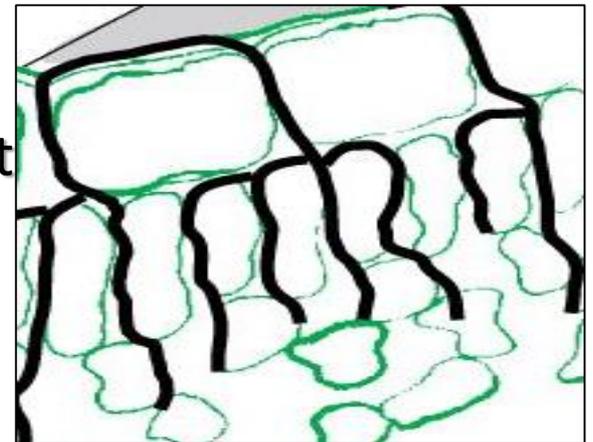
1. What is Roundup?



Without
Surfactant

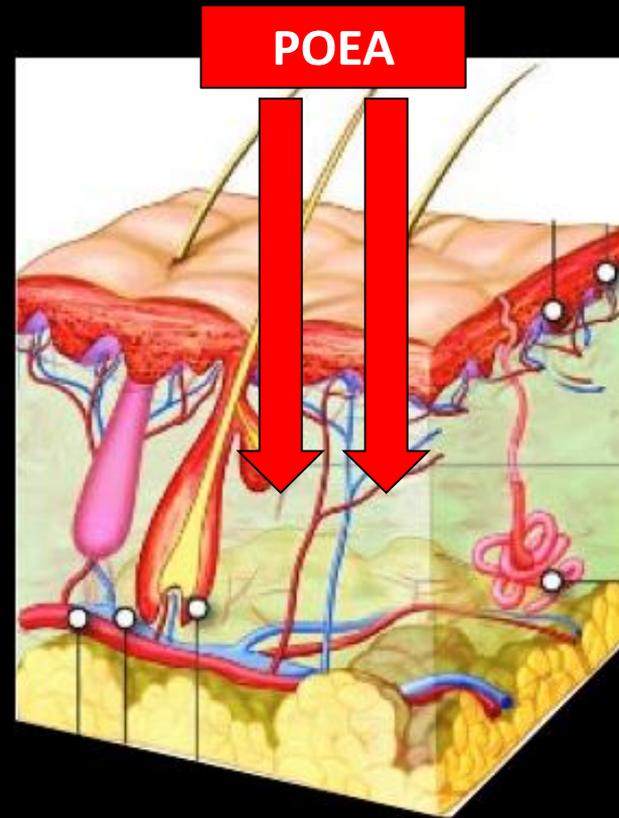
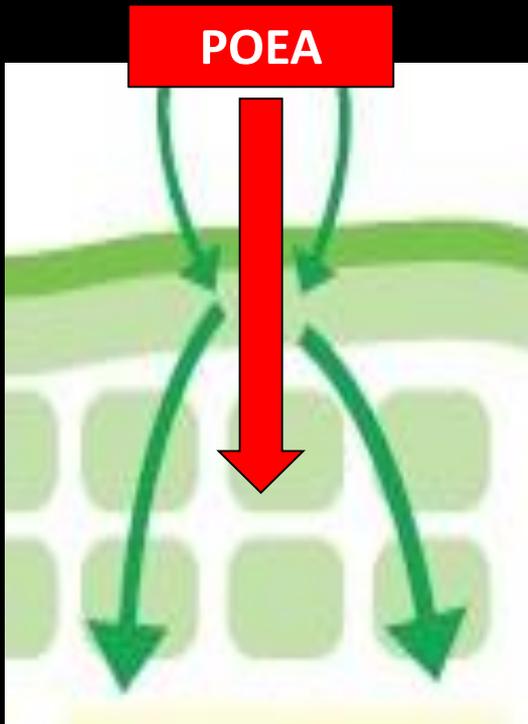


With Surfactant



1. What is Roundup?

Penetrates the surface of a leaf, but also
human skin



1. What is Roundup?

From: HEYDENS, WILLIAM F [AG/1000]
Sent: Thursday, August 06, 2015 9:55 AM
To: 'Ashley Roberts Intertek'; FARMER, DONNA R [AG/1000]
Subject: RE: Keith

Ashley,
I think the short answer is no. The focus of this is what is the carcinogenic potential of glyphosate.

That said, the surfactant in the formulation will come up in the tumor promotion skin study because we think it played a role there.

-----Original Message-----

From: Ashley Roberts Intertek [redacted]@intertek.com]
Sent: Thursday, August 06, 2015 09:47 AM Central Standard Time
To: FARMER, DONNA R [AG/1000]; HEYDENS, WILLIAM F [AG/1000]
Subject: Keith

Hi Donna/Bill,

Just received a question from Keith in response to my email message on the exposure piece this morning.

He has asked if we need to give any consideration to exposures of formulants in the commercial product, at least in applicators? I was under the impression these were inert but reading a response this morning in the Ecologist makes it sound like it is the combination that is toxic!!!

What do you think?



Plaintiff Exhibit

0366

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2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
2. Mechanistic Data
3. Epidemiology

Plaintiff's Experts

Christopher Portier, PhD.



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

- Ph.D. in Biostatistics, University of North Carolina School of Public Health (1981). Thesis addressed the best way to design a two-year rodent study to assess the ability of a chemical to cause cancer.
- Former Associate Director of the National Toxicology Program (NTP)
- Former Associate Director of National Institutes of Health
- Former Director of the National Center for Environmental Health (NCEH) at the Centers for Disease Control and Prevention (CDC)
- Former Director of the Agency for Toxic Substances and Disease Registry (ATSDR)

Plaintiff's Experts

Alfred Neugut, M.D., PhD.



- Professor of Cancer Research and Professor of Medicine and Epidemiology at Columbia University
- Director of Junior Faculty Development for the Department of Epidemiology at Columbia University
- Medical oncologist with a Ph.D. in Pathology (1977) and M.P.H. in Epidemiology (1983) from the University of Columbia
- Published over 500 peer reviewed chapters and papers and received over \$50 million in funding from the National Cancer Institute, American Cancer Society, and Department of Defense



2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
2. Mechanistic Data
3. Epidemiology

2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
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2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies



Glyphosate only

Long term – typically, 2 years

Control	Low Dose	Mid Dose	High Dose
---------	----------	----------	-----------

- Significant increases in tumors
- Replication
- Dose response
- Cross-species
- Rare tumors

2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies

Admission No. 7

Monsanto admits that it did not conduct any further long-term carcinogenicity animal studies after 1991.

- Significant increases in tumors
- Replication
- Dose response
- Cross-species
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2. Can Roundup cause cancer?



1. Animal Carcinogenicity Studies

Mice Studies – Tumor Chart

Knezevich & Hogan (1983)	Atkinson (1993)	Sugimoto (1997)	Wood (2009)	Kumar (2001)
Kidney carcinomas or adenomas	Malignant lymphoma	Kidney carcinomas or adenomas	Malignant lymphoma	Kidney carcinomas or adenomas
Spleen composite lymphosarcoma	Hemangiosarcoma	Malignant lymphoma	Mul. malignant tumors or neoplasms	Malignant lymphoma
		Hemangiosarcoma	Lung adenocarcinoma	Hemangioma
		Hemangioma		
		Mul. malignant tumors or neoplasms		
		Harderian gland adenoma		

2. Can Roundup cause cancer?



1. Animal Carcinogenicity Studies

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2. Can Roundup cause cancer?



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2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies



George Study (2010)

- Applied to skin 3x week
- 40% of mice exposed to glyphosate had tumors in skin
- 0% of control group had tumors in skin



Evidence that glyphosate is a
tumor **promoter**

2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies



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Rat Studies – Tumor Chart

Lankas (1981)	Stout & Ruecker (1990)	Atkinson (1993)	Enemoto (1997)	Suresh (1996)	Brammer (2001)	Wood (2009)
Testicular interstitial cell tumors	Thyroid C-Cell carcinomas or adenomas	Thyroid follicular carcinomas or adenomas	Kidney carcinomas or adenomas		Hepatocellular carcinomas or adenomas	Skin kera-toacanthoma
Thyroid C-Cell carcinomas or adenomas	Pancreatic islet cell tumors	Skin kera-toacanthoma	Skin kera-toacanthoma			Mammary gland carcinomas or adenomas
Pancreatic islet cell tumors	Hepatocellular carcinomas or adenomas		Basal cell tumors			Pituitary adenomas
	Adrenal cortical carcinomas					
	Skin kera-toacanthoma					

2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies



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Thyroid C-Cell carcinomas or adenomas	Pancreatic islet cell tumors	Skin keratoacanthoma	Skin keratoacanthoma			Mammary gland carcinomas or adenomas
Pancreatic islet cell tumors	Hepatocellular carcinomas or adenomas		Basal cell tumors			Pituitary adenomas
	Adrenal cortical carcinomas					
	Skin keratoacanthoma					

2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies

2. Mechanistic Data

3. Epidemiology



2. Can Roundup cause cancer?

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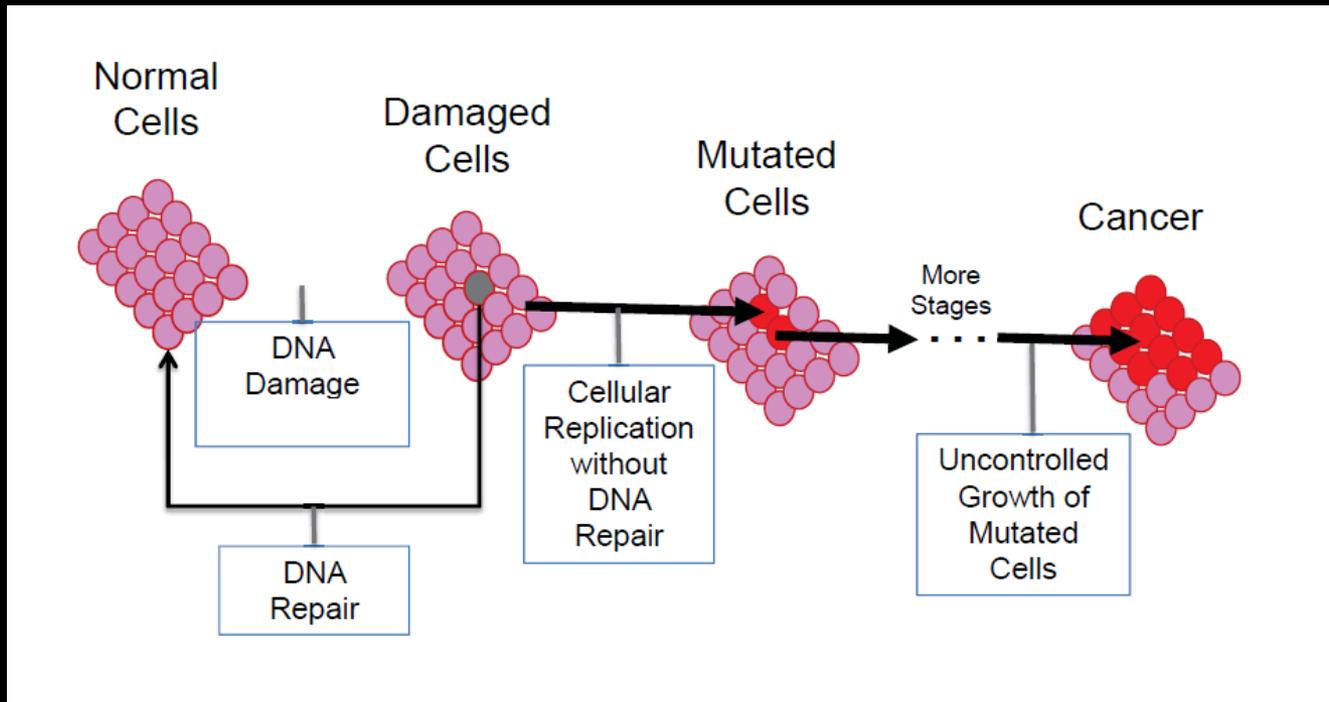


2. Can Roundup cause cancer?

2. Mechanistic Data

Mechanistic Data:

Refers to the way in which a substance can cause cancer.



2. Can Roundup cause cancer?

2. Mechanistic Data

Genotoxicity:

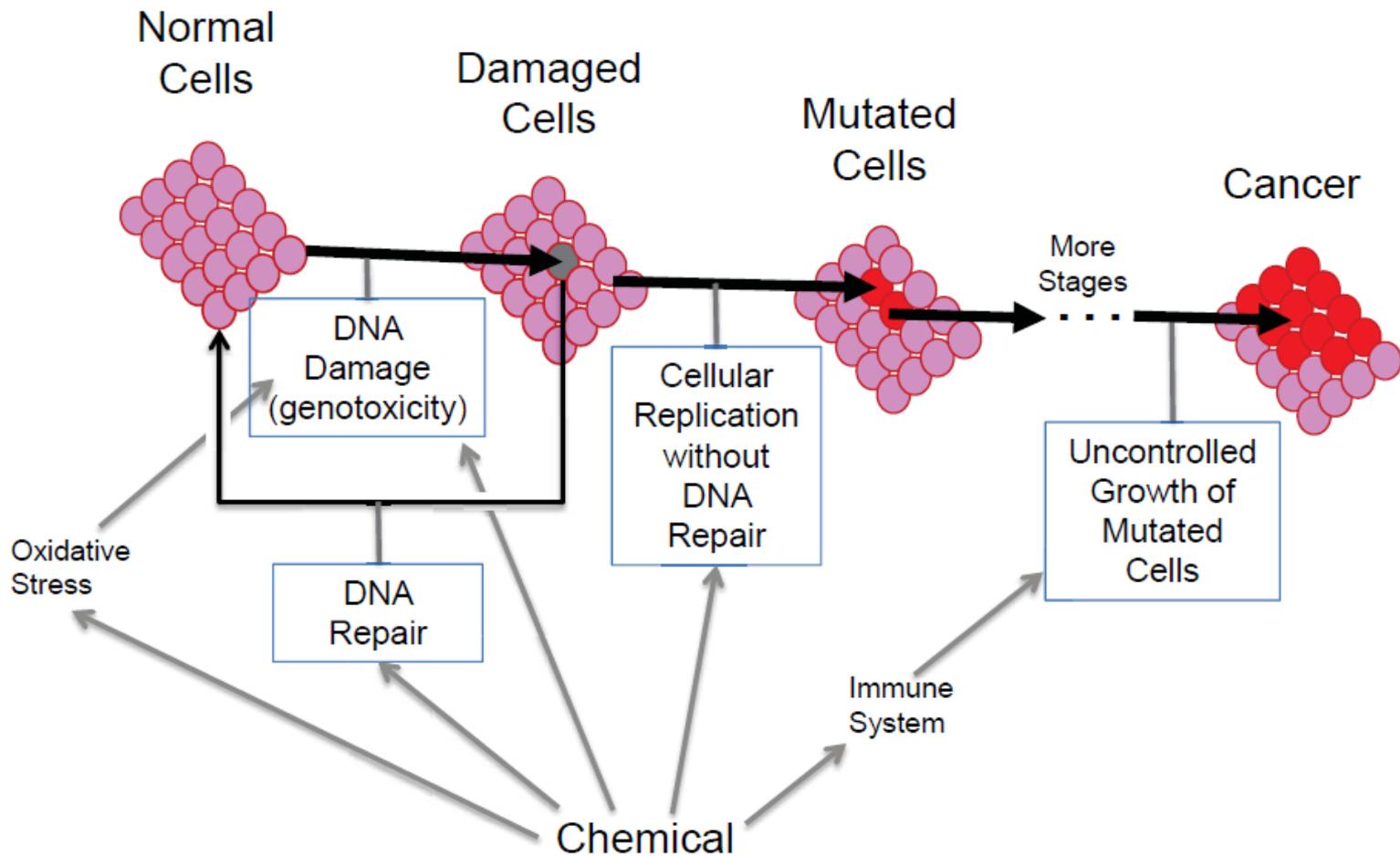
The property of chemical agents that damage the genetic information within a cell that can cause mutations.

Oxidative Stress:

An imbalance between the production of free oxygen particles and the ability of the body to counteract their harmful effects with antioxidants.

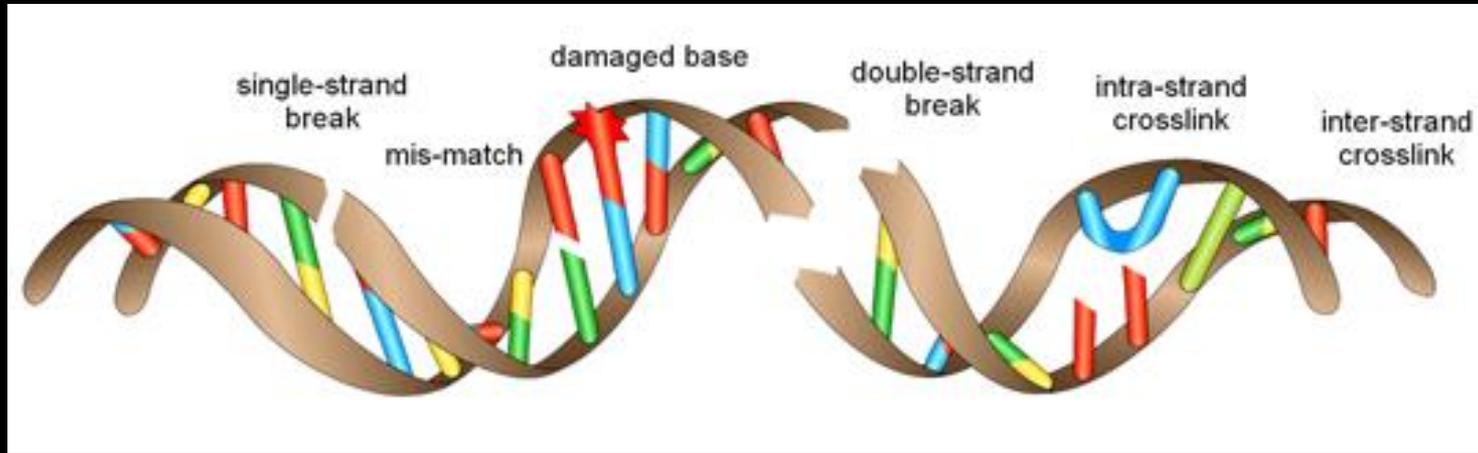
2. Can Roundup cause cancer?

2. Mechanistic Data



2. Can Roundup cause cancer?

2. Mechanistic Data



Different methods of testing DNA damage

Over 100 different studies

- Both Roundup & glyphosate
- In humans (*vivo* & *vitro*)
- Non-human mammals (*vivo* & *vitro*)
- Non-mammals (*vivo* & *vitro*)

In vivo:

In a living organism.

In vitro:

In glass, as in a test tube.

2. Can Roundup cause cancer?

2. Mechanistic Data

In the 1990's four published genotoxicity studies
Rank, Bolognesi, Lioi, & Peluso
prompted Monsanto to hire an independent genotox expert

Jan
1992

Rank study shows that Roundup exposure, as opposed to glyphosate alone, causes elevated increases of DNA damage.

Abstracts: Health, 9(11) 21-24, 1992
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GENOTOXICITY

Genotoxicity testing of the herbicide Roundup and its active ingredient glyphosate isopropylamine using the mouse bone marrow micronucleus test, Salmonella mutagenicity test, and Allium tripartite-toxicity test

J. Rank, A.-G. Jensen, B. Slos, L.H. Pedersen and K. Jensen

Department of Environment, Forestry and Food Policy, Danish Veterinary Research

Received 11 October 1991
Accepted 10 November 1991

Keywords: Roundup; Glyphosate isopropylamine; Genotoxicity; Micronucleus; Allium, *Salmonella*

SUMMARY

The general potential of the herbicide Roundup and its active agent, glyphosate isopropylamine, was studied in three different assays. No chromosome aberrations were found in the mouse bone marrow micronucleus test for either of the two agents. In the *Salmonella* assay only Roundup was tested. It showed a weak mutagenic effect for the concentrations 100 µg/plate in TAY test and 100 and 250 µg/plate in TA98 tests. These concentrations are close to the tank level. The *Allium tripartite*-toxicity test showed no effect for the glyphosate isopropylamine, but a significant increase in chromosome aberrations appeared after treatment with Roundup at concentrations of 1.0 and 2.0 mg/l when calculated as glyphosate isopropylamine. The most frequent aberration observed could be characterized as disturbance of the spindle.

Roundup is a relatively new herbicide first marketed in the USA in 1976. The active agent is Roundup or glyphosate (3-phosphomethyl phosphonic acid) which is considered as non-toxic to humans (1, 2), or even to *Allium tripartite* (3). The herbicide Roundup is commonly used in agriculture, forestry and gardens of most of the world and is expected to be used even more in the future.

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glyphosate in Roundup showed up already at a concentration of 200 µg/plate, which equals 200 µg/l tank of glyphosate.

In another study (Rank, 1977) glyphosate was tested, together with other nitrogenous pesticides, in the *Salmonella* mutagenicity test after reaction with sodium nitrite in acidic solution. Glyphosate was the only agent out of six tested, for which an extract of the reaction mixture showed a significant mutagenic activity in *Salmonella typhimurium* strain TA98. Other herbicides were detected in the reaction extract but the mutagenicity could be due to other glyphosate or some unknown pesticide components.

A positive effect of Roundup in the SCE assay was reported by Vagstad and Vise (1988). Although the authors describe the effect as weak compared with the stronger response of other pesticides, Roundup at a concentration of 0.2 x 10⁻⁶ M showed an increase in the number of SCEs to that observed by 100 µg/l a concentration of 10⁻⁶ M. No dose related effect was shown for the other concentrations of Roundup, when the highest dose, 5 x 10⁻⁶ M, inhibited cell growth completely.

A genotoxicity test was also done in the fish *Jako* assay (Naga and Gupta, 1981). No chromosome aberrations were found, but it was observed that Roundup (20 mg/l) induced pyric acid and pyruvic acid formation in rainbow trout erythrocytes after 120 min exposure, indicating some effect on the mitochondria.

Plato and Papp (1987) found that Roundup, at a concentration of 1%, suppressed the deglutathionylation process during the formation of the interphase nucleus. They also found inhibition of chromosomal migration during mitosis.

The present study shows that Roundup, which is a mixture of several agents, and among these 300 g glyphosate per liter, can induce weak mutagenicity in *Salmonella typhimurium* TAY and TA98, and induce chromosome aberrations in allium root meristems and in erythrocytes close to the level of toxicity. As a genotoxicity test with Roundup and glyphosate, the micronucleus test and the *Salmonella* mutagenicity test could be used to test other ingredients in Roundup. Merck et al. (1991) reported that the

formulation of Roundup contains 15% polyphosphonic esters, with an acid 15.2, while in the range of 1000-8000 mg/L, which could explain the higher toxicity of Roundup compared with glyphosate. In our knowledge there are no published genotoxicity data on these surfactants.

The conclusion of the present study is that we found no significant effect to test the active agent in a formulated product. Because of the possibility of additional mutagenic effects, it is not as desirable to investigate the complete product as well as the other ingredients of the product.

ACKNOWLEDGEMENTS

We wish to thank Per Hørmann, Inspector for his assistance with the statistics.

REFERENCES

Arns, S.N., J. McEwen and E. Yonushoff (1975) Methods for detecting chromosome and mutation with the micronucleus test. *Environmental Mutagenesis* 7, 347-356.
Arns, S.N. (1978) Toxicology of glyphosate. In: *Glyphosate: A Unique Herbicide* (Ed. by D. Johnson), pp. 11-21. John Wiley & Sons, New York.
Baker, A.C. (1976) Mutagenicity of Roundup. *Mutagenesis* 1, 105-107.
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Plaintiff Exhibit
0852

Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup

Claudia Bolognesi,* Stefania Bonatti, Paolo Degari, Elena Gallerani, Marco Peluso, Roberta Rabboni, Paola Roggeri, and Angelo Abbondandolo

Centro Nazionale per lo Studio dei Tumori di Origine Ambientale, Istituto Nazionale per la Ricerca sul Cancro, Largo Rosanna Benzi 10, 16132 Genova, Italy

Glyphosate (*N*-phosphonomethylglycine) is an effective herbicide acting on the synthesis of aromatic amino acids in plants. The genotoxic potential of this herbicide has been studied: the results available in the open literature reveal a weak activity of the technical formulation. In this study, the formulated commercial product, Roundup, and its active agent, glyphosate, were tested in the same battery of assays for the induction of DNA damage and chromosomal effects *in vivo* and *in vitro*. Swiss CD1 mice were treated intraperitoneally with test substances, and the DNA damage was evaluated by alkaline elution technique and 8-hydroxydeoxyguanosine (8-OHdG) quantification in liver and kidney. The chromosomal damage of the two pesticide preparations was also evaluated *in vivo* in bone marrow of mice as micronuclei frequency and *in vitro* in human lymphocyte culture as SCE frequency. A DNA-damaging activity as DNA single-strand breaks and 8-OHdG and a significant increase in chromosomal alterations were observed with both substances *in vivo* and *in vitro*. A weak increment of the genotoxic activity was evident using the technical formulation.

Keywords: Pesticides; *in vivo* genotoxicity; *in vitro* genotoxicity; SCE; micronucleus test; alkaline elution; DNA oxidative damage

INTRODUCTION

Roundup, an extremely effective nonselective post-emergence herbicide, is a combination of an active ingredient, the isopropylamine salt of glyphosate, and a surface-active agent that enhances the spreading of

1985), but Roundup has been identified as a cause of irritation phenomenon or contact dermatitis, respectively, in occupationally exposed agricultural workers (1980).

The formulated commercial product, Roundup, s

Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup

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Keywords: Pesticides; *in vivo* genotoxicity; *in vitro* genotoxicity; SCE; micronucleus test; alkaline elution; DNA oxidative damage

INTRODUCTION

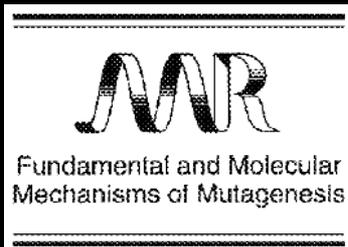
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Jul
1998



Lioi study shows that
glyphosate induces cell
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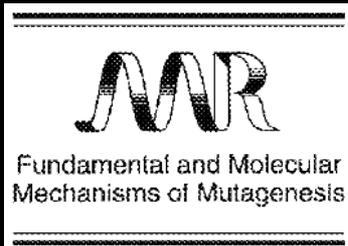


Dec
1998



Peluso study shows that Roundup exposure induces “dose dependent” DNA damage in mice.

Jul
1998



Lioi study shows that glyphosate induces cell stress in animal cells.



Reply Separator

Subject: Actions from 1/17 meeting re Mutagenicity
Author: [REDACTED]
Date: 12/22/88 1:01 PM

e) Agreed an external global network of genotox experts needs to be developed.

As EA has an immediate need and is a critical area now it was agreed that [REDACTED] would contact Dr. Parry next week to discuss with him his participation in the support of glyphosate, glyphosate-based formulations genotox issues.

after initial contact, if Dr. Parry is agreeable then [REDACTED] will be included in discussion to outline issues/needs etc.

For North America - [REDACTED] will be here in early February as part of the CANFOX project. [REDACTED] as previously agreed to join in those discussions.

=====

2) Unfortunately our time ran out but [REDACTED] and [REDACTED] stayed a little while longer and discussed the [REDACTED] papers:

- The data are very unusual and suspect (i.e. the results may reflect an artifact of some procedural error and/or inexperience in scoring) but may be extremely difficult to refute based simply on the contents of the paper.

- It is a real concern that these papers may create an even bigger problem for us than the [REDACTED] paper. Therefore we do some things quickly!

- The results of the human lymphocyte test by [REDACTED] do not agree with

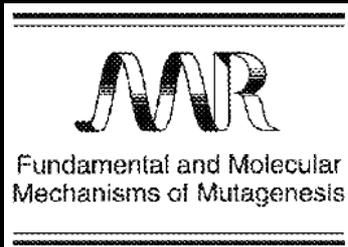


Dec
1998

Plaintiff Exhibit
0842

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Jul
1998



Dec
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Monsanto's Reaction:
Need to hire an expert to refute these studies, so Monsanto reaches out to Dr. James Parry.

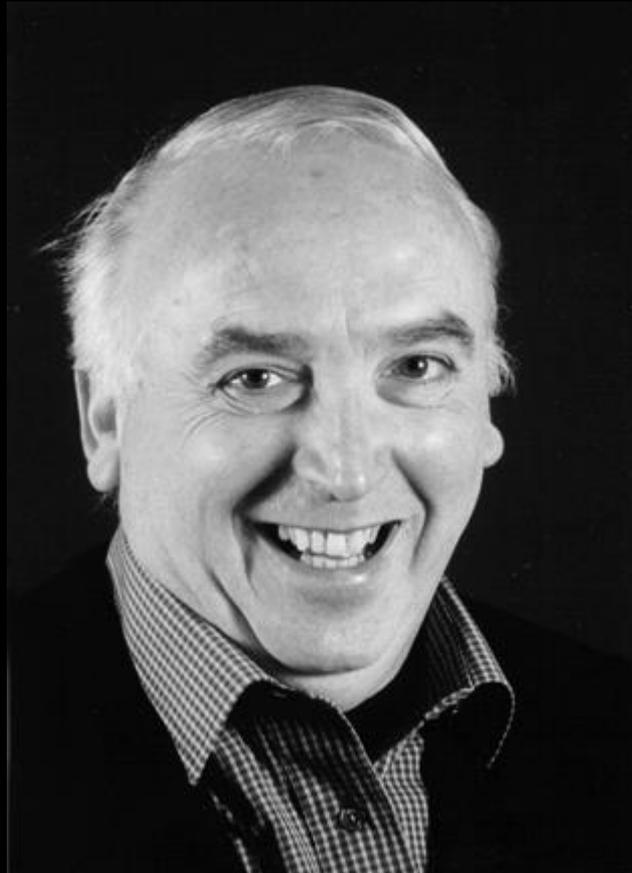
Lioi study shows that glyphosate induces cell stress in animal cells.

Plaintiff Exhibit
0809

Plaintiff Exhibit
0215



Dr. James Parry



1940 - 2010



Swansea University
Prifysgol Abertawe

- Author of two influential textbooks “Comparative Genetic Toxicology” and “Principles and Methods of Genetic Toxicology”
- Published over 300 papers on toxicology
- Founder of Journal “Mutagenesis” and the “European Journal of Molecular Genetics and Toxicology”
- President of the European Environmental Mutagen Society

Dr. James Parry

Monsanto Unsure About Dr. Parry



Plaintiff Exhibit

0263

6). External global network of genotox experts:

- EU

- While Dr. Parry is a recognized genotox expert what is not known is how he views some of the "non-standard endpoints" (such as SCE, DNA P-32 postlabelling, Comet assays etc) evaluated in the genotox articles by Rank, Bolognesi etc.
- Therefore it was recommended that before we ask him to get more deeply involved (reviewing all the literature, glyphosate data; represent us as a consultant with regulators, etc) we would ask him to review a subset of the articles.
- It was proposed that [REDACTED] would contact Dr. Parry and ask him for a written review the articles by Rank, Bolognesi, Peluso & Lioi
- Based on his critique of the the genotox papers a decision would be made as to expanding or terminating his involvement.
- Regarding [REDACTED], no further contact will be made at this time. When a clear role has been identified for [REDACTED] Alan will contact him.
- Money for this initial consultation will come from [REDACTED] budget. A bigger initiative will require additional funds to be located.

- NA

- Expanded discussions with Dr. Gary Williams on genotox issues will occur as part of the CANTOX meetings (2/5,6&7). Dr. Williams is recognized internationally as a genotox expert and might be used in Europe on a contingency basis.

- LA/SEA - no action at this time

7). There is a concern that the papers by Lioi et al, may present an even bigger problem because the studies are with glyphosate and are on a more standard endpoints. The results of the human lymphocyte test by Lioi do not agree with the toxicity and data in the human lymphocyte study by Agrichem at NOTOX therefore it was recommended that:

- Larry Kier will finalize his rebuttal
- Include the Lioi papers in the articles to be reviewed by Dr. Parry
- Bill/Donna will draft for Larry a letter to the editor or a short publication to be submitted to the journal upon receipt of Parry's evaluation

8). While there is \$90K in the glyphosate toxicology testing budget for mutagenicity testing, this may not be enough. Further

6). External global network of genotox experts:

- EU



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Dr. James Parry

- 4) The development of a "positive" press release was requested. Please comment on the DRAFT below:

DRAFT DRAFT DRAFT DRAFT

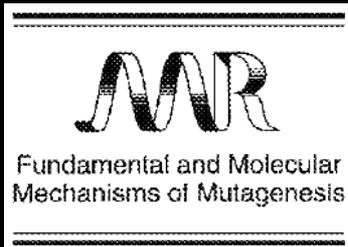
"Several genotoxicity studies have been conducted on glyphosate, the surfactants in glyphosate formulations, and other closely-related surfactants. Studies have also been performed on Roundup herbicide and other glyphosate formulations. None of these studies have shown any adverse findings. Based on all these results, we are confident that glyphosate herbicide products are not genotoxic and therefore to not present a mutagenic or carcinogenic risk to humans and animals. We will continue to diligently consider concerns raised in this area and will support our conclusions on the safety of Roundup herbicides with appropriate scientific

Dec
1998

Plaintiff Exhibit
0842

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Jul
1998



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Lioi study shows that glyphosate induces cell stress in animal cells.

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Plaintiff Exhibit
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Miriambo Eutene
Parc Scientifique Fleming
Rue Laid Barriel 5
B-1348 Louvain-La-Neuve
Belgium

11 February 1999

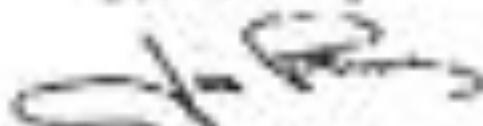
Dear [REDACTED]

You will find enclosed my evaluation of the four papers you provided concerning the potential genotoxicity of glyphosate and Roundup. Although each of the papers have weaknesses, I have avoided a report which attempts to focus upon these weaknesses. Rather, I have attempted to "pull out" the data which provide an aid to the understanding of the potential mechanisms of glyphosate genotoxicity and indicated how you might clarify these mechanisms. It has been my experience with Regulatory Agencies that a positive attitude to published data is a more productive approach than just criticizing individual studies.

I assume that you will already have in house data for some of the suggested experiments. In my view the *in vitro* micronucleus work suggested would be the most productive way of clarifying the question of mechanisms. I would be happy to provide you with further suggestions as to detailed protocols for such studies. They would make a rather nice Ph.D project for a graduate student if you could find the funding.

I have enclosed my invoice for the evaluation.

Yours sincerely



at equivalent concentrations to that in Roundup, failed to increase activity. These data provide some evidence to support the concept that any *in vivo* activity of Glyphosate may be prevented by other components of the Roundup mixture.

The overall data provided by the four publications provide evidence to support a model that Glyphosate is capable of producing genotoxicity both *in vivo* and *in vitro* by a mechanism based upon the production of oxidative damage. If confirmed, such a mechanism

of genetic damage would be expected to be produced at high concentrations of the herbicide and would be relevant only when the anti-oxidant protective mechanisms of the cell are overwhelmed. Thus, I would conclude that if the mechanism of action can be proved to be based upon oxidative damage then hazard and risk assessment could be based upon a non-linear model with a threshold of activity at low doses.

Questions raised by the studies

- 1) Role of components of mixture which leads to high levels of activity of Roundup?
- 2) Is the genotoxic activity observed due to oxidative damage?
- 3) Can the genotoxic activity be reduced by anti-oxidant?

Recommendation for further work to clarify the potential genotoxic activity of

based upon relative damage than based and risk assessment could be based upon a non-linear model with a threshold of activity at low doses.

Questions raised by the studies

- i) Role of components of mixtures which leads to high levels of activity of Brevibacterium?
- ii) Is the genotoxic activity observed due to oxidative damage?
- iii) Can the genotoxic activity be reduced by anti-oxidants?

Recommendation for further work to clarify the potential genotoxic activity of Glycyrrhizin

Bacteria

I recommend a repeat of Salmonella studies particularly with Brevibacterium. It would be helpful if these data are not already available in-house.

Cytogenetics

I recommend an *in vitro* micronucleus study preferably in human lymphocytes. It combined with analyses of the micronuclei for the presence and absence of centromeric DNA this study would indicate whether Glycyrrhizin induces predominantly chromosome structural

or numerical damage.

The *in vitro* microassay would allow both:

- a) The assessment of the potential influence of anti-oxidants upon the genotoxic potential of Glyphosate - Note the assessment of the effect of anti-oxidants as a genetic endpoint is a critical deficiency in the Lai et al (1998) study.

- b) Assessment of the individual components of the Roundup mixture to determine whether there is any component(s) which are synergistically to increase the potential genotoxicity of Glyphosate. Each study could be designed to investigate a panel of mixtures leaving one one component of the mix. In each individual experiment.

In vivo studies

In view of the limitations of the Delgado et al (2011) study i.e.

- limited number of animals
- single dose of compound
- low spontaneous micronucleus frequency

it would be worth repeating the study in a more comprehensive design.

To assess both the DNA strand breaks and animal work would require very large

*From
Simpson-Louis
Studies*

Feb
1999

Dr. Parry submits his first internal report, concluding glyphosate is genotoxic.

Apr
1999

Monsanto Reaction:
Monsanto decides to give Dr. Parry more data with the hope of turning him around.

UNIVERSITY OF WALES
PHILIPPOU CHRYSTAKIS
 Department of Food Science
 Faculty of Agriculture, University of Wales, Bangor, Gwynedd, LL57 2UW

11 February 1999

Dear [redacted]

The full text and an evaluation of the four papers are provided... I am sure that you will already have a better idea of the... I have enclosed my report for the evaluation...

Yours sincerely
 Philippos Chrystakis

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 Philippos Chrystakis

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Yours sincerely
 Philippos Chrystakis

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Plaintiff Exhibit
0216

There have been... I have enclosed my report for the evaluation...

Yours sincerely
 Philippos Chrystakis

4) Global experts

Review Dr. Parry's analysis - what is our next step?
Dr. Parry concluded on his evaluation of the four articles that glyphosate is capable of producing genotoxicity both in vivo and in vitro by a mechanism based upon the production of oxidative damage.

The data that Dr. Parry evaluated is limited and is not consistent with other better conducted studies. In order to move Dr. Parry from his position we will need to provide him with the additional information as well as asking him to critically evaluate the quality of all the data including the open literature studies.

As a followup Mark will contact Dr. Parry, discuss with him the existence of additional data and ask him to evaluate the full package. Mark will also explore his interest (if we can turn his opinion around) in being a spokesperson for us for these type of issues.

Larry as well as others will be available to discuss the data with Parry as needed by e-mail, phone or in person or all the above.

Dr. Williams - discuss the outcome of the caucus meeting

The panel concluded that glyphosate and Roundup were not mutagenic. That in the evaluation of these types of studies criteria should be set... up front in the evaluation process as to what makes an acceptable study and what does not - this is to be included in the manuscript as well as a weight of evidence approach.

5) Last followup

Feb
1999

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Apr
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UNIVERSITY OF WALES
PHYSIOLOGICAL CHEMISTRY
 Department of Physiology and Biochemistry
 School of Health Sciences
 Faculty of Health Sciences, S4COT
 Singleton Park, Swansea, SA2 8PP

11 February 1999

Dear [redacted]

The full text and an evaluation of the four papers you provided concerning the genotoxic potential of glyphosate and Roundup. Although most of the papers have been reviewed, I have not had a chance to review the other three. The authors' findings are summarized in the attached report. The report also includes a list of references and a list of questions for you to answer. I would appreciate it if you could provide answers to these questions as soon as possible. The report is attached to this email. I would appreciate it if you could provide answers to these questions as soon as possible. The report is attached to this email.

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Yours sincerely
 Professor John M. Parry

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UNIVERSITY OF WALES
 UNIVERSITY OF WALES SWANSEA
 School of Food Science
 Singleton Park, Swansea, SA2 8PP

11 February 1999

Dear [redacted]

The full text of your report on the results of the four papers was provided to the University of Wales Swansea on 10 February 1999. Although we are grateful for the information you have provided, I have not had a chance to read your report. I am sorry that I cannot provide you with a more detailed response at this time. I will be happy to discuss your report with you in person if you wish. I will be happy to discuss your report with you in person if you wish.

I have enclosed a copy of the report for your information.

Yours sincerely,
 Professor John H. Parry

at appropriate concentrations to the B. thuringiensis strain in various studies. These are given in the enclosed report to ensure that the use of the B. thuringiensis strain is not prevented in other countries of the B. thuringiensis strain.

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Aug
1999

Dr. Parry submits second
comprehensive report.



Aug
1999



Dr. Parry submits second
comprehensive report.

Clastogen:

A clastogen is an agent that can induce mutation by disrupting or damaging chromosomes.

Aug
1999

Dr. Parry submits second
comprehensive report.

Dr. Parry concludes **glyphosate is
clastogenic.**

12

- 17) None of the surfactants demonstrated any mutagenic activity in bacteria.
- 18) There are no adequate data to evaluate the *in vitro* clastogenic activity of surfactants.
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the study of Liot *et al* (1998a and 1998b) I conclude that glyphosate is a potential clastogenic *in vivo*. The study of Bolognesi *et al* (1997) indicates that this clastogenic activity may be reproduced *in vivo* in somatic cells. However, the dominant lethal assay (of limited sensitivity) indicates that this genotoxic activity is not reproduced in germ cells. The work of Bolognesi *et al* (1997) and Liot *et al* (1998a and 1998b) suggests that the genotoxicity observed may be derived from the generation of oxidative damage in the presence of glyphosate.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of adequate data no evaluation of the clastogenic potential *in vitro* of glyphosate mixtures is possible. In the absence of a micronucleus study to the protocol of that used by Bolognesi *et al* (1997) no adequate assessment of the potential activity of glyphosate mixtures in bone marrow is possible. The available studies do not provide any evidence of genotoxicity in rodent bone marrow. There is some evidence from *Drosophila* to suggest that glyphosate mixtures may have some germ cell activity.

The studies of Bolognesi *et al* (1997) suggests that glyphosate mixtures may be capable of inducing oxidative damage *in vivo*.

Specific evaluation of surfactants

Key Issues concerning the potential genotoxicity of glyphosate, glyphosate formulations and surfactants; recommendations for future work.

James M. Parry

Centre for Molecular Genetics and Toxicology
School of Biological Sciences
University of Wales Swansea
Swansea SA2 8PP, UK

Key Questions

1. Is glyphosate an *in vitro* clastogen? Can the positive studies of Liot *et al* (1998a, 1998b) be reproduced?
2. Is glyphosate an *in vivo* clastogen? Can the positive studies of Bolognesi *et al* (1997) be reproduced?
3. If glyphosate is an *in vitro* and *in vivo* clastogen, what is its mechanism of action and does the mechanism lead to other types of genotoxic activity *in vivo* such as point mutation induction?
4. Does glyphosate produce oxidative damage?
5. Can we explain the reported genotoxic effects of glyphosate on the basis of the induction of oxidative damage?
6. If glyphosate is an *in vivo* genotoxin is its mechanism of action thresholded? Under what conditions of exposure are the antioxidant defences of the cell overwhelmed?
7. Are there differences in the genotoxic activities of glyphosate and glyphosate formulations?
8. Do any of the surfactants contribute to the reported genotoxicity of glyphosate formulations?

Plaintiff Exhibit

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If the genotoxic activity of glyphosate and its formulations is confirmed it would be advisable to determine whether there are exposed individuals and groups within the human population. If such individuals can be identified then the extent of exposure should be determined and their lymphocytes analysed for the presence of chromosome aberrations. In

inducing activity with the surfactant MON0818.

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The studies of Bolognesi *et al* (1997) suggests that glyphosate mixtures may be capable of inducing oxidative damage *in vivo*.

Specific evaluation of surfactants

None of the surfactants were capable of inducing mutations in bacteria. No adequate data available to evaluate the *in vitro* or *in vivo* clastogenicity of the surfactants.

Aug
1999

Dr. Parry submits second
comprehensive report.

Dr. Parry concludes **glyphosate is
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12

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Specific evaluation of surfactants

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Key Issues concerning the potential genotoxicity of glyphosate, glyphosate formulations and surfactants; recommendations for future work.

James M. Parry

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Sent: 9/16/1999 6:18:36 PM
To: [REDACTED] 'KIER, LARRY D [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=33322]; 'FARMER, DONNA R [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=180070]
CC: 'HEYDENS, WILLIAM F [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=230737]
Subject: RE: Parry report

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However, let's step back and look at what we are really trying to achieve here. We want to find/develop someone who is comfortable with the genotox profile of glyphosate/Roundup and who can be influential with regulators and Scientific Outreach operations when genotox. issues arise. My read is that Parry is not currently such a person, and it would take quite some time and \$\$\$/studies to get him there. We simply aren't going to do the studies Parry suggests. [REDACTED] do you think Parry can become a strong advocate without doing this work Parry? If not, we should **seriously** start looking for one or more other individuals to work with. Even if we think we can eventually bring Parry around closer to where we need him, we should be currently looking for a second/back-up genotox. supporter. We have not made much progress and are currently very vulnerable in this area. We have time to fix that, but only if we make this a high priority now.

Bill



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Admission No. 26

Monsanto admits that it has no record of submitting Dr. Parry's Reports to the EPA.

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5. Can we explain the reported genotoxic effects of glyphosate on the basis of the induction of oxidative damage?
6. If glyphosate is an *in vivo* genotoxin is its mechanism of action thresholded? Under what conditions of exposure are the antioxidant defences of the cell overwhelmed?
7. Are there differences in the genotoxic activities of glyphosate and glyphosate formulations?
8. Do any of the surfactants contribute to the reported genotoxicity of glyphosate formulations?

If the genotoxic activity of glyphosate and its formulations is confirmed it would be advisable to determine whether there are exposed individuals and groups within the human population. If such individuals can be identified then the extent of exposure should be determined and their lymphocytes analysed for the presence of chromosome aberrations. In

RY D
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improve the report.
develop someone who is
regulators and Scientific
a person, and it would take
do you
think Parry can become a strong advocate without doing this work Parry? If not, we should **seriously** start looking for one or more other individuals to work with. Even if we think we can eventually bring Parry around closer to where we need him, we should be currently looking for a second/back-up genetox. supporter. We have not made much progress and are currently very vulnerable in this area. We have time to fix that, but only if we make this a high priority now.

Bill



Plaintiff Exhibit
0220

Plaintiff Exhibit
0221

Aug
1999

Dr. Parry submits second comprehensive report.

Dr. Parry concludes **glyphosate is clastogenic.**

Sept
1999

Monsanto Reaction:
“We simply are not going to do the studies Parry suggests.”

12

17) None of the surfactants demonstrated any mutagenic activity in bacteria.

18) There are no adequate data to evaluate the *in vitro* clastogenic activity of surfactants.

19) One limited bone marrow micronucleus assay failed to detect any micronucleus inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the study of Lioi *et al* (1998a and 1998b) I conclude that glyphosate is a potential clastogenic *in vivo*. The study of Bolognesi *et al* (1997) indicates that this clastogenic activity may be reproduced *in vivo* in somatic cells. However, the dominant lethal assay (of limited sensitivity) indicates that this genotoxic activity is not reproduced in germ cells. The work of Bolognesi *et al* (1997) and Lioi *et al* (1998a and 1998b) suggests that the genotoxicity observed may be derived from the generation of oxidative damage in the presence of glyphosate.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of adequate data no evaluation of the clastogenic potential *in vitro* of glyphosate mixtures is possible. In the absence of a micronucleus study to the protocol of that used by Bolognesi *et al* (1997) no adequate assessment of the potential activity of glyphosate mixtures in bone marrow is possible. The available studies do not provide any evidence of genotoxicity in rodent bone marrow. There is some evidence from *Drosophila* to suggest that glyphosate mixtures may have some germ cell activity.

The studies of Bolognesi *et al* (1997) suggests that glyphosate mixtures may be capable of inducing oxidative damage *in vivo*.

Specific evaluation of surfactants

Plaintiff Exhibit
0220

Key Issues concerning the potential genotoxicity of glyphosate, glyphosate formulations and surfactants; recommendations for future work.

James M. Parry
Centre for Molecular Genetics and Toxicology
School of Biological Sciences
University of Wales Swansea
Swansea SA2 8PP, UK.

Key Questions

1. Is glyphosate an *in vitro* clastogen? Can the positive studies of Lioi *et al* (1998a, 1998b) be reproduced?
2. Is glyphosate an *in vivo* clastogen? Can the positive studies of Bolognesi *et al* (1997) be reproduced?
3. If glyphosate is an *in vitro* and *in vivo* clastogen, what is its mechanism of action and does the mechanism lead to other types of genotoxic activity *in vivo* such as point mutation induction?
4. Does glyphosate produce oxidative damage?
5. Can we explain the reported genotoxic effects of glyphosate on the basis of the induction of oxidative damage?
6. If glyphosate is an *in vivo* genotoxin is its mechanism of action thresholded? Under what conditions of exposure are the antioxidant defences of the cell overwhelmed?
7. Are there differences in the genotoxic activities of glyphosate and glyphosate formulations?
8. Do any of the surfactants contribute to the reported genotoxicity of glyphosate formulations?

If the genotoxic activity of glyphosate and its formulations is confirmed it would be advisable to determine whether there are exposed individuals and groups within the human population. If such individuals can be identified then the extent of exposure should be determined and their lymphocytes analysed for the presence of chromosome aberrations. In

Message

From: HEYDENS, WILLIAM F [FND/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]
Sent: 9/16/1999 6:18:36 PM
To: [REDACTED] 'KIER, LARRY D [NCP/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=33322]; 'FARMER, DONNA R [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=180070]
CC: 'HEYDENS, WILLIAM F [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=230737]
Subject: RE: Parry report

[REDACTED] All,

I have read the report and agree with the comments - there are various things that can be done to improve the report.

However, let's step back and look at what we are really trying to achieve here. We want to find/develop someone who is comfortable with the genotox profile of glyphosate/Roundup and who can be influential with regulators and Scientific Outreach operations when genotox. issues arise. My read is that Parry is not currently such a person, and it would take quite some time and \$\$\$/studies to get him there. We simply aren't going to do the studies Parry suggests. [REDACTED] do you think Parry can become a strong advocate without doing this work Parry? If not, we should **seriously** start looking for one or more other individuals to work with. Even if we think we can eventually bring Parry around closer to where we need him, we should be currently looking for a second/back-up genotox. supporter. We have not made much progress and are currently very vulnerable in this area. We have time to fix that, but only if we make this a high priority now.

Bill



Plaintiff Exhibit
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Apr
2000

Ghostwriting:
Dr. Heydens ghostwrites
Williams paper.



Safety Evaluation and Risk Assessment of the Herbicide Roundup¹ and Its Active Ingredient, Glyphosate, for Humans

Gary M. Williams,* Robert Kroes,[†] and Ian C. Munro![‡]

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Received December 6, 1999

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Ghostwriting:
When a company writes a favorable
publication and pays a prestigious author to
put their name on it.

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Williams, Kroes, and Munro

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Apr
2010

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served us well over the
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Glyphosate Toxicology
Activities
Supporting Registration
Reviews

David Saltmiras, PhD, DABT
CPTLT December 10, 2010

From: SALTMIRAS, DAVID A [AG/1000]
 Sent: Wednesday, December 08, 2010 11:17 AM
 To: HEYDENS, WILLIAM F [AG/1000]
 Subject: Updated glyphosate activities presentation for Friday's CPTLT meeting

Bill,

Updated and attached for your comment.

Thanks.

David Saltmiras, Ph.D., D.A.B.T.
 Toxicology Manager
 Regulatory Product Safety Center
 Monsanto



Science

...e facing regulatory reviews with increased focus on
 ...e reviewed literature, irrespective of the quality of the science
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Toxicology Manager
Regulatory Product Safety Center
Monsanto

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Sent: Th
To: FISH
Cc: KOO
Subject:

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Glyphosate Toxicology Activities Supporting Registration Reviews



David Saltmiras, PhD, DABT
CPTLT December 10, 2010

Publications

- Williams et al. (2000) an invaluable asset
 - Monsanto responses to agencies
 - Scientific Affairs rebuttals
 - Regulator reviews
- More current external expert publications are now needed to support our **FTO** and Registration Reviews
 - EU Annex 1 Renewal requires extensive lit. review
 - Will weight of evidence be measured by number of publications or quality of the science???



Political Science



- Unfortunately, we are facing regulatory reviews with increased focus on
 - Claims in the peer reviewed literature, irrespective of the quality of the science
 - Stakeholder input including activist researchers
 - Political pressure on outcomes - e.g. POEAs in Germany
 - Reduced pesticide use in general
- Williams et al. (2000) has served us well in toxicology over the last decade
- We need a stronger arsenal of robust scientific papers to support the safe use of our products as we face the next set of chemistry registration reviews across the globe
- With increasing business interests in South America, a local network credible expert scientists is crucial to facilitate scientifically robust and objective regulatory evaluations of our products *We have not determined exactly what we should & could do here. I would modify bullet to reflect that we need to determine an appropriate & do-able (i.e., we can get someone to pay for it course of action here*



Apr
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2. Mechanistic Data

Recent Data Findings:



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Recent Data Findings: Ghisi (2016)

Chemosphere 145 (2016) 42–54

Contents lists available at ScienceDirect
Chemosphere
Journal homepage: www.elsevier.com/locate/chemosphere

ELSEVIER

Review

Does exposure to glyphosate lead to an increase in the micronuclei frequency? A systematic and meta-analytic review

Néda de Castilhos Ghisi ^{a,b,*}, Elton Celton de Oliveira ^b, Alberto José Prioli ^b

^a Programa de Pós-graduação em Ecologia de Ambientes Aquáticos e Continentais (PEA)/Núcleo, Universidade Estadual de Maringá (UEM), Av. Colombo, 5790, Zona 7, 87020-900, Maringá (PR), Brazil
^b Universidade Tecnológica Federal do Paraná (UTFPR), Estrada para Boa Esperança, km 4, 85660-000, Dois Vizinhos (PR), Brazil

HIGHLIGHTS

- Systematic meta-analytical review correlating glyphosate exposure and micronuclei.
- Groups exposed to glyphosate formulations have increased formation of micronuclei.
- Significant difference among glyphosate (GLY) and its commercial formulations.
- Difference in MN formation among different exposure routes of GLY.
- Difference in MN formation among different groups of vertebrates.

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Micronucleus
Mutagenesis
Pesticides
Roundup

ABSTRACT

Glyphosate-based herbicides are among the most used pesticides worldwide. Reviews on the safety of glyphosate have been conducted by several regulatory agencies and research centers, many times with contradictory results. This study is a systematic meta-analytical review of experimental studies on the relationship between exposure to the glyphosate (GLY) and its formulations with the formation of micronuclei (MN) to establish a quantitative estimate of the environmental risks. The natural logarithm (ln) of the estimated response ratio was calculated from 81 experiments. A meta-analysis was performed on the complete data set, and individual meta-analyses were conducted after stratification by test systems, class of vertebrate, exposure route, gender, endpoints, type of literature, formulation, GLY dose and exposure time. A forest plot showed an overall positive association between GLY exposure and its formulations and MN, corroborated by the cumulative effects size. Different responses were observed on mammalian and non-mammalian. Interesting results was noticed in exposure route where oral administration of GLY presented no significance. Exposure by intraperitoneal injection presented the highest MN formation. Pure GLY caused fewer effects than to commercial mixtures, but both presented mutagenic effects. The studies with males presented significant responses, while studies with females were not significant. The cumulative effects size was not clearly related to GLY dose, and was negatively related to exposure time. It can be attributed to different test systems, exposure routes and protocols analyzed. In conclusion, our results support the hypothesis that exposure to GLY and its formulations increases the frequency of MN formation.

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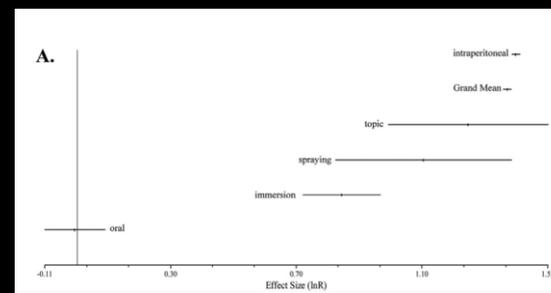
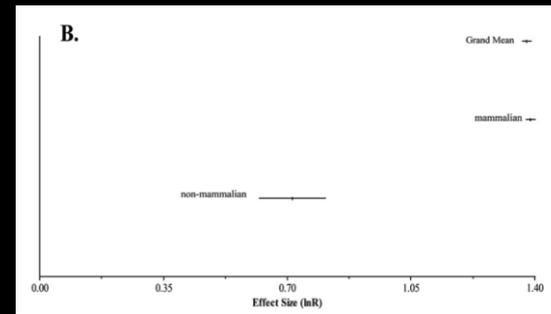
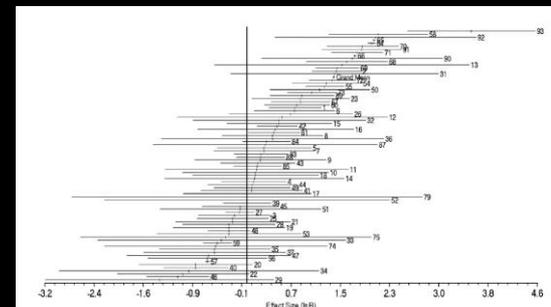
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0766





Review

Does exposure to glyphosate lead to an increase in the micronuclei frequency? A systematic and meta-analytic review



Nédia de Castilhos Ghisi^{a,b,*}, Elton Celton de Oliveira^b, Alberto José Prioli^b

^a Programa de Pós-graduação em Ecologia de Ambientes Aquáticos e Continentais (PEA)/Nupélia, Universidade Estadual de Maringá (UEM), Av. Colombo, 5790, Zona 7, 87020-900, Maringá (PR), Brazil

^b Universidade Tecnológica Federal do Paraná (UTFPR), Estrada para Boa Esperança, km 4, 85660-000, Dois Vizinhos (PR), Brazil

H I G H L I G H T S

- Systematic meta-analytical review correlating glyphosate exposure and micronuclei.
- Groups exposed to glyphosate formulations have increased formation of micronuclei.
- Significant difference among glyphosate (GLY) and its commercial formulations.
- Difference in MN formation among different exposure routes of GLY.
- Difference in MN formation among different groups of vertebrates.

A R T I C L E I N F O

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Handling Editor: Frederic Leusch

A B S T R A C T

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Review

Does exposure to glyphosate lead to an increase in the micronuclei frequency? A systematic meta-analytical review



Nédia de Castilhos

Meta-analysis:

A statistical approach that combines the results of multiple studies into a single summary estimate.

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5790, Zona 7, 87020-900, Maringá,
^b Universidade Tecnológica Federal

HIGHLIGHTS

- Systematic meta-analytical
- Groups exposed to glyphosate formulations have increased formation of micronuclei.
- Significant difference among glyphosate (GLY) and its commercial formulations.
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2. Can Roundup cause cancer?

2. Mechanistic Data

Recent Data Findings: Ghisi (2016)

Chemosphere 145 (2016) 42–54

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Néda de Castilhos Ghisi ^{a,b,*}, Elton Celton de Oliveira ^b, Alberto José Prioli ^b

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^b Universidade Tecnológica Federal do Paraná (UTFPR), Estrada para Boa Esperança, km 4, 85660-000, Dois Vizinhos (PR), Brazil

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Meta-analysis
Micronucleus
Mutagenesis
Pesticides
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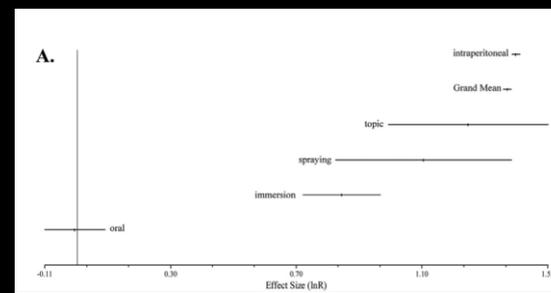
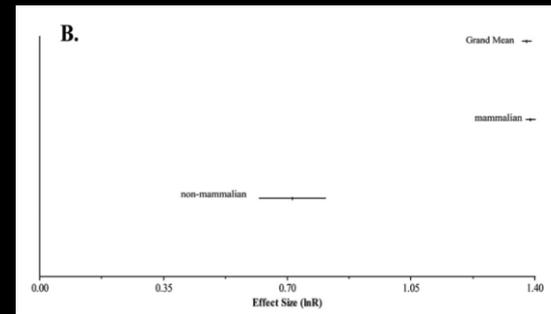
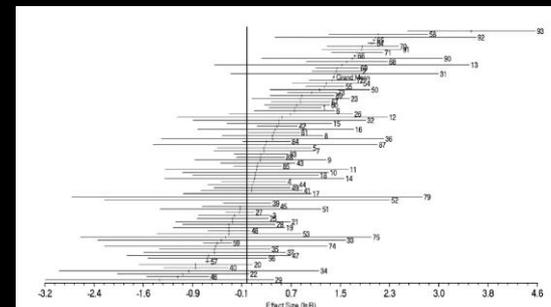
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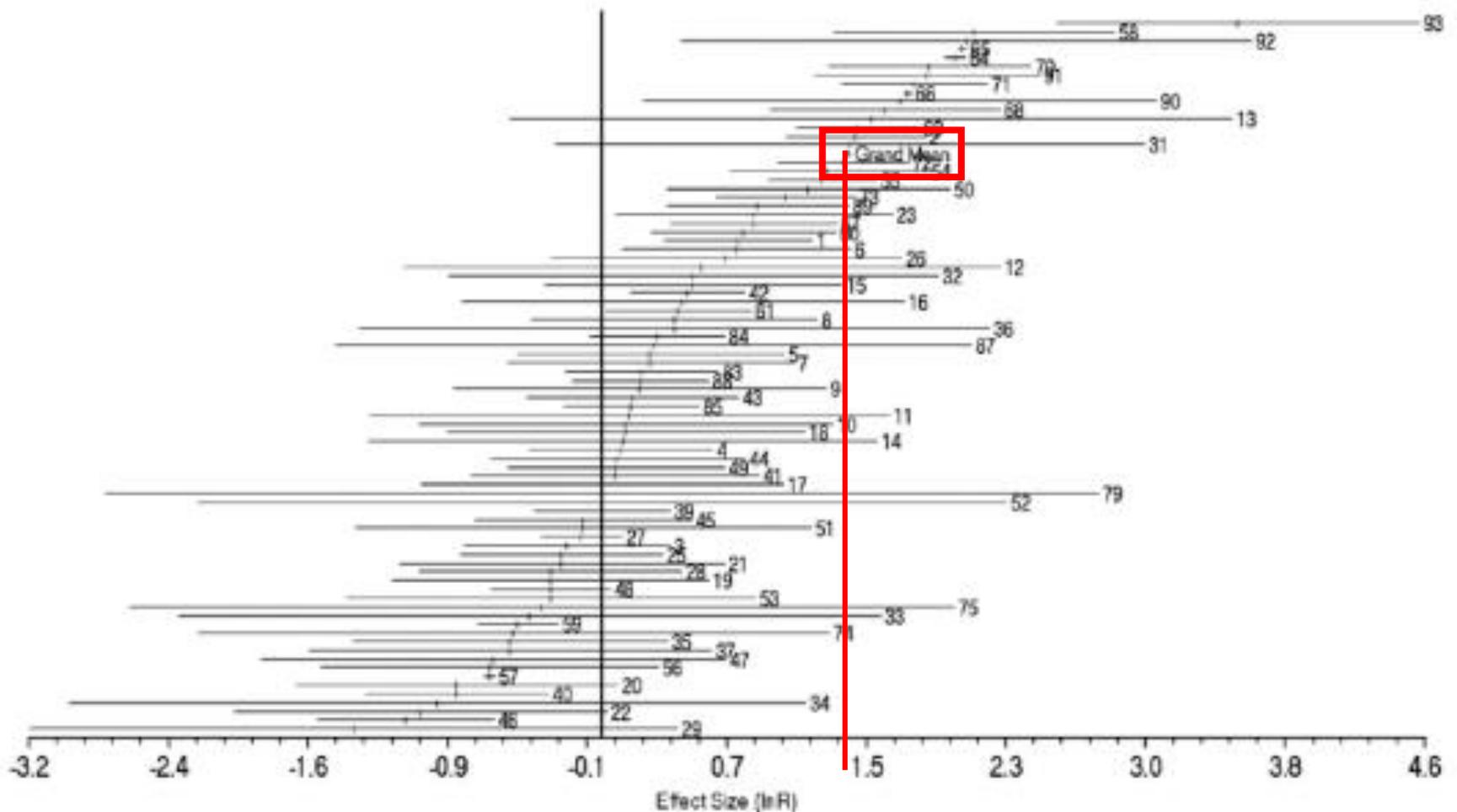
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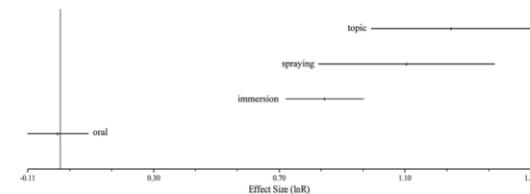


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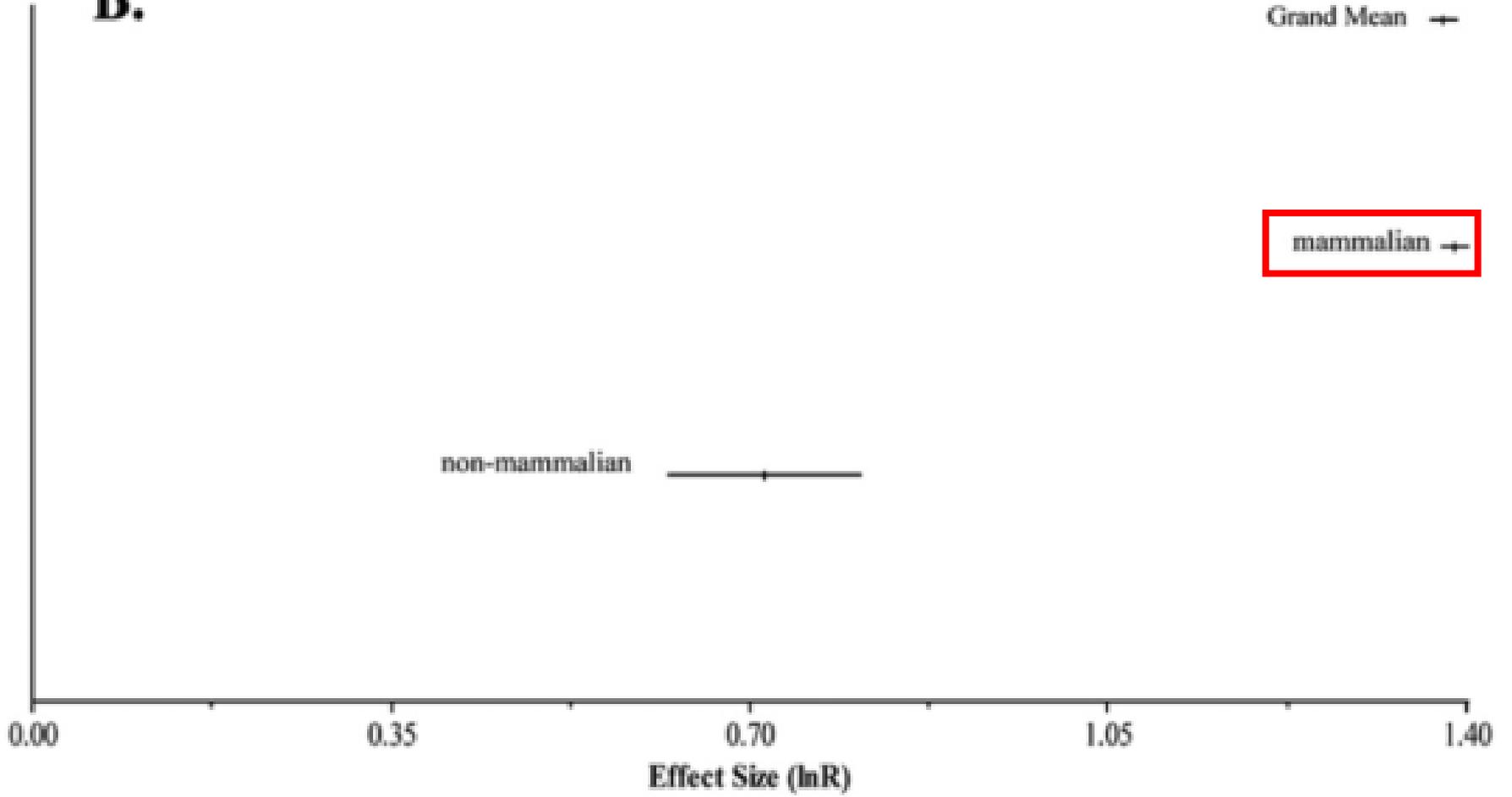
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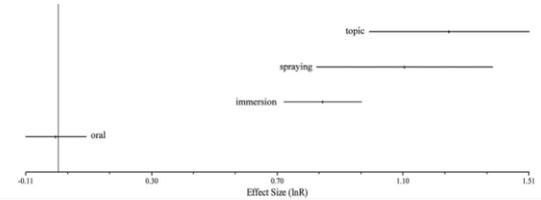


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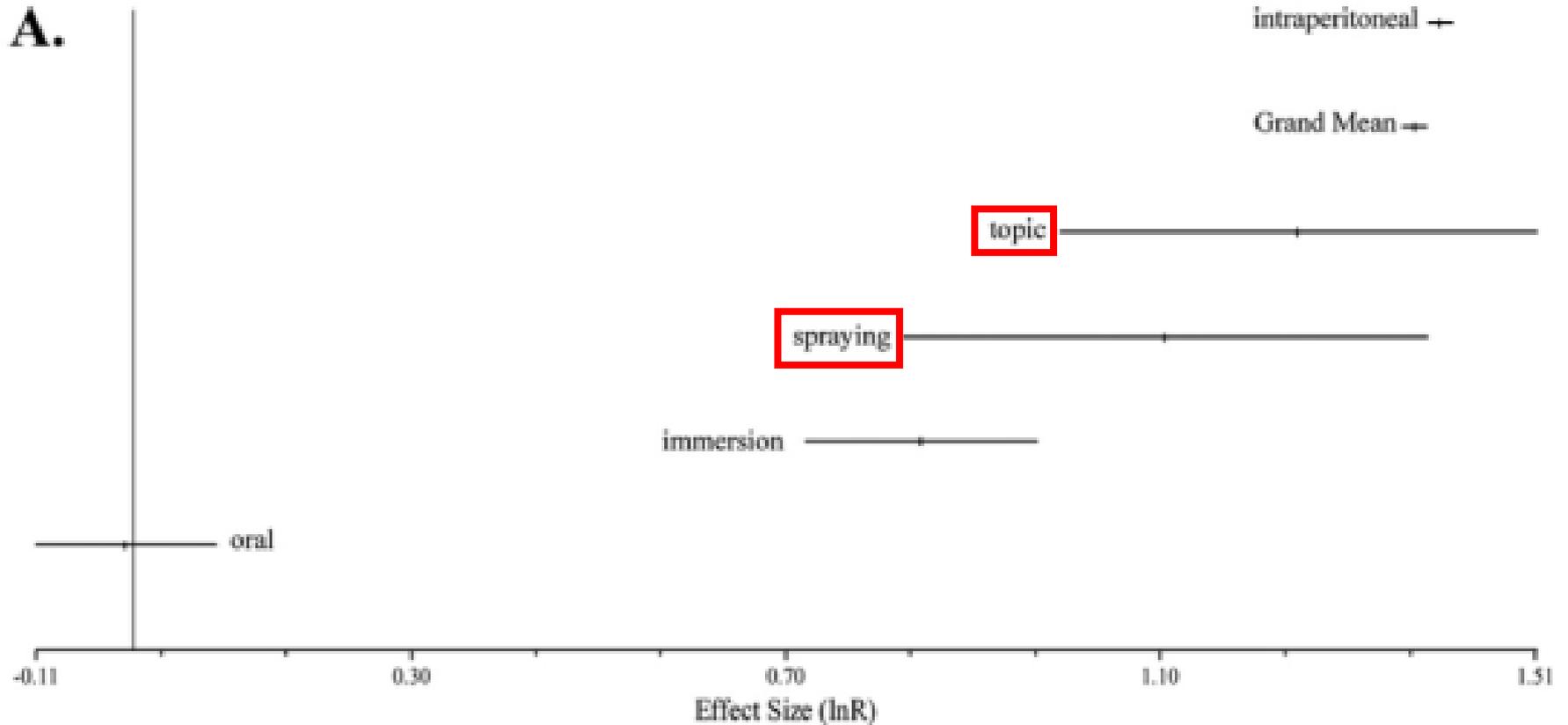
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2. Can Roundup cause cancer?



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2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies

2. Mechanistic Data

3. Epidemiology



2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies

2. Mechanistic Data

3. Epidemiology



2. Can Roundup cause cancer?

3. Epidemiology

Epidemiology:

The study of the distribution and causes of disease in human populations.

Non-Hodgkin Lymphoma-specific

2. Can Roundup cause cancer?

3. Epidemiology

Non-Hodgkin Lymphoma:

A cancer that starts in white blood cells called lymphocytes, which are part of the body's immune system.

Two types:

- B-Cell (most common)
- T-Cell (less common)

2. Can Roundup cause cancer?

3. Epidemiology

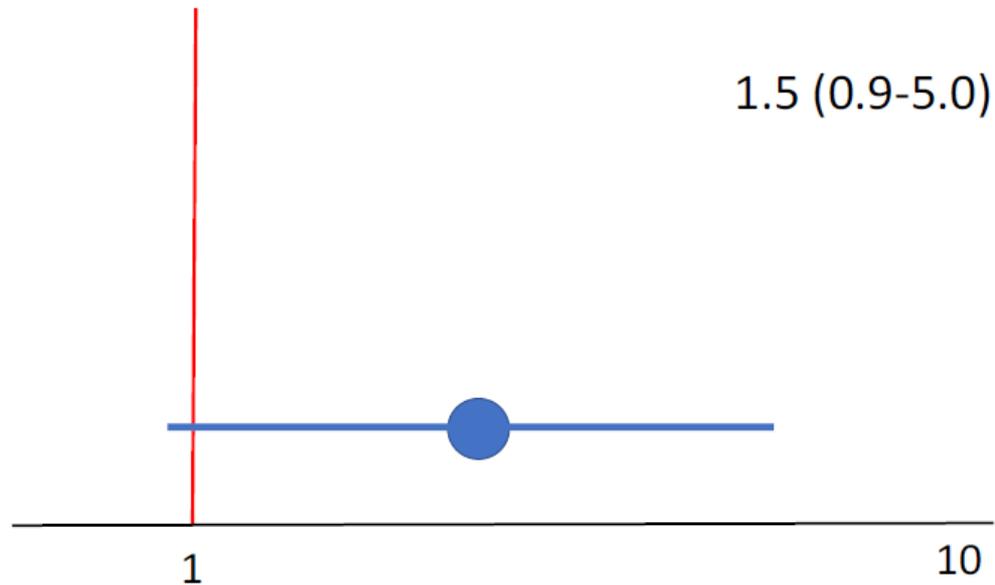
Confidence Bound:

A range of values where there is a specified probability that the true value lies within it.

2. Can Roundup cause cancer?

3. Epidemiology

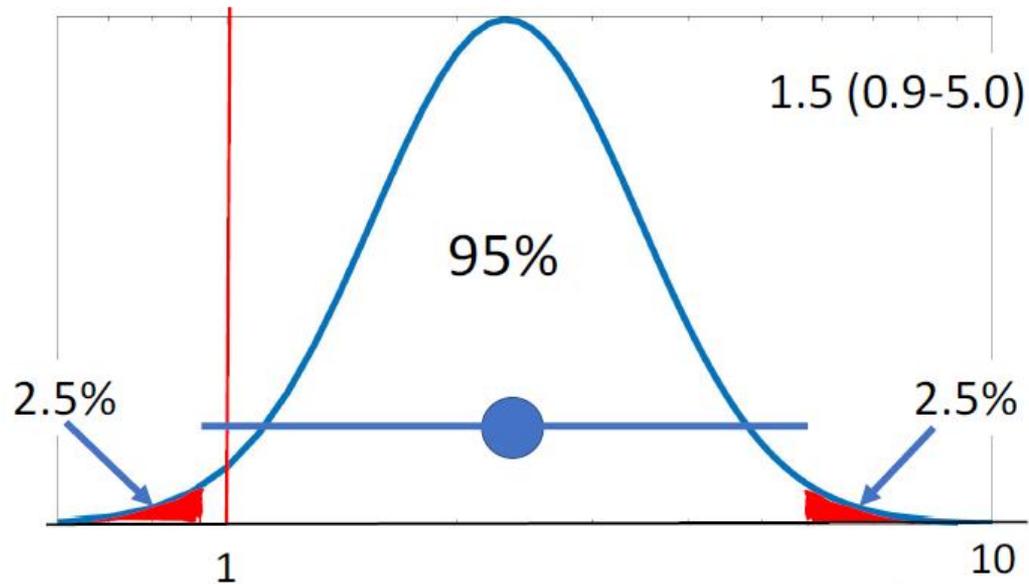
Confidence Bounds



2. Can Roundup cause cancer?

3. Epidemiology

Confidence Bounds

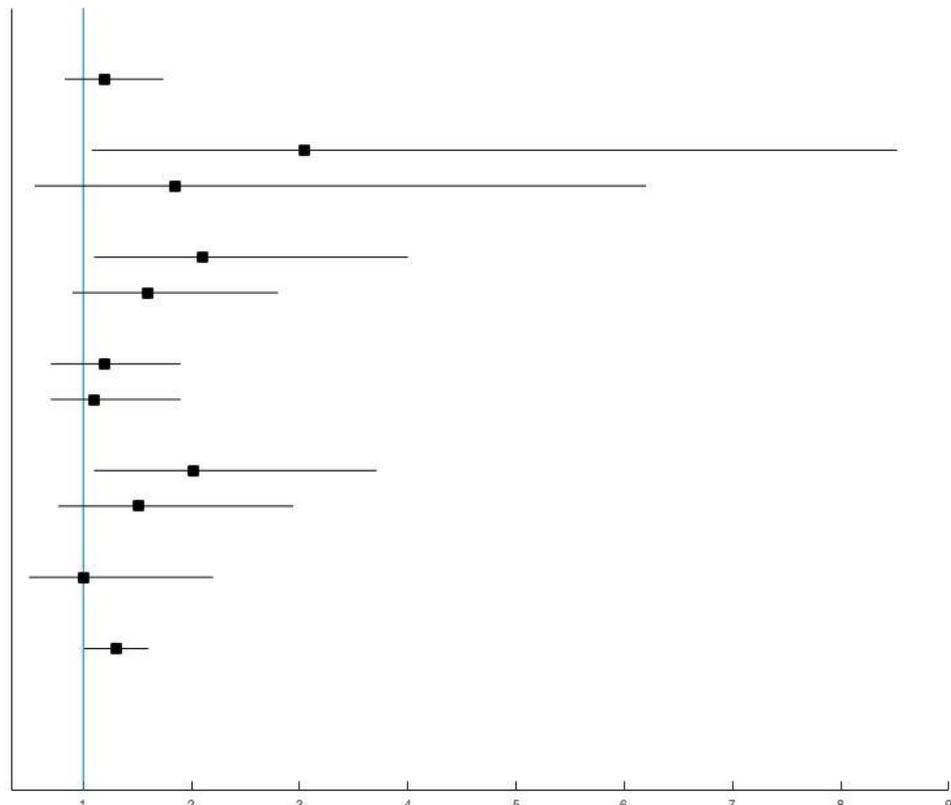


2. Can Roundup cause cancer?

3. Epidemiology

NHL – Never / Ever

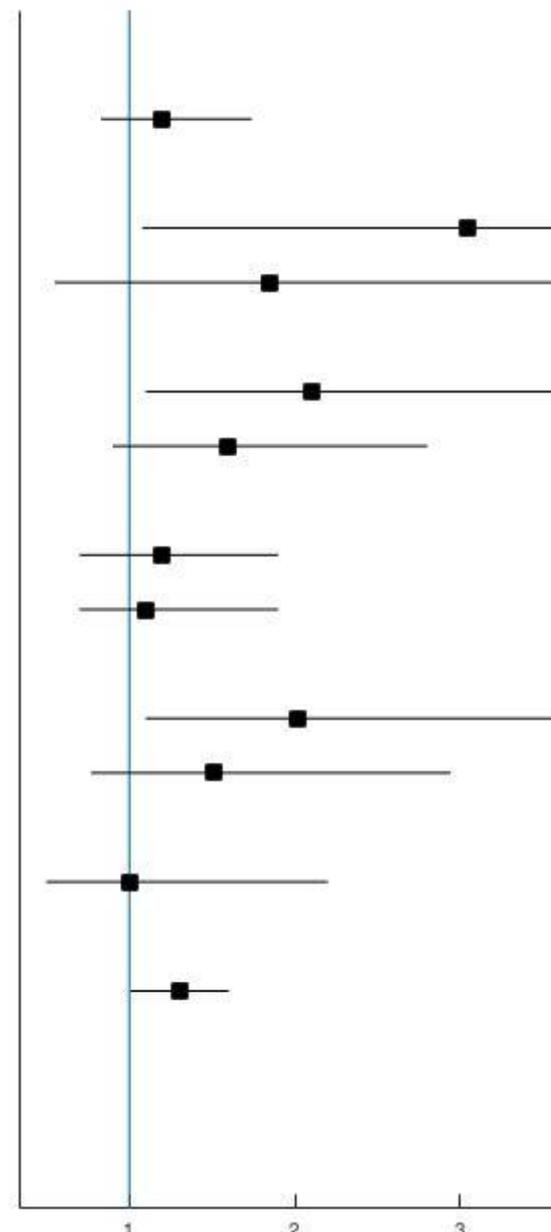
Study	RR	Lower	Upper
McDuffie et al. (2001)			
no pesticide adjustment	1.20	0.83	1.74
Hardell et al. (2002)			
no pesticide adjustment	3.04	1.08	8.52
adjusted for pesticides	1.85	0.55	6.20
De Roos et al. (2003)			
adjusted for pesticides	2.10	1.10	4.00
Bayesian modeling	1.60	0.90	2.80
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Meta-Analysis: Model 1			
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Andreotti et al. (2018)			
not provided			



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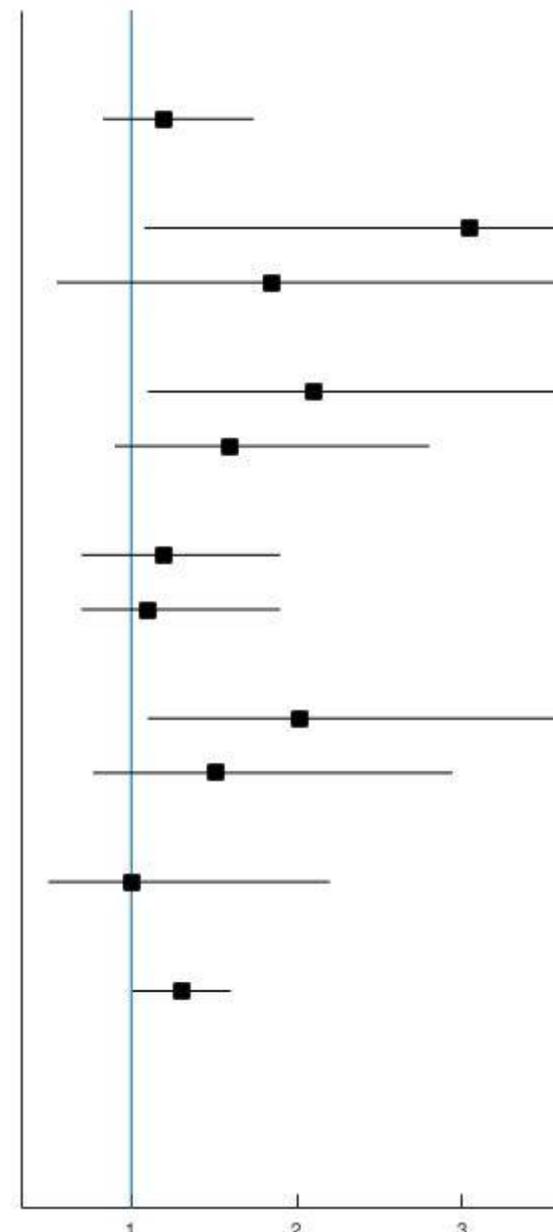
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2. Can Roundup cause cancer?

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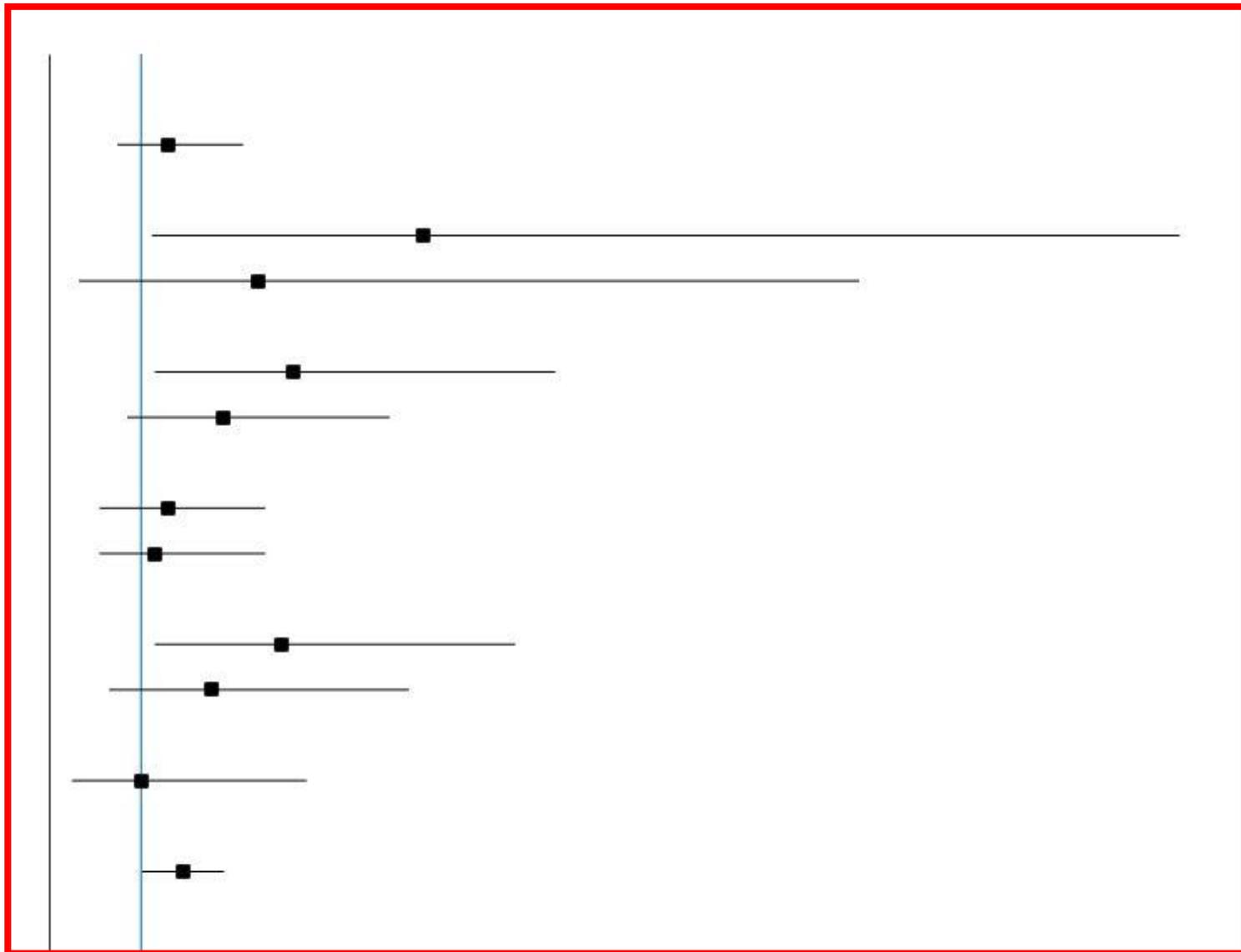
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3. Epidemiology

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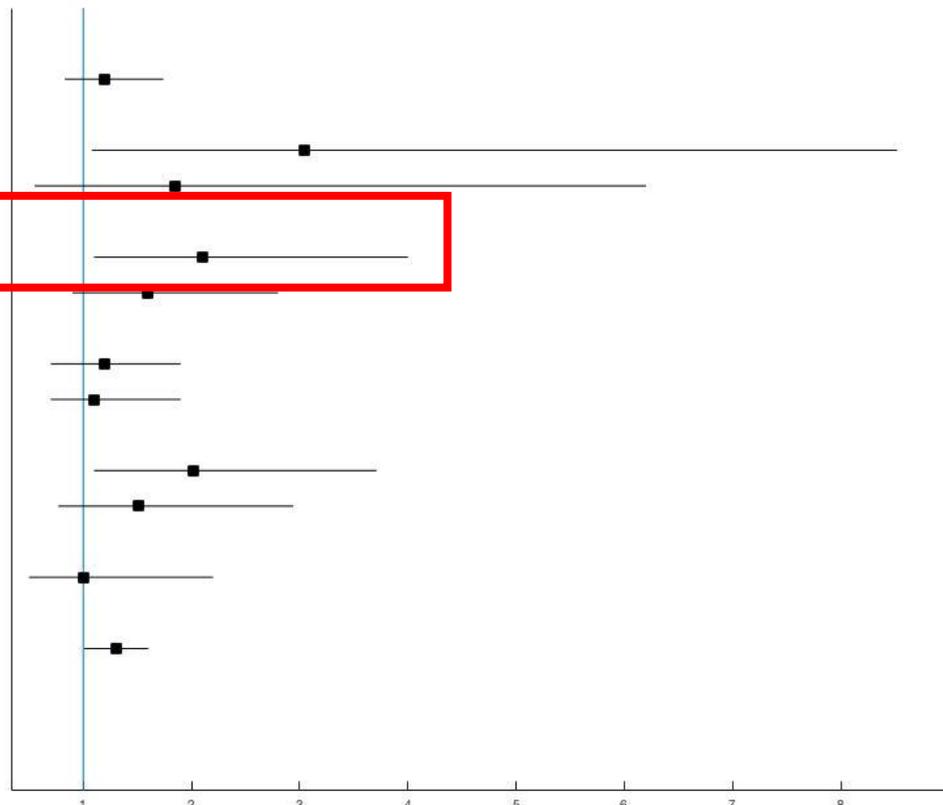
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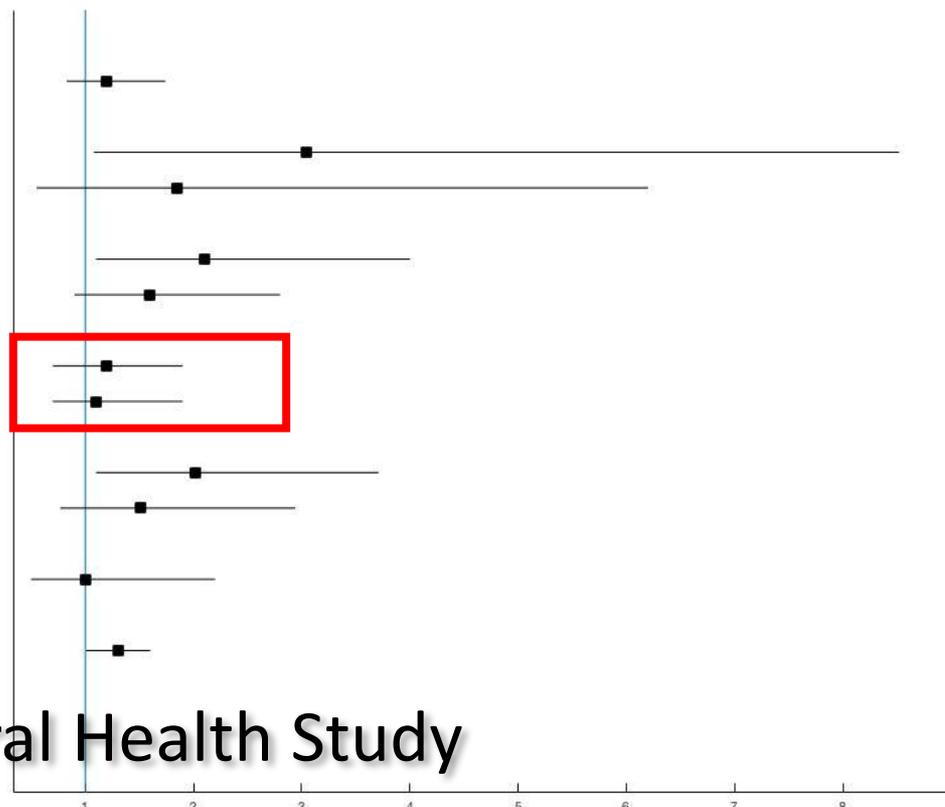


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Andreotti et al. (2018)
not provided

2. Can Roundup cause cancer?

3. Epidemiology

The Agricultural Health Study

- Large cohort study following pesticide applicators in North Carolina and Iowa
- Does not show any association for general NHL
- Does show association for T-cell NHL

2. Can Roundup cause cancer?

3. Epidemiology

The Agricultural Health Study

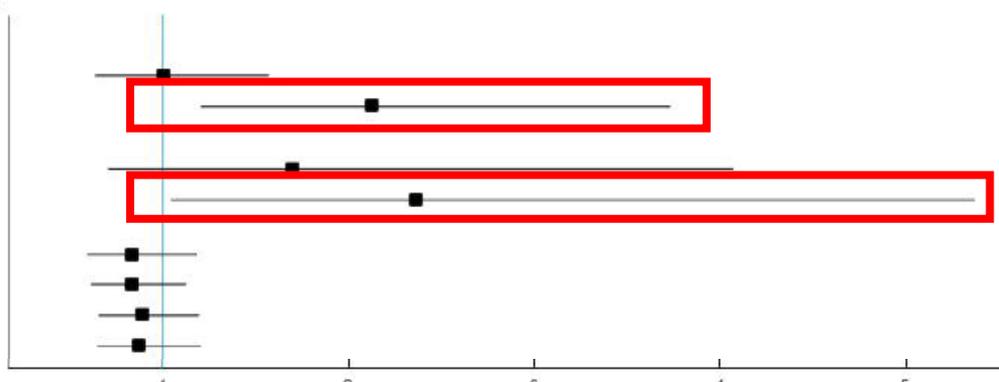
- Deeply flawed study
 - Many pesticides being studied
 - Exposure classification
 - Imputation defects
 - AHS failed to detect other known carcinogens

2. Can Roundup cause cancer?

3. Epidemiology

NHL – Exposure Duration

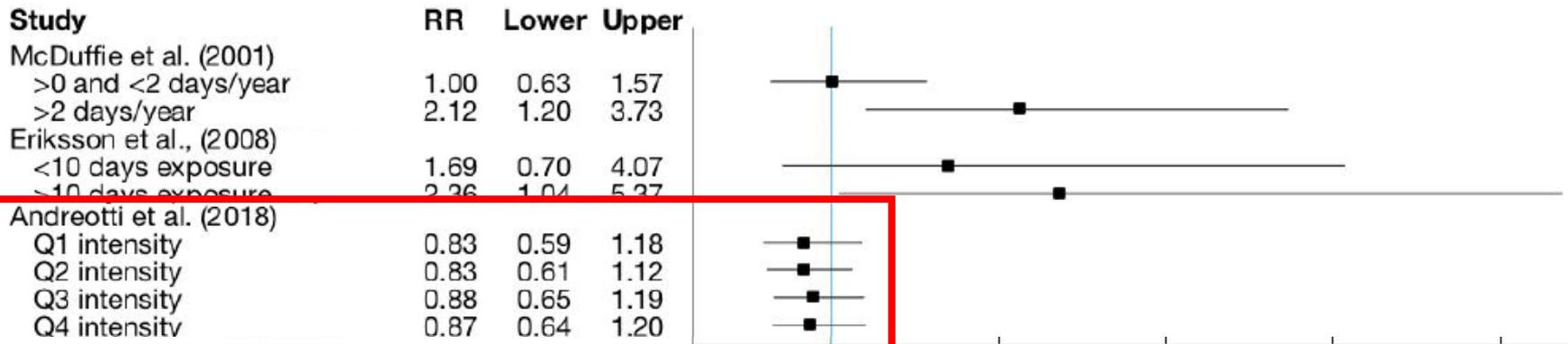
Study	RR	Lower	Upper
McDuffie et al. (2001)			
>0 and <2 days/year	1.00	0.63	1.57
>2 days/year	2.12	1.20	3.73
Eriksson et al., (2008)			
<10 days exposure	1.69	0.70	4.07
>10 days exposure	2.36	1.04	5.37
Andreotti et al. (2018)			
Q1 intensity	0.83	0.59	1.18
Q2 intensity	0.83	0.61	1.12
Q3 intensity	0.88	0.65	1.19
Q4 intensity	0.87	0.64	1.20



2. Can Roundup cause cancer?

3. Epidemiology

NHL – Exposure Duration



Mar
1999



Epidemiology:

Hardell study shows **230%**
increased risk of NHL for
glyphosate formulation.

Mar
1999

Epidemiology:
Hardell study shows **230% increased** risk of NHL for glyphosate formulation.



Apr
1999

Monsanto's Reaction:
Hardell study raises "index of concern."



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Review of:
Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999; 87:1375-1380.
By:
John Anagnostou, PhD and Donna Farmer, PhD
Monsanto Company, April 14, 1999

Executive Summary:
Hardell and Erikson conducted a case control study to look for associations between reported pesticide use and non-Hodgkin's lymphoma (NHL). The study included 604 NHL cases and 741 controls. The measure of association in the study was the odds ratio (OR), a measure for estimates of the rate of disease risk in the case (NHL) relative to exposed and unexposed populations.

The authors reported statistically significant associations for NHL with reported use of non-hexachlorocyclopentadiene (NHC) with reported use of 2,4-dichlorophenoxyacetic acid (OR = 2.7), and reported use of 2,4-dichlorophenoxyacetic acid (OR = 2.7). The major limitations of this study with the reliance on reported pesticide use (no documented exposure) information, the small number of subjects who reported use of specific pesticides, the possibility of recall bias, the absence of non-occupational sources for the 2,4-dichlorophenoxyacetic acid (approximately 43% of the pesticides use information), and the difficulty in controlling for potential confounding factors, given the small number of exposed subjects.

The authors also reported a non-significant (borderline) OR of 2.3 for glyphosate. This OR was not statistically significant and was based on only four "exposed" cases and three "unexposed" controls. This finding needs to be evaluated in light of the limitations of the study, occupational status, and the wealth of toxicologic information that has resulted in glyphosate being judged to be non-toxic and non-carcinogenic by the U.S. Environmental Protection Agency and the World Health Organization. Systematic errors or biases seem the most likely explanations for the findings reported for glyphosate in this study.

Hardell and Erikson conducted an epidemiologic study to look for associations between self-reported pesticide use and non-Hodgkin's lymphoma (NHL). The authors, for conducting this research via previous studies by the first author¹ and by investigators at the U.S. National Cancer Institute² which found associations between reported use of herbicidal agents (primarily 2,4-D) and NHL. The results of these studies were acknowledged to be inconclusive by a special Science Advisory Panel convened in the early 1980s by the U.S. Environmental Protection Agency (EPA)³.

The present study presents new data about phenocyclic acids and other commonly used pesticides. However, it reviews the methods and results of this recent study.

Study design:
Hardell and Erikson employed a case control design for their research. In case control studies, subjects are selected on the basis of their disease status. There is the disease of interest in the cases (with NHL) and the cases discuss their study participants as the controls. Information about demographic and other factors are collected from cases and controls using similar methodology.

Additional scientific evidence was not reviewed in this report when the pH was adjusted to a physiological level⁴. Also, EPA characterized the herbicide review carcinogenicity study⁵ as showing "no evidence of carcinogenicity" in the three tested and classified sulfonate as category I - no evidence for carcinogenicity in humans⁶.

The one glyphosate toxicology study cited⁷ showed weak positive findings for acute chemical toxicity in human lymphocytes in vitro. This study had many limitations and numerous, more specific, toxicologic studies have not shown positive results for glyphosate⁸. Extensive reviews of the available toxicologic data have been completed recently by the U.S. Environmental Protection Agency⁹ (EPA) and the World Health Organization¹⁰. These agencies concluded that glyphosate is not mutagenic or carcinogenic. EPA classified glyphosate as category II¹¹. This would support the biological plausibility of the findings reported by Hardell and Erikson.

In conclusion, the study by Hardell and Erikson found a modest association between NHL and several chemical pesticides - most notably, for NHCs and the collective group of hexachloro. The reported risk to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall or confounding bias. It is clear, however, that the widespread use of glyphosate and concerns about potential health effects for farmers and their families will raise the "index of concern" for glyphosate in future agricultural carcinogenic studies.

References

1. Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999;87:1375-1380.
2. Hardell L. Malignant lymphomas of the larynx to type and exposure to phenocyclic acids or alkylphenols. *Lancet* 1979;1:35-36.
3. Hardell L, Erikson M, Lerner P, Lundgren E. Malignant lymphomas and exposure to chemicals, especially organo-phosphorus, alkylphenols, and phenoxy acids: a case-control study. *Biol J Cancer* 1981;43:149-76.
4. Huse SK, Blair A, Helzlsouer TP, et al. Agricultural herbicide use and risk of lymphoma and soft tissue sarcoma. *JAMA* 1986;255:1111-1117.
5. Huse Zhan S, Weisenburger DD, Shih PA, et al. A case control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. *Epidemiology* 1991;1:48-50.
6. Environmental Protection Agency, An SAB Report: Assessment of potential 2,4-D carcinogenicity. Review of the epidemiological and other data on potential carcinogenesis of 2,4-D by the SAB/PA joint committee. EPA-SAB-ERC-94-001, Washington, DC, US EPA, 1994.
7. Mortimer DS. *Toxicological Epidemiology*. John Wiley & Sons, New York, 1985.
8. Rothman KJ, Greenland S. *Modern Epidemiology*. Second Edition. Lippincott-Raven, Philadelphia, 1998.

Mar
1999

Review of:

Hardell L, Eriksson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999, 85:1353-1360.

By:

John Acquavella, PhD, and Donna Farmer, PhD
Monsanto Company April 14, 1999

Excerpts:

pesticide
control
the

herbicide
phosphorus
pesticide

specific pesticides, the possibility of recall bias, the reliance on secondary sources (next-of-kin interviews) for approximately 43% of the pesticide use information, and the difficulty in controlling for potential confounding factors, given the small number of exposed subjects.

The authors also reported a moderately elevated OR of 2.3 for glyphosate. This OR was not statistically significant and was based on only four "exposed" cases and three "exposed" controls. This finding needs to be evaluated in light of the limitations of the study, mentioned above, and the wealth of toxicologic information that has resulted in glyphosate being judged to be non-mutagenic and non-carcinogenic by the U.S. Environmental Protection Agency and the World Health Organization. Systematic error or chance seem the most likely explanations for the findings reported for glyphosate in



between reported
cases and 741
that estimates of
ma.

ed use of any
chloro-2-methyl
not reported
to reported use of

Pla



In conclusion, the study by Hardell and Eriksson found a modest association between NHL and several chemical pesticides - most notably for MCPA and the collective group of fungicides. The reported weak to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall or confounding bias. It is clear, however, that the widespread use of glyphosate and concerns about pesticide related health effects for farmers and their families will raise the "index of concern" for glyphosate in future agricultural epidemiologic studies.

References

1. Hardell L, Eriksson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1989;85:1353-1360.
2. Hardell L. Malignant lymphomas of the histiocytic type and exposure to phenoxyacetic acids or chlorophenols. *Lancet* 1979;1:55-56.
3. Hardell L, Eriksson M, Lerner P, Lundgren H. Malignant lymphoma and exposure to chemicals.

Mar
1999

Epidemiology:
Hardell study shows **230% increased** risk of NHL for glyphosate formulation.



Apr
1999

Monsanto's Reaction:
Hardell study raises "index of concern."



Plaintiff Exhibit
0139

Review of:
Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999; 87:1375-1380.
By:
John Anagnostou, PhD and Donna Farmer, PhD
Monsanto Company, April 14, 1999

Executive Summary:
Hardell and Erikson conducted a case control study to look for associations between reported pesticide use and non-Hodgkin's lymphoma (NHL). The study included 604 NHL cases and 741 controls. The measure of association in the study was the odds ratio (OR), a measure for estimates of the rate of disease risk in the case (NHL) relative to exposed and unexposed populations.

The authors reported statistically significant associations for NHL with reported use of non-hexachlorocyclopentadiene (NHCYD) (OR = 1.5) reported use of any hexachlorocyclopentadiene (NHCYD) (OR = 2.7), and reported use of a chloro-2-methyl phenoxy acetic acid (OR = 2.7). The major limitations of this study with the reliance on reported pesticide use (no documented exposure) information, the small number of subjects who reported use of specific pesticides, the possibility of recall bias, the absence of non-occupational sources for hexachlorocyclopentadiene (approximately 43% of the pesticides use information), and the difficulty in controlling for potential confounding factors, given the small number of exposed subjects.

The authors also reported a non-significant (borderline) OR of 2.3 for glyphosate. This OR was not statistically significant and was based on only four "exposed" cases and three "unexposed" controls. This finding needs to be evaluated in light of the limitations of the study, occupational status, and the wealth of toxicologic information that has resulted in glyphosate being judged to be non-toxic and non-carcinogenic by the U.S. Environmental Protection Agency and the World Health Organization. Systematic errors or biases seem the most likely explanations for the findings reported for glyphosate in this study.

Hardell and Erikson conducted an epidemiologic study to look for associations between self-reported pesticide use and non-Hodgkin's lymphoma (NHL). The authors, for conducting this research via previous studies by the first author¹ and by investigators at the U.S. National Cancer Institute² which found associations between reported use of herbocyclic acids (primarily 2,4-D) and NHL. The results of these studies were acknowledged to be inconclusive by a special Science Advisory Panel convened in the early 1980s by the U.S. Environmental Protection Agency (EPA)³.

The present study presents new data about phenocyclic acids and other commonly used pesticides. However, it reviews the methods and results of this recent study.

Study design:
Hardell and Erikson employed a case control design for their research. In case control studies, subjects are selected on the basis of their disease status. There is the disease of interest in the cases (with NHL) or the cases' disease free study participants as the controls. Information about demographic and other factors are collected from cases and controls using similar methodology.

Additional's specific limitations were not mentioned in this report when the pH was adjusted to a physiological level⁴. Also, EPA characterized the authors' review "concomitantly made" in allowing "no evidence of carcinogenicity" in the "broad control" and identified sulfonate as category I - no evidence for carcinogenicity as follows⁵.

The one glyphosate toxicology study cited⁶ showed weak positive findings for acute chemical reactions in human lymphocytes in vitro. This study had many limitations and numerous, more specific, toxicologic studies have not shown positive results for glyphosate⁷. Extensive reviews of the available toxicologic data have been completed recently by the U.S. Environmental Protection Agency⁸ (EPA) and the World Health Organization⁹. These agencies concluded that glyphosate is not mutagenic or carcinogenic. EPA classified glyphosate as category II¹⁰. This would support the biological plausibility of the findings reported by Hardell and Erikson.

In conclusion, the study by Hardell and Erikson found a modest association between NHL and several chemical pesticides - most notably, for NHCYD and the collective group of hexachlorocyclopentadiene. The reported risk to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall or confounding bias. It is clear, however, that the widespread use of glyphosate and concerns about potential health effects for farmers and their families will raise the "index of concern" for glyphosate in future agricultural carcinogenic studies.

References

1. Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999;87:1375-1380.
2. Hardell L. Malignant lymphomas of the larynx to type and exposure to phenocyclic acids or alkylphenols. *Lancet* 1979;1:35-36.
3. Hardell L, Erikson M, Lerner P, Lundgren E. Malignant lymphomas and exposure to chemicals, especially organo-phosphorus, alkylphenols, and phenoxy acids: a case-control study. *Biol J Cancer* 1981;43:149-76.
4. Huse SK, Blair A, Helzlsouer TP, et al. Agricultural herbicide use and risk of lymphoma and soft tissue sarcoma. *JAMA* 1986;255:1111-1117.
5. Huse Zhan S, Weisenburger DD, Shih PA, et al. A case control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. *Epidemiology* 1991;1:149-156.
6. Environmental Protection Agency, An SAB Report: Assessment of potential 2,4-D carcinogenicity. Review of the epidemiological and other data on potential carcinogenesis of 2,4-D by the EMBRAP joint committee. EPA-SAB-ERC-94-001, Washington, DC, US EPA, 1994.
7. Mortimer GS. *Toxicological Epidemiology*. John Wiley & Sons, New York, 1985.
8. Rothman KJ, Greenland S. *Modern Epidemiology*. Second Edition. Lippincott-Raven, Philadelphia, 1998.

Mar
1999

Epidemiology:
Hardell study shows **230% increased** risk of NHL for glyphosate formulation.

Aug
2001

Monsanto:
Dr. Acquavella learns that Dr. Helen McDuffie plans to publish article showing NHL risk with glyphosate.



Apr
1999

Monsanto's Reaction:
Hardell study raises "index of concern."



Review of:
Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999; 87:1375-1380.
By:
John Acquavella, PhD and Donna Farmer, PhD
Monsanto Company, April 14, 1999

Executive Summary:
Hardell and Erikson conducted a case-control study to look for associations between reported pesticide use and non-Hodgkin's lymphoma (NHL). The study included 91 NHL cases and 741 controls. The measure of association in the study was the odds ratio (OR), a measure for estimates of the rate of disease risk in the case (NHL) relative to exposed and unexposed populations.
The authors reported statistically significant associations for NHL with reported use of non-herbicidal OR = 1.5 (reported use of any herbicide) OR = 1.9, and reported use of glyphosate-based herbicide versus acid OR = 2.76. The major limitations of this study were the reliance on reported pesticide use (no documented exposure) information, the small number of subjects who reported use of specific pesticides, the possibility of recall bias, the absence of accurate sources for herbicide use (approximately 45% of the pesticide use information), and the difficulty in controlling for potential confounding factors, given the small number of exposed subjects.

The authors also reported a moderately elevated OR of 2.3 for glyphosate. This OR was not statistically significant and was based on only four "exposed" cases and three "unexposed" controls. This finding needs to be evaluated in light of the limitations of the study, mentioned above, and the wealth of toxicologic information that has resulted in glyphosate being judged to be non-toxic and non-carcinogenic by the U.S. Environmental Protection Agency and the World Health Organization. Systematic error or biases seen in the most likely explanations for the findings reported for glyphosate in this study.
Hardell and Erikson conducted an epidemiologic study to look for associations between self-reported pesticide use and non-Hodgkin's lymphoma (NHL). The rationale for conducting this research was previous studies by the first author¹ and by investigators at the U.S. National Cancer Institute² which found associations between reported use of herbicidal agents (primarily 2,4-D and 4-VP) and NHL. The results of these studies were interpreted to be supportive by a special Science Advisory Panel convened in the early 1990s by the U.S. Environmental Protection Agency (EPA)³.

The present study presents new data about phenoxycarboxylic acids and other commonly used pesticides. Hence, it is review the methods and results of this recent study.
Study design
Hardell and Erikson employed a case-control design for their research. In case-control studies, subjects are selected on the basis of their disease status. There is the disease of interest in the cases (with NHL) or the disease-free, free study participants as the controls. Information about prospective risk factors are collected from cases and controls using similar methodology.
The controls in a case-control study provide an estimate of the exposure prevalence in the case (the prevalence of self-reported pesticide use) in the base population that gave rise to the cases and controls.
The exposed odds for the cases is then compared to the exposed odds for the controls. The resulting ratio

of the glyphosate biological study cited⁴ showed risk positive findings for acute chemical reactions in human lymphocytes in vitro. This study had many limitations and numerous, more specific, toxicologic studies have not shown positive results for glyphosate.⁵ Extensive reviews of the available toxicologic data have been completed recently by the U.S. Environmental Protection Agency⁶ (EPA) and the World Health Organization.⁷ These agencies concluded that glyphosate is not carcinogenic or mutagenic. EPA classified glyphosate as category II-7. This would represent the biological plausibility of the findings reported to Hardell and Erikson.

In conclusion, the study by Hardell and Erikson found a modest association between NHL and several chemical pesticides—most notably, for MCPA and the collective group of herbicides. The reported risk to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall over-reporting bias. It is clear, however, that the widespread use of glyphosate and concerns about potential related health effects for farmers and their families will raise the "index of concern" for glyphosate to those agricultural pesticide studies.

References

1. Hardell L, Erikson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999;87:1375-1380.
2. Hardell L. Malignant lymphoma of the testis: type and exposure to phenoxyacetic acids or alkylphenols. *Lancet* 1979;1:35-36.
3. Hardell L, Erikson M, Lerner P, Lundgren E. Malignant lymphomas and exposure to chemicals, especially organic solvents, alkylphenols, and phenoxy acids: a case-control study. *Biol J Cancer* 1981;43:149-70.
4. How SK, Blair A, Helzlsouer TP, et al. Agricultural herbicide use and risk of lymphoma and soft tissue sarcoma. *JAMA* 1996;276:1111-1117.
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6. Environmental Protection Agency. An SAB Report. Assessment of potential 2,4-D carcinogenicity. Review of the epidemiological and other data on potential carcinogenicity of 2,4-D in the RABBIT joint contract. EPA-SAB-ERC-94-001. Washington, DC: US EPA, 1994.
7. Miettinen OS. *Theoretical Epidemiology*. John Wiley & Sons, New York, 1985.
8. Rothman KJ. *Causal Inference: Modern Epidemiology*. Second Edition. Lippincott-Raven, Philadelphia, 1998.

risk of NHL including mecoprop, malathion, DDT, carbaryl, aldrin, and lindane. When the authors controlled for personal factors including antecedent cancer, family history of cancer, personal history of mesothelioma, and allergy/desensitization treatments, the only pesticide that was significantly related to NHL was mecoprop (a.k.a. MCPP 2-(4-chloro-2-methylphenoxy) propanoic acid).
Additional analyses found significant relationships for more than 2 days use/year for glyphosate (odds ratio 2.1, 95% CI 1.2-3.7) and mecoprop (odds ratio 2.1, 95% CI 1.2-3.6). The full range of confounding factors was not considered in these analyses, but one presumes that again only mecoprop would remain associated with NHL in a multivariate analysis.
Since the organizers of the ISEE meeting asked me to chair the pesticide session which included this paper, I had the opportunity to spend some time with the author. She struck me as a reasonable person, I was expecting [redacted] but Dr. McDuffie is [redacted] she doesn't seem to have any preconceived notions about glyphosate, she agreed to share her paper with me when it is ready for submission for publication. She also agreed to come and present her work to an industry audience (ACFA, us, etc.). I gave her a copy of the Gaitton glyphosate review and told her of our ongoing Farm Family Exposure Study (FFES). She was extremely interested in the FFES and asked to be kept informed of the results from this program. We obviously need to establish a relationship with Dr. McDuffie because her research program will be generating findings for the next few



analysis was to look for region relationships between pesticide use and NHL. The authors showed variable findings by province authors reported a significant British Columbia, but not elsewhere in Canada (see table). (note - As is typical with epidemiologists, only the British Columbia finding was included in the meeting abstract.)

significantly related to NHL was mecoprop (diethyl ester of (4-chloro-2-methylphenoxy) propanoic acid).

Additional analyses found significant relationships for more than 2 days use/year for glyphosate (odds ratio 2.1, 95% CI 1.2-3.7) and mecoprop (odds ratio 2.1, 95% CI 1.2-3.6). The full range of confounding factors was not considered in these analyses, but one presumes that again only mecoprop would remain associated with NHL in a multivariate analysis.

Since the organizers of the ISEE meeting asked me to chair the pesticide session which included this paper, I had the opportunity to spend some time with the author. She struck me as a reasonable person. I was expecting a [REDACTED] but Dr. McDuffee is [REDACTED]. She doesn't seem to have any preconceived notions about glyphosate. She agreed to share her paper with me when it is ready for submission for publication. She also agreed to come and present her work to an industry audience (ACPA, us,

etc.). I gave [REDACTED] told her of our [REDACTED] She was extremely [REDACTED] informed of the [REDACTED] to establish a [REDACTED] research program [REDACTED] years. The FFE [REDACTED] equitable share [REDACTED]



glyphosate review and [REDACTED] Study (FFES). [REDACTED] asked to be kept [REDACTED] We obviously need [REDACTED] because her [REDACTED] for the next few [REDACTED] is for an [REDACTED]

It remains to [REDACTED] eventual publication [REDACTED] up selectively [REDACTED] finding that [REDACTED] we need to be [REDACTED] information. I [REDACTED]

ated in the [REDACTED] whether anyone picks [REDACTED] glyphosate [REDACTED] abstract. Obviously, [REDACTED] limited [REDACTED] follow-up plans below.

Mar
1999

Epidemiology:
Hardell study shows **230% increased** risk of NHL for glyphosate formulation.

Aug
2001

Monsanto:
Dr. Acquavella learns that Dr. Helen McDuffie plans to publish article showing NHL risk with glyphosate.



Apr
1999

Monsanto's Reaction:
Hardell study raises "index of concern."



Review of:
Hardell L, Eriksson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999; 87:1375-1380.
By:
John Acquavella, PhD and Donna Farmer, PhD
Monsanto Company, April 14, 1999

Executive Summary:
Hardell and Eriksson conducted a case-control study to look for associations between reported pesticide use and non-Hodgkin's lymphoma (NHL). The study included 91 NHL cases and 741 controls. The measure of association in the study was the odds ratio (OR), a measure for estimates of the rate of disease risk in the case (NHL) relative to exposed and unexposed populations.

The authors reported statistically significant associations for NHL with reported use of herbicides (OR = 1.5) reported use of any pesticides (OR = 1.3), and reported use of glyphosate (OR = 2.3). The major limitations of this study were the reliance on reported pesticide use (no documented exposure), the small number of subjects who reported use of specific pesticides, the possibility of recall bias, the absence of accurate sources for herbicide use (approximately 45% of the pesticide use information), and the difficulty in controlling for potential confounding factors, given the small number of exposed subjects.

The authors also reported a moderately elevated OR (2.3) for glyphosate. This OR was not statistically significant and was based on only four "exposed" cases and three "unexposed" controls. This finding needs to be evaluated in light of the limitations of the study, mentioned above, and the wealth of toxicologic information that has resulted in glyphosate being judged to be non-toxic and non-carcinogenic by the U.S. Environmental Protection Agency and the World Health Organization. Significant error or omissions seen in the most likely explanations for the findings reported for glyphosate in this study.

Hardell and Eriksson conducted an epidemiologic study to look for associations between self-reported pesticide use and non-Hodgkin's lymphoma (NHL). The rationale for conducting this research was previous studies by the first author¹ and by investigators at the U.S. National Cancer Institute² which found associations between reported use of herbicides and NHL (primarily 2,4-D) and NHL. The results of these studies were acknowledged to be inconsistent by a special Science Advisory Panel convened in the early 1990s by the U.S. Environmental Protection Agency (EPA)³.

The present study presents new data about phenoxycarboxylic acids and other commonly used pesticides. Hence, it is review the methods and results of this recent study.

Study design

Hardell and Eriksson employed a case-control design for their research. In case-control studies, subjects are selected on the basis of their disease status. There is the disease of interest in the cases (with NHL) and the cases' disease free study participants as the controls. Information about prospective risk factors are collected from cases and controls using similar methodology.

The controls in a case-control study provide an estimate of the exposure prevalence in the case (the prevalence of self-reported pesticide use) in the base population that gave rise to the cases and controls.⁴ The exposure odds for the cases is then compared to the exposure odds for the controls. The resulting ratio

of herbicide use (odds) was not statistically in this study when the OR was adjusted to a physiological level.⁵ Also, EPA characterized the herbicide (glyphosate) study as "inconclusive" or "inconclusive of carcinogenicity"; "the three 'control' and identified herbicide in category I - no evidence for carcinogenicity in humans."⁶

The one glyphosate toxicology study cited⁷ showed risk-positive findings for acute chemical reactions in human lymphocytes in vitro. This study had many limitations and numerous, more specific, toxicologic studies have not shown positive results for glyphosate.⁸ Extensive reviews of the available toxicologic data have been completed recently by the U.S. Environmental Protection Agency⁹ (EPA) and the World Health Organization.¹⁰ These agencies concluded that glyphosate is not carcinogenic or mutagenic. EPA classified glyphosate as category II.¹¹ This would represent the biological plausibility of the findings reported to Hardell and Eriksson.

In conclusion, the study by Hardell and Eriksson found a modest association between NHL and self-reported pesticide use, mostly for MCPA and the collective group of herbicides. The reported risk to moderate associations for glyphosate are not statistically significant and could be due to chance or to recall overreporting bias. It is clear, however, that the widespread use of glyphosate and concerns about potential related health effects for farmers and their families will raise the "index of concern" for glyphosate to those agricultural pesticide studies.

References

1. Hardell L, Eriksson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. *Cancer* 1999;87:1375-1380.
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5. Hux Zhan S, Weisenburger DD, Shihbi PA, et al. A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. *Epidemiology* 1995;6:149-156.
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8. Rothman KJ. *Conceptual Epidemiology*. Second Edition. Lippincott-Raven, Philadelphia, 1998.



risk of NHL including mecoprop, malathion, DDT, carbaryl, aldrin, and lindane. When the authors controlled for personal factors including antecedent cancer, family history of cancer, personal history of mesothelioma, and allergy/desensitization treatments, the only pesticide that was significantly related to NHL was mecoprop (a.k.a. MCPP 2-(4-chloro-2-methylphenoxy) propanoic acid).

Additional analyses found significant relationships for more than 2 days use/year for glyphosate (odds ratio 2.1, 95% CI 1.2-3.7) and mecoprop (odds ratio 2.1, 95% CI 1.2-3.6). The full range of confounding factors was not considered in these analyses, but one presumes that again only mecoprop would remain associated with NHL in a multivariate analysis.

Since the organizers of the ISEE meeting asked me to chair the pesticide session which included this paper, I had the opportunity to spend some time with the author. She struck me as a reasonable person, I was expecting

but Dr. McDuffie is the doesn't seem to have any preconceived notions about glyphosate, she agreed to share her paper with me when it is ready for submission for publication. She also agreed to come and present her work to an industry audience (ACFA, us, etc.). I gave her a copy of the Gaitors glyphosate review and told her of our ongoing Farm Family Exposure Study (FFES). She was extremely interested in the FFES and asked to be kept informed of the results from this program. We obviously need to establish a relationship with Dr. McDuffie because her research program will be generating findings for the next few



analysis was to look for region relationships between pesticide use and NHL. The authors showed variable findings by province authors reported a significant British Columbia, but not elsewhere in Canada (see table). (note - As is typical with epidemiologists, only the British Columbia finding was included in the meeting abstract.)



British Journal of Cancer (1998) 77(11), 2048–2052
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Plaintiff Exhibit

0818

Nov
2001



Epidemiology:

McDuffie study shows
212% increased risk of NHL
when using Roundup more
than 2 days a year.

British Journal of Cancer (1998) 77(11), 2048–2052
© 1998 Cancer Research Campaign

Plaintiff Exhibit
0818

Nov
2001

Epidemiology:
McDuffie study shows
212% increased risk of NHL
when using Roundup more
than 2 days a year.

Nov
2001

Monsanto's Reaction:
Celebrate the fact that
glyphosate is not
mentioned in the abstract.



From: FARMER, DONNA R [AG/2001] [D=MONSANTO/OU=NA-1000-EL/OU=RECIPIENTS/OU=US0070]
Sent: 11/29/2001 2:07:23 PM
To: ACCIARIELLA, JOHN F [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=US0405]
CC: GOLDSTEIN, DANIEL A [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=527246]; ARMSTRONG, JARICE M [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=597137]; PEYDENS, WILLIAM F [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=249793]
Subject: RE: the McDuffie article about - glyphosate not mentioned in the abstract

John,

I know we don't know yet what it says in the "small print", ...but the fact that glyphosate is no longer mentioned in the abstract is a huge step forward - it removes it from being picked up by abstract searches!

Donna

-----Original Message-----
From: ACCIARIELLA, JOHN F [AG/2001]
Sent: Thursday, November 29, 2001 7:54 am
To: FARMER, DONNA R [AG/2001]
CC: GOLDSTEIN, DANIEL A [AG/2001]; AM
Subject: the McDuffie article re: glyphosate
Importance: High

The McDuffie article ap
journal Cancer Epidemic
abstract below). Unlike
International Society f
August 1999, Glyphosate
factor in the abstract.
what it says in "the small print".

John

Plaintiff Exhibit
0312

Donna

-----Original Message-----

From: ACQUAVELLA, JOHN F [AG/1000]
Sent: Thursday, November 29, 2001 7:54 AM
To: FARMER, DONNA R [AG/1000]
Cc: GOLDSTEIN, DANIEL A [AG/1000]; ARMSTRONG, JANICE M [AG/1000]; HEYDENS, WILLIAM F [AG/1000]
Subject: the McDuffee article appears - glyphosate not mentioned in the abstract
Importance: High

The McDuffee article appeared in the November issue of the journal *Cancer Epidemiology, Biomarkers, and Prevention* (see abstract below). Unlike the abstract presented at the International Society for Environmental Epidemiology meeting August 1999, Glyphosate is no longer mentioned as a risk factor in the abstract. I'll have to get the article and see what it says in "the small print."

John



Message

From: FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]
Sent: 11/29/2001 2:07:25 PM
To: ACQUAVELLA, JOHN F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=145465]
CC: GOLDSTEIN, DANIEL A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=527246]; ARMSTRONG, JANICE M [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=597137]; HEYDENS, WILLIAM F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]
Subject: RE: the McDuffee article appears - glyphosate not mentioned in the abstract

John,

I know we don't know yet what it says in the "small print" - but the fact that glyphosate is no longer mentioned in the abstract is a huge step forward - it removes it from being picked up by abstract searches!

Donna

-----Original Message-----

From: ACQUAVELLA, JOHN F [AG/1000]
Sent: Thursday, November 29, 2001 7:54 AM
To: FARMER, DONNA R [AG/1000]
Cc: GOLDSTEIN, DANIEL A [AG/1000]; ARMSTRONG, JANICE M [AG/1000]; HEYDENS, W
Subject: the McDuffee article appears - glyphosate not mentioned in the abstract
Importance: High



The McDuffee article appeared in the November
journal Cancer Epidemiology, Biomarkers, and Prevention (see

British Journal of Cancer (1998) 77(11), 2048–2052
© 1998 Cancer Research Campaign

Plaintiff Exhibit
0818

Nov
2001

Epidemiology:
McDuffie study shows
212% increased risk of NHL
when using Roundup more
than 2 days a year.

Nov
2001

Monsanto's Reaction:
Celebrate the fact that
glyphosate is not
mentioned in the abstract.



From: FARMER, DONNA R [AG/2001] [D=MONSANTO/OU=NA-1000-EL/OU=RECIPIENTS/OU=US0070]
Sent: 11/29/2001 2:07:23 PM
To: ACCIARIELLA, JOHN F [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=US0405]
CC: GOLDSTEIN, DANIEL A [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=527246]; ARMSTRONG, JARICE M [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=597137]; PEYDENS, WILLIAM F [AG/2001] [D=MONSANTO/OU=NA-1000-01/OU=RECIPIENTS/OU=249793]
Subject: RE: the McDuffie article about - glyphosate not mentioned in the abstract

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John

Plaintiff Exhibit
0312

British Journal of Cancer (1998) 77(11), 2048–2052
© 1998 Cancer Research Campaign

Plaintiff Exhibit
0818

Nov
2001

Epidemiology:
McDuffie study shows
212% increased risk of NHL
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May
2002

Epidemiology:
Another Hardell
study shows **306%
increased** risk of
NHL for Roundup.

Nov
2001

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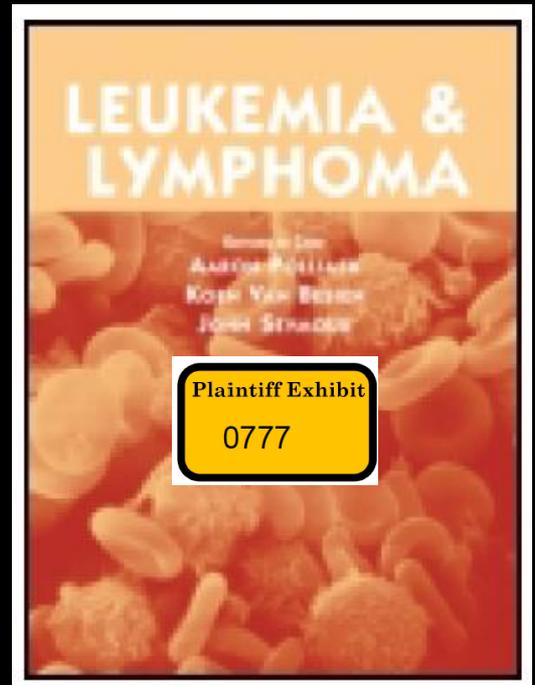
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50 **Williams GM**, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Regul Toxicol Pharmacol* 2000;**31**:117-65.

Glyphosate, commercially sold as Roundup, is a commonly used herbicide in the United States, both on crops and on non-cropland areas.¹⁰ An association of glyphosate with NHL was observed in another case-control study, but the estimate was based on only four exposed cases.¹¹ A recent study across a large region of Canada found an increased risk of NHL associated with glyphosate use that increased by the number of days used per year.¹² These few suggestive findings provide some impetus for further investigation into the potential health effects of glyphosate, even though one review concluded that the active ingredient is non-carcinogenic and non-genotoxic.¹³

Much attention in NHL research has focused on the herbicide 2,4-D as a potential risk factor and several studies have observed positive associations with 2,4-D exposure.¹⁴⁻¹⁶ Whereas an indicated effect of 2,4-D exposure on NHL was reported in NCI's Nebraska and Kansas studies,¹⁴ a meta-analysis of the pooled data found no association with 2,4-D.¹⁵ The null association does not result from confounding by other pesticides, missing data, or from

Plaintiff Exhibit
0710

Sept
2003

Monsanto's Reaction:
Dr. Acquavella warns that
the De Roos study could
add fuel to the fire.



Message

From: ACQUAVELLA, JOHN F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=145465]
Sent: 9/2/2003 2:29:00 PM
To: CABR, KATHERINE H [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=43435]; GOLDSTEIN, DANIEL A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=527246]; FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]; [REDACTED]
cc: [REDACTED] KRONENBERG, JOEL M [AG/1000]
[REDACTED] WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=1195231]; [REDACTED]
[REDACTED] HEYDENS, WILLIAM F [AG/1000]
[REDACTED] DANHAUS, ROY G [AG/1000]
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Plaintiff Exhibit
0482

See
20

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A [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=527246; FARMER, DONNA R [AG/1000]
L [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]; [REDACTED]
[REDACTED] KRONENBERG, JOEL M [AG/1000]
L [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=501517]
CC: V [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523]; [REDACTED]
[REDACTED] HEYDENS, WILLIAM F [AG/1000]
L [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]; DANHAUS, ROY G [AG/1000]
L [AG/1000] /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=218231]
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Plaintiff Exhibit
0482

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Jan
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Epidemiology:
De Roos publishes first
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Plaintiff Exhibit
0482

Plaintiff Exhibit

0758

Jul
2008

Epidemiology:

Eriksson study shows 202% increased risk of NHL for Roundup. Also shows 236% increased risk of NHL when used for more than 10 days a year.

Plaintiff Exhibit

0758

Jul
2008

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Eriksson study shows **202% increased** risk of NHL for Roundup. Also shows **236% increased** risk of NHL when used for more than 10 days a year.

Oct
2008

Monsanto's Reaction:
"How do we combat this?"



Epidemiology:

Message

From: FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]
Sent: 10/14/2008 6:31:44 PM
To: Nasser Dean [REDACTED]; Scott Kohne [REDACTED@bayercropscience.com]; Karen Ca
[REDACTED@bayercropscience.com]; GOUGH, GEORGE N [AG/1230] [/O=MONSANTO/OU=NA-1000-
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CC: McAllister, Ray [REDACTED@croplifeamerica.org]; MITCHELL, BRADLEY C [AG/1000] [/O=MONSANTO/C
01/CN=RECIPIENTS/CN=BCMITC1]
Subject: RE: Study Shows Herbicides Increase Risk of Non-Hodgkin's Lymphoma - Beyond Pesticides, October 14



Nassar,

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Here is their bottom line...how do we combat this?

Avoid carcinogenic herbicides in foods by supporting organic agriculture, and on lawns by using non-toxic land care strategies that rely on soil health, not toxic herbicides.

Regards,

Donna

Plaintiff Exhibit

0758

Jul
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Oct
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Plaintiff Exhibit
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International Journal of
**Environmental Research and
Public Health**

Plaintiff Exhibit
0861

Apr
2014

Epidemiology:
Schinasi & Leon meta analysis reveals Roundup **increases overall NHL risk by 150%.**

Oct
2008

Monsanto's Reaction:
"How do we combat this?"

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Regards,
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Plaintiff Exhibit
0513



Plaintiff Exhibit
0758

Jul
2008

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International Journal of
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Public Health**

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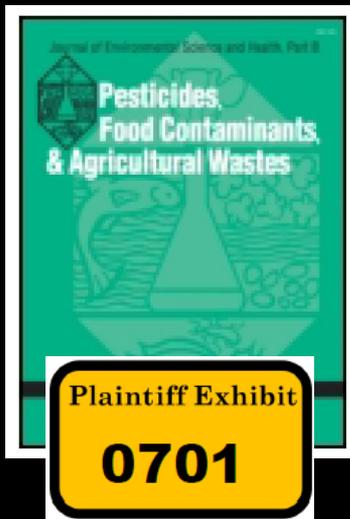
Plaintiff Exhibit
0513



Oct
2016

Epidemiology:

Monsanto-sponsored meta-analysis shows a **130% increased** risk of NHL from Roundup use.



Oct
201



	None	161	1.00 (reference)	
	Q1	136	0.87 (0.64 to 1.19)	
	Q2	126	0.88 (0.66 to 1.17)	
	Q3	137	0.93 (0.71 to 1.23)	
	Q4	144	1.00 (0.74 to 1.34)	.43
Hodgkin lymphoma				
	None	7	1.00 (reference)	
	M1	7	0.59 (0.17 to 2.11)	
	M2	11	0.90 (0.25 to 3.24)	.94
Non-Hodgkin lymphoma				
	None	135	1.00 (reference)	
	Q1	113	0.83 (0.59 to 1.18)	
	Q2	304	0.83 (0.61 to 1.12)	
	Q3	112	0.88 (0.65 to 1.19)	
	Q4	111	0.87 (0.64 to 1.20)	.95
Non-Hodgkin lymphoma B cell				
	None	128	1.00 (reference)	
	Q1	102	0.79 (0.55 to 1.13)	
	Q2	93	0.78 (0.56 to 1.05)	
	Q3	106	0.88 (0.64 to 1.21)	
	Q4	103	0.86 (0.62 to 1.19)	.86
Classic lymphocytic lymphoma, small lymphocytic leukemia				
	None	36	1.00 (reference)	
	Q1	28	0.75 (0.40 to 1.43)	
	Q2	26	0.76 (0.41 to 1.43)	
	Q3	26	0.90 (0.50 to 1.63)	
	Q4	27	0.87 (0.48 to 1.58)	.71
Diffuse large B cell lymphoma				
	None	37	1.00 (reference)	
	Q1	28	1.11 (0.60 to 2.07)	
	Q2	23	0.94 (0.49 to 1.80)	
	Q3	30	1.13 (0.59 to 2.17)	
	Q4	22	0.97 (0.51 to 1.85)	.83
Marginal-zone lymphoma				
	None	4	1.00 (reference)	
	M1	6	0.39 (0.06 to 2.45)	
	M2	5	0.44 (0.09 to 2.17)	.67
Follicular lymphoma				
	None	35	1.00 (reference)	

None	7	1.00 (reference)
M1	5	0.36 (0.09 to 1.43)
M2	11	0.82 (0.23 to 2.98)

*Cancer sites are listed and presented in order of surveillance, Epidemiology and End Results Site Record ID-D-3. CI = confidence interval; RR = rate ratio; Q1-Q4 = quartiles; Q1: 1-695.5; Q2: 199-1445.5; Q3: 1650-4319.5; Q4: >4940.5; T1: 1-896.24; T2: 896.25-2963.8; T3: >2964.0. Median; M1: 1-1649.0; M2: >1649.0. Poisson regression was used to model rate ratios and confidence intervals. P values were calculated using a two-sided Wald test. All models adjusted for age, state of residence, education, cigarette smoking status, six-month family history of cancer, stroke, alcohol, metabolic, reflux

Discussion

In this updated evaluation of glyphosate use and cancer risk in a large prospective study of pesticide applicators, we observed associations between glyphosate use and overall cancer risk with total lymphohematopoietic cancers, including NHL and multiple myeloma. However, there was some evidence of an increased risk of AML for applicators, particularly in the highest category of glyphosate exposure compared with newer users of glyphosate.

Like other hematological malignancies, AML is thought to result from multiple genetic and environmental factors. Occupational farming and general pesticide exposure have been linked to leukemia [13]. In 2007, a meta-analysis of occupational pesticide exposure found a statistically significant association with AML when restricting to cohort studies (meta RR = 1.55, 95% CI 1.02 to 2.34) [14], although specific chemicals were not evaluated. One case-control study that evaluated glyphosate use found no evidence of an association with leukemia overall based on reported cases and did not report results for AML. [15]. Similar to the previous AIE analysis, there was no association with AML overall based on 32 exposed cases, and AML was not statistically associated (5). To our knowledge, our study is the first to report a possible association between glyphosate use and AML.

Risk estimates were similar in magnitude between unlagged and lagged exposure analyses for all sites ev

Oct
201

	Q2	23	0.94 (0.49 to 1.80)	
	Q3	30	1.13 (0.59 to 2.17)	
	Q4	22	0.97 (0.51 to 1.85)	83
Marginal-zone lymphoma	None	4	1.00 (reference)	
	M1	6	0.39 (0.06 to 2.45)	
	M2	5	0.44 (0.09 to 2.17)	67
Follicular lymphoma	None	16	1.00 (reference)	
	T1	21	0.89 (0.37 to 2.15)	
	T2	11	0.61 (0.23 to 1.60)	
	T3	20	0.85 (0.36 to 2.03)	95
Multiple myeloma	None	30	1.00 (reference)	
	Q1	19	0.70 (0.36 to 1.36)	
	Q2	26	0.94 (0.50 to 1.76)	
	Q3	19	0.78 (0.39 to 1.56)	
	Q4	14	0.87 (0.45 to 1.69)	84
Non-Hodgkin lymphoma T cell	None	3	1.00 (reference)	
	M1	14	4.25 (0.73 to 24.54)	
	M2	6	1.53 (0.23 to 10.38)	31

425%

(continued)

evidence of an association with leukemia overall based on pooled cases and did not report results for AML. (15). Since the previous AIES analysis, there was no association with this overall based on 32 exposed cases, and AML was not noted (5). To our knowledge, our study is the first to report a possible association between glyphosate use and AML.

Risk estimates were similar in magnitude between unlagged and lagged exposure analyses for all sites except for AML, there were elevated risks in the highest exposure groups, and statistically significant or borderline significant of trend for unlagged and lagged analyses. The latent period between relevant exposure and AML diagnosis is unknown and may vary by type of exposure and population characteristics. Most studies of established AML risk factors, such as benzene, suggest a relatively short latency period (less than five years) (16), as do studies of therapy-induced AML (five to seven years) (17). Long-term studies of radiation-exposed populations reported elevated risks of AML up to 55 years after exposure (18).

The IARC Working Group noted strong evidence of genotoxicity and oxidative stress effects from glyphosate exposure. In particular, they highlighted two studies in communities exposed to glyphosate through aerial spraying that:



Plaintiff Exhibit
0701

Christine G. Parks, Michael G. Alavanja, Debra T. Silverman, Laura E. Beane Freeman

Abstract
Glyphosate is the most commonly used herbicide worldwide, with both residential and agricultural uses. In 2015, the International Agency for Research on Cancer classified glyphosate as "probably carcinogenic to humans," citing strong mechanistic evidence and positive associations for non-Hodgkin lymphoma (NHL) in some epidemiologic studies. A previous evaluation in the Agricultural Health Study (AHS) with follow-up through 2012, found no statistically significant associations with glyphosate use and cancer at any site.

Methods: The AHS is a prospective cohort of licensed pesticide applicators from North Carolina and Iowa. Here, we updated the previous evaluation of glyphosate with cancer incidence from registry linkage through 2012. Participants (N=107,666) were categorized into quartiles of glyphosate use based on self-reported application rates and application frequency (100-1000 and 100-1000 applications per year). We stratified incident rates and hazard ratios (HRs) into 10-year exposure intervals (20) and glyphosate exposure, controlling for potential confounders, including use of other pesticides. All statistical tests were two-sided.

Results: Among 44,205 applicators, 44,912 (102.0%) used glyphosate, including 1779 incident cancer cases (39.3% of all cases). In unlagged analyses, glyphosate use was statistically significantly associated with cancer at any site. However, among applicators in the highest exposure quartile, there was an increased risk of acute myeloid leukemia (AML) compared with nonusers (HR = 4.25, 95% CI = 0.73 to 24.54, $P_{trend} = .01$), though this association was not statistically significant. Results for AML were similar with a two-year (HR_{2-year} = 2.33, 95% CI = 0.34 to 15.1, $P_{trend} = .07$) and 10-year exposure lag (HR_{10-year} = 1.96, 95% CI = 0.30 to 12.0, $P_{trend} = .86$).

Conclusions: In this large, prospective cohort study, no association was apparent between glyphosate and any solid cancer or lymphoid leukemias after several, including 10, year lags. There was some evidence of increased risk of AML, among the highest exposed group that requires confirmation.

Glyphosate was evaluated as a broad spectrum herbicide in 1974, and it quickly became one of the most heavily used herbicide worldwide with the introduction of genetically engineered Roundup herbicide.

Plaintiff Exhibit
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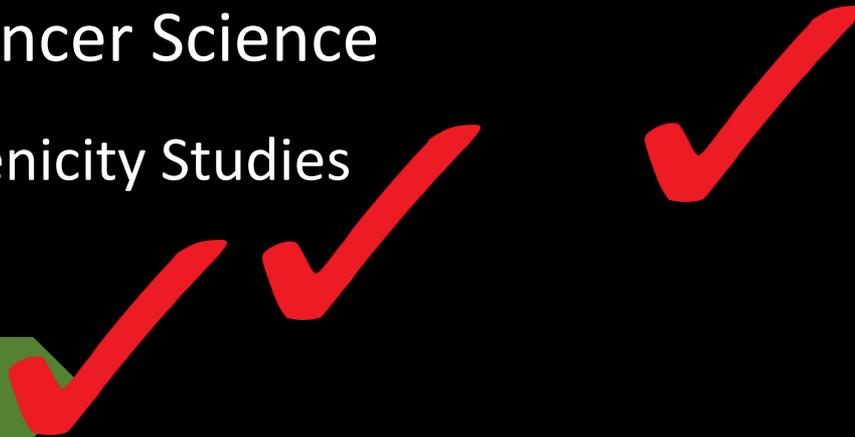
2. Can Roundup cause cancer?

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies

2. Mechanistic Data

3. Epidemiology



2. Can Roundup cause cancer?

International Agency Research on Cancer



World Health
Organization



2. Can Roundup cause cancer?



Message

From: HEYDENS, WILLIAM F [AG/1000] [REDACTED]@monsanto.com
Sent: 10/15/2014 9:08:37 PM
To: [REDACTED]@monsanto.com
CC: [REDACTED]@monsanto.com; SALTIRAS, DAVID A [AG/1000] [REDACTED]@monsanto.com; KOCH, MICHAEL S [AG/1000] [REDACTED]@monsanto.com
Subject: IARC Evaluation of Glyphosate

[REDACTED]

It is my recollection that you notified the EU-GTF of this IARC evaluation, but I am not aware that there has been any talk of approaching the GTF about providing funding to fight this because it is not considered in the remit of achieving Annex I renewal. If so, is this really the case? I thought the EU evaluation could go well into the summer of 2015, and wouldn't an adverse IARC evaluation have the real potential to impact the results of the Annex I renewal?

I really started thinking about this after our phone call yesterday with the outside epidemiology experts that Donna lined up. The bottom line of the call was that there really is no meaningful publication that we can complete prior to the February submission to positively impact the epidemiology discussion outcome in March. One has to consider that this situational timing did not happen by chance and that more than just pure bad luck is working against glyphosate.

And while we have vulnerability in the area of epidemiology, we also have potential vulnerabilities in the other areas that IARC will consider, namely, exposure, genotox, and mode of action (David has the animal onco studies under control). If there is a force working against glyphosate, there is ample fodder to string together to help the cause even though it is not scientifically justified in its purest form. Putting all this in the proper perspective will be quite resource intensive, so can't we consider approaching the GTF? Recall that the PAG already agreed to fund the onco publication 2+ years ago for this exact reason.

Thanks.

Bill

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[REDACTED]@monsanto.com; SALTMIRAS, DAVID A [AG/1000] [REDACTED]@monsanto.com; KOCH,
MICHAEL S [AG/1000] [REDACTED]@monsanto.com
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Thanks.

Bill



2. Can Roundup cause cancer?

- Leading world experts on cancer
- 17 scientists from the EPA, California EPA, and worldwide
- Over six months reviewing all peer-reviewed science on glyphosate
- Held a week-long meeting
- **Unanimous** vote

2. Can Roundup cause cancer?

Participants

- Members:
 - Aaron Blair, National Cancer Institute, USA (Overall Chair)
 - Charles W. Jameson, CWJ Consulting, LLA, USA
 - Matthew T. Martin, U.S. Environmental Protection Agency, USA
 - Lauren Zeise, California Environmental Protection Agency, USA
 - Matthew K. Ross, Mississippi State University, USA
- Invited Specialists
 - Christopher J. Portier, Agency for Toxic Substances and Disease Registry, USA
- Representatives of National and International Health Agencies
 - Jesudoss Rowland, U.S. Environmental Protection Agency, USA
- Observers
 - Thomas Sorahan, for Monsanto Company, USA
 - Patrice Sutton, for the University of California, San Francisco, Program on Reproductive Health and the Environment

2. Can Roundup cause cancer?

GLYPHOSATE

1. Exposure Data

1.1 Identification of the agent

1.1.1 Nomenclature

Chem. Abstr. Serv. Reg. No.: 1071-83-6 (acid);

also relevant:

38641-94-0 (glyphosate-isopropylamine salt)

40465-66-5 (monoammonium salt)

69254-40-6 (diammonium salt)

34494-03-6 (glyphosate-sodium)

81591-81-3 (glyphosate-trimesium)

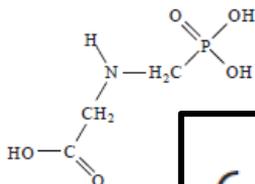
Chem. Abstr. Serv. Name: N-(phosphonomethyl)glycine

Preferred IUPAC Name: N-(phosphonomethyl)glycine

Synonyms: Glyphosate; glyphosate; glyphosate hydrochloride; glyphosate [calcium, copper (2+), dilithium, disodium, magnesium, monoammonium, monopotassium, monosodium, sodium, or zinc] salt

Trade names: Glyphosate products have been sold worldwide under numerous trade names, including: Abundit Extra; Credit; Xtreme; Glifonox; Glyphogan; Ground-Up; Rodeo; Roundup; Touchdown; Tragli; Wipe Out; Yerbimat ([Farm Chemicals International, 2015](#)).

1.1.2 Structural and molecular formulae and relative molecular mass



Molecular formula: C₃H₅O₄P

Relative molecular mass: 169.07

Additional information: Structure is also available in the PubChem database ([NCBI, 2015](#)).

1.1.3 Chemical and physical pure substance

Description: Glyphosate acid is a colourless, odourless, crystalline solid. It is formulated as a salt consisting of the deprotonated acid of glyphosate and a cation (isopropylamine, ammonium, or sodium), with more than one salt in some formulations.

Solubility: The acid is of medium solubility at 11.6 g/L in water (at 25 °C) and insoluble in common organic solvents such as acetone, ethanol, and xylene; the alkali-metal and

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
2. Mechanistic Data **Sufficient**

6.2 Cancer in experimental animals

There is *sufficient evidence* in experimental animals for the carcinogenicity of glyphosate.

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0784

2. Can Roundup cause cancer?

GLYPHOSATE

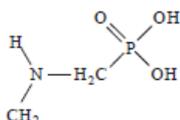
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1.1 Identification of the agent

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Chem. Abstr. Serv. Reg. No.: 1071-83-6 (acid);
also relevant:

1.1.2 Structural and molecular formulae and
relative molecular mass



Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
2. Mechanistic Data **Sufficient**

Sufficient evidence of carcinogenicity: The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide ***sufficient evidence***

Yerbimal ([Farm Chemicals International, 2015](#)).

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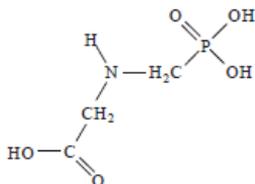
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Preferred IUPAC Name: N-(methyl)glycine

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1.1.2 Structural and molecular formulae and relative molecular mass



Molecular formula: C₃H₈NO₃P

Relative molecular mass: 169.07

Additional information on chemical structure is also available in the PubChem Compound

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies
2. Mechanistic Data **Sufficient**
3. Epidemiology **Strong**

Overall, the mechanistic data provide strong evidence for genotoxicity and oxidative stress. There is evidence that these effects can operate in humans.

ethanol, and xylene; the alkali-metal and

Plaintiff Exhibit

0784

2. Can Roundup cause cancer?

GLYPHOSATE

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1.1 Identification of the agent

1.1.1 Nomenclature

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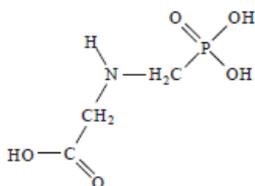
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1.1.3 Chemical and physical properties of the pure substance

Description: Glyphosate acid is a colour-

Three Pillars of Cancer Science

1. Animal Carcinogenicity Studies

2. Mechanistic Data **Sufficient**

3. Epidemiology **Strong**

Limited

Limited evidence of carcinogenicity: A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

2. Can Roundup cause cancer?

IARC Monographs on the Carcinogenic Risk to Humans, Volume 112: Some Organophosphate Insecticides and Herbicides, IARC, Lyon, France, 3-10 March 2015

March 2015:
IARC unanimously decides to list
glyphosate as a class 2A carcinogen – a
probable human carcinogen.

Plaintiff Exhibit
0182
Case No.
CGC-16-550128

2. Can Roundup cause cancer?

Monsanto's Response to IARC

STRATEGIES/TACTICS

PRE-IARC

1. Amplification of Scientific Studies

- Support the development of three new papers on glyphosate focused on epidemiology and toxicology
- Work with RPSA and Strategic Communications to amplify existing studies and new papers
 - Authors work directly with scientific journals to issue alerts and news releases on new bodies of work
 - RPSA posts blog from first-person viewpoint of Monsanto's David Saitmiras, co-author of one of the glyphosate cancer papers
 - Share resources and content with Monsanto key regions to amplify the message globally

2. Inform / Inoculate / Engage Industry Partners

- Develop a "toolkit" containing key information and resources
 - Identify any message shortcomings and address through updates to monsanto.com/glyphosate and through US and EU blog posts
- Work with RPSA, Stakeholder Outreach Team, Industry Affairs, Government Affairs, US Business, Global CE and Regulatory teams, etc. to engage industry partners
 - Tier 1: Crop Life International / European Crop Protection Association / GMO Answers / BIO – identify committees that are best to engage
 - Tier 2: Academics (AgBioChatter), Biofortified, Sense About Science, Genetic Literacy Project, Academics Review
 - Tier 3: Alert food companies via Stakeholder Engagement team (IFIC, GMA, CFI) for "inoculation strategy" to provide early education on glyphosate residue levels, describe science-based studies versus agenda-driven hypotheses
 - Tier 4: Inoculate key grower associations

3. Address New Allegations

- Respond quickly and publically to new pseudoscience cancer studies
- Identify / request third-party experts to blog, op/ed, tweet and/or link, repost, retweet, etc.

POST-IARC

4. Orchestrate Outcry with IARC Decision ~ March 10, 2015

- Industry conducts robust media / social media outreach on process and outcome
 - [Sense About Science?] leads industry response and provides platform for IARC observers and industry spokesperson
 - Joint Glyphosate Taskforce publishes press release, letter signed by leaders of each manufacturer in North America and Europe
 - Push opinion leader letter to key daily newspaper on day of IARC ruling with assistance of Potomac Group
- Monsanto responds with strong reactive statement
 - Distribute video and audio responses to IARC decision
 - Address media inquiries with company glyphosate spokesperson
 - Utilize Monsanto channels (web, FB, Twitter, blog, etc) to provide Monsanto POV
 - Corporate Engagement team packages industry and Monsanto responses, then distributes via email to ~20 most influential ag media outlets across print, radio and TV

5. Engage Regulatory Agencies

- Grower associations / growers write regulators with an appeal that they remain focused on the science, not the politically charged decision by IARC

Plaintiff Exhibit

0292

POST-IARC

4. Orchestrate Outcry with IARC Decision ~ March 10, 2015

- Industry conducts robust media / social media outreach on process and outcome
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 - CLI and other associations issue press releases
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February 23, 2015

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Plaintiff Exhibit

0292

2. Can Roundup cause cancer?

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Plaintiff Exhibit

0292

2. Can Roundup cause cancer?

Nearly 100 scientists from all over the world endorse IARC's assessment of glyphosate

Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)

Christopher J Portier,¹ Bruce K Armstrong,² Bruce C Baguley,³ Xaver Baur,⁴ Igor Belyaev,⁵ Robert Bellé,⁶ Fiorella Belpoggi,⁷ Annibale Biggeri,⁸ Maarten C Bosland,⁹ Paolo Bruzzi,¹⁰ Lygia Therese Budnik,¹¹ Merete D Bugge,¹² Kathleen Burns,¹³ Gloria M Calaf,¹⁴ David O Carpenter,¹⁵ Hillary M Carpenter,¹⁶ Lizbeth López-Carrillo,¹⁷ Richard Clapp,¹⁸ Pierluigi Cocco,¹⁹ Dario Consonni,²⁰ Pietro Comba,²¹ Elena Craft,²² Mohamed Aqiel Dalvie,²³ Devra Davis,²⁴ Paul A Demers,²⁵ Anneclaire J De Roos,²⁶ Jamie DeWitt,²⁷ Francesco Forastiere,²⁸ Jonathan H Freedman,²⁹ Lin Fritschj,³⁰ Caroline Gaus,³¹ Julia M Gohlke,³² Marcel Goldberg,³³ Eberhard Greiser,³⁴ Johnni Hansen,³⁵ Lennart Hardell,³⁶ Michael Hauptmann,³⁷ Wei Huang,³⁸ James Huff,³⁹ Margaret O James,⁴⁰ C W Jameson,⁴¹ Andreas Kortenkamp,⁴² Annette Kopp-Schneider,⁴³ Hans Kromhout,⁴⁴ Marcelo L Larramendy,⁴⁵ Philip J Landrigan,⁴⁶ Lawrence H Lash,⁴⁷ Dariusz Leszczynski,⁴⁸ Charles F Lyndh,⁴⁹ Corrado Magnani,⁵⁰ Daniele Mandrioli,⁵¹ Francis L Martin,⁵² Enzo Merler,⁵³ Paola Michelozzi,⁵⁴ Lucia Miligi,⁵⁵ Anthony B Miller,⁵⁶ Dario Mirabelli,⁵⁷ Franklin E Mirer,⁵⁸ Saloshni Naidoo,⁵⁹ Melissa J Perry,⁶⁰ Maria Grazia Petronio,⁶¹ Roberta Pirastu,⁶² Ralph J Portier,⁶³ Kenneth S Ramos,⁶⁴ Larry W Robertson,⁶⁵ Theresa Rodriguez,⁶⁶ Martin Rössli,⁶⁷ Matt K Ross,⁶⁸ Deodutta Roy,⁶⁹ Ivan Rusyn,⁷⁰ Paulo Saldiva,⁷¹ Jennifer Sass,⁷² Kai Savolainen,⁷³ Paul T J Scheepers,⁷⁴ Consolato Sergi,⁷⁵ Ellen K Silbergeld,⁷⁶ Martyn T Smith,⁷⁷ Bernard W Stewart,⁷⁸ Patrice Sutton,⁷⁹ Fabio Tateo,⁸⁰ Benedetto Terracini,⁸¹ Heinz W Thielmann,⁸² David B Thomas,⁸³ Harri Vainio,⁸⁴ John E Vena,⁸⁵ Paolo Vineis,⁸⁶ Elisabete Weiderpass,⁸⁷ Dennis D Weisenburger,⁸⁸ Tracey J Woodruff,⁸⁹ Takashi Yorifuji,⁹⁰ Il Je Yu,⁹¹ Paola Zambon,⁹² Hajo Zeeb,⁹³ Shu-Feng Zhou⁹⁴

The International Agency for Research on Cancer (IARC) Monographs Programme identifies chemicals, drugs, mixtures, occupational exposures, lifestyles and personal habits, and physical and biological

For numbered affiliations see end of article.

Correspondence to Dr Christopher J Portier, Environmental Health Consultant, Thun, CH-3200 Switzerland; cportier@

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agents that cause cancer in humans and has evaluated about 1000 agents since 1971. Monographs are written by ad hoc Working Groups (WGs) of international scientific experts over a period of about 12 months ending in an eight-day meeting. The WG evaluates all of the publicly available scientific information on each substance and, through a transparent and rigorous process,¹ decides on the scientific evidence

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supports that substance's potential to cause or not cause cancer in humans.

For Monograph 112,² 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate.³ The WG concluded that the data for glyphosate meet the criteria for classification as a *probable human carcinogen*.

The European Food Safety Authority (EFSA) is the primary agency of the European Union for risk assessments regarding food safety. In October 2015, EFSA reported⁴ on their evaluation of the Renewal Assessment Report⁵ (RAR) for glyphosate that was prepared by the Rapporteur Member State, the German Federal Institute for Risk Assessment (BfR). EFSA concluded that 'glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential'. Addendum 1 (the BfR Addendum) of the RAR⁶ discusses the scientific rationale for differing from the IARC WG conclusion.

Serious flaws in the scientific evaluation in the RAR incorrectly characterise the potential for a carcinogenic hazard from exposure to glyphosate. Since the RAR is the basis for the European Food Safety Agency (EFSA) conclusion,⁴ it is critical that these shortcomings are corrected.

THE HUMAN EVIDENCE

EFSA concluded 'that there is very limited evidence for an association between glyphosate-based formulations and non-Hodgkin lymphoma (NHL), overall inconclusive for a causal or clear associative relationship between glyphosate and cancer in human studies'. The BfR Addendum (p. ii) to the EFSA report explains that 'no consistent positive association was observed' and 'the most powerful study showed no effect'. The IARC WG concluded there is *limited evidence of carcinogenicity in humans* which means 'A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.'¹

The finding of *limited evidence* by the IARC WG was for NHL, based on high-quality case-control studies, which are

Plaintiff Exhibit
0293
Case No.
CGC-16-550128

Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)

Christopher J Portier,¹ Bruce K Armstrong,² Bruce C Baguley,³ Xaver Baur,⁴ Igor Belyaev,⁵ Robert Bellé,⁶ Fiorella Belpoggi,⁷ Annibale Biggeri,⁸ Maarten C Bosland,⁹ Paolo Bruzzi,¹⁰ Lygia Therese Budnik,¹¹ Merete D Bugge,¹² Kathleen Burns,¹³ Gloria M Calaf,¹⁴ David O Carpenter,¹⁵ Hillary M Carpenter,¹⁶ Lizbeth López-Carrillo,¹⁷ Richard Clapp,¹⁸ Pierluigi Cocco,¹⁹ Dario Consonni,²⁰ Pietro Comba,²¹ Elena Craft,²² Mohamed Aqiel Dalvie,²³ Devra Davis,²⁴ Paul A Demers,²⁵ Anneclaire J De Roos,²⁶ Jamie DeWitt,²⁷ Francesco Forastiere,²⁸ Jonathan H Freedman,²⁹ Lin Fritschi,³⁰ Caroline Gaus,³¹ Julia M Gohlke,³² Marcel Goldberg,³³ Eberhard Greiser,³⁴ Johnni Hansen,³⁵ Lennart Hardell,³⁶ Michael Hauptmann,³⁷ Wei Huang,³⁸ James Huff,³⁹ Margaret O James,⁴⁰ C W Jameson,⁴¹ Andreas Kortenkamp,⁴² Annette Kopp-Schneider,⁴³ Hans Kromhout,⁴⁴ Marcelo L Larramendy,⁴⁵ Philip J Landrigan,⁴⁶ Lawrence H Lash,⁴⁷ Robert M Luster,⁴⁸ Thomas M Maron,⁴⁹ G. Scott McEachern,⁵⁰

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 Dariusz Leszczynski,⁴⁸ Charles F Lynch,⁴⁹ Corrado Magnani,⁵⁰
 Daniele Mandrioli,⁵¹ Francis L Martin,⁵² Enzo Merler,⁵³
 Paola Michelozzi,⁵⁴ Lucia Miligi,⁵⁵ Anthony B Miller,⁵⁶
 Dario Mirabelli,⁵⁷ Franklin E Mirer,⁵⁸ Saloshni Naidoo,⁵⁹
 Melissa J Perry,⁶⁰ Maria Grazia Petronio,⁶¹ Roberta Pirastu,⁶²
 Ralph J Portier,⁶³ Kenneth S Ramos,⁶⁴ Larry W Robertson,⁶⁵
 Theresa Rodriguez,⁶⁶ Martin Röösli,⁶⁷ Matt K Ross,⁶⁸ Deodutta Roy,⁶⁹
 Ivan Rusyn,⁷⁰ Paulo Saldiva,⁷¹ Jennifer Sass,⁷² Kai Savolainen,⁷³
 Paul T J Scheepers,⁷⁴ Consolato Sergi,⁷⁵ Ellen K Silbergeld,⁷⁶
 Martyn T Smith,⁷⁷ Bernard W Stewart,⁷⁸ Patrice Sutton,⁷⁹
 Fabio Tateo,⁸⁰ Benedetto Terracini,⁸¹ Heinz W Thielmann,⁸²
 David B Thomas,⁸³ Harri Vainio,⁸⁴ John E Vena,⁸⁵ Paolo Vineis,⁸⁶
 Elisabete Weiderpass,⁸⁷ Dennis D Weisenburger,⁸⁸
 Tracey J Woodruff,⁸⁹ Takashi Yorifuji,⁹⁰ Il Je Yu,⁹¹ Paola Zambon,⁹²
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2. Can Roundup cause cancer?

Nearly 100 scientists from all over the world endorse IARC's assessment of glyphosate

Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)

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The most appropriate and scientifically based evaluation of the cancers reported in humans and laboratory animals as well as supportive mechanistic data is that glyphosate is a *probable human carcinogen*. On the basis of this conclusion and in the absence of evidence to the contrary, it is reasonable to conclude that glyphosate formulations should also be considered likely human carcinogens.

supports that substance's potential to cause or not cause cancer in humans.

For Monograph 112,² 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate.³ The WG concluded that the data for glyphosate meet the criteria for classification as a *probable human carcinogen*.

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2. Can Roundup cause cancer?



Known and Probable Human Carcinogens

In most cases, the ACS does not directly evaluate whether a certain substance or exposure causes cancer. Instead, the ACS looks to national and international organizations such as the NTP and IARC, whose mission is to evaluate environmental cancer risks based on evidence from laboratory and human research studies.

Plaintiff Exhibit

0306

2. Can Roundup cause cancer?



Glyphosate v. Roundup

No one tests "Roundup"

2. Can Roundup cause cancer?

Charles Benbrook, PhD.



- B.A. in Economics from Harvard University (1971) and Ph.D. in Agricultural Economics from the University of Wisconsin (1980).
- Former Staff Director of the Subcommittee on Department Operations, Research, and Foreign Agriculture (“DOFRA”) of the House Committee on Agriculture.
- Organized several DOFRA hearings on pesticide issues, and worked with Members of Congress in drafting potential changes in federal laws impacting the Environmental Protection Agency’s (“EPA”) Office of Pesticide Programs (“OPP”).

2. Can Roundup cause cancer?



1. The EPA does not test anything.
2. Vulnerable to political shifts.
3. EPA's "Scientific Advisory Panel" split.
4. EPA's Office of Research and Development disagrees.

Opening Statement Roadmap:

1. What is Roundup?

2. Can Roundup cause cancer?  **Yes.**

3. Did Roundup cause Mr. Johnson's cancer?

4. What are Mr. Johnson's damages?

5. Should Monsanto be punished for its conduct?

Opening Statement Roadmap:

1. What is Roundup?
2. Can Roundup cause cancer? **Yes.**
3. Did Roundup cause Mr. Johnson's cancer?
4. What are Mr. Johnson's damages?
5. Should Monsanto be punished for its conduct?

3. Did Roundup cause Mr. Johnson's cancer?

Chadi Nabhan, M.D.



- Board-Certified hematologist and medical oncologist specializing in Non-Hodgkin Lymphoma (“NHL”).
- Vice President and Chief Medical Officer of Cardinal Health Specialty Solutions.
- Former Medical Director of the Clinical Cancer Center at the University of Chicago.
- Treated thousands of lymphoma patients.



THE UNIVERSITY OF
CHICAGO

3. Did Roundup cause Mr. Johnson's cancer?

William Sawyer, PhD.



- Ph.D. in toxicology from Indiana University School of Medicine (1983).
- Diplomate of the American Board of Forensic Medicine with more than 28 years of experience in public health and forensic toxicology, including five years of governmental service.
- Former Assistant Professor (23 years) at the Department of Medicine, Upstate Medical University, Syracuse, New York.
- 14 years of experience as a licensed clinical and environmental laboratory director.



3. Did Roundup cause Mr. Johnson's cancer?

2012 – New Job at Benicia School District



3. Did Roundup cause Mr. Johnson's cancer?

Pest Management



3. Did Roundup cause Mr. Johnson's cancer?

The Label:

ATTENTION:
This specimen label is provided for general information only.

- This pesticide product may not yet be available or approved for sale or use in your area.
- It is your responsibility to follow all Federal, state and local laws and regulations regarding the use of pesticides.
- Before using any pesticide, be sure the intended use is approved in your state or locality.
- Your state or locality may require additional precautions and instructions for use of this product that are not included here.
- Monsanto does not guarantee the completeness or accuracy of this specimen label. The information found in this label may differ from the information found on the product label. You must have the EPA approved labeling with you at the time of use and must read and follow all label directions.
- You should not base any use of a similar product on the precautions, instructions for use or other information you find here.
- Always follow the precautions and instructions for use on the label of the pesticide you are using.

21225G1-13



Ranger
PRO[®] Herbicide

Complete Directions for Use

The complete broad-spectrum postemergence professional herbicide for industrial, turf and ornamental weed control.

EPA Reg. No. 524-517 2007-1

AVOID CONTACT OF HERBICIDE WITH FOLIAGE, GREEN STEMS, EXPOSED NON-WOODY ROOTS OR FRUIT OF CROPS, DESIRABLE PLANTS AND TREES, BECAUSE SEVERE INJURY OR DESTRUCTION IS LIKELY TO RESULT.

Read the entire label before using this product.
Use only according to label instructions.
It is a violation of Federal law to use this product in any manner inconsistent with its labeling.
Not all products recommended on this label are registered for use in California. Check the registration status of each product in California before using.
Read the "LIMIT OF WARRANTY AND LIABILITY" statement at the end of the label before buying or using. If terms are not acceptable, return at once unopened.
THIS IS AN END-USE PRODUCT. MONSANTO DOES NOT INTEND AND HAS NOT REGISTERED IT FOR REFORMULATION. SEE INDIVIDUAL CONTAINER LABEL FOR REPACKAGING LIMITATIONS.

1.0 INGREDIENTS

ACTIVE INGREDIENT:
*Glyphosate, N-(phosphonomethyl)glycine, 41.0%
in the form of its isopropylamine salt 59.0%
OTHER INGREDIENTS (including surfactant): 100.0%

*Contains 480 grams per liter or 4 pounds per U.S. gallon of the active ingredient glyphosate, in the form of its isopropylamine salt. Equivalent to 356 grams per liter or 3 pounds per U.S. gallon of the acid, glyphosate.
This product is protected by U.S. Patent Nos. 5,683,958; 5,703,015; 6,063,733; 6,121,199; 6,121,200. No license granted under any non-U.S. patent(s).

2.0 IMPORTANT PHONE NUMBERS

FOR PRODUCT INFORMATION OR ASSISTANCE
IN USING THIS PRODUCT,
CALL TOLL-FREE, 1-800-322-3111.
IN CASE OF AN EMERGENCY INVOLVING THIS PRODUCT,
OR FOR MEDICAL ASSISTANCE,
CALL COLLECT DAY OR NIGHT (314)-684-4000.

3.0 PRECAUTIONARY STATEMENTS

3.1 Hazards to Humans and Domestic Animals

Keep out of reach of children.
CAUTION!
CAUSES EYE IRRITATION.
Avoid contact with eyes or clothing.

FIRST AID: Call a poison control center or doctor for treatment advice.	
IF IN EYES	<ul style="list-style-type: none"> • Hold eye open and rinse slowly and gently with water for 15 - 20 minutes. • Remove contact lenses if present after the first 5 minutes then continue rinsing eye.

- Have the product container or label with you when calling a poison control center or doctor or going for treatment.
- You may also contact (314) 684-4000, collect day or night, for emergency medical treatment information.
- This product is identified as Ranger PRO[®] herbicide, EPA Registration No. 524-517.

DOMESTIC ANIMALS: This product is considered to be relatively nontoxic to dogs and other domestic animals; however, ingestion of this product or large amounts of freshly sprayed vegetation may result in temporary gastrointestinal irritation (vomiting, diarrhea, colic, etc.). If such symptoms are observed, provide the animal with plenty of fluids to prevent dehydration. Call a veterinarian if symptoms persist for more than 24 hours.

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 Personal Protective Equipment (PPE). If there are no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

When handlers use closed systems, enclosed cabs or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240 (d) (4-6)), 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. Then wash thoroughly and put on clean clothing.

3.2 Environmental Hazards

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwaters.

3.3 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 react 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.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in any manner inconsistent with its labeling. This product can only be used in accordance with the Directions for Use on this label or in separately published Monsanto Supplemental Labeling.

3. Did Roundup cause Mr. Johnson's cancer?

The Label:

Keep out of reach of children.

CAUTION!

CAUSES EYE IRRITATION.

Avoid contact with eyes or clothing.

FIRST AID: Call a poison control center or doctor for treatment advice.

IF IN EYES

- Hold eye open and rinse slowly and gently with water for 15 - 20 minutes.
- Remove contact lenses if present after the first 5 minutes then continue rinsing eye.

- Have the product container or label with you when calling a poison control center or doctor, or going for treatment.
- You may also contact (314) 694-4000, collect day or night, for emergency medical treatment information.
- This product is identified as **Ranger PRO® herbicide, EPA Registration No. 524-517.**

DOMESTIC ANIMALS: This product is considered to be relatively nontoxic to dogs and other domestic animals; however, ingestion of this product or large amounts of freshly sprayed vegetation may result in temporary gastrointestinal irritation (vomiting, diarrhea, colic, etc.). If such symptoms are observed, provide the animal with plenty of fluids to prevent dehydration. Call a veterinarian if symptoms persist for more than 24 hours.

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3. Did Round

The Label:

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3. Did Roundup cause Mr. Johnson's cancer?

Admission No. 13

Monsanto admits that it has never warned any consumer that Roundup could cause cancer

Admission No. 14

Monsanto admits that it has never warned Mr. Johnson that Roundup could cause cancer.

3. Did Roundup cause Mr. Johnson's cancer?

Personal Protection



3. Did Roundup cause Mr. Johnson's cancer?

Multiple Heavy Exposures Nov. 2014: Reports to Monsanto

Message

From: GOLDSTEIN, DANIEL A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=527246]
Sent: 11/11/2014 8:19:51 PM
To: BIEHL, PATRICIA M [AG-Contractor/1045] [/O=MONSANTO/OU=NA-1000-01/cn=Recipients/cn=208718]
Subject: RE: Ranger Pro Exposure

I will call him. The story is not making any sense to me at all.

Dan

From: BIEHL, PATRICIA M [AG-Contractor/1045]
Sent: Tuesday, November 11, 2014 2:12 PM
To: GOLDSTEIN, DANIEL A [AG/1000]
Subject: Ranger Pro Exposure



Spoke with Dewayne Johnson @ [REDACTED] and this is his story.

He told me he works for a school district in CA and about 9 months ago had a hose break on a large tank sprayer. This resulted in him becoming soaked to the skin on his face, neck and head with Ranger Pro. He said he was wearing a white exposure suit and it even went inside that. A few months after this incident he noticed a rash on his knee then on his face and later on the side of his head. He said he changed his laundry detergent, dryer sheets and used all creams available to him but nothing seemed to help. His entire body is covered in this now and doctors are saying it is skin cancer.

He is just trying to find out if it could all be related to such a large exposure to Ranger Pro since he stated his skin was always perfect until this happened. He is looking for answers.

Thanks in advance for your assistance.

Patricia Biehl
Product Support Specialist

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3. Did Roundup cause Mr. Johnson's cancer?

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Patricia Biehl
Product Support Specialist

3. Did Roundup cause Mr. Johnson's cancer?

Multiple Heavy Exposures Mar. 2015: Reports Problem Again

Message

From: Thompson, Joy [REDACTED]
Sent: 4/15/2015 7:04:57 PM
To: GRANETO, MATTHEW J [AG/1000] [REDACTED]
CC: GOLDSTEIN, DANIEL A [AG/1000] [REDACTED@m Monsanto.com]; NYANGULU, JAMES M [AG/8070] [REDACTED@m Monsanto.com]; THURSTON, RUTH M [AG/8070] [REDACTED@m Monsanto.com]; WHITE, ERIN [AG/1000] [REDACTED@m Monsanto.com]; SEIFERT-HIGGINS, SIMONE [AG/1000] [REDACTED@m Monsanto.com]; Weber, Julie [REDACTED@ssmhc.com]
Subject: March 2015 FIFRA 6(a)(2) Reports
Attachments: FIFRA March 2015.docx
Flag: Follow up

Good afternoon Matt,
Attached are the FIFRA 6(a)(2) Reports for the Monsanto Lawn & Garden and Monsanto Agricultural products for the month of March 2015.
Please call me at 314 [REDACTED] if you have any questions.

Thank you,
Joy Thompson RN, CSPI
Industry liaison
Missouri Poison Center



Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

Reporting Categories: H-A, H-B, H-C
Reporting Period: March 1, 2015 – March 31, 2015

Substance:	Ranger Pro Herbicide from Monsanto
Serial Number:	32283189
Date:	03/27/2015
Medical Outcome:	Major Effect H-B
EPA Reg. No.	524-517
Active Ingredients:	Glyphosate 41%
State:	California
History and Notes:	Caller states he has been using Ranger Pro as part of his job for 2 to 3 years. He has recently been diagnosed with cutaneous T cell lymphoma. He has concerns about continuing to use Roundup as part of his job and questions if Roundup could be a source of his cancer. As the call progressed, caller said that doctors are unsure as to how to treat his condition and they are not even sure if it is cancer. Caller states that he works with Ranger Pro using a 50 gallon tank and also using a backpack sprayer. He dilutes 10 ounces of the Roundup per gallon (3.0%) for the 50 gallon tank and 4 ounces of Roundup per gallon (1.25%) when using the backpack sprayer. He recalls having been exposed to Roundup twice in the past 2 to 3 years, both from the backpack leaking/malfunctioning. In one case, he was wearing personal protective equipment (PPE) but it soaked through the PPE and his clothing. Recently, he has had a swollen foot and the MD's cannot figure out what is going on. The caller's level of fear is rising over his continued use of Ranger Pro. He states he continues to get unexplained rashes and nodules over his body. MRPC discussed the product toxicity. The symptoms are not an expected response from the product. Advised MRPC is available, if the treating MD has any questions.

3. Did Roundup cause Mr. Johnson's cancer?

Message

From: Thompson, Joy [REDACTED]
Sent: 4/15/2015 7:04:57 PM
To: GRANETO, MATTHEW J [AG/1000]
CC: GOLDSTEIN, DANIEL A [AG/1000]
[REDACTED]@monsanto.com; ERIN [AG/1000] [REDACTED]@monsanto.com; [REDACTED]@monsanto.com]; Web
Subject: March 2015 FIFRA 6(a)(2) Reports
Attachments: FIFRA March 2015.docx
Flag: Follow up



JAMES M [AG/8070]
[REDACTED]@monsanto.com]; WHITE,
[REDACTED]

Good afternoon Matt,

Attached are the FIFRA 6(a)(2) Reports for the Monsanto Lawn & Garden and Monsanto Agricultural products for the month of March 2015.

Please call me at 314-[REDACTED] if you have any questions.

Thank you,

Joy Thompson RN, CSPI

Industry liaison

Missouri Poison Center

Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

Reporting Categories: H-A, H-B, H-C

Reporting Period: March 1, 2015 – March 31, 2015



Substance:	<u>Ranger Pro Herbicide from Monsanto</u>
Serial Number:	32283189
Date:	<u>03/27/2015</u>
Medical Outcome:	Major Effect H-B
EPA Reg. No.	524-517
Active Ingredients:	Glyphosate 41%
State:	California
History and Notes:	<p>Caller states he has been using Ranger Pro as part of his job for 2 to 3 years. He has recently been diagnosed with cutaneous T cell lymphoma. He has concerns about continuing to use Roundup as part of his job and questions if Roundup could be a source of his cancer. As the call progressed, caller said that doctors are unsure as to how to treat his condition and they are not even sure if it is cancer. Caller states that he works with Ranger Pro using a 50 gallon tank and also using a backpack sprayer. He dilutes 10 ounces of the Roundup per gallon (3.0%) for the 50 gallon tank and 4 ounces of Roundup per gallon (1.25%) when using the backpack sprayer. He recalls having been exposed to</p>

Date:	03/27/2015
Medical Outcome:	Major Effect H-B
EPA Reg. No.	524-517
Active Ingredients:	Glyphosate 41%
State:	California



History and Notes: Caller states he has been using Ranger Pro as part of his job for 2 to 3 years. He has recently been diagnosed with cutaneous T cell lymphoma. He has concerns about continuing to use Roundup as part of his job and questions if Roundup could be a source of his cancer. As the call progressed, caller said that doctors are unsure as to how to treat his condition and they are not even sure if it is cancer. Caller states that he works with Ranger Pro using a 50 gallon tank and also using a backpack sprayer. He dilutes 10 ounces of the Roundup per gallon (3.0%) for the 50 gallon tank and 4 ounces of Roundup per gallon (1.25%) when using the backpack sprayer. He recalls having been exposed to Roundup twice in the past 2 to 3 years, both from the backpack leaking/malfunctioning. In one case, he was wearing personal protective equipment (PPE) but it soaked through the PPE and his clothing. Recently, he has had a swollen foot and the MD's cannot figure out what is going on. The caller's level of fear is rising over his continued use of Ranger Pro. He states he continues to get unexplained rashes and nodules over his body. MRPC discussed the product toxicity. The symptoms are not an expected response from the product. Advised MRPC is available, if the treating MD has any questions.

3. Did Roundup cause Mr. Johnson's cancer?

Multiple Heavy Exposures 2015: Reports Problem Again

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From: Thompson, Joy [REDACTED]
Sent: 4/15/2015 7:04:57 PM
To: GRANETO, MATTHEW J [AG/1000] [REDACTED]
CC: GOLDSTEIN, DANIEL A [AG/1000] [REDACTED@m Monsanto.com]; NYANGULU, JAMES M [AG/8070] [REDACTED@m Monsanto.com]; THURSTON, RUTH M [AG/8070] [REDACTED@m Monsanto.com]; WHITE, ERIN [AG/1000] [REDACTED@m Monsanto.com]; SEIFERT-HIGGINS, SIMONE [AG/1000] [REDACTED@m Monsanto.com]; Weber, Julie [REDACTED@ssmhc.com]
Subject: March 2015 FIFRA 6(a)(2) Reports
Attachments: FIFRA March 2015.docx
Flag: Follow up

Good afternoon Matt,
Attached are the FIFRA 6(a)(2) Reports for the Monsanto Lawn & Garden and Monsanto Agricultural products for the month of March 2015.
Please call me at 314 [REDACTED] if you have any questions.

Thank you,
Joy Thompson RN, CSPI
Industry liaison
Missouri Poison Center



Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

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Reporting Period: March 1, 2015 – March 31, 2015

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3. Did Roundup cause Mr. Johnson's cancer?

While Mr. Johnson was waiting for a response from Monsanto, he continued to use Roundup and Ranger Pro for another spraying season.

His cancer got worse and worse.

Why?

Roundup can **promote** cancer.

3. Did Roundup cause Mr. Johnson's cancer?



3. Did Roundup cause Mr. Johnson's cancer?



3. Did Roundup cause Mr. Johnson's cancer?



3. Did Roundup cause Mr. Johnson's cancer?

Issues to Consider

1. Exposure
2. Latency
3. Other possible causes
4. Warning

Opening Statement Roadmap:

1. What is Roundup?

2. Can Roundup cause cancer?

Yes.

3. Did Roundup cause Mr. Johnson's cancer?

Yes.

4. What are Mr. Johnson's damages?

5. Should Monsanto be punished for its conduct?

Opening Statement Roadmap:

1. What is Roundup?
2. Can Roundup cause cancer? **Yes.**
3. Did Roundup cause Mr. Johnson's cancer? **Yes.**
4. What are Mr. Johnson's damages?
5. Should Monsanto be punished for its conduct?

4. What are Mr. Johnson's damages?

Compensatory Damages

- Economic damages
- Non-economic damages
 - physical pain



4. What are Mr. Johnson's damages?

Compensatory Damages

- Economic damages
- Non-economic damages
 - physical pain
 - mental suffering
 - loss of enjoyment of life



4. What are Mr. Johnson's damages?

Compensatory Damages

- Economic damages
- Non-economic damages
 - physical pain
 - mental suffering
 - loss of enjoyment of life
 - disfigurement
 - physical impairment



4. What are Mr. Johnson's damages?

Compensatory Damages

- Economic damages
- Non-economic damages
 - physical pain
 - mental suffering
 - loss of enjoyment of life
 - disfigurement
 - physical impairment
 - grief
 - anxiety
 - humiliation
 - emotional distress





Opening Statement Roadmap:

1. What is Roundup?
2. Can Roundup cause cancer? **Yes.**
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Net Worth:
\$6.6 Billion



5. Should Monsanto be punished for its conduct?

Message

From: FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=F
Sent: 9/21/2009 5:12:07 PM
To: COMBEST, JOHN C [AG/1000] [REDACTED]@Monsanto.com]
Subject: RE: Roundup article in Fremantle Herald

I didn't find anything on the Australian site either ...however take that is taken up it is glyphosate. It stops the synthesis of 3 amino proteins) and this "process" is also found in microbes and fungi.

5. How does Roundup work?

Roundup is taken up through the leaves and moves in the sap flow throughout the plant. It stops the production of proteins so that the plant starves. This process is found only in plants; Roundup has extremely low toxicity to humans and wildlife.

Or this - you cannot say that Roundup does not cause cancer..we have not done carcinogenicity studies with "Roundup".

2. Will Roundup harm my family or me?

Based on the results of short term and long term testing, it can be concluded that Roundup poses no danger to human health when used according to label directions. In long term exposure studies of animals, Roundup did not cause cancer, birth defects or adverse reproductive changes at dose levels far in excess of likely exposure.

I will follow up with the Monsanto folks who interface with Scotts...they are aware that Scotts does these things.

Donna



5. Should Monsanto be punished for its conduct?

1. Why did no one from Monsanto call Mr. Johnson back, even after IARC?
2. Why did Monsanto not send the Perry reports to the EPA and, instead, ghostwrite the Williams paper?
3. Why did Monsanto refuse to study the Roundup formulation, like Dr. Parry suggested 20 years ago?
4. Why did Monsanto feel the need to combat published articles raising concerns about the safety of Roundup?

5. Should Monsanto be punished for its conduct?

Dr. Kirk Azevedo
Sales Representative (former)

5. Should Monsanto be punished for its conduct?

Dr. Kirk Azevedo
Sales Representative (former)



5. Should Monsanto be punished for its conduct?

“We’re about making money, so get it straight.”



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Yes.

