

**PTO No. 94 Production:** Mr. Hardeman's draft Opening Statement slide deck.

By complying with this Court's PTO No. 94, Plaintiff is not waiving any attorney work product and/or attorney-client communication privileges. Further, this is not the final version of the slide deck displayed to the jury.

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## Overview of this case:



## Ed Hardeman v. Monsanto Corporation

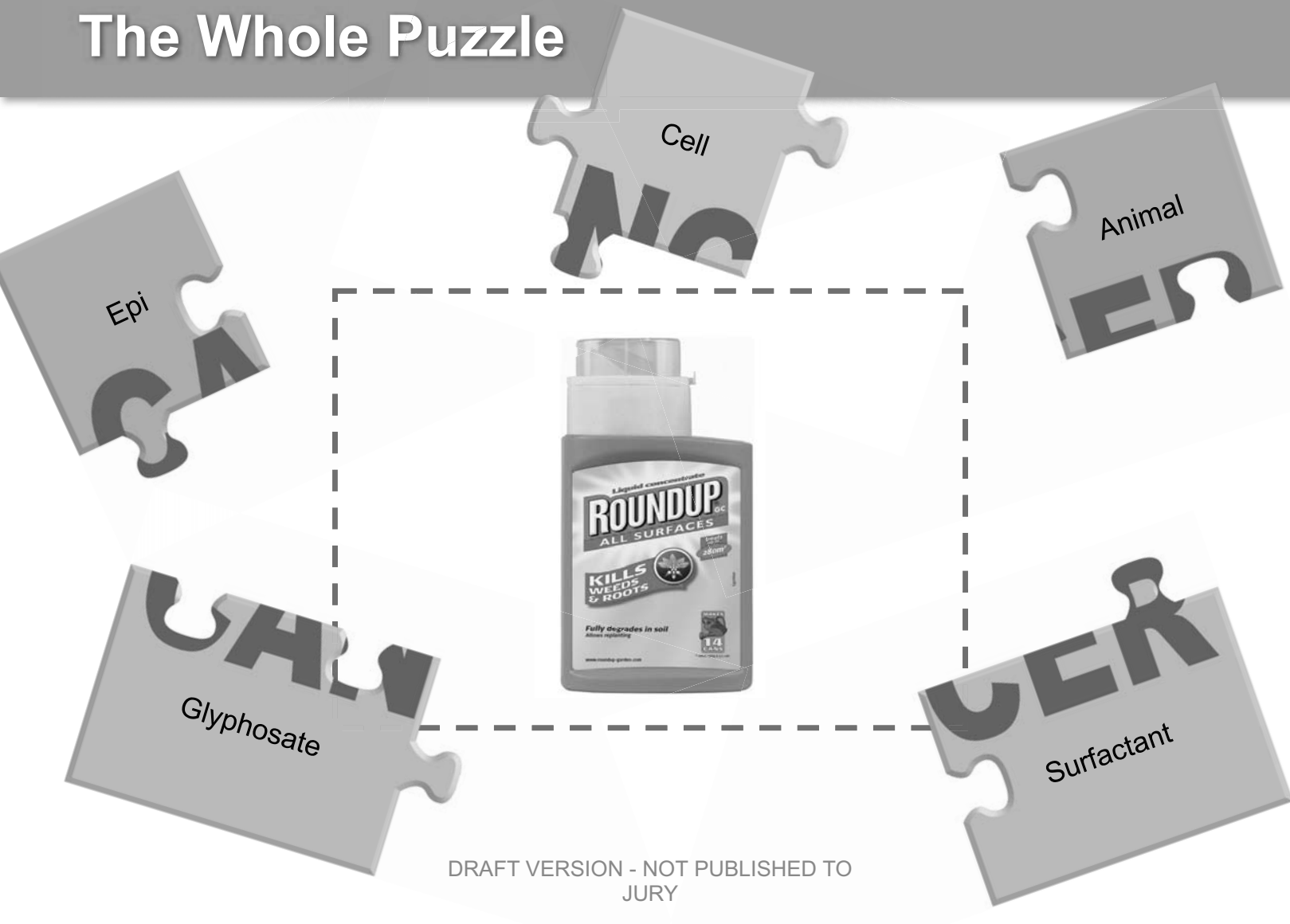
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## Ed Hardeman's cancerous tumors



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## The Whole Puzzle



## How the trial works:

### **Phase 1**

Was Mr. Hardeman's exposure to Roundup a substantial factor in causing his NHL?

### **Phase 2**

- What did Monsanto know, and when?
- Monsanto's conduct.
- Mr. Hardeman's damages.
- Should Monsanto be punished for its behavior?

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## How the Phase 1 trial works:

Opening statements

Plaintiff's case

Monsanto's case

Closing arguments

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## How the Phase 1 trial works:

Opening statements

Plaintiff's case

Monsanto's case

Closing arguments

Decide whether Mr. Hardeman's exposure to Roundup concentrate was a substantial factor in causing his non-Hodgkin's lymphoma.

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## Monsanto's current & former employees



**Dr. William Reeves**



**Dr. Daniel Goldstein**

**Monsanto's designated spokespeople**



**Dr. Donna Farmer**  
Lead Product Protections



**Any Live Witnesses?**  
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**Dr. David Saltmiras**  
Toxicology Director



## Opening Statement Roadmap Phase 1:

1. What is Roundup?
2. Can Roundup cause cancer?
3. Was Roundup exposure a substantial factor in causing Mr. Hardeman's cancer?

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## Opening Statement Roadmap Phase 1:

1. What is Roundup?
2. Can Roundup cause cancer?
3. Was Roundup exposure a substantial factor in causing Mr. Hardeman's cancer?

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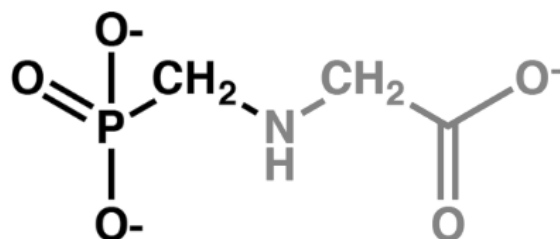
## 1. What is Roundup?



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## 1. What is Roundup?

### Glyphosate



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1. What is Roundup?

# Surfactant

## ACTIVE INGREDIENT:

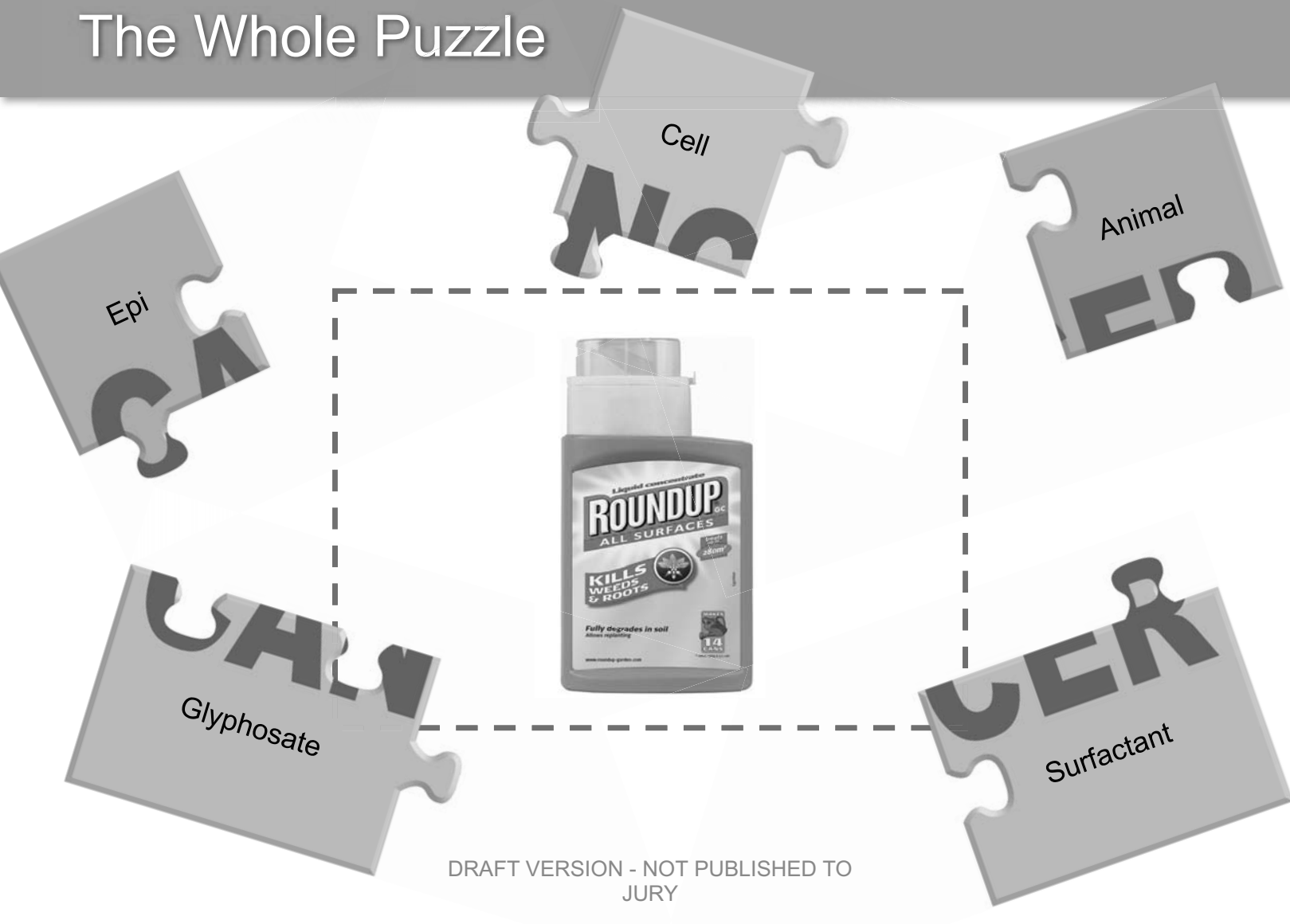
\*Glyphosate, N-(phosphonomethyl)glycine,  
in the form of its isopropylamine salt..... 41.00%

OTHER INGREDIENTS (including surfactant): ..... 58.99%  
100.0%

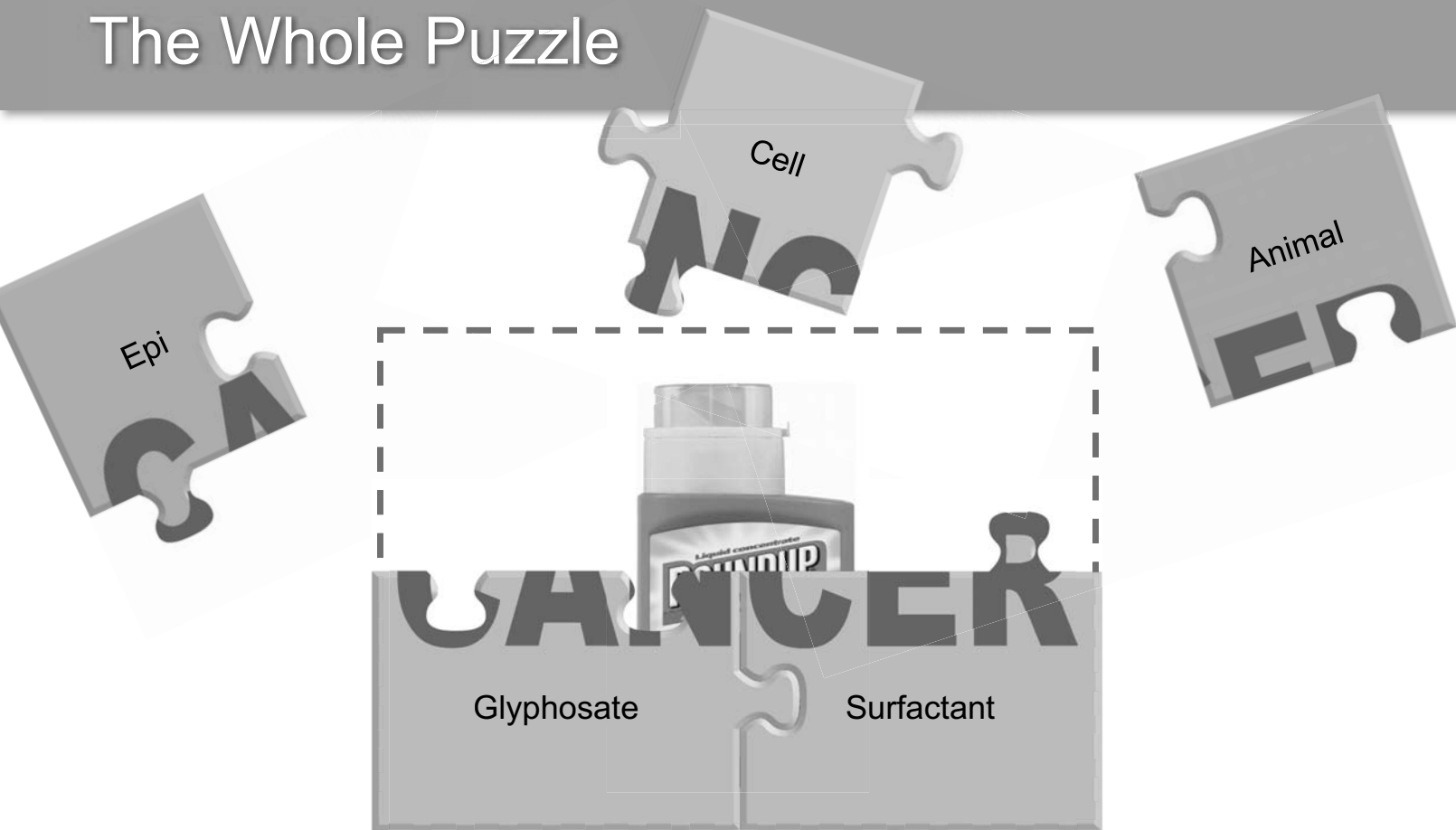
POlyEthoxylated tallow Amine (POEA)

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# The Whole Puzzle



## The Whole Puzzle



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## Opening Statement Roadmap Phase 1:

1. What is Roundup?
2. Can Roundup cause cancer?
3. Was Roundup exposure a substantial factor in causing Mr. Hardeman's cancer?

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## 2. Can Roundup cause cancer?

# Three Pillars of Cancer Science

Epidemiology studies



Animal studies



Cell data studies



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## Plaintiff's Experts: Beate Ritz, MD, Ph.D.



Professor, Departments of Epidemiology, Environmental Health, School of Public Health, and Neurology, School of Medicine, UCLA at University of California Los Angeles; Chairman of Epidemiology Department 2012-2015



- President of the International Society of Environmental Epidemiology (ISEE)
- MD after 6 years of medical school in Germany (1977-1983); M.P.H. in Epidemiology (1993) from UCLA; Ph.D. in Epidemiology (1995) from UCLA
- Chair (since 2005) and Member (since 2001) of the external advisory committee for the NCI/NIEHS Agricultural Cohort Study

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## Plaintiff's Experts: Christopher Portier, Ph.D.



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)

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## Plaintiff's Experts: Dr. Weisenburger, M.D.



**Professor and Chairman**, Department of Pathology, City of Hope Medical Center, Duarte, California



- Medical Pathologist with M.D. from University of Minnesota (1974)
- Current Notable Assignments, City of Hope Medical Center: Committee of Chairs, Medical Group Board of Directors; Cancer Center Leadership Council; Lymphoma Center Investigative Committee
- Published over 434 Peer Reviewed literature; over 613 published abstracts, and 37 book chapters

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## 2. Can Roundup cause cancer?

# Three Pillars of Cancer Science

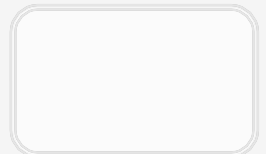
Epidemiology studies



Animal studies



Cell data studies



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## 2. Can Roundup cause cancer?

### Epidemiology studies

## **non-Hodgkin lymphoma (NHL):**

A rare disease; a blood cancer

## 2. Can Roundup cause cancer?

### NHL Epidemiology studies

## **NHL Epidemiology:**

A method to study the risk of developing NHL in humans

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## Human Epidemiological Studies

Study	Type	Size	Findings	Exposed Cases
Swedish Case-Control Study ( <i>Hardell et al., 1999</i> )	Population based case-control study	404 case, 741 control (limited power)		4 NR
Cross-Canada ( <i>McDuffie et al, 2001</i> )	Population-based case control study	517 cases, 1506 controls		51 28 23
Swedish Case-Control Study ( <i>Hardell et al., 2002</i> )	Population-based case-control study	515 cases, 1141 controls		8 8
US Midwest ( <i>De Roos et al., 2003</i> )	Pooled analysis 3 case-control studies	NHL: 650 cases, 1933 controls		36 36
Swedish Case-Control Study ( <i>Eriksson et al., 2008</i> )	Population-based case-control study	910 cases, 1016 control		29 29 12 17
France Case-Control ( <i>Orsi et al, 2009</i> )	Hospital-based case-control study	244 cases, 456 controls		12
North American Pooled Project (Frequency, U – August 31, 2015 Sao Paulo, Brazil) (Frequency, A - June 3, 2015 Ontario, Canada)	Pooled analysis 2 case-control studies (De Roos, McDuffie)	1690 cases, 5131 controls		113
Agricultural Health Study ( <i>De Roos et al., 2005</i> )	Cohort – licensed pesticide applicators	52 395 (+32 347 spouses), 92 cases, 4-8 years follow up		73
Agricultural Health Study ( <i>Andreotti et al., 2018</i> )	Cohort – licensed pesticide applicators	54 251 applicators, 575 cases		440

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A – adjusted for other pesticides as potential confounders



## 2. Can Roundup cause cancer?

### Epidemiology studies

#### **DOSE RESPONSE**

**The risk of getting NHL  
increases the more you use  
Roundup.**

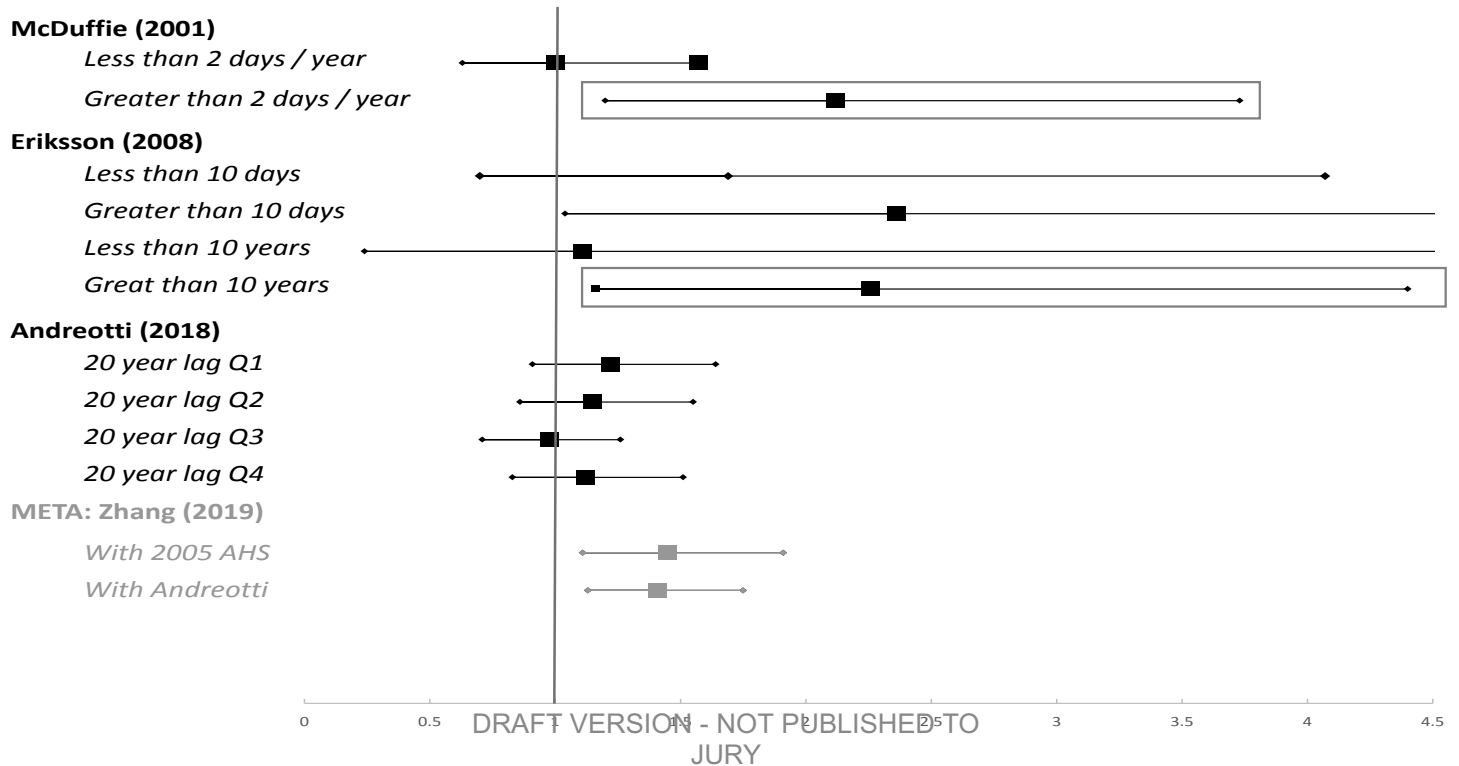
“The Dose Makes the Poison”

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## 2. Can Roundup cause cancer?

### Epidemiology studies

#### Plot Summary of NHL risk – dose response



# Non-Hodgkin's Lymphoma and Specific Pesticide Exposures in Men: Cross-Canada Study of Pesticides and Health<sup>1</sup>

Helen H. McDuffie,<sup>2</sup> Punam Pahwa,  
John R. McLaughlin, John J. Spinelli, Shirley Fincham,  
James A. Dosman, Diane Robson, Leo F. Skinner,  
Norman W. Choi<sup>3</sup>

John R. McLaugham, Diane Robson,  
Thomas A. Dosman, Diane Robinson,  
Norman W. Chan

Centre for Agricultural Medicine [H.H.M., P.P., J.A.D.], National Cancer Institute  
Saskatchewan, 578 University of Saskatchewan, Saskatoon, Ontario, M5S  
Saskatchewan, Epidemiology Unit, University of Toronto, Toronto, Ontario, M5S  
1A8 (P.C.), British Columbia, V6Z 1Y6 (J.S.), Alberta Cancer  
1483 (J.P.), Vancouver, British Columbia, Vancouver, British Columbia, V6Z 1Y6 (J.S.),  
Health Division, Epidemiology, Prevention and Screening, Edmonton, Alberta,  
Alberta, T6Z 1Z2 (J.P.), Saskatchewan Cancer Agency, Edmonton, Alberta,  
Centre, 578 University of Saskatchewan, Saskatoon, Saskatchewan, S7N 0W1 (D.R.),  
University of Saskatchewan, Saskatoon, Saskatchewan, S7N 0W1 (D.R.),  
and Manitoba Cancer Treatment and Research Foundation, Winnipeg,  
Manitoba, R3E 0V9 (N.W.C.).

**Abstract** Our objective in the study was to investigate the putative associations of specific pesticides with non-Hodgkin's Lymphoma [NHL; International Classification of Diseases, version 9 (ICD-9) 200, 202]. We conducted a Canadian multicenter population-based incident, case (n = 517)-control (n = 1506) study among men in a telephone interview for those diversity of occupations using an initial postal questionnaire followed by a telephone interview for those reporting pesticide exposure of 10 h/year or more, and a 15% random sample of the remainder. Adjusted odds ratios (ORs) were computed using conditional logistic regression stratified by the matching variables of age and province of residence, and subsequently adjusted for statistically significant medical variables (history for measles, mumps, cancer, allergy desensitization treatment, and a positive history of cancer in first-degree relatives). We found that among major chemical classes of herbicides, the risk of NHL was statistically significantly increased by exposure to phenoxyherbicides to dicamba (OR, 1.88; 95% CI, 1.32-2.68). Exposure to organophosphorus insecticides (OR, 1.73; 95% CI, 1.27-2.36), amide fungicides, and the fungitant carbon tetrachloride (OR, 2.42; 95% CI, 1.19-5.14) statistically significantly increased risk. Among individual

compounds, in multivariate analyses, the risk of NHL was statistically significantly increased by exposure to the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D; OR, 1.32; 95% CI, 1.01-1.73), mecoprop (OR, 2.33; 95% CI, 1.32-3.44), and dicamba (OR, 1.68; 95% CI, 1.00-2.81), to the insecticides malathion (OR, 1.83; 95% CI, 1.31-2.55), 1,1,1-trichloro-2,2-bis (4-chlorophenyl) ethane (DDT), carbaryl (OR, 2.11; 95% CI, 1.21-3.69), aldrin, and lindane; and to the fungicides captan and sulfur compounds. In additional multivariate models, which included exposure to other major chemical classes or individual pesticides, personal antecedent cancer history of cancer among first-degree relatives, exposure to mixtures containing dicamba (OR, 1.49-2.75) or to mecoprop (OR, 3.42; 95% CI, 1.18-1.20) and to aldrin (OR, 3.42; 95% CI, 1.18-1.20) whereas a personal history of an insignificant independent risk of cancer was not significant for NHL, whereas a personal history of an allergy desensitization treatments lowered the risk of NHL. We concluded that NHL was associated with pesticides after adjustment for other indoor predictors.

[illegible]

**Materials and Methods**

**Study Population.** We conducted a population-based case-control study among men resident in six Canadian provinces to

<sup>1</sup> This research was funded by Health Canada Grant 6608-1258, the British Columbia Health Research Foundation, and the Centre for Agricultural Medicine, Saskatoon, Saskatchewan. Correspondence should be addressed to, Centre for Agricultural Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0. Tel: (306) 966-8799.

<sup>2</sup> To whom requests for reprints should be addressed, at Centre for Hospital, Saskatchewan University of Saskatchewan.  
Hospital Drive, P. O. Box 120, Royal University Hospital, Saskatoon, Saskatchewan, Canada S4N 0W8. Phone: (306) 966-6154. Fax: (306) 966-8799.

Received 12/20/00; revised 8/13/01; accepted 8/22/01.  
The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

<sup>3</sup> Dr. Choi was a collaborator who is now deceased.

<sup>4</sup> The abbreviations used are: NHL, non-Hodgkin's lymphoma; DDT, 1,1,1-trichloro-2,2,2-tris (4-chlorophenyl) ethane; STS, soft tissue sarcoma; HD, hairy-cell leukemia; MOPP, mechlorethamine, vincristine, procarbazine, and prednisone; MCHL-2, 2-chloro-4-methylphenoxycetic acid; 2,4-D, 2,4-dichlorophenoxycetic acid; MCPA, 4-chloro-2-methylphenoxycetic acid; 2,4,5-T, 2,4,5-trichlorophenoxycetic acid; OR, odds ratio; OR<sub>adj</sub>, adjusted OR; 95% CI, 95% confidence interval.

© 2001 American Association for Cancer Research

# McDuffie

Nov. 2001

Study shows  
**212% increased risk**  
of NHL when using Roundup  
more than 2 days a year  
**Dose Response**

# Epidemiology studies

Eriksson  
July 2008

Eriksson study shows 202% increased risk of getting NHL when exposed to Roundup  
Also shows 236% increased risk of NHL when used for more than 10 days a year  
Dose Response  
10 year after first exposure – 226% increase

123, 1657-1663 (2008)  
Wiley-Liss, Inc.  
Pesticide exposure as risk factor for non-Hodgkin lymphoma including  
pathological subgroup analysis

El Eriksson<sup>1\*</sup>, Lennart Hardell<sup>2</sup>, Michael Carlberg<sup>2</sup> and Måns Åkerman<sup>3</sup>  
<sup>1</sup>Department of Oncology, University Hospital, Lund, Sweden  
<sup>2</sup>Department of Oncology, University Hospital, Örebro, Sweden  
<sup>3</sup>Department of Pathology, University Hospital, Lund, Sweden

We report a population based case-control study of exposure to pesticides as risk factor for non-Hodgkin lymphoma (NHL). Male and female subjects aged 18-74 years living in Sweden were included during December 1, 1999, to April 30, 2002. Controls were selected from the national population registry. Exposures to different agents was assessed by questionnaire. In total 910 (91%) cases and 1016 (92%) controls participated. Exposure to herbicides gave odds ratio (OR) 1.72, 95% confidence interval (CI) 1.18-2.51. Regarding phenylacetate herbicides highest risk was calculated for MCPA; OR 2.81, 95% CI 1.27-6.22, all these cases had a latency period >10 years. Exposure to glyphosate gave OR 2.26, 95% CI 1.16-4.40. Insecticides gave OR 1.28, 95% CI 0.96-1.72 and impregnating agents gave OR 1.57, 95% CI 1.07-2.30. Results are also presented for different entities of NHL. In conclusion our study confirmed an association between exposure to phenylacetate acids and NHL and the association with glyphosate was considerably strengthened.

Key words: phenylacetate acids; MCPA; glyphosate; insecticides; impregnating agents; non-Hodgkin lymphoma

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of lymphoid malignancies, where new classification systems based on immunohistochemistry, cytogenetics and evolving classification in clinical presentation and course has led to modern classification systems.<sup>1</sup> Today, it is therefore more adequate to discuss NHL as many different diseases, which share some features but also differ in several aspects.

Interest in the etiology of NHL has been strengthened by an observed substantial increase in the incidence of the disease from the 1960's to the 1980's as reported from most countries with reliable cancer registries. However, this increase has clearly leveled off in many countries since the early 1990's, i.e., in Sweden, Denmark and the USA.<sup>2</sup> The established risk factors for development of NHL include different immunosuppressive states, e.g., human immunodeficiency virus (HIV), autoimmune diseases as Sjögren's syndrome and systemic lupus erythematosus (SLE), immunodeficiency after organ transplantation and some inherited immunodeficiency states (e.g., Ref. 3). However, these causes may explain a minority of cases, with a possible exception for HIV-related increases among younger persons in certain areas.

It has been shown that Epstein-Barr virus (EBV) plays an essential role in the pathogenesis of lymphomas after organ transplantation.<sup>4</sup> A relation between lymphoma and elevated EBV-titers has been reported in a cohort.<sup>5</sup> Normally, EBV-production is held back by active cellular and humoral immune mechanisms. In immunodeficiency states this balance is disrupted and EBV-infected B-cells begin to proliferate.

During the last decades, research on the etiology of NHL has been directed towards other potential causes such as pesticides, which may explain the impressive increase in the incidence. Today, it is also reasonable to consider the leveling off in incidence as a probable consequence of a reduced carcinogenic influence related to NHL. Furthermore, our emerging knowledge concerning the spectrum of NHL subgroups makes it reasonable to investigate causative agents for these different types of disease.

for NHL and Hodgkin lymphoma (HL) in persons who had been exposed to phenylacetate herbicides or impregnating chlorophenols.<sup>6</sup> Our study was initiated by a case report.<sup>7</sup> Some of these chemicals were contaminated by dioxins, of which 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) has been recognized as a complete carcinogen by IARC.<sup>8</sup> Furthermore, these and several other related chemicals are immunotoxic.<sup>9-11</sup> Our results have been confirmed in some other studies, regarding phenylacetate herbicides from e.g., Kansas<sup>12</sup> and Nebraska<sup>13</sup>

Furthermore, in 1999 we reported on a case-control study of exposure to pesticides, where we evaluated more recent chemicals, and we could therefore not find a relation with pesticides regarding latency period.<sup>14</sup>

In that study, however, some of the chemicals used today, such as the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and the insecticide dichlorodiphenyl ether (DDT), were prohibited due to health concerns. Reporting of these chemicals in Sweden is less likely. It is also probable that protective measures have been taken to further evaluate the use of these chemicals, focus on other chemicals, and we have performed a new study we have also different histopathological classification.<sup>15</sup>

## Material and methods

The study covered 4 years, from 1999 to 2002, and was associated with the 1999-2002 Swedish Cancer Registry. Data were collected from the Swedish Cancer Registry, which was the time when the recruitment of cases was completed with another research parallel study on NHL.

## Cases

All consecutive newly diagnosed NHL, identified through pathology, were included in the study.

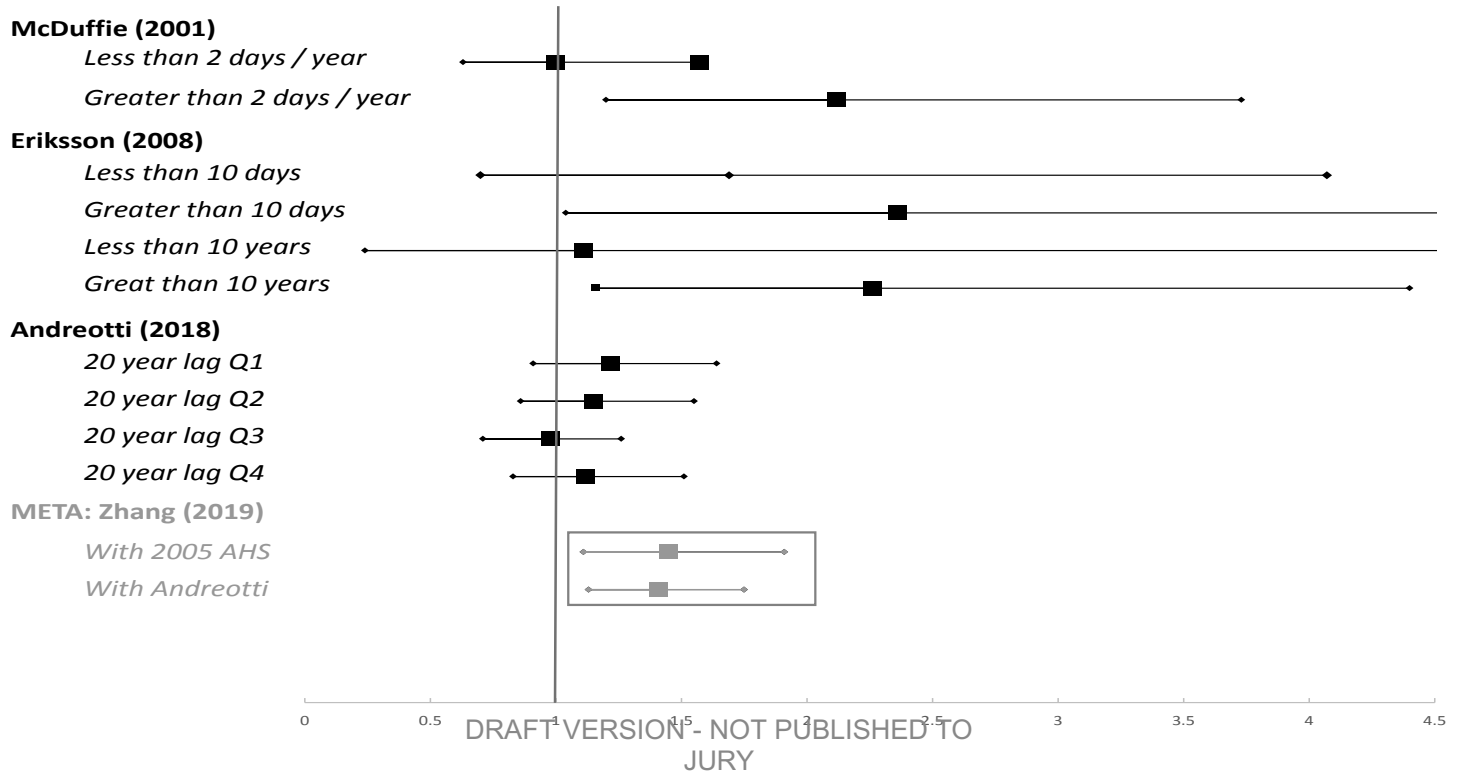
Grant sponsor: Swedish Cancer Foundation; Grant number: SE-22195 Lund, Sweden; Received 4 November 2007; Accepted 10 January 2008; DOI 10.1002/epid.13011; Published online 11 July 2008 in Wiley InterScience (www.interscience.wiley.com).

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## 2. Can Roundup cause cancer?

### Epidemiology studies

#### Plot Summary of NHL risk – dose response



## 2. Can Roundup cause cancer?

### Epidemiology studies

## The Agricultural Health Study (AHS)

- Only cohort study following pesticide applicators in North Carolina and Iowa
- Does not show any association for general NHL
- Two Relevant AHS Papers: ***De Roos 2005*** & ***Andreotti 2018***

## 2. Can Roundup cause cancer?

### Epidemiology studies

# **The Agricultural Health Study**



## ***Deeply flawed study – Glyphosate***

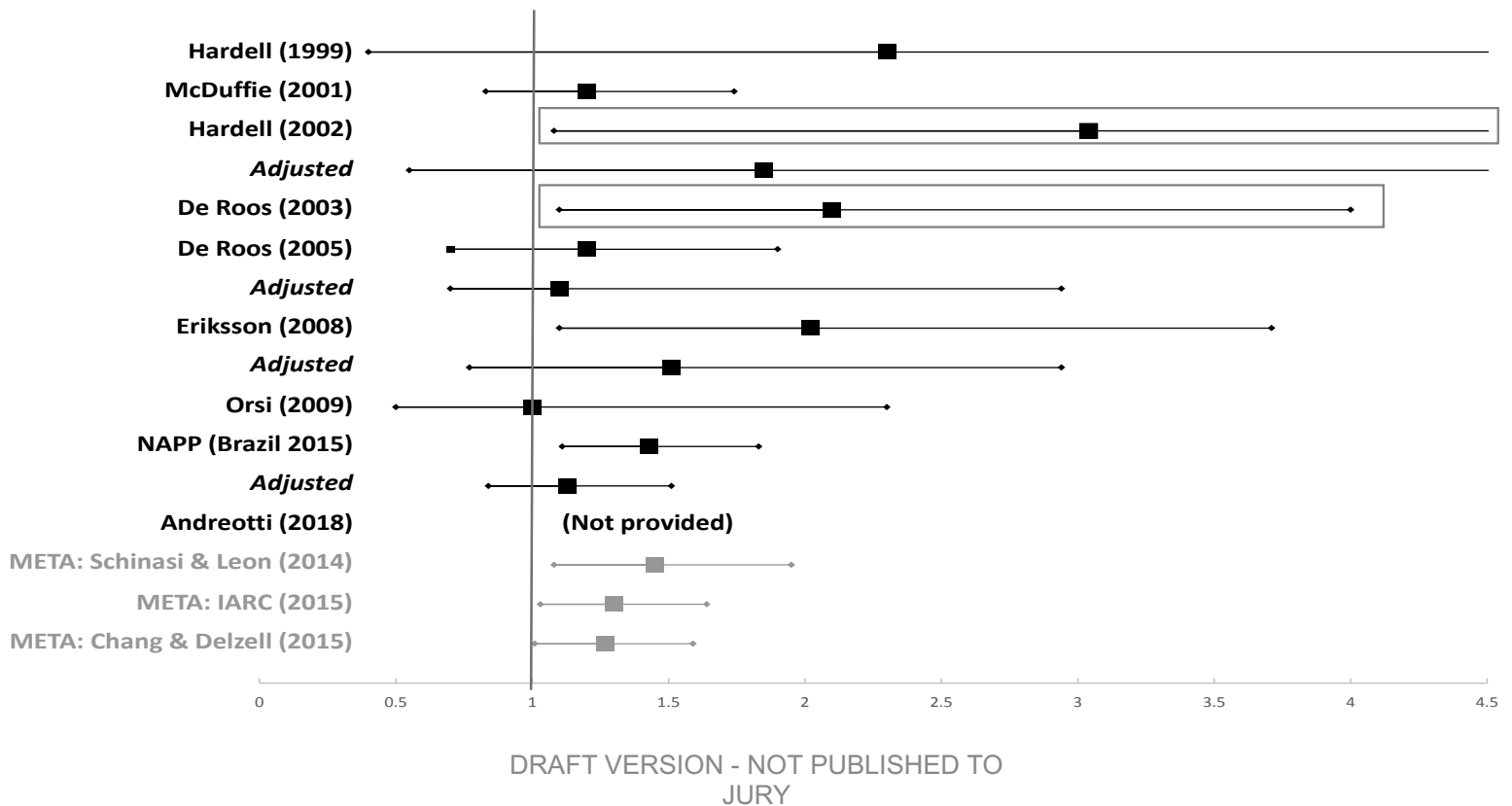
- Many pesticides being studied
- Exposure misclassification
  - Quantity over Quality
- 37% of participants disappeared
- AHS failed to detect other known carcinogens
- Finds Roundup protects from cancer

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## 2. Can Roundup cause cancer?

### Epidemiology studies

#### Plot Summary of NHL risk with ever/ never







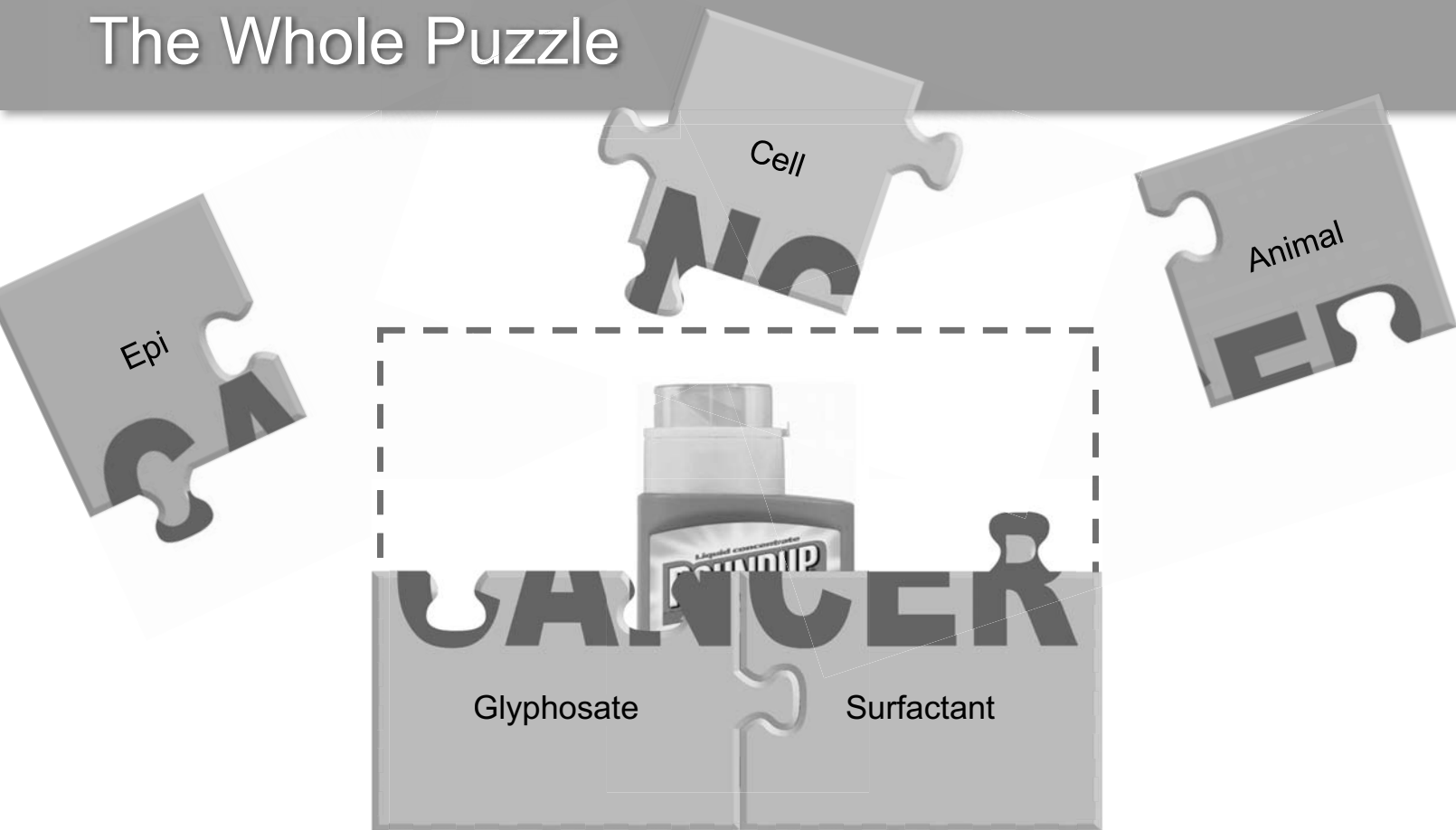
Zhang L., *et. al.* February 5, 2019:

“Overall, in accordance with evidence from experimental animal and mechanistic studies, our current meta-analysis of human epidemiological studies suggests ***a compelling link between exposure to GBH [glyphosate-based herbicides] and increased risk for NHL.***” (emphasis added).

- Zhang L, *et. al.*, Exposure to Glyphosate-Based Herbicides and Risk for Non-Hodgkin Lymphoma: A Meta-Analysis and Supporting Evidence. Mutation Research-Reviews in Mutation Research (2019).

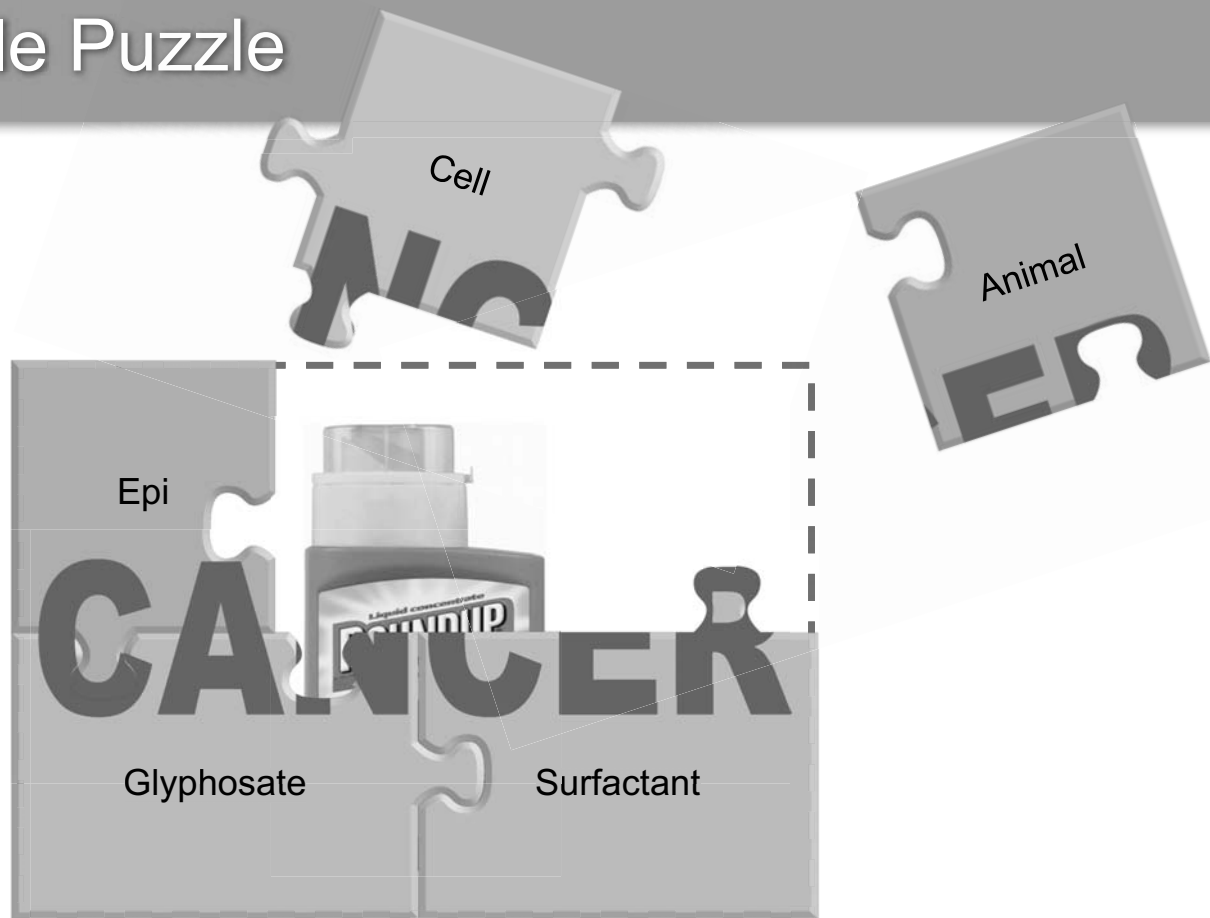
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## The Whole Puzzle



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## The Whole Puzzle



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2. Can Roundup cause cancer?

## Three Pillars of Cancer Science

Epidemiology studies

**YES**

Animal studies

Cell data studies

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## Rodent Studies

- Humans share 95% DNA with rodents
- Humans share similar pathways for toxin eradication
- Standard model for studying cancer
- Use specially bred mice and rats
- Mouse models are commonly used to develop drugs for lymphoma treatments



CD-1 Mouse



Wistar Rat

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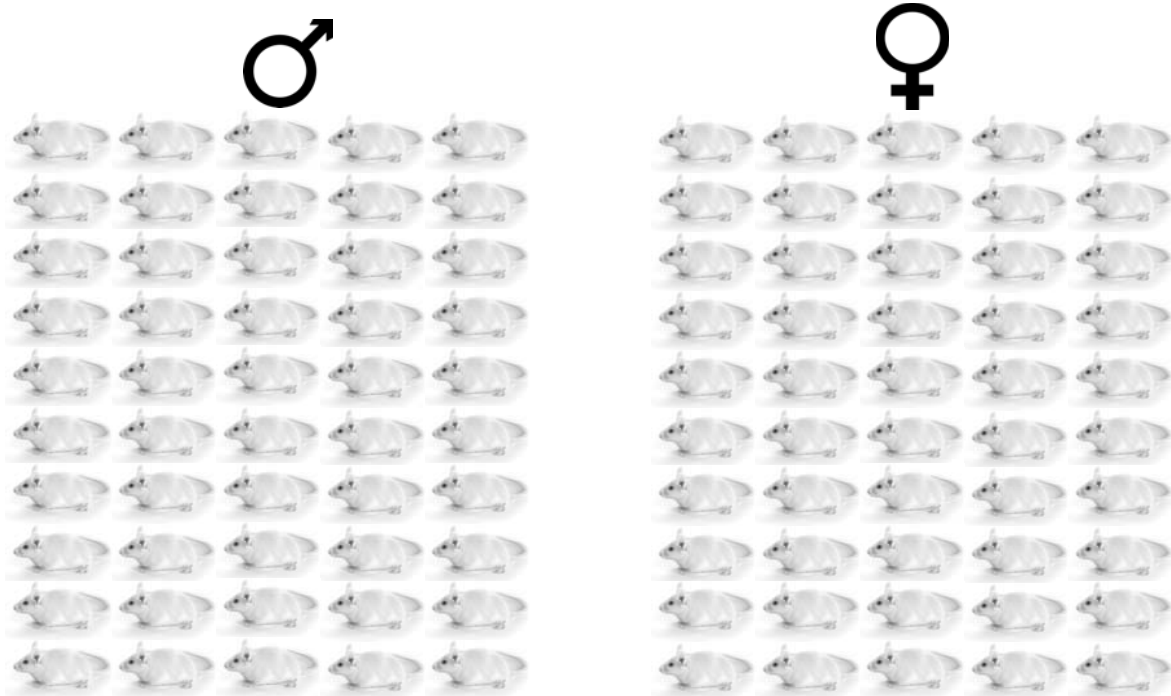
# Walkthrough of Typical Rodent (Mouse) Study



CD-1 Mouse

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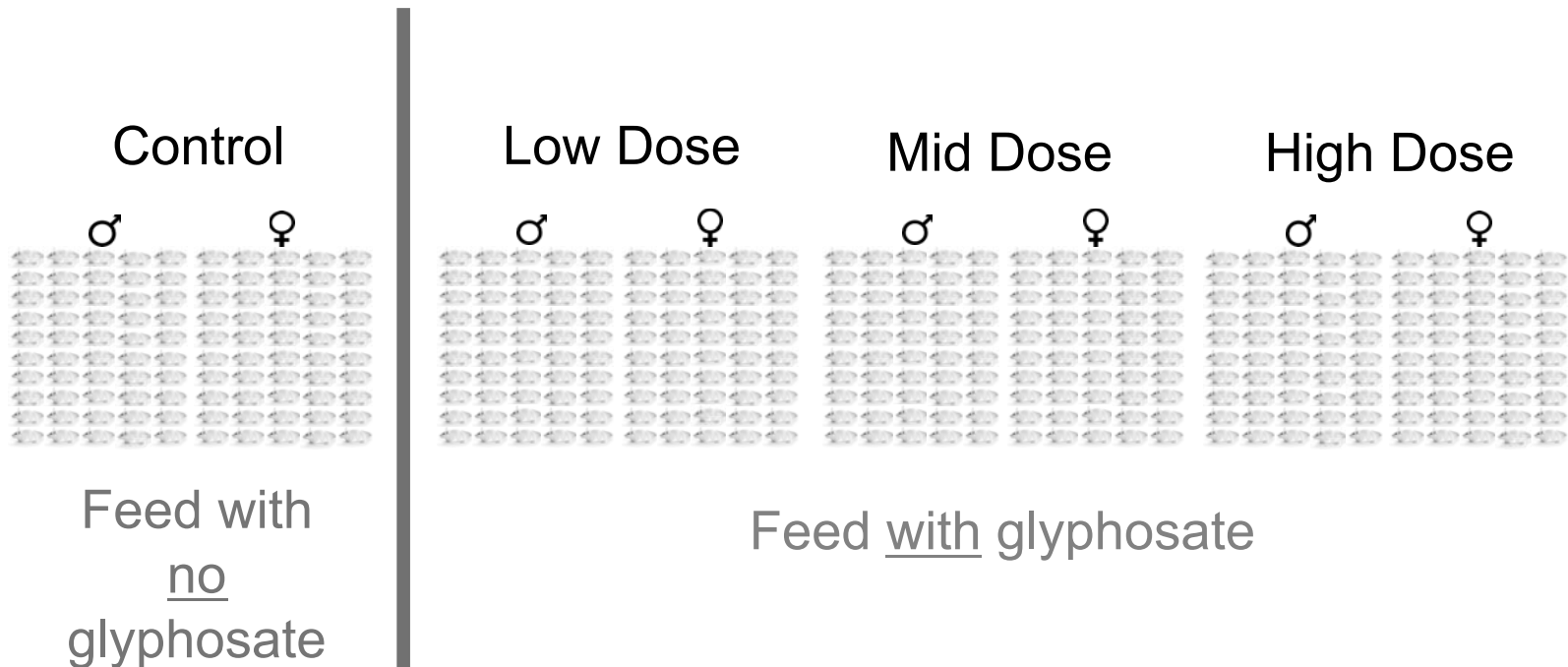
Mice are placed in groups where they are treated identically.  
Each group usually contains 50 males and 50 females.



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There are 4 treatment groups = typically 400 mice

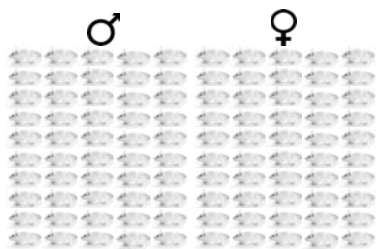


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Highest dose is usually the Maximum Tolerated Dose (MTD)

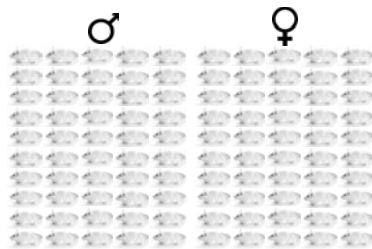


Control

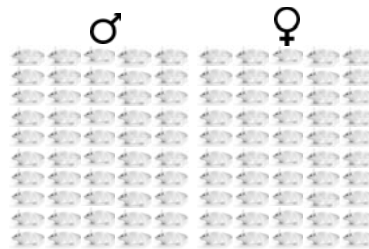


Feed with  
no  
glyphosate

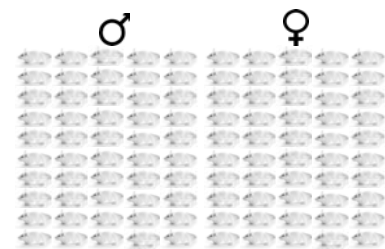
Low Dose



Mid Dose



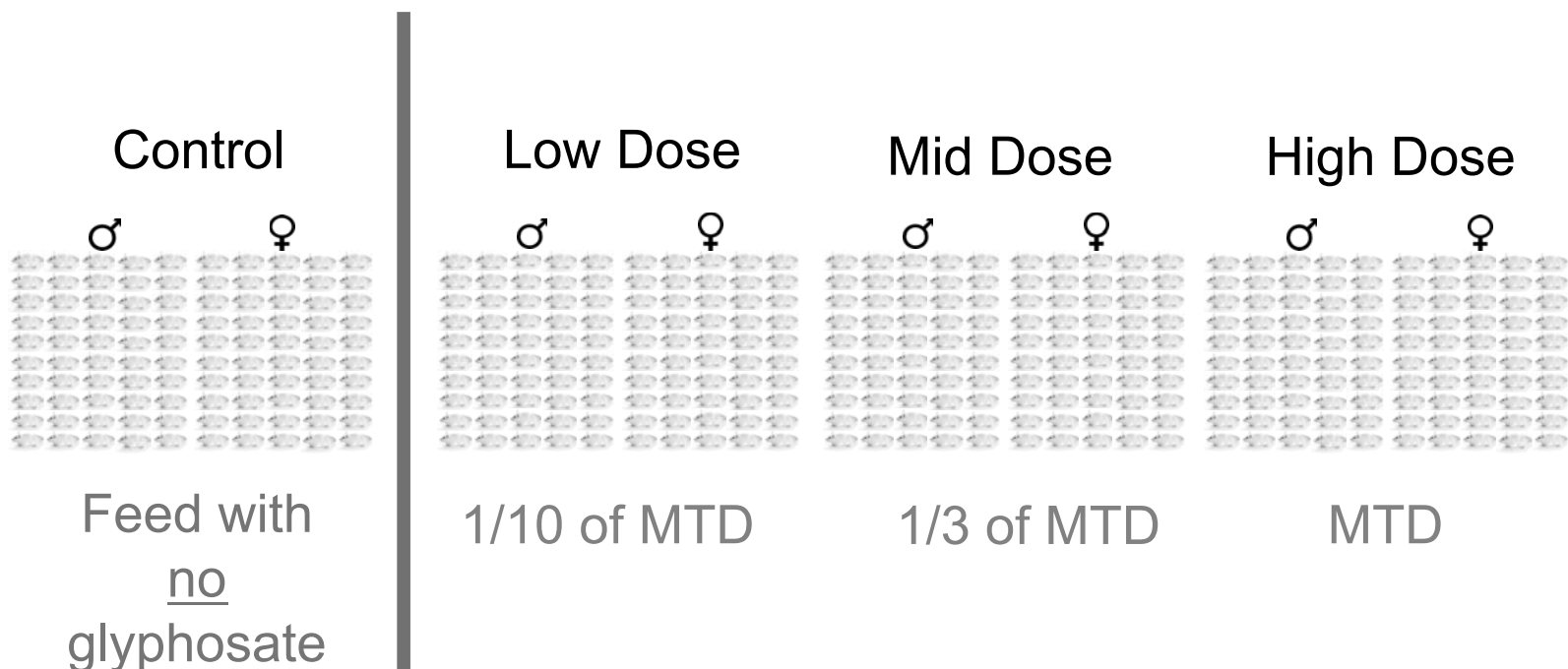
High Dose



Maximum Tolerated Dose (MTD) = The  
highest dose of glyphosate that does not  
cause toxic effects in the mice after 90 days of  
exposure

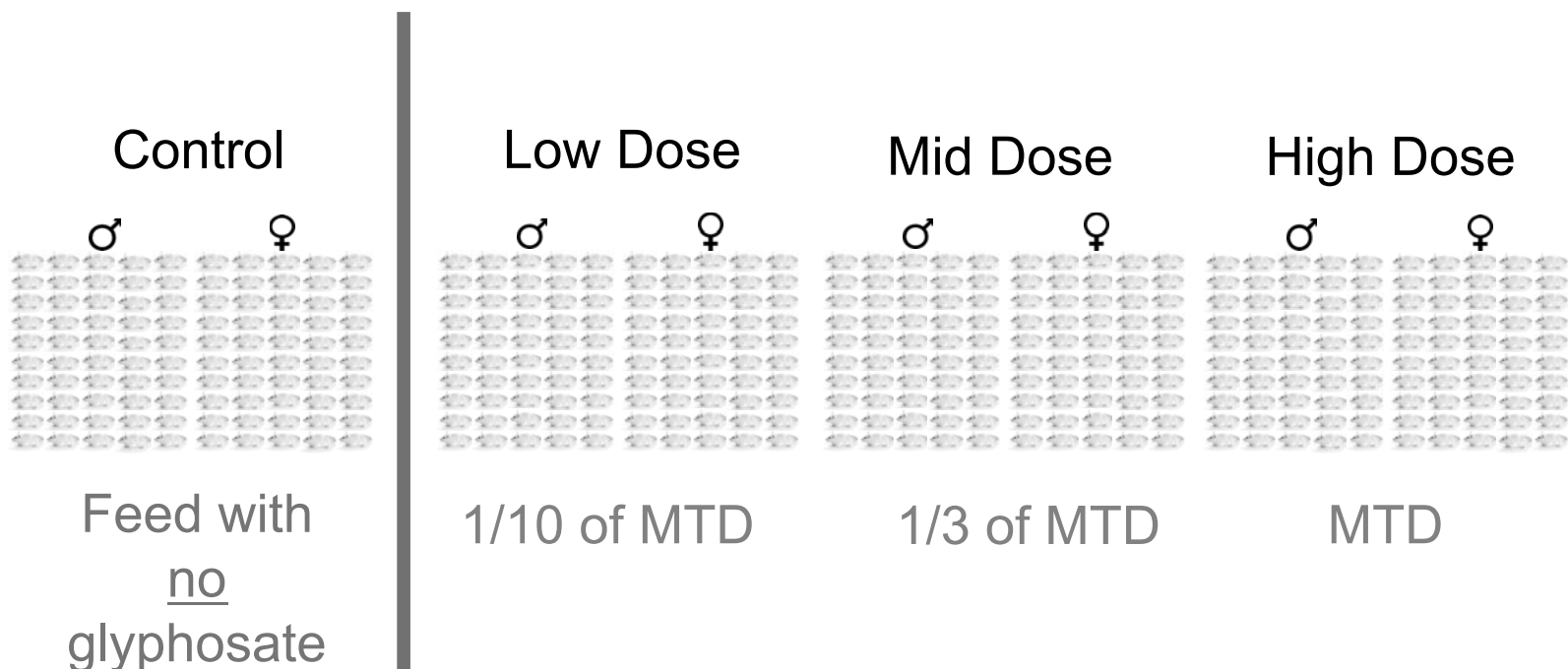
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Doses are set as fractions of the Maximum Tolerated Dose (MTD)



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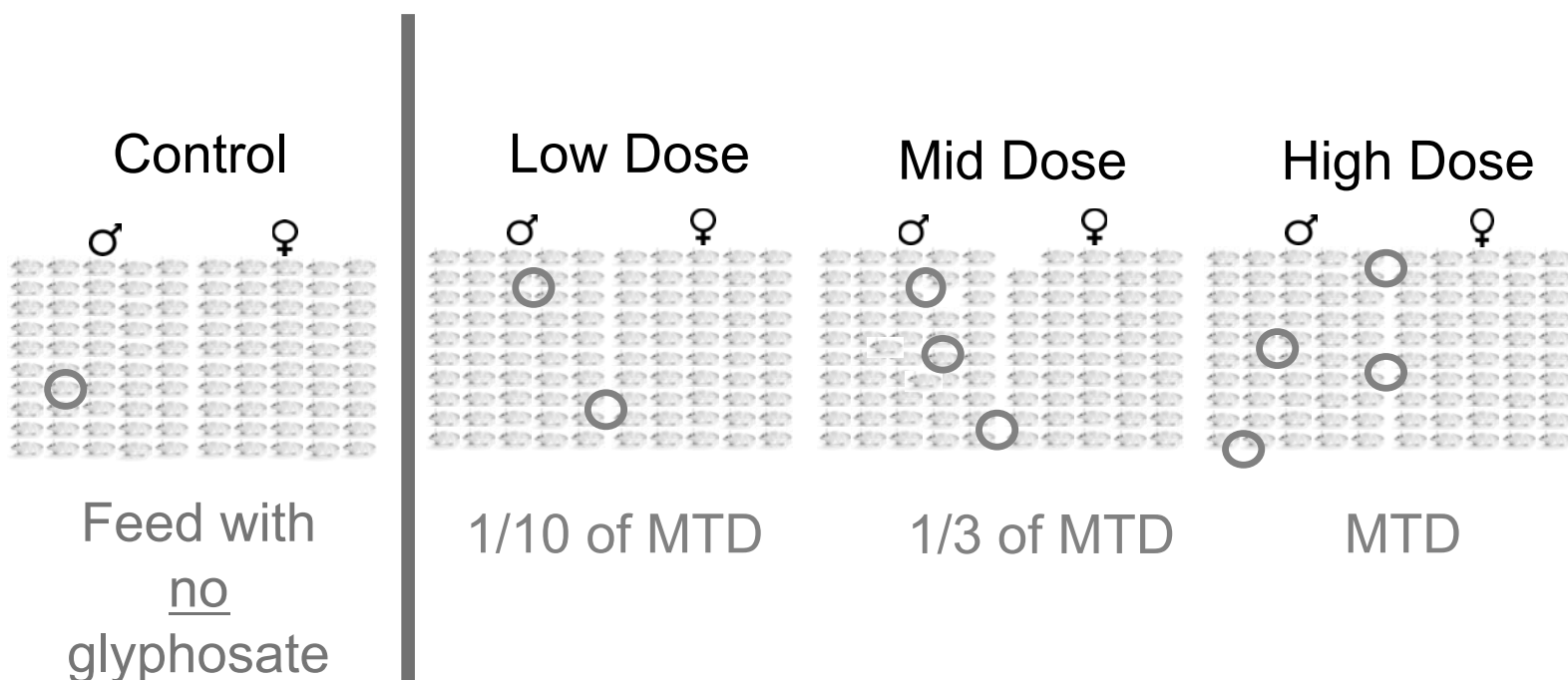
Mice are studied for entire lifetime = 6-weeks old to 2 years



At 6-weeks old, no tumors in mice

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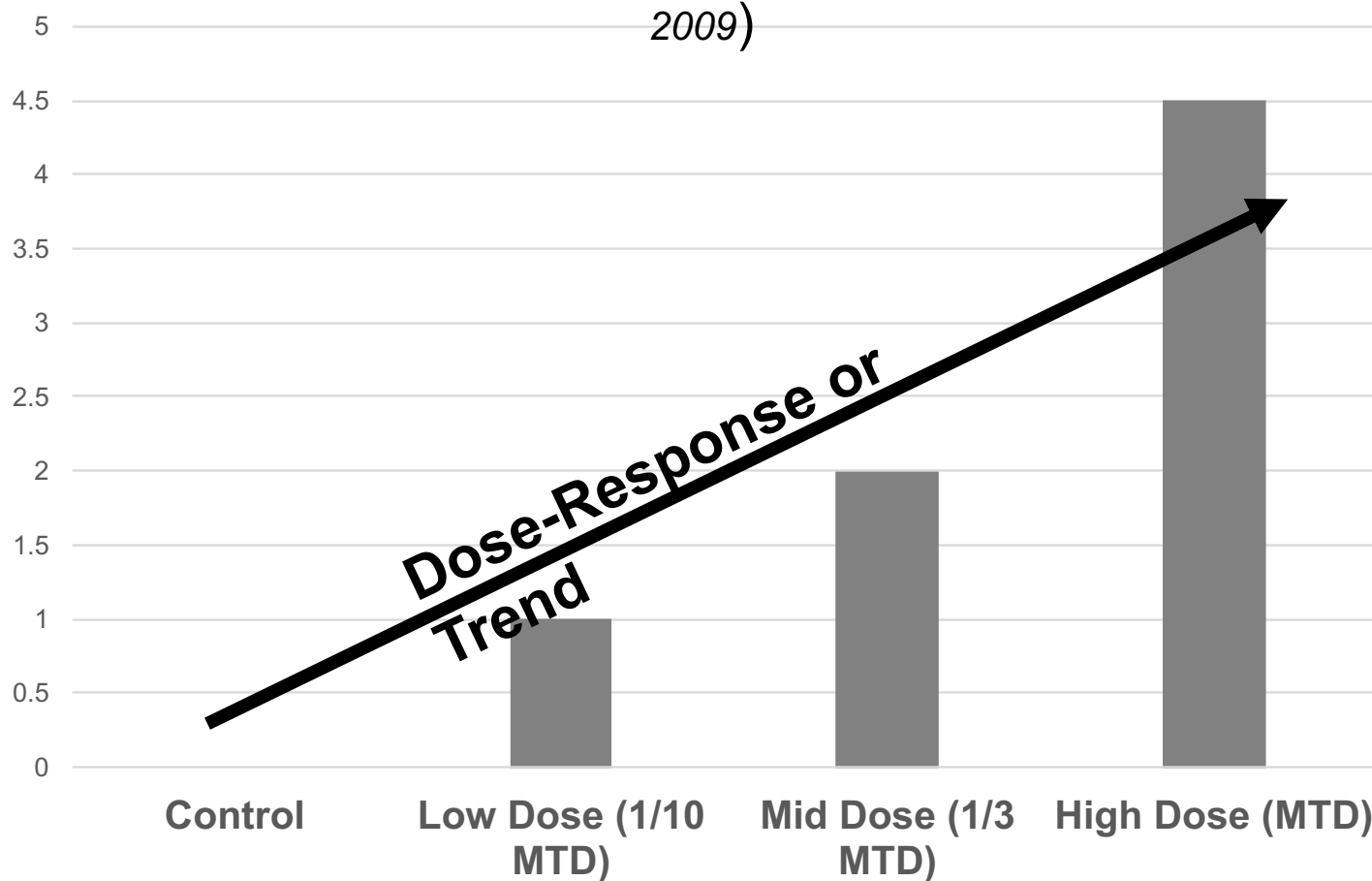
Mice are studied for entire lifetime = 6-weeks old to 2 years



At 2 years, mice are examined for tumors

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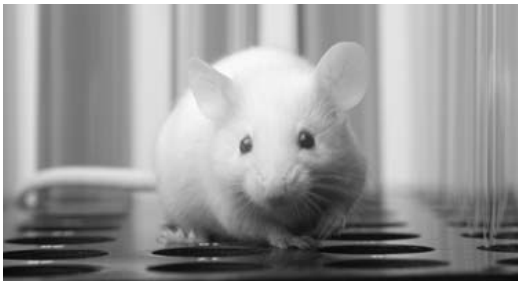
## Real Example: Malignant Lymphoma in Male CD-1 Mice (*Wood, 2009*)



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## 2. Can Roundup cause cancer?

### Animal studies



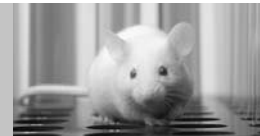
### **Animal Study Factors**

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

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## 2. Can Roundup cause cancer?

### Animal 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		

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## 2. Can Roundup cause cancer?

### Animal 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
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## 2. Can Roundup cause cancer?

### Animal studies



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		Harderian gland adenoma		

**Lymphoma**

**Lymphoma found in  
every mouse Study**

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## 2. Can Roundup cause cancer?

### Animal studies



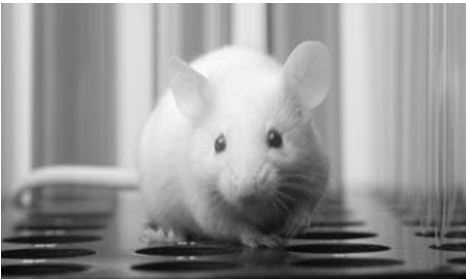
Mice Studies – Tumor Chart

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**Lymphoma found in  
every mouse Study**

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## 2. Can Roundup cause cancer?

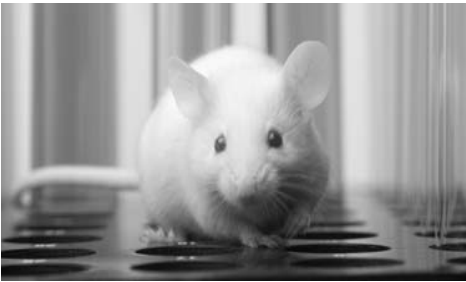


- **February 1985:** Monsanto submits Knezevich & Hogan as its only support for EPA approval.
  - Finds that rare tumor in 0-0-1-3
  - EPA makes a unanimous decision that glyphosate has an oncogenic effect- **Category C**
  - **This is bad for Monsanto's glyphosate.**
- **Monsanto: "Short of a new study or finding tumors in control groups, what can we do to get this thing off Group C?"**

Knezevich & Hogan (1983)

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## 2. Can Roundup cause cancer?

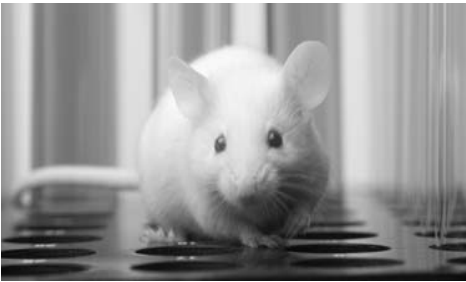


### February 1985

- **EPA:** "...a prudent person would reject the Monsanto assumption that glyphosate dosing has no effect on kidney tumor production. Another way of saying this is that if glyphosate were truly unrelated to kidney production, we would expect to see four or more tumors in less than one out of 100 experiments of the type sponsored by Monsanto. Thus, glyphosate is suspect."

Knezevich & Hogan (1983)

## 2. Can Roundup cause cancer?

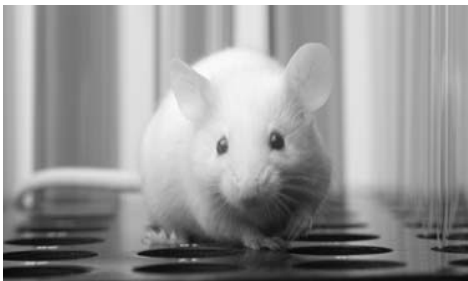


### February 1985:

- **EPA:** We disagree with the registrant's position...The registrant wishes to avoid false positives, while those concerned with the public health wish to avoid false negatives. Hence, for this reason alone, Monsanto's argument is unacceptable...viewpoint is a key issue. Our viewpoint is one of protecting the public health when we see suspicious data. It is not our job to protect registrants from false positives...We sympathize with the registrant's problem, but they will have to demonstrate that this positive result is false.

Knezevich & Hogan (1983)

## 2. Can Roundup cause cancer?



**April 3, 1985:**

**Monsanto:** Senior management at EPA is reviewing a proposal to classify glyphosate as a Class C possible human carcinogen because of kidney adenomas in male mice.

Dr. Marvin Kuschner will review kidney sections and present his evaluation of them to EPA in an effort to persuade the agency that the observed tumors are not related to glyphosate.

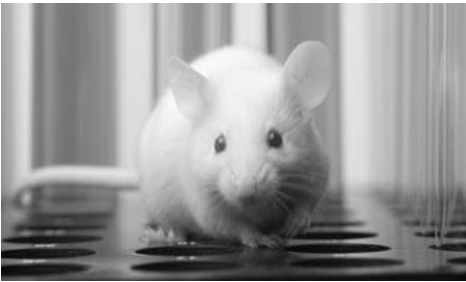


Dr. Kuschner did not receive the slides until **April 14, 1985**

## Knezevich & Hogan (1983)

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## 2. Can Roundup cause cancer?



### April 1985:

- Dr. Kushner finds a tumor in the control group
- EPA Disagrees, recuts slides – No Tumor
- EPA instructs Monsanto to redo the mouse study. Monsanto refuses and instead gives the EPA the Lankas rat study

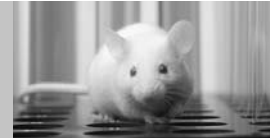
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## 2. Can Roundup cause cancer?

### Animal studies



Mice Studies – Tumor Chart

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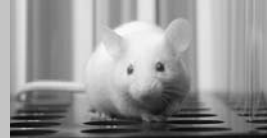
**1986:** Mr. Hardeman  
begins spraying Roundup

**Lymphoma** found in  
**every** mouse Study

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## 2. Can Roundup cause cancer?

### Animal studies



#### George Study (2010)

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

Particularly important when someone has been exposed to multiple risk factors.

Evidence that glyphosate is a tumor **promoter**




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## 2. Can Roundup cause cancer?

### Animal studies



**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	 Problem with control group	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					

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## 2. Can Roundup cause cancer?

### Animal studies



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## 2. Can Roundup cause cancer?

### Animal studies



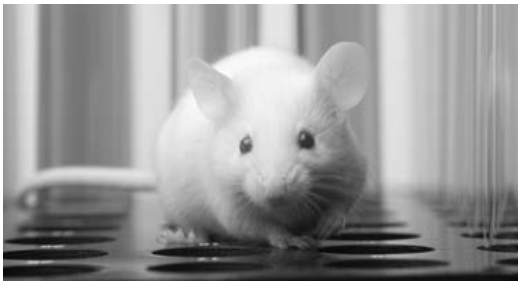
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## 2. Can Roundup cause cancer?

### Animal studies



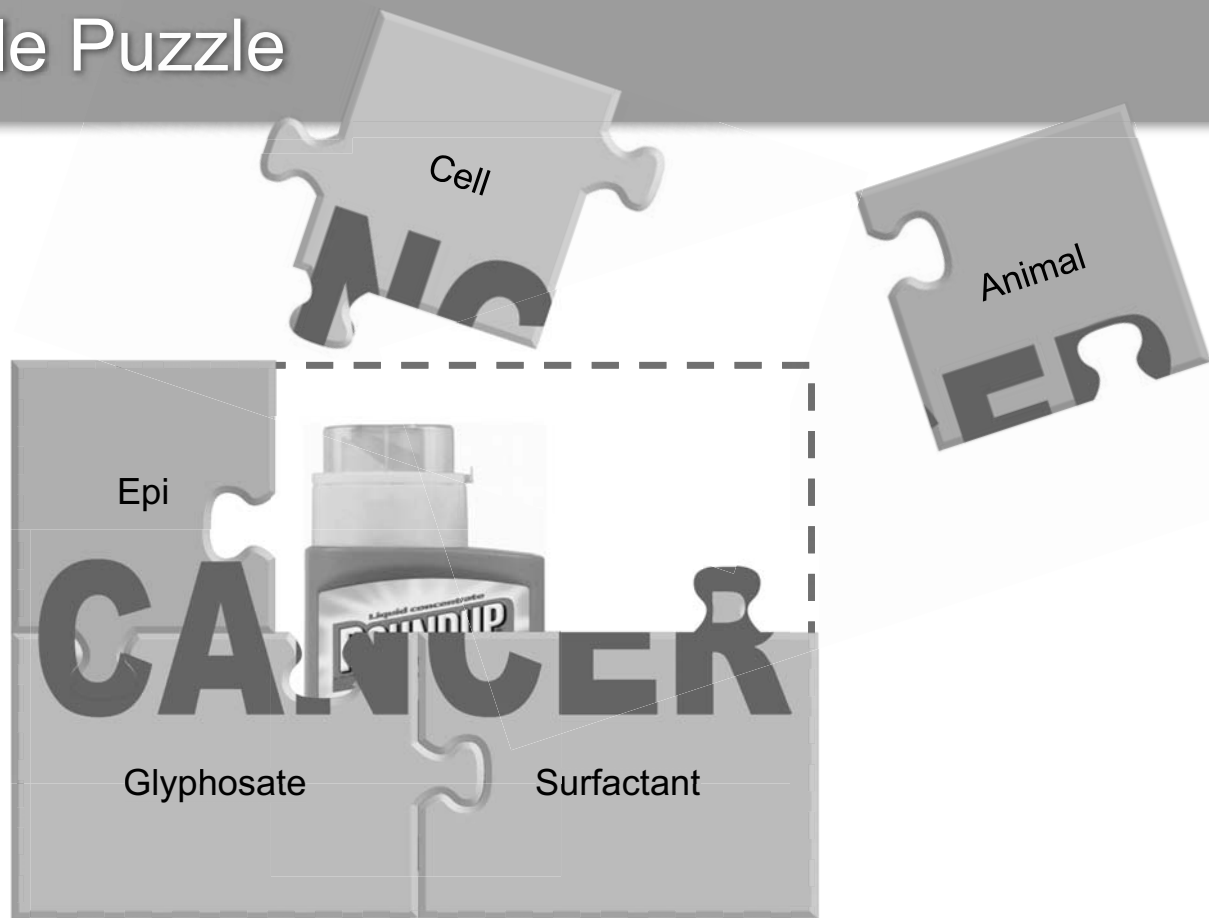
### Animal Study Factors

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



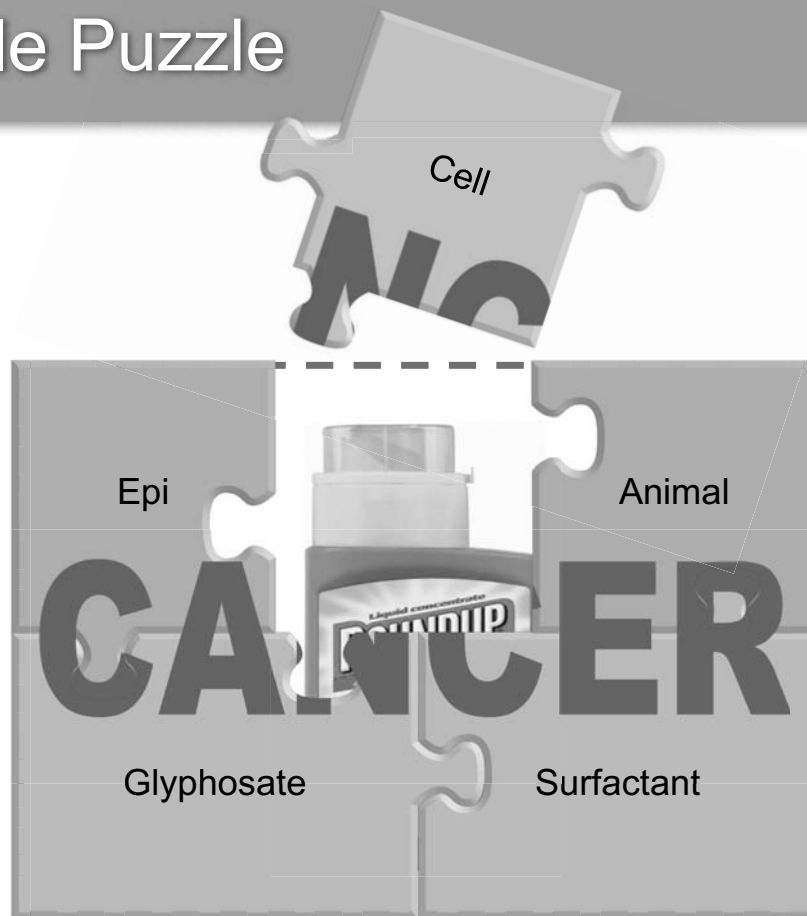
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## The Whole Puzzle



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## The Whole Puzzle



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2. Can Roundup cause cancer?

## Three Pillars of Cancer Science

Epidemiology studies

**YES**

Animal studies

**YES**

Cell data studies

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## 2. Can Roundup cause cancer?

### Cell data studies

**Genotoxic:** causes cell damage that lead to cancer.

### **Oxidative Stress:**

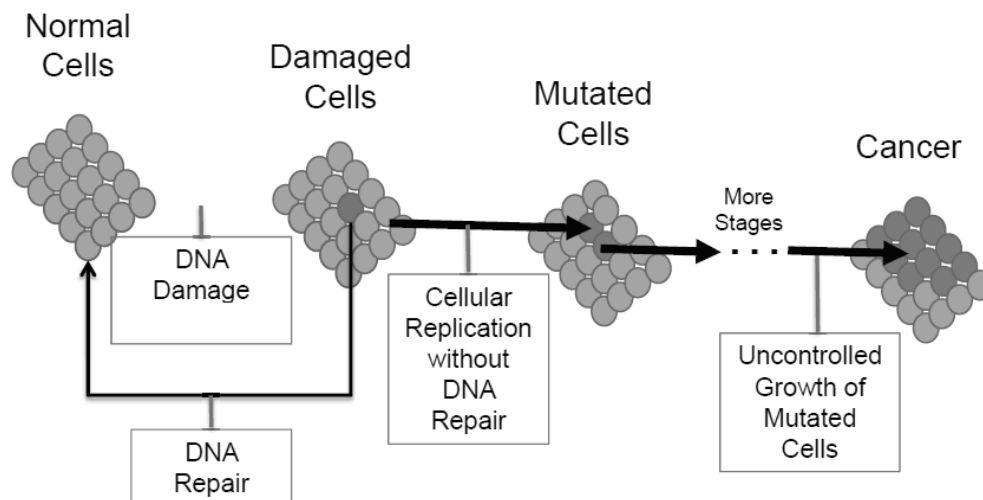
Oxygen radicals bind to the wrong thing, like DNA, and cause problems that lead to cancer.

## 2. Can Roundup cause cancer?

### Cell data studies

# Cellular Data:

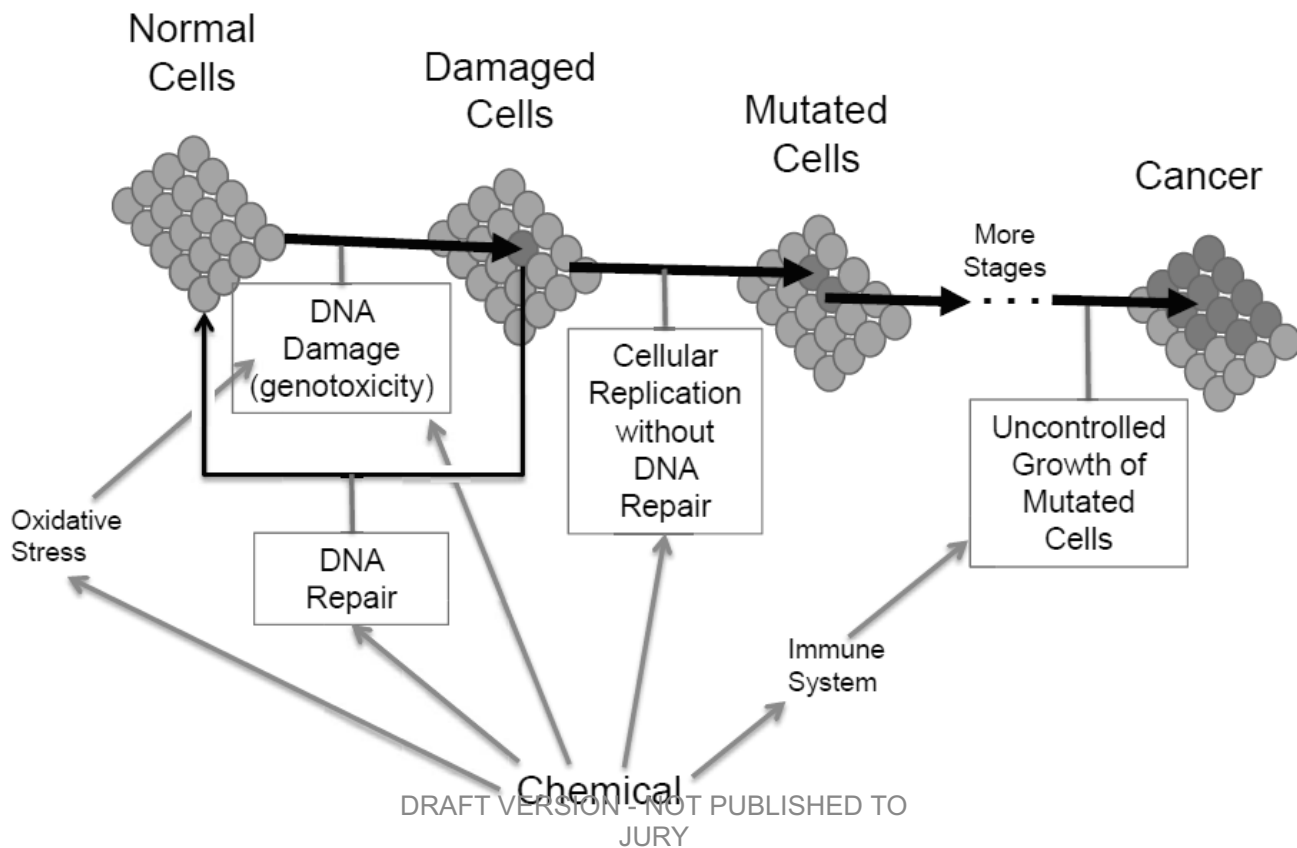
Refers to the way in which a substance can cause cancer.



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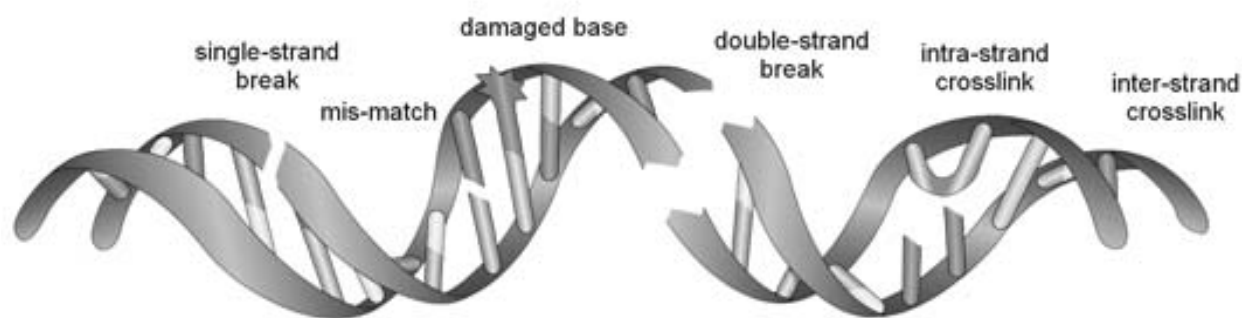
## 2. Can Roundup cause cancer?

### Cell data studies



## 2. Can Roundup cause cancer?

### Cell data studies



Different methods of testing DNA damage  
Over 100 different studies

- Both Roundup & glyphosate
- In humans (*vivo* & *vitro*)
- Non-human mammals (*vivo* & *vitro*) - Monkeys
- Non-mammals (*vivo* & *vitro*) – Fish, bacteria

**In vivo:**

In a living organism.

**In vitro:**

In a petri dish or test tube.

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# Human *In Vitro* Genotoxicity Data

Study	Glyphosate	Formulation
Vigfusson and Vyse (1980)	ND	
Bolognesi (1997)		
Lioi (1998)		ND
Lueken (2004)		ND
Monroy (2005)*		ND
Gasnier (2009)		
Manas (2009)*		ND
Mladinic (2009)		ND
Mladinic (2009)		ND
Koller (2012)		
Alvarez-Moya (2014)		ND

+ = Positive  
 — = Negative  
 ND = No Data

UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF CALIFORNIA

TRIAL EXHIBIT 875

Case No. 3:16-cv-0525-VC

Date Entered \_\_\_\_\_

By \_\_\_\_\_  
Deputy Clerk

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# Recent *In Vitro* Human Genotoxicity Data

Study	Glyphosate	Formulation
Townsend (2017)		ND
Luo (2017)	ND	
Kwiatkowska (2017)		ND
Kasuba (2017)		ND
Wozniak (2018)		
Santovito (2018)		ND
De Almeida (2018)		
Anifandis (2018)		ND

+ = Positive  
 — = Negative  
 ND = No Data

UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF CALIFORNIA

TRIAL EXHIBIT 876

Case No. 3:16-cv-0525-VC

Date Entered \_\_\_\_\_

By \_\_\_\_\_  
Deputy Clerk

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# Human *In Vitro* Oxidative Stress Data

Study	Glyphosate	Formulation
Gehin (2005)		
Mladinic (2009)		ND
Elie-Caille (2010)		ND
George and Shukla (2013)	ND	
Chaufan (2014)		
Coalova (2014)	ND	
Kwiatkowska (2014)		ND
Luo (2017)	ND	
Kasuba (2017)		ND
Wozniak (2018)		

+ = Positive  
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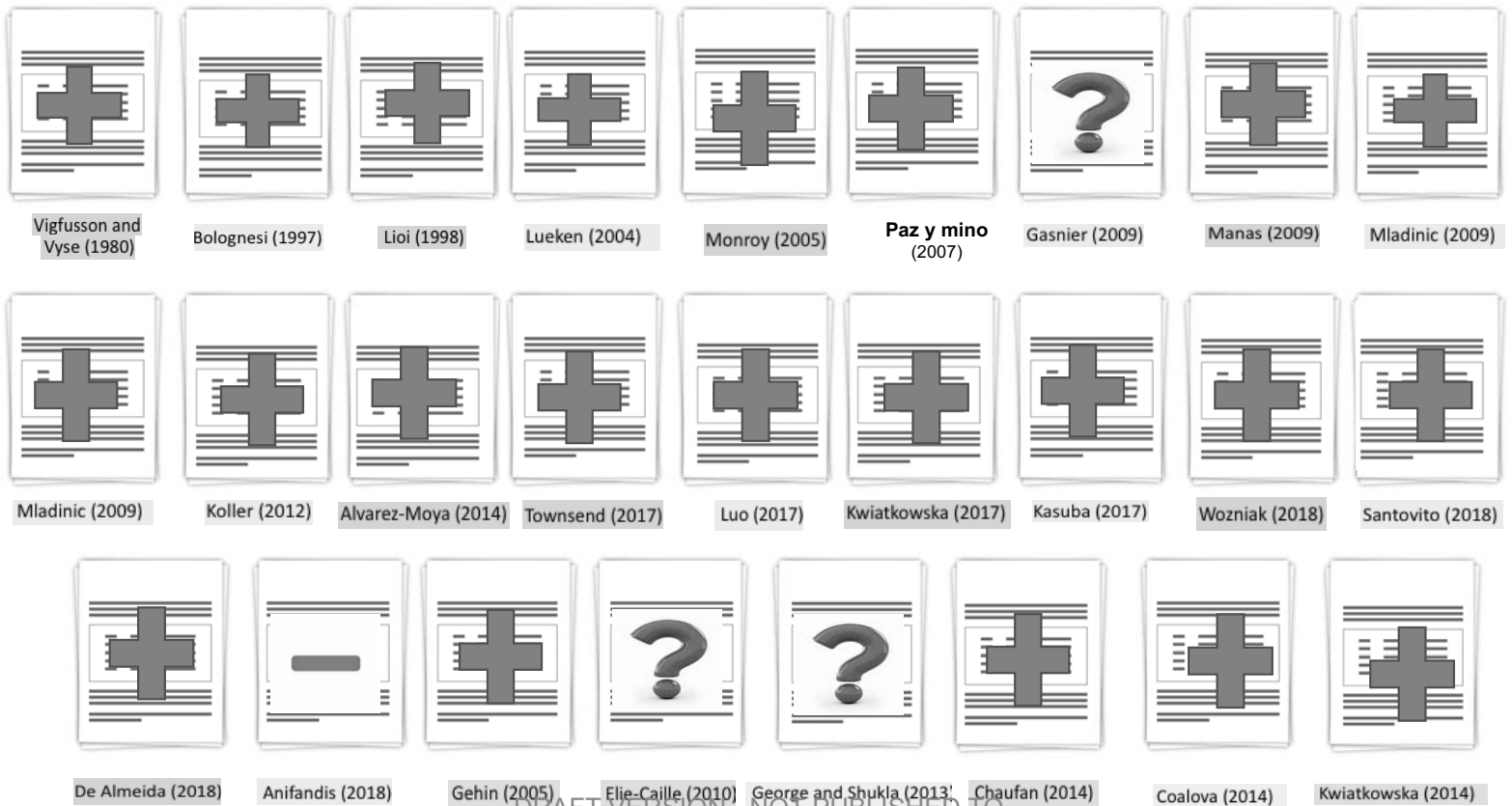
UNITED STATES DISTRICT COURT  
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 By \_\_\_\_\_  
 Deputy Clerk

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## 2. Can Roundup cause cancer?

### Cell data studies



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2. Can Roundup cause cancer?

## Three Pillars of Cancer Science

Epidemiology studies

**YES**

Animal studies

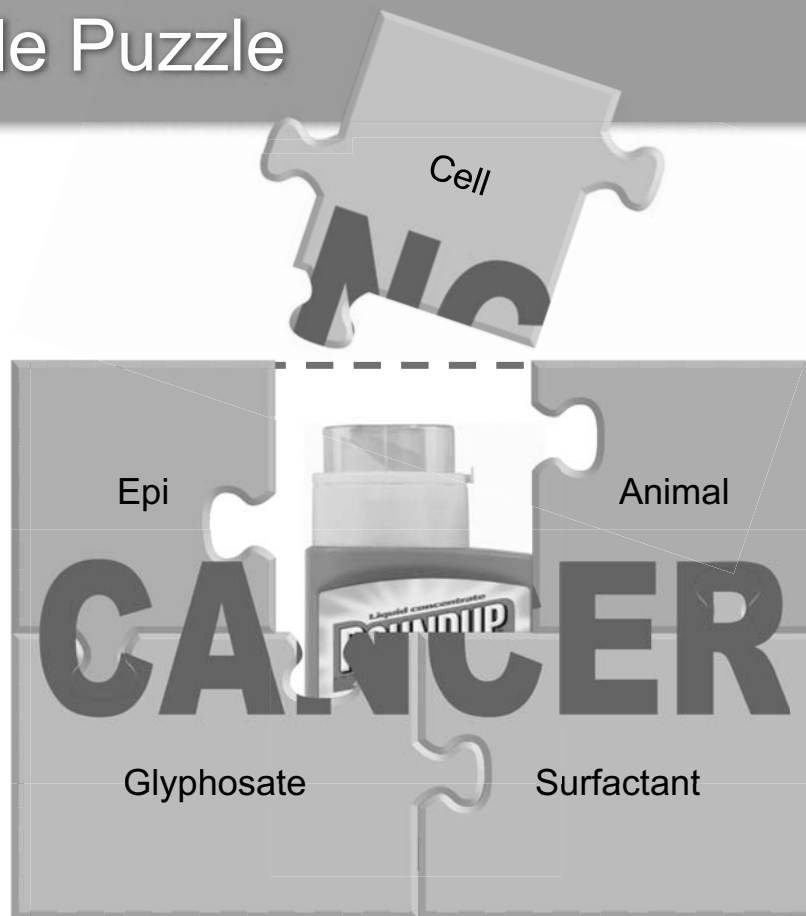
**YES**

Cell data studies

**YES**

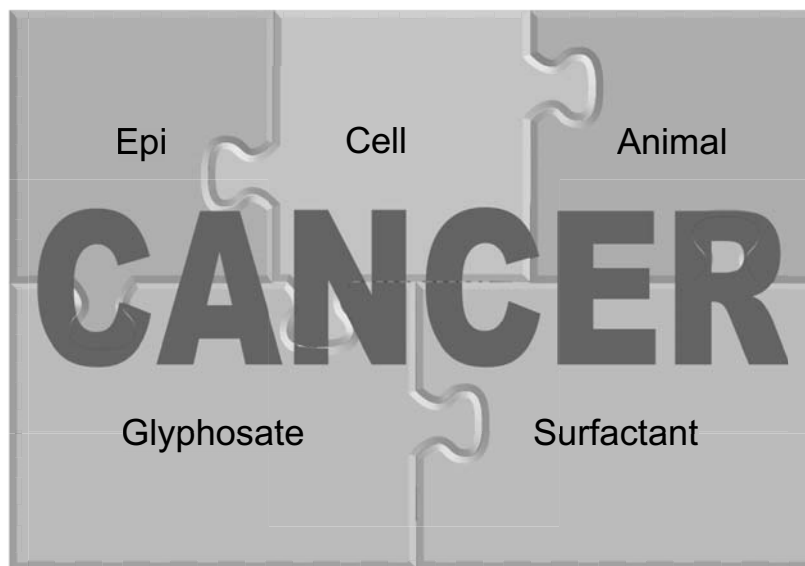
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## The Whole Puzzle



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## The Whole Puzzle



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# The Whole Puzzle



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## 2. Can Roundup cause cancer?

# International Agency Research on Cancer



**World Health  
Organization**



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## 2. Can Roundup cause cancer?

### IARC's 2014-2015 Review of Glyphosate

- Leading world experts on cancer
- 17 scientists from the EPA, California EPA, and worldwide
- Monsanto sent observer and participated in program
- Over six months reviewing all peer-reviewed science on glyphosate
- Held a week-long meeting in France
- **Unanimous** vote – Class 2a

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2. Can Roundup cause cancer?

# IARC's analysis of the same Three Pillars of Cancer Science

Epidemiology studies “Limited” evidence

**YES**

Animal studies “Sufficient” evidence

**YES**

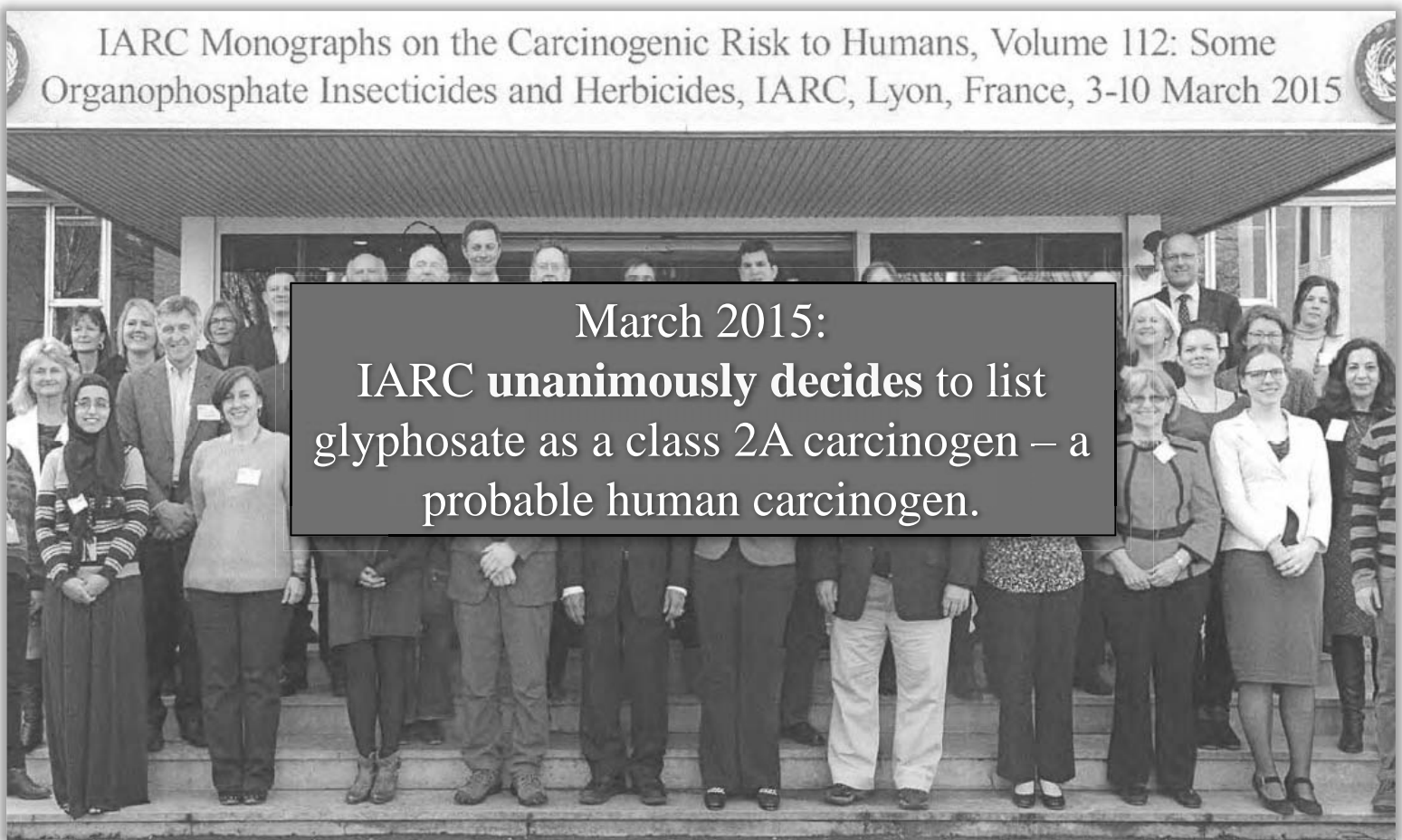
Cell data studies “Strong” evidence

**YES**

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## 2. Can Roundup cause cancer?



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## Monsanto's Position



**Dr. William Reeves:**  
Monsanto's  
Chosen Spokesperson

- Q. Monsanto's position, to be clear, is that there is no evidence to support Roundup causing cancer in people?
- A. It's that there is no evidence that glyphosate or glyphosate-based formulations cause cancer under the conditions that people are expose to.

- Transcript, 30:5-10.

**Monsanto's Position on January 23, 2019**

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## 2. Can Roundup cause cancer?



# Glyphosate v. Roundup

No one tests “Roundup”

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## 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. Divisions within EPA disagree.

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## Opening Statement Roadmap Phase 1:

1. What is Roundup?

2. Can Roundup cause cancer?

**YES**

3. Was Roundup exposure a substantial factor in causing Mr. Hardeman's cancer?

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## Mr. Hardeman's Kaiser Treating Physicians

### Oncologists:



Dr. Turk



Dr. Turley



Dr. Ye

**February 14, 2015: Stage 3 Aggressive Cancer**  
6 rounds of CHEMO

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## Epidemiology studies

**Eriksson**

**2008**

Non-Hodgkin's Lymphoma and Specific Pesticide Exposures in Men:  
Cross-Canada Study of Pesticides and Health<sup>1</sup>

202% increased risk of  
getting NHL when  
exposed to Roundup  
Also shows 236%  
increased risk of NHL  
when used for more  
than 10 days a year  
Dose Response  
10 year after first  
exposure – 226%  
increase

**McDuffie**

**2001**

Study shows

**212% increased risk**  
of NHL when using Roundup  
more than 2 days a year  
**Dose Response**

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Association for Cancer Research.

## Differential for NHL

Known Risk Factors for NHL	Mr. Hardeman's Risk Factors for NHL	Substantial Factor Causing Hardeman's NHL
Age		
Sex		
Race		
Family history of hematologic malignancies		
Pesticide use		
Obesity		
Viral infections		
Bacterial infections		
Immunodeficiency		
Immunosuppression		
Autoimmune diseases		
Chronic inflammation		
Solvent use		

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## Differential for NHL

Known Risk Factors for NHL		Mr. Hardeman's Risk Factors for NHL	Substantial Factor Causing Hardeman's NHL
Age	NO		
Sex	NO		
Race	NO		
Family history of hematologic malignancies	NO		
Pesticide use		Roundup	
Obesity		Obesity	
Viral infections		Hepatitis B Hepatitis C	
Bacterial infections	NO		
Immunodeficiency	NO		
Immunosuppression	NO		
Autoimmune diseases	NO		
Chronic inflammation	NO		
Solvent use	NO		

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Sex	NO		
Race	NO		
Family history of hematologic malignancies	NO		
Pesticide use		Roundup	Roundup
Obesity		Obesity	
Viral infections		Hepatitis B Hepatitis C	
Bacterial infections	NO		
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## Opening Statement Roadmap Phase 1:

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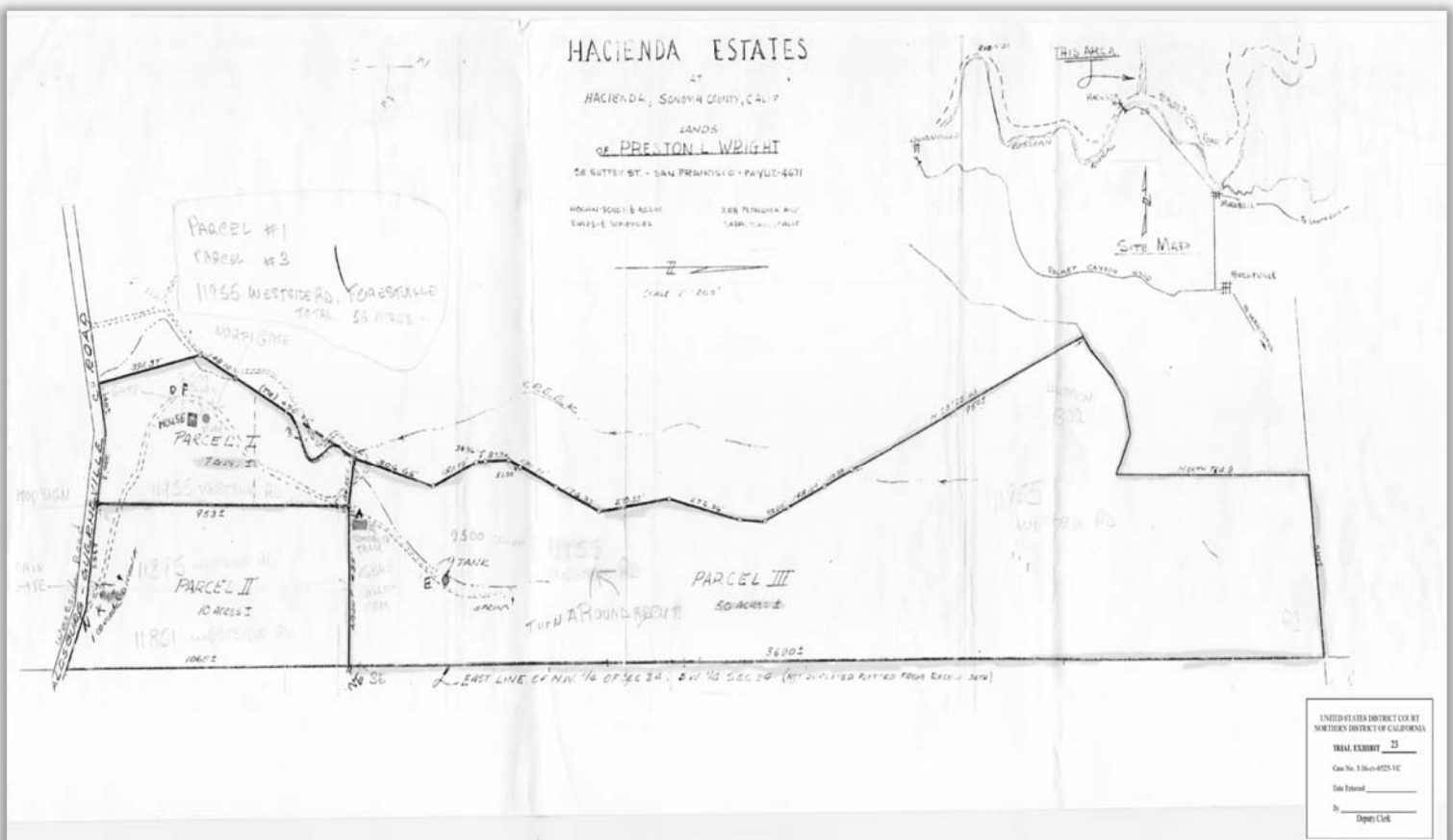
## Monsanto Admission

### Monsanto ADMISSION No. 13

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

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# Roundup Exposure: 1986–2012 (approx. 26 yrs)



56 Acres

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## Mr. Hardeman's Roundup Exposure

- High dose spraying on 56 acres for 26 years: 1986-2012
  - Poison oak infestation
  - Hiking trails and road ways
- Mr. Hardeman read the labels, and complied with all warnings.
- Diagnosed with aggressive stage 3 cancer in 2015.



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