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

DEWAYNE JOHNSON,  
  
Plaintiff,

vs.

MONSANTO COMPANY,  
  
Defendant.

Case No. CGC-16-550128

**EXHIBITS 1 THROUGH 15 TO THE  
DECLARATION OF SANDRA A.  
EDWARDS IN SUPPORT OF  
MONSANTO'S MOTIONS *IN LIMINE*  
NOS. 6-30**

Trial Date: June 18, 2018  
Time: 9:30 p.m.  
Department: TBD

ELECTRONICALLY  
**FILED**  
Superior Court of California,  
County of San Francisco  
**05/24/2018**  
Clerk of the Court  
BY: VANESSA WU  
Deputy Clerk

# **EXHIBIT 1**

# **An Update on FDA's Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies Proposed Rule**

SOT: Regulatory and Safety Evaluation Specialty Section Webinar  
September 29, 2017

Mark Seaton, Ph.D., DABT, FDA/CDER/OTS/OSIS

# Disclaimer

The views expressed in this presentation are those of the speaker, and do not necessarily reflect the official views of the Food and Drug Administration (FDA)

# GLP for Nonclinical Laboratory Studies

## Proposed Rule

### Outline

- A Brief History of GLP Regulations
- Background for Notice of Proposed Rulemaking (NPRM)
- Highlights of Proposed Changes

Good Laboratory Practice (GLP) for  
Nonclinical Laboratory Studies  
Proposed Rule

# A BRIEF HISTORY OF GLP REGULATIONS



# GLPs: How did we get here?



Printed in Collier's magazine, 11 articles in 1905, by Samuel Hopkins Adams on fraud in the pharmaceutical industry. The publication so outraged the public that Congress was finally able to enact the first of several pure food and drug laws in 1906. In the 1920's the U.S. Food & Drug Administration was established to regulate the Nation's food and drug industry.

# History – 1900's

## Pure Food and Drug Act, 1906

- Banned foreign and interstate traffic in adulterated or mislabeled food and drug products.
- Directed the U.S. Bureau of Chemistry to inspect products and refer offenders to prosecutors.
- Required that active ingredients be placed on the label of a drug's packaging and that drugs could not fall below purity levels.
- Drug labels had to list any of 10 ingredients that were deemed "addictive" and/or "dangerous" on the product label if they were present, including alcohol, morphine, opium, cannabis.
- Did not require **safety** or **efficacy** testing.

# History – 1930's

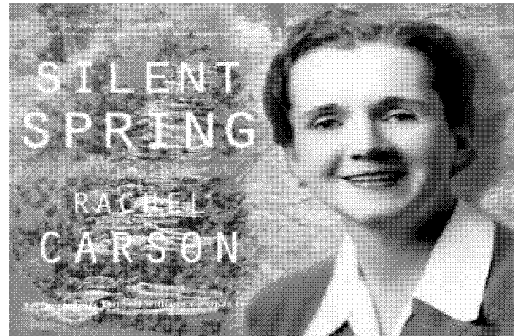
## Federal Food, Drug & Cosmetic Act, 1938

- Gave FDA authority to oversee the safety of food, drugs and cosmetics.
  - Included cosmetics and medical devices.
  - Required drugs be labeled with adequate directions for safe use.
  - Prohibited false therapeutic claims for drugs.
  - Mandated pre-market approval of all new drugs, **including proving safety.**



# History – 1960's

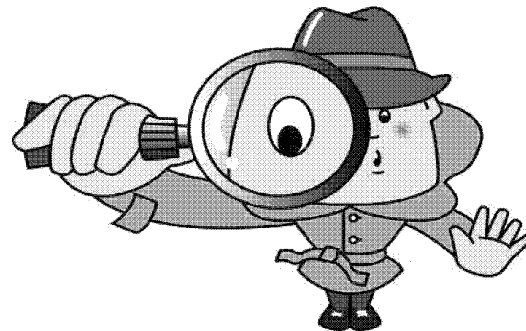
- 1962, “Silent Spring” by Rachel Carson detailed the negative impact on the environment of indiscriminate pesticide use.



- 1970, Formation of EPA
  - Requirement for **more safety testing** studies and **more labs** in which to conduct those studies.

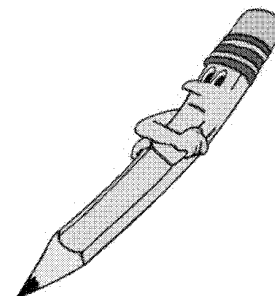
# Industrial Bio-Test Laboratories (IBT)

- 1975, FDA received a tip that there were problems with tests submitted to FDA.
- The medical officer found study data was ‘unbelievably clean’, no rats on 2 year study developed cancer.
- The medical officer found enough deficiencies to warrant an inspection.
- Visit to IBT in April 1976: “What we found there is enough to make your hair stand up”.



## “Magic Pencil Study”

- Terminal blood and urine samples were not collected.
- Draft data tables for the blood and urine assessments were blank, as expected.
- However, the final report not only had values reported, but had the technical writer’s name written in.  
All of those results had been fabricated.



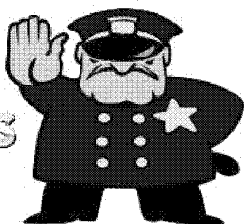
## “The Swamp”

- System designed for automatic watering and flushing waste from cages rarely worked properly.
- Faulty nozzles sprayed the room with a continuing mist. The floor was at times submerged under 4 inches of water.
- Technicians only entered the room wearing rubber boots.
- Clogged water nozzles and drain hoses drenched some rats in a cold spray, while others died of thirst.



# Regulatory Action

- FDA and EPA reviewed compounds that relied on IBT for data in support of safety.
- Called into question the reviews of more than 200 pesticides, many were retested at manufacturer's expense.
- 618 of 867 (71%) of studies audited by the FDA were invalidated for having "numerous discrepancies between the study conduct and data".



## HISTORY -1970's

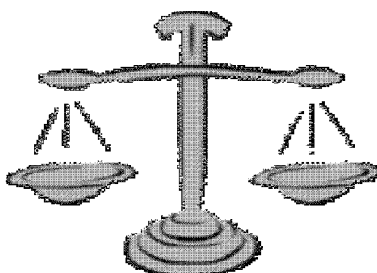
- Congress proposed and enacted the Good Laboratory Practice Regulations for FDA as part of the Federal Food, Drug, and Cosmetic Act (FD&C).
- 21 CFR Part 58 Good Laboratory Practices For Nonclinical Studies
- The *proposed* regulations for Good Laboratory Practice were published in the Federal Register on November 19, 1976.
- The Good Laboratory Practice Regulations, Final Rule was published in the Federal Register on December 22, 1978.

# History – 1980s

- Federal Register of October 29, 1984 (49 FR 43530), FDA published a proposal to amend the agency's regulations in 21 CFR Part 58.
- 33 commenters.
- Revised Good Laboratory Practice Regulations, Final Rule was published in the Federal Register on September 4, 1987.
  - Significant changes in the provisions with respect to quality assurance, protocol preparation, test and control article characterization, and retention of specimens and samples

## History – 2000's

- 2003, Coulston Foundation was disqualified by the FDA
  - TFM and QAU deficiencies
  - Study records deficiencies
- Warning letters December 22, 1999 and October 11, 2001 led to consent agreement
- “Notice of Opportunity for a Hearing” letter March 18, 2003



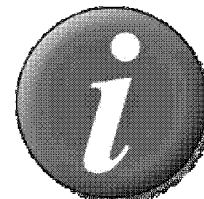


## Primary References

- *Faking It, The Case Against Industrial Bio-Test Laboratories*, The Amicus Journal, Spring 1983
- *Creative Penmanship in Animal Testing Prompts FDA Controls*, Science, 23Dec1977
- *Taste of Raspberries, Taste of Death, the 1937 Elixir Sulfanilamide Incident*, FDA website
- *The Murky World of Toxicity Testing*, Science, 10Jun83
- *The Bressler Report*,  
[www.mpwhi.com/complete \*\*bressler report.pdf\*\*](http://www.mpwhi.com/complete_bressler_report.pdf)
- Coulston NOH:  
[www.fda.gov/downloads/RegulatoryInformation/FOI/ElectronicReadingRoom/UCM144540.pdf](http://www.fda.gov/downloads/RegulatoryInformation/FOI/ElectronicReadingRoom/UCM144540.pdf)

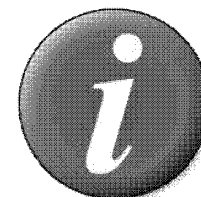
Good Laboratory Practice (GLP) for  
Nonclinical Laboratory Studies  
Proposed Rule

## BACKGROUND



# Background

- GLP Working Group
  - Included all FDA Centers, ORA, OGCP, NCTR, OCC.
  - Included other Federal Agencies.
    - EPA, NIH/OLAW, USDA/APHIS
- Advanced Notice of Proposed Rulemaking (ANPRM)
  - Published in December 2010 (75 FR 80011).
  - Approximately 90 commenters responded.



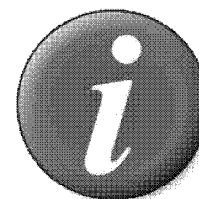
# Background

- ANPRM Areas (request for comments):
  - GLP Quality System
  - Multisite Studies
  - Electronic/Computerized Systems
  - Sponsor Responsibilities
  - Animal Welfare
  - Information on Quality Assurance Inspectional Findings
  - Process-Based Systems Inspections
  - Test and Control Article Information
  - Sample Storage Container Retention



# Background

- Notice of Proposed Rulemaking (NPRM)
  - Published on August 24, 2016 (81 FR 58342)
  - Considered ANPRM comments and consistency with relevant OECD documents
  - Comment period closed on January 21, 2017
    - 90 day comment period
    - 60 day extension
  - 78 commenters
  - Multiple comments per submission



Good Laboratory Practice (GLP) for  
Nonclinical Laboratory Studies  
Proposed Rule

# HIGHLIGHTS OF PROPOSED CHANGES



# Highlights of Proposed Changes

- Enhance (require) the existing quality system approach.
- Reflect current practices such as multisite studies.
- Incorporate wording consistent with domestic and international (OECD) guidelines or regulations.

Specifically,

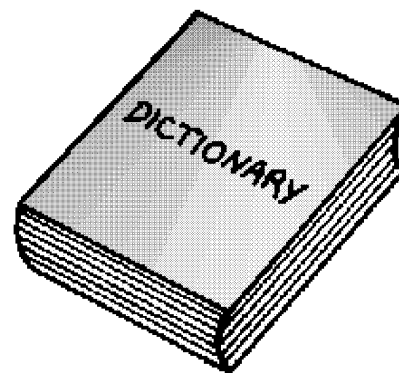
- Expand scope
- Add definitions
- Clarify GLP roles and responsibilities
- Add animal welfare provisions
- Request comment on Animal Rule studies

# Proposed § 58.1 Scope

- Proposed expansion includes:
  - Toxicity studies
  - Tobacco products
  - Devices (to include veterinary)
- Proposed changes:
  - “Applications and Submissions” – not just for research or marketing
- Animal Rule
  - Requested comment on inclusion of certain Animal Rule studies in GLP scope

# Proposed § 58.3 Definitions

- Test Site
- Contracted Person
- Test Facility Management with Executive Responsibility
- Attending Veterinarian
- Contributing Scientist
- Principal Investigator



# Proposed § 58.5 Sponsor Responsibilities

- Proposed responsibilities relating to the protocol:
  - Meets requirements in § 58.120
  - Provides for humane care of animals
  - Review, approve, sign, and date each protocol and amendment
- Proposed responsibilities relating to accredited and qualified persons
- Proposed responsibilities relating to study communication:
  - Ensure appropriate lines of communication are established
  - Document communications

# Proposed § 58.5 Sponsor Responsibilities

- Proposed responsibilities relating to test, control, and reference articles:
  - Document characterization,
  - Provide characterization information to study director as soon as available,
  - Inform study director of any known potential risks of the test article.
- Proposed responsibilities related to statement of compliance
  - the final study report and amendments to the final report must include a statement of compliance or noncompliance.

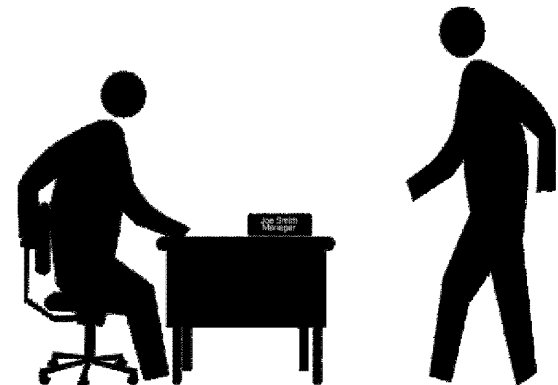
# Proposed § 58.15 Inspections

- Clarification of FDA's inspection authority to include any person that conducts a phase of a nonclinical laboratory study.
- Includes any contracted or subcontracted person that agrees to assume any regulatory responsibility.

\* Person includes an individual, partnership, corporation, association, scientific or academic establishment, government agency, or organizational unit thereof, and any other legal entity.

# Proposed § 58.31 Testing Facility Management with Executive Responsibility (TFMWER)

- “Management with executive responsibility is ultimately responsible for the GLP Quality System and must establish policy and objectives for a GLP Quality System and a commitment to quality, as defined in § 58.3.”

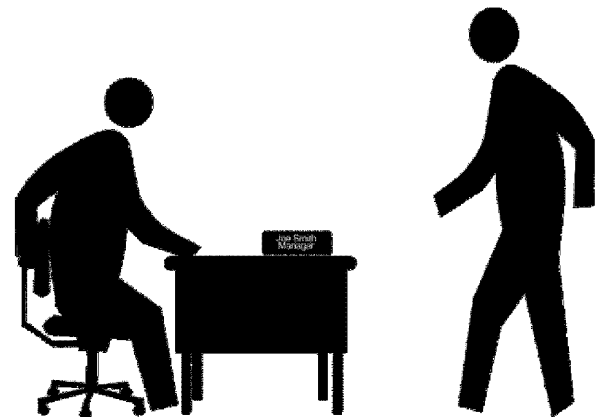


# Proposed § 58.31 TFMWER

- Propose new responsibilities related to:
  - GLP Quality System
    - review at specified intervals
    - appoint management representative
  - Multisite studies
    - all persons are trained and follow equipment SOPs
  - Master schedule
    - individual, not necessarily QAU
  - Protocol review

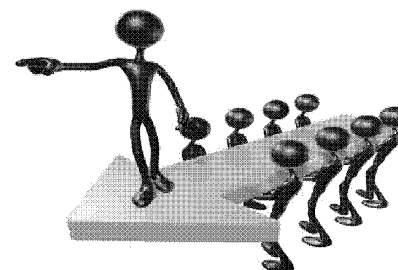
# Proposed § 58.31 TFMWER

- Propose new responsibilities related to:
  - QAU review
  - SOPs



# Proposed § 58.33 Study Director

- “The study director represents the single point of study control and has overall responsibility, which cannot be delegated, for...
  - ...Implementation of procedures to ensure adequate communication among all study personnel and with the study sponsor, as applicable...”
  - Document communications with all persons conducting a phase of the nonclinical study and with the sponsor.

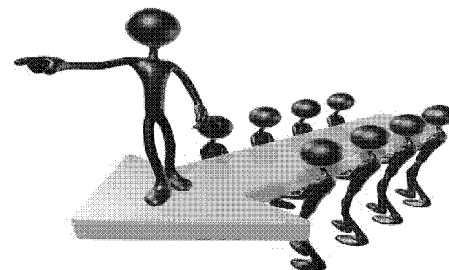


# Proposed § 58.33 Study Director

- Proposed new requirements:
  - Consult with attending veterinarian during review of proposed study protocol,
  - Defer to attending veterinarian on animal welfare decisions.
  - For multisite studies:
    - Document qualifications of any person conducting a phase of the nonclinical study,
    - Determine and document the need for a principal investigator.

# Proposed § 58.33 Study Director

- Proposed new requirements:
  - Archive all raw data, documentation, protocols, specimens, reserve samples and final reports no later than 2 weeks after the study completion.



# Proposed § 58.35 Quality Assurance Unit (QAU)

- For studies conducted entirely at the testing facility, the QAU can:
  - Consist of personnel at the facility itself; or,
  - Be a separately contracted unit.
- For multisite studies:
  - A Lead QAU must be designated by TFMWER, and
  - Provide QA oversight for the entire study.
- Requirements for Lead QAU included throughout proposed 58.35

## Proposed § 58.35 QAU

- QAU inspections can include:
  - Study-based inspections
  - Facility-based inspections
  - Process-based inspections
    - If a person conducting a phase of a nonclinical laboratory study chooses to conduct process-based inspections, that person must prepare a written certification...whenever a process-based inspection reveals problems.

# Proposed § 58.37 Contributing Scientist

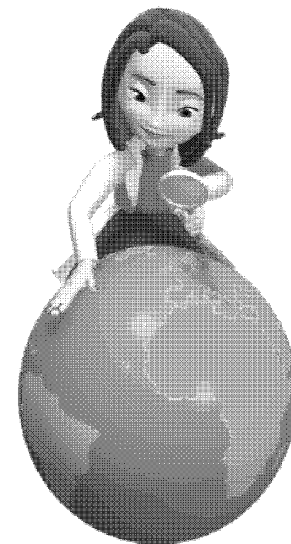
- Proposed responsibilities:
  - For those phases for which the contributing scientist is responsible:
    - Comply with Part 58,
    - Provide a signed and dated report of all phases to include in final study report,
    - Both original and amended versions of reports from all contributing scientists be appended to the final study report.
    - Permit oversight by the designated QAU.

# Proposed § 58.37 Contributing Scientist

- Independent contributing scientist - Proposed responsibilities include:
  - Date and sign the study protocol to indicate agreement to comply with the protocol requirements,
  - Maintain and update documentation of their education, training, and experiences,
  - Archiving responsibilities.

## Proposed § 58.39 Principal Investigator (PI)

- The study director can delegate to the PI responsibility for phases of a nonclinical laboratory study but not responsibility for an entire study.
- Proposed responsibilities include:
  - Verify study conducted according to Part 58,
  - Report deviations to study director.



# Proposed § 58.105 Test, control, and reference article characterization

- Analyses must be performed by the sponsor or by a contracted person either:
  - Before study initiation; or,
  - Concomitantly according to written SOPs.
- Results must be provided to the study director as soon as available.



# Proposed § 58.130 Conduct of a nonclinical laboratory study

Proposed requirements for:

- Demonstration that all analytical methods are accurate, sufficiently precise, and sensitive enough to result in accurate and reproducible data
- Considering the humane care and ethical treatment of animals,
  - Consulting the attending veterinarian regarding the impact of the protocol on the welfare of test animals,
  - Deferring to the attending veterinarian on animal welfare decisions.

# Proposed § 58.180 Data quality and integrity

- All data generated during the conduct of a nonclinical laboratory study must be ALCOA
  - Accurate
  - Legible
  - Contemporaneous
  - Original, and
  - Attributable

# Proposed § 58.180 Data quality and integrity

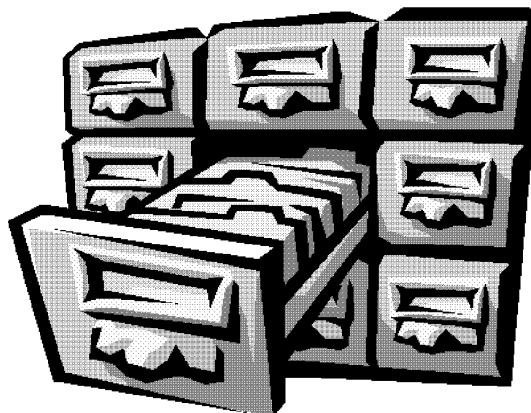
- Any change to any entry must:
  - be made so as not to obscure the original entry,
  - indicate the reason for the change,
  - indicate when the change was made,
  - must identify who made the change.
- Use of an electronic records system must be fully compliant with applicable regulations.
- All data accrued as required in this section must be included in the final study report.

# Proposed § 58.185 Reporting of Nonclinical Laboratory Study Results

- A signed and dated report from each person conducting an analysis or evaluation of study data or specimens after data generation was completed,
- the study director provide with the final study report a statement about the study's extent of compliance with part 58, including any study deviations,
- For discontinued studies, the study director to write, sign, and date a short written summary report closing the study and discussing why the study was discontinued

# Proposed § 58.190 Storage and retrieval of records and data

- All study material must be archived no later than 2 weeks after the study completion date.
- SOPs regarding archiving, required in 58.81(b)(13), must include specific procedures for the removal of study materials from the archives, including maximum timeframes material can remain outside of the archives.



## Proposed § 58.202

- “FDA may disqualify any person conducting a phase of a nonclinical laboratory study upon finding that person repeatedly or deliberately failed to comply with one of more of the regulations set forth in this part...or repeatedly or deliberately submitted false information in any required report”

Person includes an individual, partnership, corporation, association, scientific or academic establishment, government agency, or organizational unit thereof, and any other legal entity.

## Link to NPRM

[www.federalregister.gov/documents/2016/08/24/2016-19875/good-laboratory-practice-for-nonclinical-laboratory-studies](http://www.federalregister.gov/documents/2016/08/24/2016-19875/good-laboratory-practice-for-nonclinical-laboratory-studies)

# Contact Information

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(301)-796-3408





# **EXHIBIT 2**

## **Texas firm probed for residue studies**

■ **WASHINGTON**— Regulators and federal prosecutors are investigating allegations that a Texas company falsified data used to determine pesticide residues on food, the Environmental Protection Agency said Friday.

The agency said it did not believe there was any risk to consumers or the environment.

The data were submitted to the EPA by pesticide manufacturers who had hired Craven Laboratories of Austin to determine how much pesticide remains on fruits, vegetables and grains in the marketplace.

These studies are used to help determine how much pesticide may be applied and how much may be allowed on the foods going to the consumer. They are a small part of the massive work on farmworker exposure, toxicity of the pesticide, its persistence in the environment and other topics needed to determine pesticide safety.

Linda Fisher, EPA assistant administrator for pesticides and toxic substances, said the agency had asked all 262 companies that had ever submitted residue data to tell the agency of any work submitted to the agency and done by Craven.

# **EXHIBIT 3**

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

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)  
DEWAYNE JOHNSON, )  
 )  
Plaintiff, )  
 )  
vs. ) Case No.  
 ) CGC-16-550128  
MONSANTO COMPANY, )  
 )  
Defendant. )  
----- )

VIDEOTAPED DEPOSITION OF  
DEWAYNE ANTHONY LEE JOHNSON  
Vallejo, California  
Wednesday, December 6, 2017  
Volume I

Reported by: SUZANNE F. GUDELJ  
CSR No. 5111  
Job No. 2770165  
PAGES 1 - 458

1 Vallejo, California; Thursday, December 7, 2017

2 9:24 a.m.

3 ---o0o---

4

5 VIDEO OPERATOR: Good morning. We are 09:24:14  
6 going on the record at 9:24 on December 8th [sic] of  
7 the year 2107. This is the beginning of disk 1,  
8 Volume 1 in the videoed deposition of Dewayne  
9 Johnson taken by counsel for defendant in the matter  
10 of Dewayne Johnson v the Monsanto Company. It's 09:24:39  
11 filed in the Superior Court, the State of  
12 California, County of San Francisco, Case  
13 CGC-16-550128.

14 We are at the Courtyard Marriott at 1000  
15 Fairgrounds Drive in Vallejo, California. My name 09:25:00  
16 is Kevin Four. I'm from Veritext. I'm here with  
17 court reporter Suzanne Gudelj, also from Veritext.

18 Please understand that mics are very  
19 sensitive and may pick up whispering, private  
20 conversations and cell interference. Audio and 09:25:18  
21 video recording will continue to take place unless  
22 all parties agree to go off the record.

23 I'm not related to any party, nor am I  
24 financially interested in the outcome.

25 Will counsel please state their 09:25:31

Page 8

1 appearances.

2 MR. COPLE: William Cople of Hollingsworth  
3 LLP and Stephanie Salek also of Hollingsworth LLP  
4 and Sandra Edwards of Farella Braun all representing  
5 Monsanto Company. 09:25:47

6 MR. LITZENBURG: Timothy Litzenburg from  
7 The Miller Firm for the plaintiff, Mr. Johnson.

8 VIDEO OPERATOR: Thank you. If the court  
9 reporter will please swear the witness, we can  
10 begin. 09:26:08

11  
12 DEWAYNE ANTHONY LEE JOHNSON,  
13 having been administered an oath, was examined and  
14 testified as follows:

15 09:26:09

16 EXAMINATION

17 BY MR. COPLE:

18 Q Good morning, Mr. Johnson.

19 A Good morning.

20 Q We have not met previously until just a 09:26:15  
21 moment ago, correct?

22 A Correct.

23 Q And your name is Dewayne Lee Johnson;  
24 that's your full name?

25 A Dewayne Anthony Lee Johnson. Anthony is in 09:26:27

Page 9

1 you claim from being on the job were based on  
2 what -- what responsibilities the school district  
3 gave you as part of hiring you; is that right?

4 A So my job was a pretty broad job. It  
5 started out as a integrated pest manager is what 09:31:24  
6 it's called, and then I have also some duties as far  
7 as groundsman or a regular landscaper.

8 Q We'll talk in more detail about all those  
9 duties. Just trying to make sure I understand  
10 that -- that at least one part of your job was to 09:31:41  
11 apply Ranger PRO.

12 A Exactly. That was the main part. It was  
13 to be a -- to start a program that was supposed to  
14 stop the use of Ranger PRO and use more natural and  
15 more controlling things where we're not putting down 09:31:58  
16 chemicals.

17 Q That was your responsibility?

18 A Yeah, as the integrated pest manager, I was  
19 supposed to keep up with that type of stuff.

20 Q And you started applying Ranger PRO in 09:32:08  
21 June 2012?

22 A Around that time.

23 Q And the last time that you applied Ranger  
24 PRO as part of your job at the school district would  
25 have been in January 2015? 09:32:18

1 applicable laws.

2 BY MR. COPLE:

3 Q Now, the second incident that you referred  
4 to, is this an incident that occurred in April of  
5 2014? 10:00:29

6 A April 2014? I don't know exactly the date.

7 Q Is this -- is the second incident an  
8 occasion when you have said that you were splashed  
9 on the face with Ranger PRO? Was that the second  
10 incident? 10:00:48

11 A The splashing on the face didn't really  
12 have a specific date. That thing was coming with  
13 that spraying all the time. You feel a little bit  
14 of drift here and there because there was no way to  
15 control the drift. I didn't wear a face mask. I 10:00:59  
16 wore goggles, and I wore a helmet, like a sort of  
17 pullover type of thing, a hoodie, nothing to totally  
18 close my face.

19 Q Do you recall that you went to see a  
20 doctor, Dr. Carrie Chanson, in July 2014 about an 10:01:10  
21 eruption on your skin?

22 A Is that the dermatologist? She's from --  
23 from Solano Dermatology?

24 (Reporter clarification.)

25 The dermatologist from Solano Dermatology? 10:01:24

1 Q If you go to page 2 of this Exhibit 5, and  
2 it says, section No. 4, "First Aid Measures," and  
3 first thing it says is:

4 "Use personal protection  
5 recommended in section 8."

12:31:32

6 You followed that, right?

7 A Yes.

8 Q You followed that, right?

9 A Yes.

10 Q Okay. And if you go to section 8, which is 12:31:43  
11 over -- it's two more pages, under "Exposure  
12 Controls/Personal Protection," if you go down to  
13 section 8.3.2, it says "Skin protection," right?

14 A Which one is that?

15 Q Skin protection, 8.3.2.

12:32:05

16 A Yeah.

17 Q And it says, "No special requirement when  
18 used as recommended" meaning when the product is  
19 used as recommended, correct?

20 A Yep.

12:32:15

21 Q But you -- you did use -- anyway, you used  
22 the Tyvek suit?

23 A Yep.

24 Q And you did, as it says, wear chemical  
25 resistant clothes; you had that?

12:32:25

1 A Yes.

2 Q And you had the boots?

3 A The boots and everything.

4 Q And the mask?

5 A And the paper mask. 12:32:30

6 Q And the goggles?

7 A And the goggles.

8 Q Okay. And if you go -- if you go back to  
9 section 4, "First Aid Measures," and we just talked  
10 about personal protection. If you go down a little 12:32:45  
11 further under "Description of first aid measures,"  
12 it's 4.1. And further down from there is "Skin  
13 contact," 4.1.2. Do you see that?

14 A Mm-hmm.

15 Q It says: 12:33:01

16 "Take off contaminated clothing.

17 Rinse skin immediately with plenty of

18 water for 15-20 minutes. Call a poison

19 control center or doctor for treatment

20 advice." 12:33:15

21 So on the -- you didn't read this every day  
22 because you already knew what this said; is that  
23 why?

24 A No.

25 Q Why didn't you read it every day? 12:33:26

1 now.

2 And it's just trial and error, push and  
3 pull until I get to the point where I just take the  
4 treatments down there at Kaiser. Took my pills  
5 through the week until I can get out of the hole 06:45:29  
6 that I'm in right now.

7 BY MR. LITZENBURG:

8 Q Do you -- are you familiar with -- well, do  
9 you see signs -- living in California, do you see  
10 signs out that say there's a chemical here that's 06:45:38  
11 known in the state of California to cause cancer or  
12 birth defects?

13 A Yeah.

14 MR. COPLE: Objection. Lacks foundation.

15 BY MR. LITZENBURG: 06:45:47

16 Q Have you ever seen one for -- for Roundup?

17 MR. COPLE: Objection. Calls for  
18 speculation.

19 THE WITNESS: No, not directly for Roundup.

20 BY MR. LITZENBURG: 06:45:54

21 Q I'm going to represent --

22 A Except that commercial that I saw.

23

24

25

Confidential

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I, DEWAYNE ANTHONY LEE JOHNSON, do hereby  
declare under penalty of perjury that I have read  
the foregoing transcript of my deposition; that I  
have made such corrections as noted herein, in ink,  
initialed by me, or attached hereto; that my  
testimony as contained herein, as corrected, is true  
and correct.

EXECUTED this \_\_\_\_\_ day of \_\_\_\_\_,  
2017, at \_\_\_\_\_, \_\_\_\_\_.  
(City) (State)

\_\_\_\_\_  
DEWAYNE ANTHONY LEE JOHNSON  
Volume I

1 I, the undersigned, a Certified Shorthand  
2 Reporter of the State of California, do hereby  
3 certify:

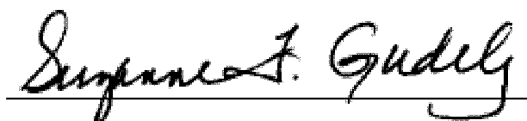
4 That the foregoing proceedings were taken  
5 before me at the time and place herein set forth;  
6 that any witnesses in the foregoing proceedings,  
7 prior to testifying, were duly sworn; that a record  
8 of the proceedings was made by me using machine  
9 shorthand which was thereafter transcribed under my  
10 direction; that the foregoing transcript is a true  
11 record of the testimony given.

12 Further, that if the foregoing pertains to  
13 the original transcript of a deposition in a Federal  
14 Case, before completion of the proceedings, review  
15 of the transcript [ ] was [ ] was not requested.

16 I further, certify I am neither financially  
17 interested in the action nor a relative or employee  
18 of any attorney or party to this action.

19 IN WITNESS WHEREOF, I have this date  
20 subscribed my name.

21 Dated: December 18, 2017

22  
23 

24 SUZANNE F. GUDELJ

25 CSR No. 5111

# **EXHIBIT 4**

ARTICLE

# Glyphosate Use and Cancer Incidence in the Agricultural Health Study

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## Abstract

**Background:** 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,” noting 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 2001 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 linkages through 2012 (North Carolina)/2013 (Iowa). Lifetime days and intensity-weighted lifetime days of glyphosate use were based on self-reported information from enrollment (1993–1997) and follow-up questionnaires (1999–2005). We estimated incidence rate ratios (RRs) and 95% confidence intervals (CIs) using Poisson regression, controlling for potential confounders, including use of other pesticides. All statistical tests were two-sided.

**Results:** Among 54 251 applicators, 44 932 (82.8%) used glyphosate, including 5779 incident cancer cases (79.3% of all cases). In unlagged analyses, glyphosate was not 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 never users (RR = 2.44, 95% CI = 0.94 to 6.32,  $P_{\text{trend}} = .11$ ), though this association was not statistically significant. Results for AML were similar with a five-year (RR<sub>Quartile 4</sub> = 2.32, 95% CI = 0.98 to 5.51,  $P_{\text{trend}} = .07$ ) and 20-year exposure lag (RR<sub>Tertile 3</sub> = 2.04, 95% CI = 1.05 to 3.97,  $P_{\text{trend}} = .04$ ).

## Conclusions:

There was some evidence of increased risk of AML among the highest exposed group that requires confirmation.

Glyphosate was introduced as a broad-spectrum herbicide in 1974, and it quickly became one of the most heavily used herbicides worldwide. With the introduction of genetically

engineered glyphosate-tolerant crops, glyphosate use increased dramatically in the late-1990s and 2000s. In addition to agricultural uses, glyphosate is one of the most common residential

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# **EXHIBIT 5**

## Genotoxic Potential of Glyphosate Formulations: Mode-of-Action Investigations

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DONNA R. FARMER<sup>†</sup>

Monsanto Company, St. Louis, Missouri 63167; Pfizer Company, St. Louis, Missouri 63167;  
Buena Vista, Colorado 81211; Tibotec BVBA, B-3210 Mechelen, Belgium; and  
Lexicon Genetics Inc., The Woodlands, Texas 77381

A broad array of in vitro and in vivo assays has consistently demonstrated that glyphosate and glyphosate-containing herbicide formulations (GCHF) are not genotoxic. Occasionally, however, related and contradictory data are reported, including findings of mouse liver and kidney DNA adducts and damage following intraperitoneal (ip) injection. Mode-of-action investigations were therefore undertaken to determine the significance of these contradictory data while concurrently comparing results from ip and oral exposures. Exposure by ip injection indeed produced marked hepatic and renal toxicity, but oral administration did not. The results suggest that ip injection of GCHF may induce secondary effects mediated by local toxicity rather than genotoxicity. Furthermore, these results continue to support the conclusion that glyphosate and GCHF are not genotoxic under exposure conditions that are relevant to animals and humans.

**KEYWORDS:** Glyphosate; genotoxicity; mode of action

### INTRODUCTION

The potential genotoxicity of glyphosate has been tested in a wide variety of in vitro and in vivo assays. No genotoxicity was observed in standard assays conducted according to international guidelines and Good Laboratory Practice (GLP) Standards. These assays are described briefly in Williams et al. (1), and the results have led to the conclusion that glyphosate does not pose a risk for the production of heritable or somatic mutations in humans (1–6). The original Roundup formulation and subsequent glyphosate-containing herbicide formulations (GCHF) have also been evaluated for genotoxic responses in several assays. Although a number of studies conducted according to international guidelines and GLP Standards show that these materials are not genotoxic (1), a few other studies have reported positive effects.

Apparent evidence of DNA adducts in the liver and kidneys of CD-1 mice was reported (7) when a formulation that was identified as “Roundup” (30.4% glyphosate, purchased from Monsanto, Italy) was administered intraperitoneally (600 mg/kg) using dimethyl sulfoxide (DMSO)/olive oil as a vehicle.

However, no DNA adducts were observed following intraperitoneal (ip) injection of isopropylamine salts of glyphosate. In contrast, ip injection of CD-1 mice with analytical grade glyphosate or the same “Roundup” formulation resulted in an increased incidence of alkali-labile sites in DNA from liver and kidney (8). The effects reported in the latter study (8) were observed at 300 mg/kg with glyphosate and at 900 mg/kg for GCHF, including a dramatic increase in the number of 8-hydroxydeoxyguanine (8-OHdG) residues in DNA from liver cells after treatment with glyphosate but not the GCHF; opposite results were found in the kidney. All of these changes were observed only under unrealistic exposure conditions (very high dose levels administered by an irrelevant route of exposure for an agricultural herbicide).

To better understand the significance of these results (7, 8), four separate but inter-related assays were undertaken to determine if high-dose ip administration produces toxicity that may be responsible for the observed changes via secondary effects, rather than direct genotoxicity, and whether a more relevant (oral) route of exposure produces the same toxic responses as those seen with ip administration. The first assay was performed to understand the relevance of findings reported by Bolognesi et al. (8) by investigating the degree of liver and kidney toxicity that occurred under the dosing conditions used by those investigators. Similarly, another assay was conducted to understand the relevance of findings reported by Peluso et al. (7); this assay also examined whether the vehicles used in their studies (DMSO/olive oil) contributed to the hepatic

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Table 1. Overall Study Experimental Design

study/test material	GCHF <sup>a</sup> dose (mg/kg)	route of dosing	necropsy: h after dosing	group size	evaluations conducted			
					CC <sup>b</sup>	pathology	NMO <sup>c</sup>	8-OHdG <sup>d</sup>
Group 1								
isotonic saline	0	ip <sup>e</sup>	24	10	+	O, G <sup>g</sup>	+	—
isotonic saline	0	ip	24	8	+	O, G	+	+
GCHF in isotonic saline	600	ip	24	8	+	O, G	+	—
isotonic saline	0	ip	4	10	+	O, G	—	—
GCHF in isotonic saline	600	ip	4	10	+	O, G, M <sup>h</sup>	+	+
Group 2								
DMSO/OO <sup>i</sup>	—	ip	24	10	+	O, G, M	+	—
GCHF/DMSO/OO	600	ip	24	10	+	O, G, M	+	—
Group 3								
GCHF/DMSO/OO	600	ip	24	10	+	O, G	—	—
GCHF without glyphosate/DMSO/OO	600	ip	24	10	+	O, G	—	—
Group 4								
isotonic saline	0	ip	24	10	+	O, G, M	+	+
GCHF in isotonic saline	900	ip	24	10	+	O, G, M	+	+
isotonic saline	0	oral	24	10	+	O, G, M	—	—
GCHF/DMSO/OO	600	oral	24	10	+	O, G, M	—	—

<sup>a</sup> GCHF, glyphosate-containing herbicide formulation. <sup>b</sup> CC, clinical chemistry. <sup>c</sup> NMO, NADPH menadione oxidoreductase mRNA. <sup>d</sup> 8-OHdG, 8-hydroxydeoxyguanosine. <sup>e</sup> Intraperitoneal injection. <sup>f</sup> Organ weights obtained. <sup>g</sup> Gross pathology examination. <sup>h</sup> Microscopic pathology examination. <sup>i</sup> Dimethylsulfoxide. <sup>j</sup> Olive oil.

and renal toxicity. A third assay was performed to investigate the relationship of glyphosate and the other GCHF ingredients to the marked toxicity observed in the second study. Finally, a fourth assay was conducted to determine if the marked toxicity observed in the studies using ip administration of the GCHF/DMSO/olive oil mixture was also produced after oral administration, the more relevant route of exposure for herbicides.

## MATERIALS AND METHODS

The assay design and the parameters evaluated by group are outlined in Table 1. Each assay was conducted at the same laboratory by the same group of investigators. The sex and strain of the animals used, animal housing and handling procedures, in-life observations, dosing methods (oral by gavage or ip injection), animal sacrifice procedures, and analytical procedures were the same in all of the assays.

**Animals.** Male Crl:CD-1(ICR)BR mice were obtained from Charles River Laboratory (Raleigh, NC). The animals, 8–10 per group, were 7–8 weeks of age at the start of the studies. Following 3–10 days of acclimatization, the mice were computer randomized by body weight and were then allocated to dosing groups so that individual animal body weights were within  $\pm 20\%$  of the group mean.

**Housing.** The mice were housed individually in stainless steel cages with wire mesh bottoms. Food (Certified Rodent Diet no. 5002, PMI Feeds, Inc., St. Louis, MO) and water (public water supply, St. Louis, MO) were available ad libitum. Animal room temperature and relative humidity were targeted to be within 64–74 °F and 30–70%, respectively. A 12/12 h light/dark cycle was observed. Animal housing and husbandry were performed in accordance with the provisions of the *Guide for the Care and Use of Laboratory Animals* (9).

**In-Life Observations.** Mortality checks were conducted at least once daily during the assays. The mice were also observed daily at 6–7 h postdosing and/or at the time of terminal sacrifice for overt signs of toxicity. Nonfasted body weights were taken prior to randomization, on the morning of dosing, and just prior to sacrifice.

**Test Materials.** The following materials were used in these assays: (a) the formulated herbicide product (Roundup, Monsanto Co., St. Louis, MO) that was the same GCHF reported to be used by Peluso et al. (7) and Bolognesi et al. (8) and that contained an isopropylamine salt (IPA) of glyphosate (~30% by weight) and an alkyl sulfate surfactant; (b) the same GCHF minus the IPA glyphosate; (c) 1% DMSO in olive oil (DMSO/OO) (both from Sigma Chemical Co., St. Louis, MO); and (d) isotonic saline solution (Phoenix Scientific, Inc.).

**Dosing Methods.** The mice received the appropriate test or control GCHF by ip injection or orally by gavage. In each case, a single dose

was administered at a volume of 10 mL/kg of body weight. The test material was administered as a suspension in DMSO/OO or as a solution in isotonic saline. Vehicle control groups received DMSO/OO or isotonic saline only.

**Scheduled Sacrifice.** All animals were sacrificed by CO<sub>2</sub> asphyxiation at 4  $\pm$  0.5 h or 24  $\pm$  2 h after dosing. This was the same sacrifice schedule used by Peluso et al. (7) and Bolognesi et al. (8). Blood was collected from the posterior vena cava into serum microvette clot tubes. All sacrificed animals were necropsied, and the livers and kidneys were removed, observed grossly, rinsed in saline, blotted dry, and weighed. Sections from the left lateral and median lobes of the liver and sections from each kidney (hilus, cortex, and medulla from the right kidney; pelvis, cortex, and medulla from a longitudinal section of the left kidney) were placed in cassettes and retained in 10% neutral-buffered formalin for microscopic evaluation. Five-micrometer histological sections were prepared from the formalin-fixed tissues, stained with hematoxylin and eosin, and examined microscopically. The remainder of the liver and kidneys was divided for the various assays, snap frozen in liquid nitrogen, and stored until analyzed.

**Clinical Chemistry.** The collected serum was analyzed for alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and sorbitol dehydrogenase (SDH). A Hitachi clinical analyzer was used for these analyses.

**Other Liver and Kidney Analyses.** *8-Hydroxydeoxyguanosine (8-OHdG).* Frozen liver and kidney tissues were transferred on dry ice for analysis to the Medicinal Chemistry and Pharmacognosy group at the University of Illinois, Chicago. Tissue samples were weighed, placed in cell-lysing buffer, and homogenized. The sample solution was centrifuged, and the nuclei pellet was retained. RNA contaminants were digested with RNases and washed away from the DNA pellet. Next, a mixture of DNase and phosphodiesterase was added to hydrolyze the DNA to nucleosides, which were purified using C<sub>18</sub> solid-phase extraction. Deoxyguanosine was quantified by UV absorbance at 260 nm. 8-OHdG was measured using LC-MS-MS in multiple-reaction-monitoring mode with [<sup>13</sup>C<sub>10</sub>, <sup>15</sup>N<sub>5</sub>]-8-OHdG as internal standard.

*NADPH Menadione Oxidoreductase (NMO) mRNA.* Total RNA was isolated from frozen tissues and quantified using a UV spectrophotometer at 260 nm. Four hundred nanograms of RNA was reverse transcribed into cDNA using reverse transcriptase and amplified by real-time Polymerase Chain Reaction (PCR) using AmpliTaq Gold DNA polymerase and PCR primers and fluorescent dye-labeled probes specific for each mRNA, as described elsewhere (10, 11). The first doubling cycle at which product may be detected above a threshold level (C<sub>T</sub>, the cycle threshold) was determined by real-time RT-PCR. C<sub>T</sub> values were converted to relative expression levels in individual

**Table 2.** Terminal Body Weights and Organ Weights for CD-1 Mice (Groups 1 and 4) Following Intraperitoneal Administration of Isotonic Saline or GCHF<sup>a</sup> in Isotonic Saline

dose group (8 or 10 mice/group)	body wt (g)	liver wt (g)	liver-to-body wt ratio ( $\times 100$ )	kidney wt (g)	kidney-to-body wt ratio ( $\times 100$ )
Group 1					
isotonic saline control, 4 h sacrifice	30.5 $\pm$ 1.4	1.61 $\pm$ 0.19	5.27 $\pm$ 0.42	0.519 $\pm$ 0.039	1.70 $\pm$ 0.12
GCHF (600 mg/kg), 4 h sacrifice	30.3 $\pm$ 1.3	1.55 $\pm$ 0.22	5.12 $\pm$ 0.66	0.502 $\pm$ 0.053	1.66 $\pm$ 0.20
isotonic saline control, 24 h sacrifice	32.5 $\pm$ 3.2	1.91 $\pm$ 0.24	5.88 $\pm$ 0.39	0.578 $\pm$ 0.065	1.78 $\pm$ 0.14
GCHF (600 mg/kg), 24 h sacrifice	29.5 $\pm$ 2.4 <sup>b</sup>	1.53 $\pm$ 0.22 <sup>c</sup>	5.23 $\pm$ 0.81	0.505 $\pm$ 0.057 <sup>b</sup>	1.71 $\pm$ 0.15
Group 4					
isotonic saline control, 24 h sacrifice	32.3 $\pm$ 1.3	1.65 $\pm$ 0.17	5.12 $\pm$ 0.43	0.546 $\pm$ 0.063	1.69 $\pm$ 0.17
GCHF (900 mg/kg), 24 h sacrifice	31.6 $\pm$ 1.0	1.43 $\pm$ 0.14 <sup>b</sup>	4.52 $\pm$ 0.36 <sup>c</sup>	0.442 $\pm$ 0.086 <sup>b</sup>	1.40 $\pm$ 0.27 <sup>c</sup>

<sup>a</sup> Glyphosate-containing herbicide formulation. <sup>b</sup> Statistically significantly different from control,  $p \leq 0.05$ . <sup>c</sup> Statistically significantly different from control,  $p \leq 0.01$ .

animals by adjusting for expression levels of the housekeeping gene cyclophilin, average expression levels in control animals, and the doubling of product that occurs at each PCR cycle. Detailed calculation methods are described elsewhere (12). Group means of individual animal relative expression levels were also calculated.

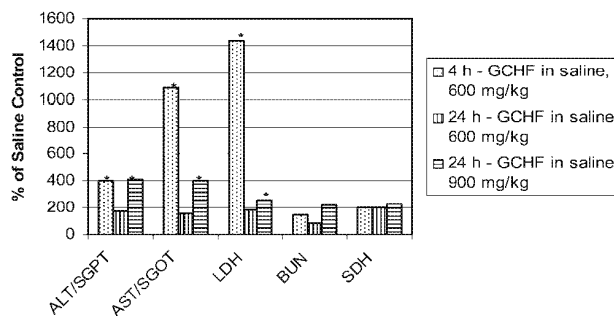
**Statistical Analyses.** Results are presented as the mean  $\pm$  standard deviation (SD) for the number of animals indicated. Comparisons between respective control and treated animals were made with Student's *t* test or Dunnett's multiple-comparison test (13, 14). These were used to evaluate mRNA expression of NMO, 8-OHdG levels, and body weights. Fisher's exact test (15) was used to evaluate the incidences of microscopic lesions. Terminal body weights, absolute organ weights, organ/body weight ratios, and clinical chemistry data were evaluated by a decision-tree statistical analysis that, depending on the results of tests for normality and homogeneity of variances (Bartlett–Box test) (16), used either parametric (Dunnett's test and linear regression) (17) or nonparametric [Kruskal–Wallis (18), Jonckheere's (19), and/or Mann–Whitney (20)] test routines to detect group differences and analyze for trend. Grubbs' test (21, 22) was used to identify outliers for cell proliferation and for 8-OHdG. Due to assay variability, Grubbs' test was not run on results from the NMO reductase mRNA analyses. All tests were evaluated at  $p < 0.05$  and  $p < 0.01$ .

## RESULTS

**Evaluation of Toxicity Following Intraperitoneal Injection of the GCHF in Saline.** Terminal body weights were unaffected in treated animals sacrificed 4 h after dosing (Table 2). The body weights of animals given the GCHF at 600 mg/kg were statistically significantly reduced (9% below control mean) at the 24 h time point. However, in a separately run experiment (see Table 1 for a description of the overall testing program), the highest dose group, 900 mg/kg, sacrificed 24 h after dosing, no such decrease was observed. The reason for the decreased body weights in the 600 mg/kg animals is unknown. Absolute liver and kidney weights were decreased (13–20 and 13–19%, respectively) in both the 600 and 900 mg/kg dose groups compared to control groups at the 24 h time point. Also, statistically significant reductions in liver and kidney-to-body weight ratios were observed at the 900 mg/kg dose level.

Intraperitoneal injection of the GCHF resulted in several statistically significant changes in clinical chemistry values. Four hours after a dose of 600 mg/kg, substantial increases in clinical chemistry values were observed, most notably ALT, AST, and LDH (406, 1087, and 1433% of controls, respectively) (Figure 1). Most of these values returned to near control levels by 24 h postdosing in mice treated with 600 mg/kg. However, statistically significant elevations in ALT, AST, and LDH (218–410% of controls) were still observed at 24 h in other mice given a 900 mg/kg dose.

No microscopic alterations in liver or kidney were observed in the 600 mg/kg dose group mice sacrificed 4 h after treatment. The only notable histopathology finding from the 600 mg/kg dose group sacrificed at 24 h was the deposition of fibrin/



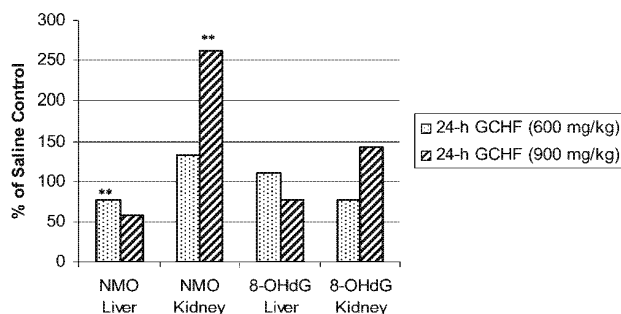
**Figure 1.** Comparison of clinical chemistry values for CD-1 mice following intraperitoneal administration of GCHF for 4 and 24 h at 600 or 900 mg/kg. The values presented are shown as the percentage of clinical chemistry values for the treatments with herbicide formulation compared to saline controls. ALT/SGPT, alanine aminotransferase; AST/SGOT, aspartate aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; SDH, sorbitol dehydrogenase. An asterisk indicates statistically significant difference from control,  $p \leq 0.05$ .

amorphous material on the capsule of the kidneys in three mice. This lesion was also observed in one mouse from the saline control group. There were no abnormal findings in the liver.

Several microscopic changes occurred in the kidneys and livers of mice given the GCHF at the 900 mg/kg dose level. Renal changes consisted of vacuolization of cortical tubules in three of the treated mice. Degeneration and necrosis also occurred in the medulla of the kidneys from one mouse. Acute inflammation of the renal capsule and deposition of amorphous material on the renal capsule occurred in a different mouse. Hepatic changes included a generalized increase in hepatocellular vacuolization, subcapsular necrosis, and subcapsular hepatocellular vacuolization; these lesions occurred in 6 of 10, 4 of 10, and 5 of 10 mice, respectively. None of these kidney and liver lesions occurred in any of the control animals.

Evidence of oxidative stress was observed in the kidneys of animals given the GCHF at a dose of 900 mg/kg but not at 600 mg/kg. A statistically significant increase in NMO (relative expression level of  $2.66 \pm 0.79$  versus  $1.02 \pm 0.20$  or 261% of controls) was seen in the kidney of the 900 mg/kg group of animals (Figure 2). There was no statistically significant increase in 8-OHdG, although the level in kidneys of mice given an ip injection of the GCHF at 900 mg/kg was 143% of the control value [mean degree of oxidation ( $\times 10^5$ ) was  $0.28 \pm 0.05$  for control and  $0.40 \pm 0.28$  for treated].

**Evaluation of Toxicity Following Intraperitoneal Injection of DMSO/OO and the GCHF/DMSO/OO Mixture.** The ip administration of DMSO/OO alone did not produce any significant evidence of toxicity. Terminal body weights and liver and kidney weights, as well as organ-to-body weight ratios, were unchanged for animals sacrificed at 24 h when treated animal



**Figure 2.** Evaluation of expression of NADPH menadione oxidoreductase (NMO) and 8-hydroxydeoxyguanosine (8-OHdG) in the liver and kidney of CD-1 mice exposed for 24 h to GCHF at 900 and 600 mg/kg by intraperitoneal administration. Values are presented as the percent of saline control. A double asterisk indicates statistically significant difference,  $p \leq 0.01$ .

were compared to control animals (Table 3). The DMSO/OO vehicle did not alter clinical chemistry values (Figure 3), and the only notable microscopic finding was the occurrence of renal capsule fibrosis in three animals. There was no statistically significant increase in liver or kidney NMO values (liver relative expression level of  $1.44 \pm 1.86$  versus  $1.04 \pm 0.29$  or 138% of controls and kidney relative expression level of  $1.03 \pm 0.24$  versus  $1.03 \pm 0.26$  or 100% of controls, Figure 4).

In contrast to the findings for DMSO/OO alone, the ip administration of the GCHF/DMSO/OO mixture at 600 mg/kg produced a significant effect. Whereas liver weights were unaffected in these animals (group 2, Table 3), absolute and relative liver weights were reduced (14 and 13%, respectively, below controls) in another group of mice (group 3, Table 4) given the same test material. Significant decreases in absolute and/or relative kidney weights were observed in both groups of animals (group 2, 11 and 9%, Table 3; and group 3, 19 and 18%, Table 4, respectively). Dramatic, statistically significant increases in clinical chemistry values were also observed. Serum ALT, AST, LDH, BUN, and SDH levels in treated animals were 151–1065% (Figure 3). In addition, pathology examinations revealed several changes in the capsule or subcapsular tissue in both livers and kidneys. The changes included deposition of fibrin and an amorphous material on the capsule of livers and kidneys, inflammation, and hemorrhage involving the renal capsule. The deposition of the fibrin/amorphous material on the surface of the liver was accompanied by necrosis of hepatocytes immediately subjacent to the capsule along with acute inflammation in subcapsular regions. In addition, there was vacuolization of hepatocytes in most subcapsular regions. Oxidative stress was also observed (Figure 4) in the kidneys of animals given the GCHF/DMSO/OO mixture as indicated by a statistically significant increase in NMO (relative expression level of  $3.09 \pm 1.53$  versus  $1.03 \pm 0.24$  or 300% of controls; liver was  $0.48 \pm 0.22$  versus  $1.04 \pm 0.29$  or 46% of controls).

**Comparison of Toxicity Produced by the GCHF/DMSO/OO Mixture with and without Glyphosate.** The toxicity produced by the GCHF/DMSO/OO mixture was further evaluated by directly comparing effects produced by that mixture to those observed after administration of a surfactant/DMSO/OO mixture. This “formulation blank” contained all of the same components of the GCHF in DMSO/OO except glyphosate. Reductions in absolute and relative organ weights were very similar for both test materials (Table 4). For example, reductions in absolute liver weights for animals given the test material with and without glyphosate were 14 and 15%; for kidney weights,

the values were 19 and 22%, respectively. Similar results were obtained for serum clinical chemistry values. As seen in Figure 5, serum enzyme levels from mice given the GCHF blank were generally comparable to values from animals given the test material with glyphosate. Gross necropsy evaluations showed the presence of a white particulate material adhering to the surface of tissues (i.e., liver, kidneys, spleen, and small intestines) in the peritoneal cavity in a majority of animals in both treated groups (data not shown).

**Evaluation of Toxicity Following Oral Administration of the GCHF/DMSO/OO Mixture.** Administration of the GCHF/DMSO/OO mixture by the oral route of exposure produced essentially no evidence of toxicity. Terminal body weights and absolute and relative kidney weights were unaffected by oral treatment with the GCHF at 600 mg/kg in DMSO/OO for animals sacrificed at 24 h when treated animals were compared to control animals (Table 5). Although absolute and relative hepatic weights were statistically significantly decreased, the changes were considered to be of little or no consequence due to their small magnitude (7.6 and 6.8% below controls, respectively). Serum chemistry parameters were not elevated for oral exposure in comparison with ip exposure (Figure 6), and no histopathological lesions were observed in the liver or kidneys (data not shown).

## DISCUSSION

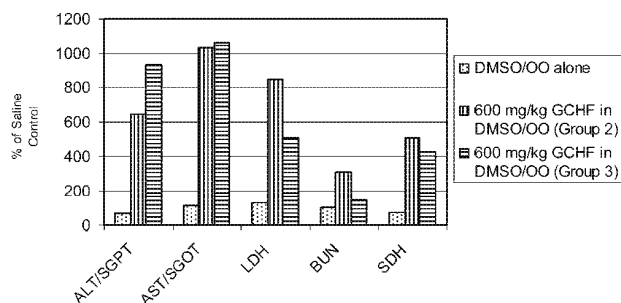
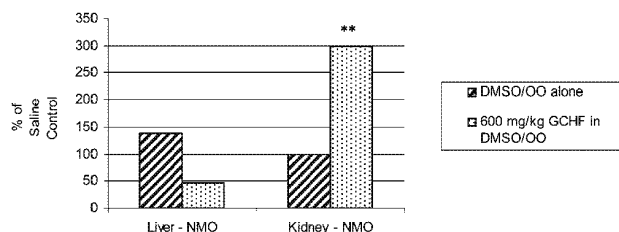
**Evaluation of Toxicity Following Intraperitoneal Injection of the GCHF in Saline.** Bolognesi et al. (8) reported that a single 900 mg/kg dose of the GCHF administered intraperitoneally produced DNA damage, as evidenced by the induction of DNA single-strand breaks and 8-OHdG. The levels of DNA single-strand breaks were statistically significantly increased in both liver and kidneys (2.5- and 2.3-fold, respectively) from animals sacrificed 4 h after administration of the GCHF. By 24 h postdosing, there were no statistically significant differences in the levels of DNA strand breaks, although the values for livers and kidneys from treated animals remained numerically elevated above control levels (1.5- and 1.6-fold, respectively). The reported increases in the numbers of 8-OHdG residues were somewhat more pronounced. Levels of 8-OHdG were significantly increased (2.7-fold) only in kidneys 4 h after dosing; by 24 h, increases in both liver and kidneys (2.8- and 3.1-fold) were observed, although only the kidney value was statistically significantly different from controls.

The work described herein demonstrated that the ip injection of the GCHF in saline resulted in significant toxicity. Four hours after a single 600 mg/kg dose, substantial increases in clinical chemistry values were observed. Most of these values returned to near control levels by 24 h postdosing. However, statistically significant elevations were still observed at 24 h in mice given a 900 mg/kg dose. Although clinical chemistry values were not evaluated at 4 h in the 900 mg/kg group, results from the 600 mg/kg group at this time point indicate that substantial elevations occurred in the higher dose group. Histopathological lesions noted in the livers (hepatocellular vacuolization, subcapsular vacuolization, and necrosis) and kidneys (cortical tubule vacuolization, medullary necrosis, and acute capsular inflammation) of mice given the 900 mg/kg dose also indicate significant organ toxicity. The statistically significant increase in NMO observed in the kidneys of animals given the GCHF at a dose of 900 mg/kg was evidence of oxidative stress. These data provide a strong indication that the dosing conditions used by Bolognesi et al. (8) produced marked hepatic and renal toxicity. The induction of DNA damage in liver and kidneys produced under

**Table 3.** Terminal Body Weights and Organ Weights for CD-1 Mice (Group 2) Following Intraperitoneal Administration of Isotonic Saline, DMSO<sup>a</sup>/OO<sup>b</sup>, or GCHF<sup>c</sup> in DMSO/OO

dose group (8 or 10 mice/group)	body wt (g)	liver wt (g)	liver-to-body wt ratio ( $\times 100$ )	kidney wt (g)	kidney-to-body wt ratio ( $\times 100$ )
isotonic saline control, 24 h sacrifice	30.0 $\pm$ 1.1	1.63 $\pm$ 0.24	5.42 $\pm$ 0.74	0.533 $\pm$ 0.045	1.77 $\pm$ 0.12
DMSO/OO, 24 h sacrifice	29.7 $\pm$ 1.3	1.54 $\pm$ 0.14	5.19 $\pm$ 0.31	0.522 $\pm$ 0.060	1.75 $\pm$ 0.15
GCHF (600 mg/kg) in DMSO/OO, 24 h sacrifice	29.6 $\pm$ 0.9	1.54 $\pm$ 0.09	5.20 $\pm$ 0.24	0.476 $\pm$ 0.039	1.61 $\pm$ 0.13 <sup>d</sup>

<sup>a</sup> Dimethyl sulfoxide. <sup>b</sup> Olive oil. <sup>c</sup> Glyphosate-containing herbicide formulation. <sup>d</sup> Statistically significantly different from control,  $p \leq 0.05$ .

**Figure 3.** Clinical chemistry values for CD-1 mice following intraperitoneal administration of GCHF in DMSO/OO (600 mg/kg, 24 h) or DMSO/OO only. The values presented are shown as the percentage of clinical chemistry values for the treatments (GCHF in DMSO/OO or DMSO/OO only) compared to saline controls. ALT/SgPT, alanine aminotransferase; AST/SgOT, aspartate aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; SDH, sorbitol dehydrogenase.**Figure 4.** Evaluation of expression of NADPH menadione oxidoreductase (NMO) in the liver and kidney of CD-1 mice exposed for 24 h to GCHF at 600 mg/kg in DMSO/OO and to DMSO/OO alone by intraperitoneal administration. Values are presented as the percent of saline control. A double asterisk indicates statistically significant difference,  $p \leq 0.01$ .

conditions of substantial organ toxicity via an ip route of exposure is of doubtful biological relevance.

By definition, an increase in 8-OHdG is not an indicator of interaction with DNA, but rather is an event that occurs secondarily to oxidative effects. It should be noted that the increases in 8-OHdG reported by Bolognesi et al. (8) (in one group of three mice) were not observed in the present study. There was no statistically significant increase in 8-OHdG in either liver or kidney, and the highest value observed (kidneys, 900 mg/kg dose group) in any treated group was only 143% of the control value. The reason for this discrepancy is not apparent. Certainly the sample size used in this study (two groups of five mice each) should have been sufficient to reproduce effects that Bolognesi et al. (8) reported in a single group of three mice. Therefore, because of the more robust nature of the present investigation, the previous report is not considered to be sufficient to conclude that high-dose ip administration of the GCHF causes oxidative damage to DNA.

**Evaluation of Toxicity Following Intraperitoneal Injection of DMSO/OO, GCHF, and the GCHF/DMSO/OO Mixture.** Peluso et al. (7) reported that the GCHF, when administered in a DMSO/OO mixture, induced DNA adduct formation in the liver and kidneys of mice injected intraperitoneally at

doses of 400–600 mg/kg. The present study investigated the potential for different components of this GCHF to produce hepatic and renal toxicity. The administration of the DMSO/OO vehicle only produced no apparent adverse effects 24 h after treatment. As discussed above, the GCHF administered in a saline vehicle at 600 mg/kg produced only slight increases in some clinical chemistry values at 24 h after dosing. In contrast, administration of the GCHF at 600 mg/kg in a DMSO/OO vehicle produced marked toxicity at 24 h after treatment as evidenced by dramatic increases in clinical chemistry values (Figure 3). In addition, pathology examinations of the animals that received the 600 mg/kg GCHF/DMSO/OO mixture revealed deposition of fibrin on the capsule of livers and kidneys, renal inflammation and hemorrhage, and hepatocellular inflammation and necrosis. From these data it is clear that the unusual combination of GCHF, DMSO, and OO is required to produce the substantial toxicity observed.

**Comparison of Toxicity Produced by the GCHF/DMSO/OO Mixture with and without Glyphosate.** To assess the contribution of glyphosate to the GCHF toxicity observed, another assay was performed in which the toxicity produced by the injection of the GCHF/DMSO/OO mixture was directly compared to that observed following administration of a “formulation blank,” consisting of DMSO/OO mixed with the components (primarily a surfactant system) of the GCHF except glyphosate. These two test materials produced essentially the same severe, adverse effects. The results support the conclusion that substantial toxicity is caused by the surfactant/DMSO/OO mixture used by Peluso et al. (7) and that glyphosate contributes little, if anything, to the adverse effects observed.

As noted above, Peluso et al. (7) reported that the GCHF/DMSO/OO mixture induced a dose-dependent formation of DNA adducts in the liver and kidneys of mice injected intraperitoneally at doses of 400, 500, and 600 mg/kg. The relative adduct levels (RAL, expressed as adducts per  $10^9$  nucleotides) reported at these dose levels were 8, 15, and 17, respectively, in liver and 19, 22, and 30, respectively, in kidneys. The significance of these RALs should not be taken at face value, however, and should instead be assessed within the context of the formation of endogenous adducts that arise from natural metabolic processes and environmental factors.

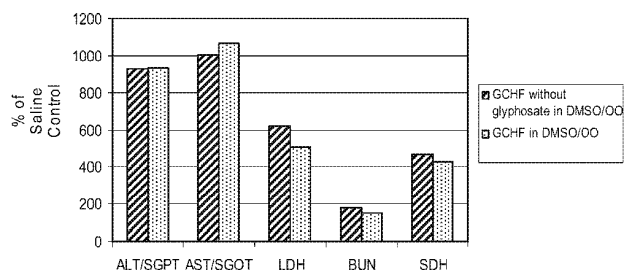
For example, upper range RAL values for several types of normal endogenous adducts have been reported to be 70–2100 cyclic adducts/ $10^9$  nucleotides in human liver and 1400 alkylated bases/ $10^9$  nucleotides in human lung (23), and levels of oxidized bases arising from natural oxidants are much higher still (e.g., 700–23000 oxidized bases/ $10^9$  in human white blood cells). Therefore, the levels of adducts reported by Peluso et al. (7) (8–17 and 19–30 adducts/ $10^9$  nucleotides in liver and kidney, respectively) are very low compared to typical levels of endogenous adducts, and their biological relevance is consequently suspect, especially considering the fact that the adducts were produced after relatively large doses of a complex test material mixture that was injected directly into the intraperitoneal cavity.

Another consideration in evaluating the significance of the study conducted by Peluso et al. (7) is that the identification of

**Table 4.** Terminal Body Weights and Organ Weights for CD-1 Mice (Group 3) Following Intraperitoneal Administration of Isotonic Saline, GCHF<sup>a</sup> in DMSO/<sup>b</sup>OO<sup>c</sup>, or GCHF without Glyphosate in DMSO/OO

dose group (8 or 10 mice/group)	body wt (g)	liver wt (g)	liver-to-body wt ratio ( $\times 100$ )	kidney wt (g)	kidney-to-body wt ratio ( $\times 100$ )
isotonic saline control, 24 h sacrifice	29.7 $\pm$ 1.2	1.88 $\pm$ 0.17	6.33 $\pm$ 0.44	0.547 $\pm$ 0.057	1.84 $\pm$ 0.19
GCHF (600 mg/kg) in DMSO/OO, 24 h sacrifice	29.4 $\pm$ 1.8	1.61 $\pm$ 0.15 <sup>d</sup>	5.49 $\pm$ 0.42 <sup>d</sup>	0.444 $\pm$ 0.062 <sup>d</sup>	1.51 $\pm$ 0.20 <sup>d</sup>
GCHF (without glyphosate) in DMSO/OO, 24 h sacrifice	29.3 $\pm$ 1.8	1.60 $\pm$ 0.13 <sup>d</sup>	5.46 $\pm$ 0.40 <sup>d</sup>	0.429 $\pm$ 0.059 <sup>d</sup>	1.47 $\pm$ 0.23 <sup>d</sup>

<sup>a</sup> GCHF, glyphosate-containing herbicide formulation. <sup>b</sup> Dimethyl sulfoxide. <sup>c</sup> Olive oil. <sup>d</sup> Statistically significantly different from control,  $p \leq 0.01$ .

**Figure 5.** Comparison of clinical chemistry values for CD-1 mice following intraperitoneal administration of GCHF (600 mg/kg, 24 h) in DMSO/OO and GCHF without glyphosate (600 mg/kg, 24 h) in DMSO/OO. The values presented are shown as the percentage of clinical chemistry values for the treatments compared to saline controls. ALT/SGPT, alanine aminotransferase; AST/SGOT, aspartate aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; SDH, sorbitol dehydrogenase.

adducts was not performed. It is known that the <sup>32</sup>P-postlabeling methodology used can label certain compounds and mimic the behavior of DNA adducts. For example, the labeling of bile salts causes them to appear as adduct-like spots (24). There are also cases of adducts having been formed from endogenous metabolites arising from normal metabolic processes, including cases in which treatment has induced increases in adducts derived from endogenous metabolites (23, 25). In addition to the potential to label endogenous compounds, it is possible that one or more of the formulation/test material ingredients might be capable of becoming labeled and therefore have an adduct-like appearance. Finally, it is conceivable that adducts were derived from lipid peroxidation products, induced by an oxidative toxic response caused by the dosing regimen used. The inclusion of appropriate controls or the characterization of adducts could have tested these possibilities, but it does not appear that these were done. In the absence of these controls, it cannot be definitively concluded that DNA adducts were actually produced or if adducts were produced that reflect covalent DNA binding of formulation components or metabolites of formulation components.

**Comparison of Toxicity Following Intraperitoneal and Oral Administration of the GCHF/DMSO/OO Mixture.** In contrast to the marked hepatic and renal toxicity observed following ip injection of the GCHF/DMSO/OO mixture, there was no evidence of adverse effects following oral administration. This is best illustrated by the sharp contrast between the occurrence of numerous histopathological lesions and large increases in serum enzyme levels (Figure 6) following ip injection compared to the complete lack of such effects after

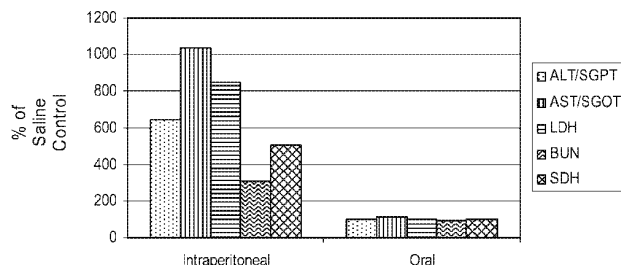
oral dosing. Oral ingestion is a more relevant route of exposure for the general population that consumes agricultural products and/or food derived from such products following the agricultural use of herbicides. Because the human consumption of glyphosate in food occurs only at extremely low levels (1, 26) and oral administration of the GCHF in mice produced no adverse effects at levels exceeding this intake by several orders of magnitude, it is concluded that results from studies using ip injection have no real significance for human risk assessment.

**Summary and Conclusions.** In a series of four inter-related assays as described herein, it was determined that high-dose ip administration of a GCHF produced significant liver and kidney toxicity. This suggests that methodology involving ip injection of GCHF may induce secondary effects mediated by local toxicity rather than genotoxicity. Importantly, there was no evidence of adverse effects following oral administration of GCHF. The experimental methods (high-dose, ip injection) used by Bolognesi et al. (8) and Peluso et al. (7) also produced marked hepatic and renal toxicity from exposure to a GCHF. Furthermore, the location and nature of the lesions resulting from this exposure scenario (i.e., direct injection into the intraperitoneal cavity) indicate that they, too, are most likely responses to local deposition of the GCHF rather than systemic toxicity. Thus, these experimental conditions (7, 8) do not assess the potential in vivo genotoxicity of the GCHF from the perspective of real-life exposure scenarios, and the DNA findings reported should not, therefore, be considered to constitute convincing evidence of relevant genotoxic activity for glyphosate or glyphosate formulations. The occurrence of severe hepatic and renal toxicity under these extreme conditions strongly indicates, instead, that effects on DNA, such as strand breaks and the formation of oxidized bases, if they do occur, may represent a secondary effect related to toxicity. Furthermore, current results indicate that some combination of the surfactant/DMSO/OO mixture is responsible for the effects reported by Peluso et al. (7) and, thus, such effects would not occur under actual use conditions of the GCHF. The large increases in 8-OHdG reported by Bolognesi et al. (8) were not reproduced here. Because of the more robust nature of the present investigation, the previous studies do not appear to provide sufficient evidence to conclude that high-dose ip administration of glyphosate causes oxidative damage to DNA. Oral administration, a route of exposure most relevant to the general human population, did not produce the hepatic or renal toxicity that occurred after ip injection. Thus, effects on DNA that are secondary to cytotoxicity would not occur following a more

**Table 5.** Terminal Body Weights and Organ Weights for CD-1 Mice (Group 4) Following Oral Administration of Isotonic Saline or GCHF<sup>a</sup> in DMSO/<sup>b</sup>OO<sup>c</sup>

dose group (8 or 10 mice/group)	body wt (g)	liver wt (g)	liver-to-body wt ratio ( $\times 100$ )	kidney wt (g)	kidney-to-body wt ratio ( $\times 100$ )
isotonic saline control, 24 h sacrifice	32.2 $\pm$ 1.2	1.71 $\pm$ 0.12	5.32 $\pm$ 0.37	0.555 $\pm$ 0.043	1.72 $\pm$ 0.11
GCHF (600 mg/kg) in DMSO/OO, 24 h sacrifice	31.8 $\pm$ 1.3	1.58 $\pm$ 0.13 <sup>d</sup>	4.96 $\pm$ 0.34 <sup>d</sup>	0.558 $\pm$ 0.050	1.76 $\pm$ 0.19

<sup>a</sup> Glyphosate-containing herbicide formulation. <sup>b</sup> Dimethyl sulfoxide. <sup>c</sup> Olive oil. <sup>d</sup> Statistically significantly different from control,  $p \leq 0.05$ .



**Figure 6.** Comparison of clinical chemistry values for CD-1 mice following oral and intraperitoneal administration of GCHF in DMSO/OO (600 mg/kg, 24 h). The values presented are shown as the percentage of clinical chemistry values for the treatments compared to saline controls. ALT/SGPT, alanine aminotransferase; AST/SGOT, aspartate aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; SDH, sorbitol dehydrogenase. Statistical analyses were not performed.

likely actual exposure scenario, that is, dietary intake. The results from these studies continue to support the conclusion that glyphosate and GCHF are not genotoxic under exposure conditions that are relevant to humans.

#### ABBREVIATIONS USED

8-OHdG, 8-hydroxydeoxyguanosine; ALT/SGPT, alanine aminotransferase; AST/SGOT, aspartate aminotransferase; BUN, blood urea nitrogen; DMSO/OO, DMSO in olive oil; GCHF, glyphosate-containing herbicide formulations; GLP, Good Laboratory Practice; ip, intraperitoneal; IPA, isopropylamine; LDH, lactate dehydrogenase; NMO, NADPH menadione oxidoreductase; PCR, Polymerase Chain Reaction; SD, standard deviation; SDH, sorbitol dehydrogenase

#### LITERATURE CITED

- (1) Williams, G. M.; Kroes, R.; Munro, I. C. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Reg. Toxicol. Pharmacol.* **2000**, *31*, 117–165.
- (2) JMPR. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues: Rome, Italy, Sept 20–29, 2004.
- (3) Li, A. P.; Long, T. J. An evaluation of the genotoxic potential of glyphosate. *Fundam. Appl. Toxicol.* **1988**, *10*, 537–546.
- (4) European Commission. Report for the active substance glyphosate, Directive 6511/VI/99, Jan 21, 2002.
- (5) U.S. EPA. Re-registration Eligibility Decision (RED): Glyphosate. U.S. Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances: Washington, DC, 1993.
- (6) WHO. *Glyphosate. Environmental Health Criteria 159*; World Health Organization: Geneva, Switzerland, 1994.

- (7) Peluso, M.; Munnia, A.; Bolognesi, C.; Parodi, S. <sup>32</sup>P-Postlabeling detection of DNA adducts in mice treated with the herbicide Roundup. *Environ. Mol. Mutagen.* **1998**, *31*, 55–59.
- (8) Bolognesi, C.; Bonatti, S.; Degan, P.; Gallerani, E.; Peluso, M.; Rabboni, R.; Roggieri, P.; Abbondandolo, A. Genotoxic activity of glyphosate and its technical formulation Roundup. *J. Agric. Food Chem.* **1997**, *45*, 1957–1962.
- (9) National Research Council. *Guide for the Care and Use of Laboratory Animals*; 1996.
- (10) Chomczynski, P. A reagent for the single-step simultaneous isolation of RNA, DNA and proteins from cell and tissue samples. *BioTechniques* **1993**, *15*, 532–537.
- (11) PE Applied Biosystems. *ABI PRISM 7700 Sequence Detection System User's Manual*; 1996.
- (12) PE Applied Biosystems. *A Dialog on Real-Time Quantitative PCR*; 1997.
- (13) Dunnett, C. W. A multiple comparison procedure for comparing several treatments with a control. *J. Am. Stat. Soc.* **1955**, *50*, 1096–1121.
- (14) Dunnett, C. W. New tables for multiple comparisons with a control. *Biometrics* **1964**, *20*, 482–491.
- (15) Fisher, R. A. *Statistical Methods for Research Workers*; Oliver and Boyd: Edinburgh, U.K., 1946.
- (16) Bartlett, M. S. *J. R. Stat. Soc. (Suppl.)* **1937**, *4*, 137.
- (17) Draper, N. R.; Smith, H. *Applied Regression Analysis*; Wiley: New York, 1966.
- (18) Breslow, N. A generalized Kruskal–Wallis test for comparing K-samples subject to unequal patterns of censorship. *Biometrika* **1970**, *57*, 579–594.
- (19) Hollander, M.; Wolfe, D. A. *Nonparametric Statistical Methods*; Wiley: New York, 1973.
- (20) Mann, H. B.; Whitney, D. R. On a test of whether one of two variables is stochastically larger than the other. *Ann. Math. Stat.* **1947**, *18*, 50.
- (21) Grubbs, F. E. Procedure for detecting outlying observations in samples. *Technometrics* **1969**, *11*, 1–21.
- (22) Grubbs, F. E.; Beck, G. Extension of sample sizes and percentage points for significance tests of outlying observations. *Technometrics* **1972**, *14*, 847–854.
- (23) Gupta, R. C.; Spencer-Beach, G. Natural and endogenous DNA adducts as detected by <sup>32</sup>P-postlabeling. *Regul. Toxicol. Pharmacol.* **1996**, *23*, 14–21.
- (24) Vulimiri, S. V.; Smith, C. V.; Rnaderath, E.; Randerath, K. <sup>32</sup>P-Postlabeling of bile components: bulky adduct like behavior in polyethyleneimine-cellulose thin layer chromatography. *Carcinogenesis* **1994**, *15*, 2061–2064.
- (25) Marnett, L. J.; Burcham, P. C. Endogenous DNA adducts—potential and paradox. *Chem. Res. Toxicol.* **1993**, *6*, 771–785.
- (26) U.S. EPA. Glyphosate; pesticide tolerance. *Fed. Regist.* **2000**, *65*, 57957–57966.

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# **EXHIBIT 6**

# Cancer Incidence among Glyphosate-Exposed Pesticide Applicators in the Agricultural Health Study

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Glyphosate is a broad-spectrum herbicide that is one of the most frequently applied pesticides in the world. Although there has been little consistent evidence of genotoxicity or carcinogenicity from *in vitro* and animal studies, a few epidemiologic reports have indicated potential health effects of glyphosate. We evaluated associations between glyphosate exposure and cancer incidence in the Agricultural Health Study (AHS), a prospective cohort study of 57,311 licensed pesticide applicators in Iowa and North Carolina. Detailed information on pesticide use and other factors was obtained from a self-administered questionnaire completed at time of enrollment (1993–1997). Among private and commercial applicators, 75.5% reported having ever used glyphosate, of which > 97% were men. In this analysis, glyphosate exposure was defined as *a*) ever personally mixed or applied products containing glyphosate; *b*) cumulative lifetime days of use, or “cumulative exposure days” (years of use  $\times$  days/year); and *c*) intensity-weighted cumulative exposure days (years of use  $\times$  days/year  $\times$  estimated intensity level). Poisson regression was used to estimate exposure–response relations between glyphosate and incidence of all cancers combined and 12 relatively common cancer subtypes. Glyphosate exposure was not associated with cancer incidence overall or with most of the cancer subtypes we studied. There was a suggested association with multiple myeloma incidence that should be followed up as more cases occur in the AHS. Given the widespread use of glyphosate, future analyses of the AHS will allow further examination of long-term health effects, including less common cancers. **Key words:** cancer, cohort study, farming, glyphosate, pesticide. *Environ Health Perspect* 113:49–54 (2005). doi:10.1289/ehp.7340 available via <http://dx.doi.org/> [Online 4 November 2004]

Glyphosate [*N*-(phosphonomethyl)glycine], commonly sold in the commercial formulation named Roundup (Monsanto Company, St. Louis, MO), has been a frequently used herbicide on both cropland and noncropland areas of the world since its introduction in the 1970s (Williams et al. 2000). Roundup is a combination of the active ingredient and other chemicals, including a surfactant (polyoxyethyleneamine) that enhances the spreading of spray droplets when they contact foliage. Glyphosate is a broad-spectrum herbicide of which the primary mechanism is inhibition of the enzyme 5-enolpyruvylshikimate 3-phosphate synthase, which is essential for the formation of aromatic amino acids in plants (Steinrucken and Amrhein 1980). Because this specific biologic pathway operates only in plants and microorganisms, the mechanism is not considered to be a risk for humans. Nevertheless, genotoxic, hormonal, and enzymatic effects in mammals have been reported (Bolognesi et al. 1997; Daruich et al. 2001; El Demerdash et al. 2001; Hietanen et al. 1983; Lioi et al. 1998a, 1998b; Olorunsogo et al. 1979; Peluso et al. 1998; Walsh et al. 2000; Yousef et al. 1995).

Results from genotoxicity studies of glyphosate have been conflicting. Glyphosate did not show any genotoxic activity in a

battery of assays (Garry et al. 1999; Grisolia 2002; Li and Long 1988; Wildeman and Nazar 1982). However, other studies observed that glyphosate treatment of human lymphocytes *in vitro* resulted in increased sister chromatid exchanges (Bolognesi et al. 1997), chromosomal aberrations (Lioi et al. 1998b), and indicators of oxidative stress (Lioi et al. 1998b). Some studies found slightly greater toxicity of the Roundup formulation compared with glyphosate, in terms of both acute toxicity (Folmar et al. 1979; Martinez et al. 1990; Mitchell et al. 1987) and genotoxicity (Bolognesi et al. 1997; Vigfusson and Vyse 1980). Roundup was associated with increased DNA adducts in mice (Peluso et al. 1998) and a weak mutagenic effect in the *Salmonella* assay (Kale et al. 1995; Moriya et al. 1983; Rank et al. 1993), whereas glyphosate alone did not show these effects. Chronic feeding studies of glyphosate have not provided evidence of a carcinogenic effect in mice or rats (Williams et al. 2000).

The U.S. Environmental Protection Agency (U.S. EPA 1993) and the World Health Organization (WHO 1994) reviewed the toxicology data on glyphosate and concluded that glyphosate is not mutagenic or carcinogenic. The U.S. EPA classified glyphosate as category E, indicating “evidence

of noncarcinogenicity for humans” (U.S. EPA 1993). Despite this conclusion, three recent case–control studies suggested an association between reported glyphosate use and the risk of non-Hodgkin lymphoma (NHL) (De Roos et al. 2003b; Hardell and Eriksson 1999; Hardell et al. 2002; McDuffie et al. 2001). Considering the widespread and frequent use of glyphosate in both the United States and the rest of the world, ongoing risk assessment is of importance. We studied site-specific cancer incidence associated with glyphosate use among pesticide applicators in the Agricultural Health Study (AHS) cohort.

## Materials and Methods

**Cohort enrollment and follow-up.** The AHS is a prospective cohort study in Iowa and North Carolina, which includes 57,311 private and commercial applicators who were licensed to apply restricted-use pesticides at the time of enrollment. Recruitment of the applicators occurred between 1993 and 1997 (Alavanja et al. 1996). Cohort members were matched to cancer registry files in Iowa and North Carolina for case identification and to the state death registries and the National Death Index (National Center for Health Statistics 1999) to ascertain vital status. Incident cancers were identified for the time period from the date of enrollment until 31 December 2001 and were coded according to the *International Classification of Diseases*, 9th Revision (WHO 1977). If cohort members had moved from the state, they were censored in the year they left. The median time of follow-up was 6.7 years.

**Exposure assessment.** Using a self-administered enrollment questionnaire, we collected comprehensive-use data on 22 pesticides, ever/never use information for 28 additional pesticides, and general information on pesticide application methods, personal protective equipment, pesticide mixing, and equipment repair. Data were also collected on basic demographic

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on the exposure-day component; therefore, only results for cumulative exposure days are shown further. When using never exposed as the referent, the association between glyphosate use and multiple myeloma was more pronounced, with more than 4-fold increased risk associated with the highest tertile of cumulative exposure days (tertile 1: RR = 2.3; 95% CI, 0.6–8.9; tertile 2: RR = 2.6; 95% CI, 0.6–11.5; tertile 3: RR = 4.4; 95% CI, 1.0–20.2; *p*-value for trend = 0.09). Although the myeloma cases were sparsely distributed in analyses of quartiles and quintiles, the highest increased risks were observed in the highest exposure categories (full set of results not shown: upper quartile vs. never exposed: RR = 6.6; 95% CI, 1.4–30.6; *p*-value for trend across quartiles = 0.01).

## Discussion

There was no association between glyphosate exposure and all cancer incidence or most of the specific cancer subtypes we evaluated, including NHL, whether the exposure metric was ever used, cumulative exposure days, or intensity-weighted cumulative exposure days. The most consistent finding in our study was a suggested association between multiple myeloma and glyphosate exposure, based on a small number of cases.

Although our study relied on self-reported exposure information, farmers have been shown to provide reliable information regarding their personal pesticide use (Blair et al. 2002; Blair and Zahm 1993; Duell et al. 2001; Engel et al. 2001; Hoppin et al. 2002).

Investigators have used pesticide supplier reports (Blair and Zahm 1993) and self-reported pesticide use information provided earlier (Engel et al. 2001) to assess the validity of retrospectively reported pesticide use data. Among farmers in the AHS, Blair et al. (2002) reported high reliability for reports of ever use of a particular pesticide (ranging from 70 to > 90%). Agreement for duration and frequency of use was lower but generally 50–60% for specific pesticides. Hoppin et al. (2002) have demonstrated that farmers provide plausible data regarding lifetime duration of use, with fewer than 5% reporting implausible values for specific chemicals.

There were rather few cases of NHL for inclusion in this analysis (*n* = 92); nevertheless,

**Table 3.** Association of glyphosate exposure (cumulative exposure days and intensity-weighted exposure days) with common cancers<sup>a</sup> among AHS applicators.

Cancer site	Cumulative exposure days <sup>b</sup>				Intensity-weighted exposure days <sup>c</sup>			
	Tertile cut points	No.	RR (95% CI) <sup>d</sup>	<i>p</i> -Trend	Tertile cut points	No.	RR (95% CI) <sup>d</sup>	<i>p</i> -Trend
All cancers	1–20 21–56 57–2,678	594 372 358	1.0 1.0 (0.9–1.1) 1.0 (0.9–1.1)	0.57	0.1–79.5 79.6–337.1 337.2–18,241	435 436 438	1.0 0.9 (0.8–1.0) 0.9 (0.8–1.1)	0.35
Lung	1–20 21–56 57–2,678	40 26 26	1.0 0.9 (0.5–1.5) <sup>e</sup> 0.7 (0.4–1.2) <sup>e</sup>		0.1–79.5 79.6–337.1 337.2–18,241	27 38 27	1.0 1.1 (0.7–1.9) <sup>e</sup> 0.6 (0.3–1.0) <sup>e</sup>	
Oral cavity	1–20 21–56 57–2,678	18 10 10	1.0 0.8 (0.4–1.7) 0.8 (0.4–1.7)		0.1–79.5 79.6–337.1 337.2–18,241	11 14 13	1.0 1.1 (0.5–2.5) 1.0 (0.5–2.3)	0.95
Colon	1–20 21–56 57–2,678	32 28 15	1.0 1.4 (0.9–2.4) <sup>e</sup> 0.9 (0.4–1.7) <sup>e</sup>	0.54	0.1–79.5 79.6–337.1 337.2–18,241	25 20 30	1.0 0.8 (0.5–1.5) <sup>e</sup> 1.4 (0.8–2.5) <sup>e</sup>	
Rectum	1–20 21–56 57–2,678	20 17 14	1.0 1.3 (0.7–2.5) 1.1 (0.6–2.3)	0.70	0.1–79.5 79.6–337.1 337.2–18,241	16 18 16	1.0 1.0 (0.5–2.0) 0.9 (0.5–1.9)	0.82
Pancreas	0–20 21–56 57–2,678	9 9 7	1.0 1.6 (0.6–4.1) 1.3 (0.5–3.6)	0.83	0–79.5 79.6–337.1 337.2–18,241	6 16 3	1.0 2.5 (1.0–6.3) 0.5 (0.1–1.9)	
Kidney	1–20 21–56 57–2,678	20 8 9	1.0 0.6 (0.3–1.4) 0.7 (0.3–1.6)	0.34	0.1–79.5 79.6–337.1 337.2–18,241	20 7 10	1.0 0.3 (0.1–0.7) 0.5 (0.2–1.0)	0.15
Bladder	1–20 21–56 57–2,678	23 14 17	1.0 1.0 (0.5–1.9) 1.2 (0.6–2.2)	0.53	0.1–79.5 79.6–337.1 337.2–18,241	14 8 13	1.0 0.5 (0.2–1.3) 0.8 (0.3–1.8)	
Prostate	1–20 21–56 57–2,678	239 132 145	1.0 0.9 (0.7–1.1) 1.1 (0.9–1.3)	0.69	0.1–79.5 79.6–337.1 337.2–18,241	167 169 174	1.0 1.0 (0.8–1.2) 1.1 (0.9–1.3)	0.60
Melanoma	1–20 21–56 57–2,678	23 20 14	1.0 1.2 (0.7–2.3) 0.9 (0.5–1.8)	0.77	0.1–79.5 79.6–337.1 337.2–18,241	24 16 17	1.0 0.6 (0.3–1.1) 0.7 (0.3–1.2)	
All lymphohematopoietic cancers	1–20 21–56 57–2,678	48 38 36	1.0 1.2 (0.8–1.8) 1.2 (0.8–1.8)	0.69	0.1–79.5 79.6–337.1 337.2–18,241	38 40 43	1.0 1.0 (0.6–1.5) 1.0 (0.7–1.6)	0.90
NHL	1–20 21–56 57–2,678	29 15 17	1.0 0.7 (0.4–1.4) 0.9 (0.5–1.6)	0.73	0.1–79.5 79.6–337.1 337.2–18,241	24 15 22	1.0 0.6 (0.3–1.1) 0.8 (0.5–1.4)	
Leukemia	1–20 21–56 57–2,678	9 14 9	1.0 1.9 (0.8–4.5) <sup>e</sup> 1.0 (0.4–2.9) <sup>e</sup>	0.61	0.1–79.5 79.6–337.1 337.2–18,241	7 17 8	1.0 1.9 (0.8–4.7) <sup>e</sup> 0.7 (0.2–2.1) <sup>e</sup>	0.11
Multiple myeloma	1–20 21–56 57–2,678	8 5 6	1.0 1.1 (0.4–3.5) <sup>e</sup> 1.9 (0.6–6.3) <sup>e</sup>	0.27	0–79.5 79.6–337.1 337.2–18,241	5 6 8	1.0 1.2 (0.4–3.8) <sup>e</sup> 2.1 (0.6–7.0) <sup>e</sup>	

<sup>a</sup>Cancers for which at least 30 subjects had sufficient information for inclusion in age-adjusted analyses. <sup>b</sup>Numbers of subjects in analyses vary depending on missing observations for cumulative exposure days and some covariates (models adjusted for demographic and lifestyle factors include 36,823 subjects; models additionally adjusted for other pesticides include 30,699 subjects). <sup>c</sup>Numbers of subjects in analyses vary depending on missing observations for intensity-weighted cumulative exposure days and some covariates (models adjusted for demographic and lifestyle factors include 36,509 subjects; models additionally adjusted for other pesticides include 30,613 subjects). <sup>d</sup>Relative rate ratios and 95% CIs from Poisson regression analyses. <sup>e</sup>Estimates adjusted for other pesticides are shown because inclusion of other pesticide variables in the model changed the effect estimate for glyphosate by at least 20%.

the available data provided evidence of no association between glyphosate exposure and NHL incidence. This conclusion was consistent across analyses using the different exposure metrics and in analyses using either never exposed or low exposed as the referent. Furthermore, there was no apparent effect of glyphosate exposure on the risk of NHL in analyses stratified by state of residence or in analyses of highly exposed groups comparing the highest with the lowest quintile of exposure. These findings conflict with recent studies. The first report of an association of glyphosate with NHL was from a case-control study, but the estimate was based on only four exposed cases (Hardell and Eriksson 1999). A pooled analysis of this initial study with a study of hairy cell leukemia showed a relationship between glyphosate exposure and an increased risk of disease [unadjusted analysis: odds ratio (OR) = 3.0; 95% CI, 1.1–8.5] (Hardell et al. 2002). A more extensive study conducted across a large region of Canada found an elevated risk of NHL associated with glyphosate use more frequent than 2 days/year (OR = 2.1; 95% CI, 1.2–3.7) (McDuffie et al. 2001). Similarly, increased NHL risk in men was associated with having ever used glyphosate (OR = 2.1; 95% CI, 1.1–4.0) after adjustment for other commonly used pesticides in a pooled analysis of National Cancer Institute-sponsored case-control studies conducted in Nebraska, Kansas, Iowa, and Minnesota (De Roos et al. 2003b). These previous studies were retrospective in design and thereby potentially susceptible to recall bias of exposure reporting. Our analysis of the AHS cohort had a prospective design, which should largely eliminate the possibility of recall bias. Differences in recall bias could account for discrepant study results; however, evaluation of the potential for recall bias in case-control studies of pesticides among farmers has not uncovered evidence that it occurred (Blair and Zahm 1993).

Our finding of a suggested association of multiple myeloma incidence with glyphosate exposure has not been previously reported, although numerous studies have observed increased myeloma risk associated with farming occupation (Boffetta et al. 1989; Brownson et al. 1989; Cantor and Blair 1984; Cerhan et al. 1998; Cuzick and De Stavola 1988; Eriksson and Karlsson 1992; Figgs et al. 1994; Gallagher et al. 1983; La Vecchia et al. 1989; Nandakumar et al. 1986, 1988; Pasqualetti et al. 1990; Pearce et al. 1985; Pottern et al. 1992; Reif et al. 1989; Vagero and Persson 1986). A possible biologic mechanism of how glyphosate might act along the causal pathway of this plasma cell cancer has not been hypothesized, but myeloma has been associated with agents that cause either DNA damage or immunosuppression (De Roos et al. 2003a).

The association we observed was with ever use of glyphosate and cumulative exposure days of use (a combination of duration and frequency), but not with intensity of exposure. Estimated intensity of glyphosate exposure was based on general work practices that were not glyphosate specific, including the percentage of time spent mixing and applying pesticides, application method, use of personal protective equipment, and repair of pesticide application equipment (Dosemeci et al. 2002). Information on work practices specific to glyphosate use would clarify whether intensity of exposure contributes to myeloma risk.

The number of myeloma cases in our study was small, and it is plausible that spurious associations arose by chance; however, several aspects of our results argue against a chance association. The findings were internally consistent, with increased risk observed in both states. Adding to the credibility of the association, there was some indication of a dose-response relationship, with risk estimates increasing across categories of increasing exposure and stronger associations observed when using never-exposed subjects as the referent (as opposed to low exposed). Another possible explanation for spurious associations is unadjusted confounding. Our risk estimates were adjusted for some demographic and lifestyle factors and other pesticides. Of the other pesticides included in the fully adjusted model, only diazinon and trifluralin were important confounders of the glyphosate–myeloma association. It is certainly possible that an unknown risk factor for myeloma could have confounded our results; however, any unknown confounder would have to be linked with glyphosate use. Finally, the increased myeloma risk associated with glyphosate use could be due to bias resulting from a selection of subjects in adjusted analyses that differed from subjects included in unadjusted analyses. Table 1 shows that 54,315 subjects were included in age-adjusted models, whereas because of missing data for covariates, only 40,719 subjects were included in fully adjusted analyses. The association of glyphosate with myeloma differed between the two groups, even without adjustment for any covariates, with no association among the full group and a positive association among the more restricted group. Subjects who answered all the questions and were thus included in adjusted analyses differed from those who dropped out of such analyses in that they were more likely to be from Iowa (71.8% in included group vs. 44.6% in dropped group), were younger (average age, 51.5 vs. 57.9 years), and were more highly educated (46.7% educated beyond high school graduate vs. 30.2%); however, the two groups were similar in their use of glyphosate (75.9% vs. 74.5%). The increased risk associated with glyphosate in adjusted analyses may

be due to selection bias or could be due to a confounder or effect modifier that is more prevalent among this restricted subgroup and is unaccounted for in our analyses. Further follow-up of the cohort and reevaluation of the association between glyphosate exposure and myeloma incidence after a greater number of cases develop will allow more detailed examination of the potential biases underlying the association.

Certain limitations of our data hinder the inferences we can make regarding glyphosate and its association with specific cancer subtypes. Although the AHS cohort is large, and there were many participants reporting glyphosate use, the small numbers of specific cancers occurring during the follow-up period hindered precise effect estimation. In addition, most applicators were male, precluding our ability to assess the association between glyphosate exposure and cancer incidence among women, for both non-sex-specific cancers and sex-specific cancers (e.g., of the breast or ovary). Our analysis provides no information on the timing of pesticide use in relation to disease, limiting the ability to sufficiently explore latency periods or effects resulting from glyphosate exposure at different ages. Despite limitations of our study, certain inferences are possible. This prospective study of cancer incidence provided evidence of no association between glyphosate exposure and most of the cancers we studied, and a suggested association between glyphosate and the risk of multiple myeloma. Future analyses within the AHS will follow up on these findings and will examine associations between glyphosate exposure and incidence of less common cancers.

## REFERENCES

- Alavanja MC, Sandler DP, McMaster SB, Zahm SH, McDonnell CJ, Lynch CF, et al. 1996. The Agricultural Health Study. *Environ Health Perspect* 104:362–369.
- Blair A, Tarone R, Sandler D, Lynch CF, Rowland A, Wintersteen W, et al. 2002. Reliability of reporting on lifestyle and agricultural factors by a sample of participants in the Agricultural Health Study from Iowa. *Epidemiology* 13:94–99.
- Blair A, Zahm SH. 1993. Patterns of pesticide use among farmers: implications for epidemiologic research. *Epidemiology* 4:55–62.
- Boffetta P, Stellman SD, Garfinkel L. 1989. A case-control study of multiple myeloma nested in the American Cancer Society prospective study. *Int J Cancer* 43:554–559.
- Bolognesi C, Bonatti S, Degan P, Gallerani E, Peluso M, Rabboni R, et al. Genotoxic activity of glyphosate and its technical formulation Roundup. *J Agric Food Chem* 45:1957–1962.
- Brownson RC, Reif JS, Chang JC, Davis JR. 1989. Cancer risks among Missouri farmers. *Cancer* 64:2381–2386.
- Cantor KP, Blair A. 1984. Farming and mortality from multiple myeloma: a case-control study with the use of death certificates. *J Natl Cancer Inst* 72:251–255.
- Cerhan JR, Cantor KP, Williamson K, Lynch CF, Torner JC, Burmeister LF. 1998. Cancer mortality among Iowa farmers: recent results, time trends, and lifestyle factors (United States). *Cancer Causes Control* 9:311–319.
- Cuzick J, De Stavola B. 1988. Multiple myeloma—a case-control study. *Br J Cancer* 57:516–520.
- Daruich J, Zirulnik F, Gimenez MS. 2001. Effect of the herbicide

# **EXHIBIT 7**

REVIEW ARTICLE

# Review of genotoxicity studies of glyphosate and glyphosate-based formulations

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## Abstract

An earlier review of the toxicity of glyphosate and the original Roundup™-branded formulation concluded that neither glyphosate nor the formulation poses a risk for the production of heritable/somatic mutations in humans. The present review of subsequent genotoxicity publications and regulatory studies of glyphosate and glyphosate-based formulations (GBFs) incorporates all of the findings into a weight of evidence for genotoxicity. An overwhelming preponderance of negative results in well-conducted bacterial reversion and *in vivo* mammalian micronucleus and chromosomal aberration assays indicates that glyphosate and typical GBFs are not genotoxic in these core assays. Negative results for *in vitro* gene mutation and a majority of negative results for chromosomal effect assays in mammalian cells add to the weight of evidence that glyphosate is not typically genotoxic for these endpoints in mammalian systems. Mixed results were observed for micronucleus assays of GBFs in non-mammalian systems. Reports of positive results for DNA damage endpoints indicate that glyphosate and GBFs tend to elicit DNA damage effects at high or toxic dose levels, but the data suggest that this is due to cytotoxicity rather than DNA interaction with GBF activity perhaps associated with the surfactants present in many GBFs. Glyphosate and typical GBFs do not appear to present significant genotoxic risk under normal conditions of human or environmental exposures.

## Keywords

Formulation, genotoxicity, glyphosate, mutagenicity, Roundup™

## History

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## Introduction

Glyphosate is an active ingredient (a.i.) in very widely used herbicide formulations. Accordingly, the toxicity of glyphosate and glyphosate-based formulations (GBFs) has been extensively studied. An earlier extensive review of glyphosate and glyphosate formulation safety and risk assessment included descriptions and analyses of genetic toxicology studies of glyphosate and Roundup™-branded and other

# **EXHIBIT 8**

1 UNITED STATES DISTRICT COURT  
2 NORTHERN DISTRICT OF CALIFORNIA

3 IN RE: ROUNDUP )  
4 PRODUCTS LIABILITY ) MDL No. 2741  
LITIGATION )  
\_\_\_\_\_) Case No.  
5 THIS DOCUMENT RELATES ) 16-md-02741-VC  
TO ALL CASES )

6  
7 THURSDAY, JANUARY 12, 2017

8 CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

9 - - -

10 Videotaped deposition of Donna  
11 Farmer, Ph.D., Volume II, held at the offices  
12 of HUSCH BLACKWELL, L.L.C., 190 Carondelet  
13 Plaza, Suite 600, St. Louis, Missouri,  
14 commencing at 9:07 a.m., on the above date,  
15 before Carrie A. Campbell, Registered  
16 Diplomate Reporter, Certified Realtime  
17 Reporter, Illinois, California & Texas  
18 Certified Shorthand Reporter, Missouri &  
19 Kansas Certified Court Reporter.

20 - - -

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2

3     V I D E O G R A P H E R :

          DAN LAWLOR,

4           Golkow Technologies, Inc.

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1                   VIDEOGRAPHER: We are now on  
2                   the record. My name is Dan Lawlor.  
3                   I'm a videographer with Golkow  
4                   Technologies. Today's date is  
5                   January 12, 2017, and the time is  
6                   9:07 a.m.

7                   This video deposition is being  
8                   held in St. Louis, Missouri, in the  
9                   matter of In Re: Roundup Products  
10                  Liability Litigation. The deponent is  
11                  Donna Farmer, Ph.D.

12                  And, Dr. Farmer, I remind you  
13                  that you're still under oath from  
14                  yesterday.

15                  THE WITNESS: Okay.

16                  VIDEOGRAPHER: Counsel, please  
17                  proceed.

18                  CROSS-EXAMINATION

19                  QUESTIONS BY MR. JOHNSTON:

20                  Q.        Good morning, Dr. Farmer.

21                            My name is Robert Johnston, and  
22                  I represent Monsanto in this litigation.

23                            We've met before, correct?

24                  A.        Yes.

25                  Q.        I want to review your

1     also have different needs. We have an IT&O  
2     market. We have a consumer market. We have  
3     an agricultural market. So those  
4     formulations can be different.

5                     We also have some that have  
6     different -- you know, the way that we can  
7     put it in containers. So we have different  
8     salts that go along with them. We have  
9     different weed species that we have to deal  
10    with.

11                    So the formulated product is --  
12    what you're looking at is what is the need to  
13    control the vegetation, what sector, and then  
14    you develop formulations to be efficacious in  
15    those groups.

16            Q.     And did I understand your  
17    testimony to be that for each of those  
18    formulations sold in the United States you  
19    have to do what you called a six-pack of  
20    tests?

21            A.     Yes, we do.

22            Q.     Have you been involved in the  
23    conduct of that six-pack of tests for US  
24    formulations?

25            A.     I have, yes.

1           Q.       What do those test results show  
2 generally?

3           A.       For the Roundup-branded  
4 products, that they are practically and  
5 slightly nontoxic. We have very little low  
6 acute, dermal and inhalation toxicity. We  
7 have low eye and skin irritation and that  
8 they are not sensitizers.

9           Q.       Has Monsanto done any testing  
10 other than or in addition to that six-pack  
11 testing on any formulated products?

12          A.       We have done some gene tox  
13 testing on some of our formulated products.

14          Q.       Do you know how many genotox  
15 studies that Monsanto has undertaken on its  
16 formulated products roughly?

17          A.       I'd say a couple dozen.

18          Q.       And is there any consistent  
19 results from those genotoxicity studies?

20          A.       Those studies are conducted  
21 according to the guidelines that the  
22 regulatory agencies require us, and they have  
23 been no evidence of genotoxicity or  
24 mutagenicity.

25          Q.       Now, are those studies required

1 by the EPA?

2 A. No, they're not.

3 Q. Well, why would Monsanto do  
4 additional genotoxicity testing on its  
5 formulated products that is not required by  
6 the EPA?

7 A. We would have people asking  
8 about the profile. Knowing that we know the  
9 surfactants are not genotoxic and that  
10 glyphosate isn't, we feel very comfortable  
11 that the formulated product would not be.  
12 But we would go ahead and then do those  
13 studies according to the EPA's guidelines.

14 Q. But why?

15 A. To answer questions if people  
16 have concerns. We want to be able to give  
17 them the data that they can have to evaluate  
18 the safety.

19 Q. You remember yesterday  
20 Mr. Miller asked you some questions about a  
21 Dr. Parry from 1999 and 2000.

22 Do you remember that?

23 A. Yes, I do.

24 Q. And he was a genotox expert  
25 that Monsanto worked with in that period?

1           A.       Correct.

2           Q.       And he pointed out in several  
3 documents that Dr. Parry wanted Monsanto to  
4 conduct some additional genotoxicity studies?

5           A.       Yes.

6           Q.       Did Monsanto ever conduct any  
7 of the sorts of studies that Dr. Parry was  
8 recommending?

9           A.       Yes, we did. Dr. Parry was  
10 concerned about the findings from the Peluso  
11 and Bolognesi studies, and so we did an in  
12 vivo study with the formulated product in  
13 those studies to evaluate and answer the  
14 questions that Dr. Parry was concerned about.

15                   (Farmer Exhibit 1-61 marked for  
16 identification.)

17 QUESTIONS BY MR. JOHNSTON:

18           Q.       I've handed you a document that  
19 I've marked as Exhibit 1-61.

20                   Have you ever seen this  
21 document before?

22           A.       Yes, I have.

23           Q.       And can you tell us what the  
24 title of this document is?

25           A.       "Genotoxic potential of

21 Q. So does that mean that when you  
22 have done your testing on technical  
23 glyphosate, that that testing also accounts  
24 for the presence of impurities at standard  
25 percentage doses in those tests?



1     carcinogenicity studies done with glyphosate?

2             A.        Yes.

3             Q.        And has Monsanto conducted any  
4     of those studies?

5             A.        Yes, we have.

6             Q.        Okay. Let me have you look at  
7     what was marked yesterday as 1-8. And  
8     Mr. Miller highlighted this sentence here,  
9     "Or this, you cannot say that Roundup does  
10    not cause cancer. We have not done  
11    carcinogenicity studies with Roundup."

12                    Is that what you wrote?

13            A.        Yes.

14            Q.        So do you recall why you were  
15    writing this e-mail?

16            A.        Yes, because what I wanted to  
17    point out was that it's -- we have done -- as  
18    I had talked about yesterday, that we have  
19    done carcinogenicity studies with glyphosate.  
20    Roundup is a brand name. Represents not just  
21    one formulation anymore, but many  
22    formulations. And so we have done a number  
23    of carcinogenicity studies with glyphosate.

24                    And as you had heard earlier,  
25    the EPA sees no evidence of carcinogenicity

1 with the surfactants. So this should have  
2 been really that we have done carcinogenicity  
3 studies with glyphosate, but with Roundup we  
4 don't believe that it causes cancer based on  
5 the lack of carcinogenicity within glyphosate  
6 and lack of carcinogenicity within the  
7 surfactants.

8 Q. So you weren't saying that no  
9 carcinogenicity studies have been done. You  
10 were just saying they hadn't been done on the  
11 formulated product, correct?

12 A. Correct. Yes.

13 Q. Okay. And then there was  
14 another document that was marked as  
15 Exhibit 1-48 yesterday.

16 And 1-48, do you remember this  
17 document?

18 A. Yes, I do.

19 Q. And Mr. Miller asked you about  
20 this, correct?

21 A. Yes.

22 Q. And it's a document by --  
23 authored by Christian {sic} Portier and, as  
24 Mr. Miller pointed out repeatedly, 94 other  
25 scientists, correct?

CERTIFICATE

I, CARRIE A. CAMPBELL, Registered Diplomat Reporter, Certified Realtime Reporter and Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, Donna Farmer, Ph.D. was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

---

CARRIE A. CAMPBELL,  
NCRA Registered Diplomat Reporter  
Certified Realtime Reporter  
California Certified Shorthand  
Reporter #13921  
Missouri Certified Court Reporter #859  
Illinois Certified Shorthand Reporter  
#084-004229  
Texas Certified Shorthand Reporter #9328  
Kansas Certified Court Reporter #1715  
Notary Public  
Dated: January 16, 2017

1 INSTRUCTIONS TO WITNESS

2

3 Please read your deposition over  
4 carefully and make any necessary corrections.  
5 You should state the reason in the  
6 appropriate space on the errata sheet for any  
7 corrections that are made.

8 After doing so, please sign the  
9 errata sheet and date it. You are signing  
10 same subject to the changes you have noted on  
11 the errata sheet, which will be attached to  
12 your deposition.

13 It is imperative that you return  
14 the original errata sheet to the deposing  
15 attorney within thirty (30) days of receipt  
16 of the deposition transcript by you. If you  
17 fail to do so, the deposition transcript may  
18 be deemed to be accurate and may be used in  
19 court.

20

21

22

23

24

25

ACKNOWLEDGMENT OF DEPONENT

I, \_\_\_\_\_, do  
hereby certify that I have read the  
foregoing pages, and that the same is  
a correct transcription of the answers  
given by me to the questions therein  
propounded, except for the corrections or  
changes in form or substance, if any,  
noted in the attached Errata Sheet.

\_\_\_\_\_  
DONNA FARMER, PH.D.

DATE

Subscribed and sworn  
to before me this

\_\_\_\_\_ day of \_\_\_\_\_, 20\_\_\_\_.

My commission expires: \_\_\_\_\_

\_\_\_\_\_  
Notary Public

# **EXHIBIT 9**

Message

---

**From:** BELVAUX, XAVIER [AG/5040] [/O=MONSANTO/OU=EA-5041-01/CN=RECIPIENTS/CN=234727]  
**Sent:** 3/5/2013 10:33:07 AM  
**To:** GARDETTE, SOPHIE [AG/5170] [/O=MONSANTO/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=SGARD]  
**CC:** SALTMIRAS, DAVID A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=DASALT]  
**Subject:** RE: Dossiers d'homologation Mon 79351et Mon 79376

Yes it should be sufficient if you properly inform them that the long term toxicity is covered by studies on the active ingredient.

**From:** GARDETTE, SOPHIE [AG/5170]  
**Sent:** Tuesday, March 05, 2013 11:29 AM  
**To:** BELVAUX, XAVIER [AG/5040]  
**Cc:** SALTMIRAS, DAVID A [AG/1000]  
**Subject:** RE: Dossiers d'homologation Mon 79351et Mon 79376

Ok, thanks for this additional information

I have already forward the review report of glyphosate to the Tunisian authorities.

I could imagine that it must be sufficient => what do you think ?

Sophie GARDETTE

Regulatory Affairs Manager - Monsanto SAS

Eden Park - 1 rue Buster Keaton 69800 St Priest

tel : +33 (0)4 72 14 41 39

Mob : +33 (0)6 33 71 43 82

**From:** BELVAUX, XAVIER [AG/5040]  
**Sent:** Tuesday, March 05, 2013 11:27 AM  
**To:** GARDETTE, SOPHIE [AG/5170]  
**Cc:** SALTMIRAS, DAVID A [AG/1000]  
**Subject:** RE: Dossiers d'homologation Mon 79351et Mon 79376

Sophie,

We do not conduct sub-chronic, chronic or teratogenicity studies with our formulations. The long term exposure has been assessed according to the regulatory requirements in chronic and carcinogenicity studies conducted with the active ingredient glyphosate. Based on review of chronic rat and mouse studies, EU Commission concluded in 2002 of "no evidence of carcinogenicity for the glyphosate. This was also confirmed by other international regulatory reviews (WHO/FAO 2004, US EPA 1993).

Do you need these tox studies conducted with the glyphosate?

Best regards,

Xavier

**From:** GARDETTE, SOPHIE [AG/5170]  
**Sent:** Tuesday, March 05, 2013 10:55 AM  
**To:** BELVAUX, XAVIER [AG/5040]  
**Subject:** FW: Dossiers d'homologation Mon 79351et Mon 79376

Hello

La Tunisie me demande des études de toxicité sub-chroniques, chroniques et tératogénicité. pour les Mon 79376 et Mon 79351 qu'on veut déposer

A date je leur ai transmis la copie des dossiers d'homolo déposés pour la France

Est-ce qu'on a quelque chose d'autres à transmettre à ton avis ?

Sinon : comment on le justifie ?

A+

Sophie GARDETTE

Regulatory Affairs Manager - Monsanto SAS

Eden Park - 1 rue Buster Keaton 69800 St Priest

tel : +33 (0)4 72 14 41 39

Mob : +33 (0)6 33 71 43 82

**From:** atlasagricole@planet.tn [mailto:atlasagricole@planet.tn]

**Sent:** Monday, March 04, 2013 10:10 AM

**To:** GARDETTE, SOPHIE [AG/5170]

**Cc:** DELUOL, PHILIPPE [AG/5170]

**Subject:** Dossiers d'homologation Mon 79351et Mon 79376

Bonjour Mme Gardette,

Suite à l'e-mail de M. Mabrouk, je vous envoie, ci-après, les remarques concernant les 2 dossiers d'homologation:

**Mon 79376**

-Dossier biologique: 14 annexes ont été cités à la fin du rapport mais sans contenu, y a-t-il des éléments oubliés ou bien il faut supprimer ces titres?

-Dossier toxicologique: les études qui figurent dans le dossier concernant la toxicité aigüe, pourriez-vous nous envoyer les études de toxicité sub-chroniques, chroniques, térotogénicité...

-Certificat d'analyse du produit formulé: nous ne l'avons pas encore reçu (références: **lot n°A2A210910A/ exp: 23/01/2017**)

-Certificat d'analyse du standard analytique: le certificat ne peut pas être accepté par le ministère, il faudra nous envoyer comme vous avez précisé un certificat de réanalyse (références: **lot n°GLP-0810-19515-A/ exp: 31/01/2013**)

**Mon 79351**

-Dossier toxicologique: les études qui figurent dans le dossier concernant la toxicité aigüe, pourriez-vous nous envoyer les études de toxicité sub-chroniques, chroniques, térotogénicité...

-Certificat d'analyse du produit formulé: nous ne l'avons pas encore reçu (références: **lot n°A2L072310A/ exp: 07/11/2017**)

-Dossier analytique: l'analyse du Mon79351 est manquante (vous l'avez déjà précisé)

Cordialement  
Walid SALHI

# **EXHIBIT 10**

Message

**From:** ADAMS, STEPHEN A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=113797]  
**Sent:** 12/14/2010 6:07:35 PM  
**To:** KLOPF, GARY J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=162545]  
**CC:** HEMMINGHAUS, JOHN W [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=521714]; DYSZLEWSKI, ANDREW D [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=102676]; LASARTE, MARTIN A [AG/5001] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=22015]; KAVANAS, DIEGO [AG/5001] [/O=MONSANTO/OU=LA-5001-01/CN=RECIPIENTS/CN=191954]; GUIBERT, MELISA [AG/5000] [/O=MONSANTO/OU=LA-5000-01/CN=RECIPIENTS/CN=661675]; WATSON, GREGORY R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=GRWATS]; HEYDENS, WILLIAM F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]; FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]; SALTMIRAS, DAVID A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=DASALT]; MORRISON, BRINNON L [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=BLMORR1]  
**Subject:** Re: Response Need - Re: Glyphosate Questions (Argentina); FW: publicaciones CASAFE en la página

All:

We have information and data to address most all of this. There are basically 2 parts that I see - 1) the chronic toxicity of glyphosate and its impurities and metabolites, and 2) the toxicity of the POEA surfactants.

With regards to the carcinogenicity of our formulations we don't have such testing on them directly but we do have such testing on the glyphosate component and some extensive tox testing on the surfactant. Since the glyphosate formulations are simply a blend of these components, I think we can address these questions in a confident manner. The biggest factor is time. With the approaching holiday season it may be several weeks before we can have the detailed response which this deserves prepared.

I have copied in the Tech Center people who would need to be involved in preparing the response and invite there comment. I will also follow-up with them.

Steve

---

**From:** KLOPF, GARY J [AG/1000]  
**To:** ADAMS, STEPHEN A [AG/1000]  
**Cc:** HEMMINGHAUS, JOHN W [AG/1000]; DYSZLEWSKI, ANDREW D [AG/1000]; LASARTE, MARTIN A [AG/5001]; KAVANAS, DIEGO [AG/5001]; GUIBERT, MELISA [AG/5000]  
**Sent:** Tue Dec 14 08:28:57 2010  
**Subject:** Response Need - Re: Glyphosate Questions (Argentina); FW: publicaciones CASAFE en la página

Steve,

Could you and/or someone else in the Regulatory group respond to the questions Martin has raised?

Thanks,

Gary (4-8784)

**From:** HEMMINGHAUS, JOHN W [AG/1000]  
**Sent:** Monday, December 13, 2010 4:58 PM  
**To:** KLOPF, GARY J [AG/1000]  
**Cc:** DYSZLEWSKI, ANDREW D [AG/1000]  
**Subject:** FW: publicaciones CASAFE en la página

**From:** LASARTE, MARTIN A [AG/5001]  
**Sent:** Monday, December 13, 2010 3:37 PM  
**To:** HEMMINGHAUS, JOHN W [AG/1000]; DYSZLEWSKI, ANDREW D [AG/1000]  
**Cc:** KAVANAS, DIEGO [AG/5001]; GUIBERT, MELISA [AG/5000]  
**Subject:** FW: publicaciones CASAFE en la página

John, Andy:

Please can you contact me with the right person to answer the bellow question regarding glyphosate formulations metabolites and potential carcinogenic properties? We also would need some comprehensive information about POEAs surfactants

The request is to assist us regarding some discussions talking place with some Universities and we don't have that kind of knowledge within the region.

Specifically we would need to understand:

- 1) Why Roundup formulations are not carcinogenic? What are their most relevant metabolites and what study showed they are not?
- 2) NNG and formaldehyde are the 2 impurities with known carcinogenic properties that we follow very closely with FAO standards. Are they also present on the metabolites?

- 3) I know from the process stand point that the AMPA is also a impurity we have under control. Is AMPA also a metabolite? Is it carcinogenic?
- 4) POEAs surfactant definition and classification. Why are they questioned?

It would be very comprehensive if there is a table showing the metabolites, their concentration on a regular basis, they carcinogenic properties and the limits

Thank you! Martin

**From:** FARINATI, JUAN M [AG/5000]

**Sent:** Lunes, 13 de Diciembre de 2010 10:45 a.m.

**To:** VILAPLANA, ADRIAN [AG/5000]; ALVAREZ ARANCEDO, MIGUEL [AG/5000]; PINA, JUAN [AG/5000]; PAVELY, CHLOE [AG/5000]

**Cc:** LASARTE, MARTIN A [AG/5001]; LIZARRAGA, DARDO S [AG/5001]

**Subject:** RE: publicaciones CASAFE en la página

Juan y Cloe estuvieron involucrados en una de las charlas de POEAs cuando salió el tema en Europa

Tb los copio a Martín y a Dardo por si nos pueden dar algo de info

SlDs

Juan M Farinati

*Monsanto Argentina S.A.I.C.*

*Maipú 1210 - Piso 11° - Buenos Aires - Argentina*

*Mob: +5491131495983*

Of: +541143162482

**From:** VILAPLANA, ADRIAN [AG/5000]  
**Sent:** Lunes, 13 de Diciembre de 2010 08:57  
**To:** ALVAREZ ARANCEDO, MIGUEL [AG/5000]  
**Cc:** FARINATI, JUAN M [AG/5000]  
**Subject:** RV: publicaciones CASAFE en la página

Mike  
Quien nos puede dar una mano con este tema?  
Gracias  
Adrian

---

**De:** Pablo Grosso <pgrosso@casafe.org>  
**Para:** FARINATI, JUAN M [AG/5000]; VILAPLANA, ADRIAN [AG/5000]  
**Enviado:** Sun Dec 12 16:26:40 2010  
**Asunto:** RV: publicaciones CASAFE en la página

Juan y Adrián,

Les mando la consulta (remarcada en el mail de abajo) para que ustedes (como los Directivos de Monsanto de mayor presencia en CASAFE) la puedan dirigir internamente con quien/quienes corresponda de la forma más urgente posible.

Los ataques de estos últimos días de una ambientalista la Dra. Gómez, ya han llegado a nivel personal (contra los Ing. Etiennot, Piazza, la Dra. Martínez del TAS) que hace que tengamos que seguir muy bien preparados y con la mejor información. Ladrán Sancho....!!!

También, me interesa tener la mayor Info posible sobre: el **AMPA y el POEA**

Abrazo.

Pablo.

**De:** Augusto Piazza [mailto:aupiazza@speedy.com.ar]  
**Enviado el:** Viernes, 10 de Diciembre de 2010 10:11 p.m.  
**Para:** 'Pablo Grosso'; ricardo.pancelli@basf.com; Etiennot particular Tato

**CC:** 'Juan C JAIME'; Jorge Perez Lissarrague; juan.pina@monsanto.com

**Asunto:** RE: publicaciones CASAFE en la página

Estimados

El informe de la Universidad del Litoral clasifica clase III el glifosato para SENASA y clase III para la organización Mundial de la salud.

Yo estoy 100 % que SENASA es Clase IV, que pasa en la OMS? Porque lo habrán puesto mal en la UNL?

Ahora entiendo porque este tipo de la UBA nos llama mentirosos, por favor, podrían verificar en la OMS

Además necesitaríamos las otras preguntas que hicimos oportunamente:

¿si existe un método para verificar que se trata de intoxicaciones con glifosato?¿qué debería encontrarse suponiendo que provoque cáncer? ¿cuál sería el residuo/metabolito/activo en el caso de malformaciones u otros?

Alberto: podrías hablar con el profe de Sanidad, Sánchez, para ver qué pasó con esto. Si usamos el informe de la UNL, y tiene errores puede sinceramente afectarnos.

Saludos

Augusto

Ing. Agr. Augusto Piazza

Cel.: 15-5022-6869

# **EXHIBIT 11**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



OFFICE OF PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

Date: April 3, 2009

**MEMORANDUM**

**SUBJECT:** Alkyl Amine Polyalkoxylates (JITF CST 4 Inert Ingredients). Human Health Risk Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as Inert Ingredients in Pesticide Formulations.

**PC Code:** 790402

**Decision No.:** 389251

**Petition No.:** 8E7382

**Risk Assessment Type:** Single Chemical Aggregate

**TXR No.:** NA

**MRID No.:** 46902001, 46902005, 46902007, 46914604, 46918001, 46918002, 46918003, 46918004, 46930503, 47041301, 47041302, 47066302, 47097401, 47193901, 47405101

**DP Barcode:** D360944

**Registration No.:** NA

**Regulatory Action:** Inert Tolerance Exemption

**Case No.:** NA

**CAS No.:** 61791-26-2, 61791-31-9, 70955-14-5, 68213-26-3

**40 CFR:** 180.920, 180.930

**FROM:** Donna S. Davis, Risk Assessor, RAB VII  
Alexandra LaMay, Biologist, RAB VII  
Matthew Lloyd, Industrial Hygienist, RAB VII  
Christine L. Olinger, Chemist, RAB VII  
Sheila Piper, Dietary Exposure Assessor, RAB VI  
Deborah Smegal, Toxicologist, RAB VII  
Linda Taylor, Toxicologist, RAB VII  
Health Effects Division (7509P)

**THROUGH:** Michael S. Metzger, Chief  
Risk Assessment Branch VII  
Health Effects Division (7509P)

**TO:** Kerry Leifer, Team Leader  
PV Shah, Chief  
Inert Ingredient Assessment Branch  
Registration Division (7505P)

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## 1.0 Executive Summary

The Joint Inert Task Force (JITF) Cluster Support Team Number 4 (CST4) has submitted a petition proposing to establish exemptions from the requirement of a tolerance for the following clusters of compounds when used as inert ingredients in pesticide formulations.

N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl) content is 2 – 60 moles.

N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) content is 2 – 60 moles.

The compounds, referred to as alkyl amine polyalkoxylates (AAPs), are not discrete compounds, but are a mixture of compounds formed from the reaction of fatty acid derived amines with either ethylene oxide or propylene oxide. The AAPs are used primarily as surfactants in pesticide formulations. The petitioner is proposing to limit the maximum amount of the inert in any end-use product to no more than 10% in fungicide and insecticide products and no more than 25% in herbicide formulations.

The toxicology database is adequate to support the use of the alkyl amine polyalkoxylates when used as inert ingredients. The AAPs are not acutely toxic by the oral and dermal routes of exposure, or via inhalation under normal use conditions. Concentrated materials are generally corrosive, eye and skin irritants and may be dermal sensitizers. There is no evidence that the AAPs are neurotoxic, mutagenic, or clastogenic.

There is no clear target organ identified across the AAPs. Following subchronic exposure to rats, some gastrointestinal irritation was observed, but no specific target organ toxicity or neurotoxicity was seen. In subchronic studies in rats and/or dogs, the most sensitive effects noted were increased mortality, clinical signs (salivation, wheezing, emesis, and/or soft feces), cataracts, cellular changes in the stomach, and liver effects characterized by enzyme induction, and pigment accumulation in Kupffer cells and bile canaliculi. There was no increased susceptibility to the offspring of rats following *in utero* exposure in two prenatal developmental toxicity studies. However, there is evidence of increased susceptibility in a reproductive screening study in rats. The points of departure (PoDs) selected for the dietary assessments are lower than the doses at which offspring toxicity occurred in the rat reproduction study and are protective of offspring toxicity occurring at higher doses. There were no residual concerns and the Food Quality Protection Act (FQPA) safety factor was reduced to 1X.

Sufficient data were provided on the chemical identify of the AAPs, however, limited data are available on the metabolism and environmental degradation of the AAPs; further, no residue data were provided. The Agency relied collectively on information provided on the representative chemical structures, the generic cluster structures, the submitted physicochemical EPI Suite™ data, structure-activity relationship information,

# **EXHIBIT 12**

UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF CALIFORNIA

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)  
IN RE: ROUNDUP PRODUCTS ) MDL No. 2741  
LIABILITY LITIGATION ) Case No. 16-md-02741-VC  
-----)

)  
This document relates to: )  
)  
ALL ACTIONS )  
)  
-----

VIDEOTAPED DEPOSITION OF DR. CHADI NABHAN  
Waukegan, Illinois  
Wednesday, August 23, 2017

Reported by:  
PAULA CAMPBELL, CSR, RDR, CRR, CRC  
JOB NO. 127897

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August 23, 2017  
9:07 A.M.

Videotaped discovery deposition of  
DR. CHADI NABHAN, held at the offices of  
CARDINAL HEALTH, 3651 Birchwood Drive,  
Waukegan, Illinois, pursuant to notice before  
Paula Campbell, CSR, RDR, CRR, CRC.

A P P E A R A N C E S:

THE MILLER FIRM

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A P P E A R A N C E S:

HOLLINGSWORTH

Attorneys for the Defendant Monsanto Company

1350 I Street, N.W.

Washington, D.C. 20005

BY: KIRBY GRIFFIS, ESQ.

STEPHANIE SALEK, ESQ.

ALSO PRESENT:

Robert Zellner, Videographer

1 VIDEOGRAPHER: Good morning. This is the  
2 start of tape labeled No. 1 of the videotape  
3 deposition of Dr. Chadi Nabhan in the matter of  
4 In re: Roundup Products Liability Litigation in  
5 the United States District Court for the  
6 Northern District of California, bearing MDL  
7 No. 2741, Case No. 16-md-02741-VC.

8 This deposition is being held Cardinal  
9 Health at 3651 Birchwood Drive in Waukegan,  
10 Illinois 60085, on Wednesday, August 23rd,  
11 2017, at approximately 9:07 A.M.

12 My name is Robert Solomon from TSG  
13 Reporting, Inc., and I'm the legal video  
14 specialist. And the court reporter is Paula  
15 Campbell, in association with TSG Reporting.

16 And will counsel now please introduce  
17 yourselves for the record.

18 MR. LITZENBURG: Timothy Litzenburg for the  
19 plaintiffs.

20 MS. TABATABAIE: Tara Tabatabaie for the  
21 plaintiffs.

22 MR. GRIFFIS: Kirby Griffis for -- with  
23 Hollingsworth, LLP, for Monsanto.

24 MS. SALEK: Stephanie Salek with  
25 Hollingsworth, LLP, for Monsanto.

1 VIDEOGRAPHER: Thank you. And will the  
2 court reporter --

3 MS. ROBERTSON: Pearl Robertson with  
4 Weitz & Luxenberg for the plaintiff.

5 REPORTER: I'm sorry. I didn't -- can you  
6 repeat?

7 MS. TABATABAIE: Can you repeat that?

8 MS. ROBERTSON: Yes. Pearl Robertson with  
9 Weitz & Luxenberg for plaintiff.

10 VIDEOGRAPHER: Thank you.

11 And will the court reporter please swear in  
12 the witness.

13 REPORTER: Would you please raise your  
14 right hand.

15 C H A D I N A B H A N,

16 called as a witness, having been duly sworn,  
17 was examined and testified as follows:

18 VIDEOGRAPHER: I may be picking up a cell  
19 phone in your pocket. If you have one, if you  
20 wouldn't mind putting it off to the side, as  
21 far as you can do it. Thank you so much.

22 Thank you.

23 EXAMINATION

24 BY MR. GRIFFIS:

25 Q. Good morning, sir.

1 association; however, one of the coauthors of this  
2 work was employed by Monsanto and provided  
3 ghostwriting, making my question the credibility of  
4 this work."

5 Correct?

6 A. Correct.

7 Q. That's the only thing you say about Greim  
8 in your whole expert report?

9 A. Correct.

10 Q. Right?

11 And nowhere in your expert report do you  
12 assess the actual content of this article; right?

13 MR. LITZENBURG: Object to form.

14 A. Well, I read the paper. And, again, I  
15 bring it up here because the conclusion or the  
16 output of that paper suggests lack of association.  
17 And I mentioned why the credibility of the paper was  
18 of low value to me as a clinician, as a researcher,  
19 because I'll have to wonder whether it was really  
20 fair and balanced.

21 It's a fair thing for me to question the  
22 evidence based on the authors. We do that all the  
23 time.

24 Q. How did you form the opinion that one of  
25 the authors was involved in ghostwriting?

1           A. Well, two things. The -- if you look at  
2 David Saltmiras --

3           Q. Yes, sir.

4           A. -- affiliation is Monsanto and glyphosate  
5 task force. And I think I'm trying to remember  
6 where I read that it is possible that he had a lot  
7 of contribute -- I mean, he's a coauthor; so he, you  
8 know, again, as a coauthor of the -- whether you  
9 call this ghostwriting or not ghostwriting, I mean,  
10 but he's a coauthor that's employed by the company  
11 that makes glyphosate.

12                 So I guess, you know, I mean, you'll have  
13 to wonder whether the opinions in the paper were  
14 fair and balanced and free of bias.

15           Q. Did you discount the opinions expressed in  
16 the paper on the grounds that one of the authors was  
17 employed by Monsanto?

18                 MR. LITZENBURG: Objection. Asked and  
19 answered.

20           A. It made me question the conclusion. I  
21 think if you were me, you would probably have the  
22 same question.

23                 Again, you know, how likely is an employee  
24 of the company that makes a compound is going to go  
25 on the record in a peer review and say "The compound

1 chance, bias, or confounding cannot be ruled out  
2 without reasonable confidence; is that right?

3 A. If this is what the IARC said, then I do  
4 agree with that.

5 Q. And with regard to any cancer other than  
6 non-Hodgkin's lymphoma, they didn't even find  
7 limited evidence; right? They found no evidence?

8 MR. LITZENBURG: Objection. Beyond the  
9 scope.

10 A. Again, I -- I -- I did not really evaluate  
11 what evidence they looked at outside. I mean, I  
12 looked at the non-Hodgkin lymphoma.

13 Q. Okay. You're not giving the opinion that  
14 glyphosate is associated with any cancer other than  
15 non-Hodgkin's lymphoma; right?

16 A. I'm just talking about non-Hodgkin  
17 lymphoma, correct.

18 Q. And when you say that glyphosate is  
19 associated with non-Hodgkin's lymphoma, do you say  
20 that it is also associated with every single subtype  
21 of non-Hodgkin's lymphoma?

22 A. Yeah, I think it's -- it's -- it's very  
23 difficult to establish that because of how many  
24 types of lymphs there are and also because the  
25 understanding of the current classification of lymph

1 was not the same classification that we had in the  
2 mid or late '90s, et cetera. So what we knew back  
3 in the '90s about the types of lymph is not what we  
4 know today.

5 So I think you'll have to look at  
6 non-Hodgkin lymphoma as one entity when you look at  
7 this causation and association.

8 Q. And you -- you're saying that we're forced  
9 to look at non-Hodgkin's lymphoma as one entity  
10 because we don't have much data on how glyphosate  
11 might be associated or not associated with various  
12 sub types?

13 A. No, for various reasons, I think. A, the  
14 classification of lymphs was different back then  
15 versus now. I mean, even -- just to give you an  
16 idea, the -- the 2016 classification, the earlier  
17 one was '014, then was '07, and there was 1999. So,  
18 again, it changes.

19 Number 2, once you actually start looking  
20 at every single subtypes, the numbers become too  
21 small to actually be able to detect statistical  
22 significance. So when we look at causation in  
23 association with occupational exposures, you'll have  
24 to look at the actual entity as a whole in order for  
25 you to establish this such association.

## C E R T I F I C A T E

I, Paula Campbell, CSR, RDR, CRR, CRC, do hereby certify that on Wednesday, August 23, 2017 appeared before me, CHADI NABHAN.

I further certify that the said witness was first duly sworn to testify to the truth in the cause aforesaid.

I further certify that the signature of the witness to the foregoing deposition was not specified by counsel.

I further certify that I am not counsel for nor in any way related to any of the parties to this suit, nor financially interested in the action.

IN TESTIMONY WHEREOF, I have hereunto set my hand on this 23rd day of August, 2017.

---

Paula Campbell, CSR, RDR, CRR, CRC  
Certified Shorthand Reporter  
Registered Diplomate Reporter  
Certified Realtime Reporter  
Certified Realtime Captioner

1 THE WITNESS: You're welcome.

2 MR. GRIFFIS: Thank you, sir.

3 THE WITNESS: You're welcome.

4 VIDEOGRAPHER: This concludes the  
5 deposition today of Dr. Chadi Nabhan. We are  
6 off the record at 5:44 P.M.

7 (Time noted: 5:44 P.M.)

8  
9 \_\_\_\_\_

10 CHADI NABHAN

11  
12 SUBSCRIBED TO AND SWORN BEFORE ME

13 THIS \_\_\_\_\_ DAY OF \_\_\_\_\_, 20\_\_.

14 \_\_\_\_\_

(Notary Public) MY COMMISSION EXPIRES: \_\_\_\_\_

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## C E R T I F I C A T E

I, Paula Campbell, CSR, RDR, CRR, CRC, do hereby certify that on Wednesday, August 23, 2017 appeared before me, CHADI NABHAN.

I further certify that the said witness was first duly sworn to testify to the truth in the cause aforesaid.

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IN TESTIMONY WHEREOF, I have hereunto set my hand on this 23rd day of August, 2017.

---

Paula Campbell, CSR, RDR, CRR, CRC  
Certified Shorthand Reporter  
Registered Diplomate Reporter  
Certified Realtime Reporter  
Certified Realtime Captioner

# **EXHIBIT 13**

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

DEWAYNE JOHNSON,

Plaintiff,

v.

MONSANTO COMPANY,

Defendants.

Case No. CGC-16-550128

**EXPERT REPORT OF CHARLES BENBROOK**

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86. Monsanto responded to EPA's request by arguing no such study was needed. OPP/EPA responded by stating why it felt such a study was indeed essential.

87. After eight years of back and forth covered in detail in this report, Monsanto had displayed to the OPP that it would always be willing and able to take whatever next step was necessary to raise new scientific issues in need of exploration, prior to a final OPP decision on whether the 1983 Bio/dynamics study was positive or negative for cancer, or needed to be repeated.

88. Monsanto also had demonstrated multiple times both its ability and willingness to direct political pressure on the agency. The company's clout in Congress, and at senior levels in Executive Branch agencies, made it possible for Monsanto to continuously raise the stakes facing OPP/EPA, until OPP brought its evaluation of the Bio/dynamics study into alignment with Monsanto's, and as a result, changed the cancer classification of glyphosate in a way acceptable to the company.

89. In short, Monsanto convinced the OPP that it was not an effective use of the agency's limited resources to continue the fight.

90. In 1991, EPA changed its interpretation of the 1983 mouse oncogenicity study, on account of one seemingly "magic" tumor found by a Monsanto-commissioned pathologist, who had been asked to reread the kidney slides in the study. This one magic tumor in the male mouse control group turned the seemingly positive Bio/dynamics mouse study into a negative one.

91. All of the pathologists that worked for the EPA and viewed the mouse kidney slides from the Bio/dynamics study could not see, and did not agree that the magic tumor existed in the kidney of one male, control mouse.

92. All of the pathologists paid by Monsanto to assess the kidney slides for the male

#### 4. Assessing Glyphosate's Capacity to Disrupt the Endocrine System

317. The European Commission had put in place a new set of testing guidelines to assess the degree to which pesticides have the potential to disrupt the functioning of the endocrine system. Such chemicals are generally referred to as “endocrine disruptors.”

318. In April 2002 Monsanto employees in Europe report to headquarters that European regulators are working on development of a list of possible endocrine disrupting pesticides, and that some new assays might be required on glyphosate and/or formulated Roundup herbicides.

319. In response to this news, William Heydens sends an email at 7:20 a.m. on April 25<sup>th</sup> to Donna Farmer. In it, he suggests a call to “...to see if there is anything more we should be doing besides the usual ‘pay no attention to the man behind the curtain’.” He ends this email by saying “...this damn endocrine crap just doesn’t go away, does it.”

320. Farmer replies to Heydens at 8:19 a.m. (just under an hour later), and writes that the “interest[ing] point” is that published tests of possible glyphosate-endocrine disruption show that pure glyphosate has no effect, but formulated product (i.e. Roundup) does. (MONGLY00885551).

321. In response to Farmer, Heydens responds at 10:47 a.m. the same day, and reports that after discussions with other Monsanto experts, they: “...concluded, not surprisingly, that we are in pretty good shape with glyphosate but vulnerable with surfactants.”

#### **D. Patterns Emerge in OPP-Monsanto Interactions over Glyphosate's Toxicology Database**

322. Applicants seeking registration of pesticide products and/or petitioning for the establishment of tolerances routinely submit studies that satisfy OPP/EPA data requirements. Submissions of such studies typically include the applicant's interpretation of the study results,

significant implications known to both OPP and Monsanto.

361. As noted earlier, once glyphosate was classified as a possible oncogen, the OPP would no longer be able to approve any required, Section 409 food additive tolerances. Moreover, final action on any pending tolerance petitions or major, new food use registrations would likely also be delayed or denied.

362. On March 20, 1984, Monsanto submitted to OPP historical control data on the incidence of renal tubule adenomas in the control groups of CD-1 mice in past studies, as requested by Toxicology Branch Deputy Chief Bill Burman in his second conversation on January 31, 1984 with Monsanto's Lyle Gingerich.

363. Burman had suggested Monsanto submit historical control data from the same laboratory, and roughly from the same time period (i.e. within 3-4 years of the time the glyphosate mouse study was conducted). Monsanto submitted such historical control data from Bio/dynamics, as well as from two other "major" contract laboratories. (MONGLY04276057)

364. The final memo codifying Dykstra's review of the mouse oncogenicity study was sent to Taylor in the Registration Division on September 4, 1984. In its "Recommendations" section, the Toxicology Division states that "1. Glyphosate was oncogenic in male mice causing renal tubule adenomas, a rare tumor, in a dose-related manner. The study is acceptable as core-minimum data. 2. A [cancer] risk assessment by Toxicology Branch is required."

365. On February 5, 1985 Monsanto sent the Director of the OPP Registration Division another letter advancing similar arguments in support of the company's conclusion that the renal tubule adenomas in the male mice were not treatment related nor statistically significant.

366. The 2/5/85 Monsanto letter sets forth six arguments in support of the company's assertion that the observed renal tubule adenomas were not treatment related: (1) tumors were

only observed in male mice, (2) renal tubule adenomas were only present at the end of the study, suggesting they were caused by the age of the male mice, rather than exposure to glyphosate in the animal's feed, (3) Only benign tumors were observed, (4) another Bio/dynamics, 2-year chronic feeding study in the same strain of mice with N-nitrosoglyphosate (NNG) produced no renal tubule adenomas in any control or treatment group, (5) glyphosate was not mutagenic in a number of assays, and (6) a complex statistical argument suggesting that the dose-related increase in renal tubule adenomas in the male mice was not statistical significant.

367. Toxicology Branch scientists assessed the data and arguments in this Monsanto letter prior to deciding whether to re-open their consideration of the renal tubule adenoma data. The review was conducted by Herbert Lacayo, and after a complex statistical analysis, he concluded that "a prudent person would reject the Monsanto assumption that Glyphosate dosing has no effect on kidney tumor production" (2/26/1985 memo, Lacayo to Reto Engler; Benbrook files).

368. It is worth noting that the 2/5/85 Monsanto letter contains two pieces of information that actually undercut two of the points raised in it.

369. First, regarding the differential rates of renal tubule adenomas in male and female mice in the glyphosate mouse study, Monsanto reports that "Historically, this lesion is observed only in male mice [four references are cited]. Control animal data from several laboratories indicate an historical control incidence in females of zero." Accordingly, the difference in incidence in this tumor, in this strain of mice, should not have been surprising, nor a reason to call into question the study's outcome.

370. Second, in the letter's point number 4, Monsanto reports zero incidence of renal tubule adenomas in the male and female control group of Charles River CD-1 mice in a similar, Monsanto-commissioned Bio/dynamics mouse study on NNG, undercutting their effort to convince OPP that the absence of renal tubule adenomas in the male mice control group was not supported by similar control-group data from other studies.

371. This and earlier letters, and multiple contacts with Monsanto officials, had made

OPP well aware that the company was determined to reverse the OPP determination that the mouse oncogenicity study was positive. So, to determine whether there was consensus among senior EPA toxicologists and cancer experts, the OPP held a meeting on February 11, 1985 attended by eight senior scientists in the Toxicology Branch.

372. The 2/11/85 meeting's stated purpose was to "evaluate and discuss the data base on Glyphosate, and in particular the potential oncogenic response of Glyphosate." The attendees reviewed the OPP assessment of the new mouse study, as well as the arguments and data submitted by Monsanto in its February 5, 1985 letter.

373. The attendees concurred unanimously that: "In accord with EPA proposed guidelines (FR of Nov. 23, 1984) the panel has classified Glyphosate as a Category C oncogen."

374. On February 21, 1985, another, Monsanto-requested meeting was held with the OPP Toxicology Branch (TB), attended by the TB Chief Ted Farber and then-Assistant Chief Bill Burnam. Dr. Gingerich, Frank Serdy, and Fred Johannsen represented of Monsanto.

375. A February 22, 1985 memo from Dr. Gingerich to Monsanto colleagues characterized the meeting mood as "relaxed, informal, and open." The memo states that Dr. Farber called the February 11, 1985 decision by OPP to classify glyphosate as a possible oncogen "an extremely close call and that EPA remains open to any new information that would make their decision easier." (MONGLY04269072)

376. The memo sets forth Monsanto's goals for the meeting, which including: "(1) see if we could respond to their concerns [the renal tubule adenomas] before any unnecessary comments became a part of the Roundup permanent file. (2) determine exactly what their concerns are. (3) gauge the level of their concern."

377. Under the heading "Concerns of Toxicology Branch" in the February 22<sup>nd</sup> memo

by Gingerich, he reports that Dr. Farber opened the meeting by describing the conclusions of the OPP toxicology branch review of the mouse oncogenicity study. Specific points noted were: “Oncogenic in mouse, IARC ranking ‘c’ [possible human carcinogen]; Company’s letter [Monsanto’s February 5<sup>th</sup> letter] was too weak to be convincing; Biologically significant rare tumors; Historical controls [data] not helpful; Will ask to re-section tissues, consider crystal formation, etc.”

378. The meeting memo then states that “Dr. Farber indicated that a substantial re-look at tissues may cause the EPA pathologist [Dr. Kasza] to change his position. If no carcinomas are found the second time, our arguments about ‘only benign’ tumors would be stronger. I [Gingerich] read this to mean that the EPA pathologist (Kasza) is open to persuasion.”

379. Next, the memo reports on several questions raised during the meeting, and their answers. Monsanto representative FJ (Frank Johannsen) then asked OPP’s Dr. Farber “...what the EPA would be likely to do if we [Monsanto] re-sectioned the slides and found no carcinomas. Dr. Farber said that it would force them to get the internal peer review group together again.”

380. This and other questions raised during the February 21, 1985 meeting demonstrated that Monsanto acted to find some basis, any basis, to change OPP’s conclusion on the mouse oncogenicity study, and the classification of glyphosate as a possible oncogen.

### **3. OPP Dismisses Monsanto’s Historical Control Data Argument**

381. On February 5, 1985, Monsanto sent to the Director of the OPP Registration Division a four-page letter transmitting additional information related to the Bio/dynamics chronic mouse study.

382. Four days later, on February 26, 1985, a memorandum was sent to OPP

statistician Reto Engler, an individual involved in the Toxicology Branch science review of glyphosate's oncogenicity and responsible for carrying out the recommended quantitative risk assessment of glyphosate's oncogenicity. The memo was written by an OPP statistician Herbert Lacayo, and sent through and signed off by Bertram Litt, OPP's Statistics Team Leader.

383. The memo focused on whether the additional, mouse historical control data for kidney tumors submitted by Monsanto alters the OPP assessment of the significance of the reported tumors in the Bio/dynamics study. It begins by noting that Monsanto submitted "historical control data from Bio/dynamics and two other laboratories," despite Dr. Burnam's unambiguous request during the February 22<sup>nd</sup> meeting that Monsanto only consider, and submit historical control data from the same laboratory where the Bio/dynamics study was conducted, and within an appropriate window of time (3-4 years).

384. The summary of the Lacayo statistical review of the historical control data states that "... we can conclude that Glyphosate dosing has a statistically significant effect (at the  $p = .006$  level) in the production of kidney tumors in male mice" (i.e., highly statistically significant, since the usual cut-off for significance is the  $p = 0.05$  level).

385. A March 4, 1985 memo on the subject "Consensus Review of Glyphosate" codified the conclusion reached by the eight Toxicology Branch scientists, each of whom signed the consensus review document (MONGLY04269067). The signatories included the Chief of the Toxicology Branch Theodore Farber, OPP's senior pathologist who read the Bio/dynamics mouse study histopathology slides, Bertram Litt, OPP's senior statistician, and William Dykstra, author of the original OPP review of the mouse study.

386. This is an unusual memo, and clearly was written to codify in the glyphosate registration file, and communicate to Monsanto, that senior scientists in the Toxicology Branch

were united in their classification of glyphosate as a possible oncogen, despite all the back and forth with Monsanto, and the review and assessment of historical control data.

387. The memo was sent to Robert Taylor in the Registration Division, and marked the end of the beginning of a protracted debate between OPP and Monsanto over the results of the Bio/dynamics mouse study.

388. The managers and scientists in OPP's Toxicology Branch were aware of the significance of this change in glyphosate's cancer classification. The memo was prepared in anticipation of a vigorous response from Monsanto to senior officials in OPP and at political levels within EPA, and possibly as well in the White House and Congress on OPP.

#### **4. Monsanto Takes Its Case to the Director of the OPP Registration Division**

389. Only two days passed before Monsanto again wrote to OPP, this time to Douglas Campt, then Director of the OPP Registration Division. The five page, March 13, 1985 letter was sent by Frank Serdy, the Monsanto Manager, Federal and State Registration Affairs.

390. The letter recounts the recent history of OPP's evaluation of the Bio/dynamics mouse oncogenicity study, the numerous meetings and back-and-forth involving OPP and Monsanto scientists, and asserts that the renal tubule adenomas observed in the male mice in the study are not treatment related, nor statistically significant. It also restates the many Monsanto arguments advanced over the past six weeks.

391. In closing his letter to Mr. Campt, Mr. Serdy states that:

"As you know, glyphosate is an extremely important herbicide to agriculture in the U.S. and around the world. Monsanto is concerned that even the initiation of formal regulatory action would have serious negative economic repercussions which we believe are not justified by the scientific evidence."

392. In 1984, an estimated 8.9 million pounds of glyphosate active ingredient were applied nationwide by U.S. farmers and ranchers (Benbrook, C [2016]. Trends in glyphosate use

in the United States and Globally, *Environmental Sciences Europe*, Vol. 28:3; data on use in the U.S. is from Supplemental Table S18, data on global use is from S24). In 2014, agricultural use in the U.S. had risen to 249.9 million pounds, 28-times higher than the level of use in 1984.

393. Globally in 1994 (first year a global estimate is possible), an estimated 124 million pounds of glyphosate active ingredient were applied. In 2014, 1.65 billion pounds of glyphosate were applied, 13-times more than in 1994, and likely well over 25-times more than global use in 1984.

394. The “negative economic repercussions” referenced in Serdy’s letter would have included curtailment of much of the dramatic rise in glyphosate use that began in 1996 with the commercial launch of genetically engineered crops able to withstand post-emergence applications of Roundup.

395. In an April 3, 1985 memo from William Dykstra to the Registration Division’s Robert Taylor, the official Toxicology Branch judgement regarding glyphosate’s oncogenicity was stated as it had been previously: “Glyphosate was oncogenic in male mice causing renal tubule adenomas, a rare tumor, in a dose-related manner.”

## **5. Monsanto’s Next Move – Hire Another Pathologist to Re-read the Kidney Slides**

396. Also on April 3, 1985, Dr. George Levinskas, a scientist in the Monsanto Department of Medicine and Environmental Health, circulated a brief update inside the company stating that “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. [Private, consulting pathologist] 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.” (MONGLY04277789)

ground application using a tractor or spray rig (42 out of 143 total cases); hand application with a backpack sprayer or hand-pump device (100 out of 142 cases); and, other types of application (1 of 142 cases).

516. Blondell's data covered 64 applicator and 24 mixer/loader cases of eye irritation between 1981 and 1985, and 52 applicator and 7 mixer/loader skin injury cases. In addition, there were a total of 24 "Systemic" illnesses reported, 6 cases among spray rig applicators and 18 among hand applicators. Hand applicators like Dewayne Johnson had suffered the majority of total-applicator injury cases: for the eye, 44 out of 64, and for skin, 35 of 52 irritation cases.

517. A section of Blondell's report addresses the relationship between the number of physician-treated occupational illnesses in California and the total pounds of glyphosate applied. The Blondell report contains the following, surprising finding that almost certainly caught EPA's attention:

"The number of California physician-treated occupational illnesses (average per year, 1981-1985) per million pounds of glyphosate reported sold in California in 1984 was 17.0. On average, for all pesticides, we find 1.3 poisonings per million pounds sold, per year in California."

518. The scope and specificity of the worker-safety provisions required in the 1986 glyphosate Registration Standard (RS), and referenced in Attachments 2 and 3 of the 6/18/87 Exposure Assessment Branch memo are central to this case.

519. Section D, Part 4 of the glyphosate RS states that "Worker Safety Rules must appear on end-use products containing glyphosate except for those labeled for homeowner use only." (page 28). (Products marketed to homeowners contain 2% or less glyphosate; such dilute products require less stringent safety precautions for those applying the products).

520. EPA required worker-safety provisions on glyphosate products like those applied at work by Dewayne Johnson include:

11/18/87 and a memo setting forth his recommended action is dated 1/28/88.

524. Nielsen agreed to Monsanto's request to postpone additional requirements for personal protective equipment (PPE) on Roundup labels subject to two conditions. The first was that the new worker-protection PR notice would be issued "...in a reasonable time frame...", and hence lead to changes in Roundup worker safety language

525. His second condition for approval of Monsanto's deferral request stands as one of the first clear statements of OPP/EPA concern over adverse health effects suffered by some Roundup herbicide applicators. Nielsen's second condition was that: "...the submitter [Monsanto] begin investigating the high number of eye and/or skin injuries associated with glyphosate use in California."

526. Reinforcing his concern, Nielsen added in his memo to the Registration Division that: "Myself and other members of the Exposure Assessment Branch would like to meet with appropriate representatives of the Monsanto Company to discuss their response to this concern [the adverse impacts data from California] within six months. Please arrange with the submitter."

## **2. Impact of Monsanto's Refusal to Accept EPA-Required Worker Safety Rules**

527. The August 11, 1986 glyphosate RS set forth the detailed worker-safety label language quoted above. This language had to be included on Roundup product labels in commercial channels of trade as of June 20, 1988.

528. Monsanto repeatedly challenged EPA's requirements for stricter worker-safety provisions through multiple communications over several years. Some arguments were procedural (e.g., defer changes in labeling until the new, generic worker-safety labeling PR notice was issued), while others were based on Monsanto-commissioned exposure studies and risk calculations.

recommended safety precautions.

535. Both labels include this language:

**“Personal Protective Equipment (PPE)**

**Applicators and other handlers must wear:** long-sleeved shirt and long pants, shoes plus socks...[no other PPE is required]”

536. The phrase “other handlers” encompasses those mixing and loading, shipping, storing, or handling these herbicides.

537. Both labels require that PPE be kept and washed separately from other laundry, and then provide this instruction to applicators and other handlers:

“Discard clothing and other absorbent materials that have been drenched or heavily contaminated with *this product’s concentrate*. Do not reuse them.” (Emphasis added).

538. Under the heading “User Safety Recommendations,” both labels state that “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.”

539. There is also a “Non-Agricultural Use Requirement” on each label: “Keep people and pets off treated areas until spray solution has dried.”

540. During his many applications of RangerPro and Roundup ProConcentrate between 2012 and 2014, Mr. Johnson went well beyond the PPE required on the product labels. He wore a Tyvek suit, goggles, and a face mask, none of which were required on either label.

541. He reported that the Tyvek suit only went up to his throat, leaving most of his neck, and the back of his head exposed.

542. Mr. Johnson also reported that when he was applying Ranger or Roundup herbicide with a backpack sprayer, he was often exposed around the neck and on his head from spray drift, especially when the wind was blowing. In his deposition in a worker’s compensation

action against the school district he worked for, Johnson stated” “And the mist [spray drift], you know, it happened a lot, where you just – you can’t control it. One minute you’re spraying and you get a drift of wind and it’s on you, you know.” (Dewayne Johnson deposition, Dewayne Johnson vs. Benicia Unified School District, 10/28/2015, page 131).

543. He also experienced two significant exposure events to the mixed glyphosate herbicide-water solution. In one, there was a leak in the hose of his backpack sprayer, resulting in the flow of some of the spray solution down his back; the second occurred when a hose on a sprayer in the back of his truck broke and he had to fix it. As a result of the second episode, he reported being drenched with the spray mixture in the tank, and had glyphosate and surfactant on his body for hours.

544. Because of Monsanto’s refusal to add to Roundup product labels the new, worker-safety language set forth in the 1986 RS, substantial differences persisted in the worker-safety provisions on the RangerPro and Roundup ProConcentrate labels in 2012-2014, compared to the PPE and other exposure-reduction provisions called for in the RS.

545. For those mixing and loading either herbicide applied by Johnson, the provisions in the RS would have stated, as quoted above:

“HANDLE THE CONCENTRATE ONLY WHEN WEARING THE FOLLOWING PROTECTIVE CLOTHING AND EQUIPMENT.”

“Wear goggles or a face shield, chemical resistant gloves, chemical resistant apron, chemical resistant shoes, shoe coverings, or boots.”

546. The mixer/loader and applicator worker-safety requirements on both the RangerPro and Roundup ProConcentrate products that Dewayne Johnson applied: (1) did not require any gloves, let alone chemical resistant gloves; (2) did not require a chemical resistant apron; and, (3) did not require chemical resistant shoes.

547. The worker-safety language requirements for glyphosate herbicides set forth in

the 1986 RS include:

“IMPORTANT! Before removing gloves, wash them with soap and water. Always wash hands, face and arms with soap and water before smoking, eating, drinking, or toileting.”

548. In addition to not requiring any gloves, the labels on both of the products that Mr. Johnson applied lacked the above “IMPORTANT” instructions regarding washing hands, face, and arms with soap and water. Instead, the RangerPro and Roundup ProConcentrate labels only offer a recommendation that users should “wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.”

549. There is another important difference between the worker-safety language required by the 1986 glyphosate RS and the language on the labels of the glyphosate products Mr. Johnson applied. The RS language states:

“HEAVILY CONTAMINATED OR DRENCHED CLOTHING CANNOT BE ADEQUATELY DECONTAMINATED” and hence should be discarded.

550. Both RangerPro and Roundup ProConcentrate labels require that the herbicide be mixed with water prior to application. The labels provide detailed instructions regarding how much water an applicator should mix with a given volume of the formulated herbicide.

551. Both labels call for discarding clothing or other absorbent materials that “have been drenched or heavily contaminated with *this product’s concentrate*” (emphasis added).

552. Clothing, or other absorbent material, could become drenched with RangerPro or Roundup ProConcentrate *only* during the mixing/loading process, or in the event a container of the concentrate herbicide was ruptured during transport or in storage.

553. Neither label requires discarding of clothing drenched during the *application* of the products, after the herbicide is mixed with water and poured into a backpack sprayer or spray tank.

in contrast to the standard, 3% estimate relied on by EU and U.S. regulators.

589. Monsanto was worried about the potential that the study would “blow Roundup risk evaluations. (getting a much higher dermal penetration than we’ve ever seen before.” (MONGLY03738295) Therefore, they decided to stop any further work with TNO to generate new rat skin dermal penetration data.

590. To my knowledge, the results of the TNO rat skin penetration study showing 5% to 10% dermal penetration were not submitted by Monsanto to the U.S. EPA, as required under the Section 6(a)(2) “adverse effects” reporting requirement in FIFRA.

591. Nor, to my knowledge and based on the records I have reviewed, was the TNO data shared with any other regulatory agency. If the company did transmit a 6(a)(2) submission to EPA with these data, or provide it to other regulators, Monsanto will surely correct the record in deposition and/or at trial.

592. In addition, Monsanto continued for years to argue in all regulatory submissions, peer-reviewed journal publications (some with an accurate listing of authorship, others ghost-written), and in the media that the 3% estimate of glyphosate-dermal penetration in the case of Roundup products formulated with POEA *overstated* actual penetration and risks, even after the company knew that the opposite was almost certainly the case.

593. Accordingly, for many years, Monsanto consciously perpetuated possibly unsafe uses of RangerPro, Roundup ProConcentrate, and other Roundup products in three ways.

594. First, the company knowingly mislead regulators, and users of RangerPro and Roundup ProConcentrate, including Dewayne Johnson, by failing to disclose to regulators that an erroneously low dermal absorption estimate was included in worker-safety risk assessments.

595. Second, Monsanto knew that people applying Roundup products with backpack

Johnson's many exposures to the glyphosate and surfactants in the formulated herbicides he applied, and hence Mr. Johnson's risk of contracting NHL.

## **B. Cultivate Relationships with “Friendly” Scientists and Officials in EPA**

601. Monsanto invested considerable effort in establishing open channels of communication with selected scientists and decision makers in EPA. Frequent interactions helped Monsanto understand how receptive a given person in EPA would likely be, if asked to move toward Monsanto's view of a given study or issue, or at least give Monsanto a “head's up” about forthcoming agency decisions or actions.

602. My review of the record convinces me that Monsanto had established unusually close relationships with some key officials and scientists in the EPA's Office of Pesticide Programs (OPP) who were involved in either the science reviews or decisions impacting glyphosate-based herbicides. Two examples are discussed herein.

### **1. Jess Rowland**

603. Jess Rowland was the Deputy Director of the OPP Health Effects Division. He was directly involved in managing the EPA's internal assessment of glyphosate's oncogenicity, as well as the EPA's interactions with and response to the IARC review of glyphosate. He also served as a point of contact between EPA and other federal agencies, and managed CARC (Cancer Assessment Review Committee), a key, internal OPP committee that rendered judgement of whether a given pesticide poses cancer risk.

604. In a 2/20/15 email as Monsanto was preparing for the release of the IARC report on glyphosate, William Heydens writes to Dan Jenkins, his Monsanto colleague that works most closely with EPA on registration issues. The topic is “EPA Folks going to IARC” (i.e., attending

the final IARC Working Group meeting in Lyons, France March 10-14, 2015).

605. Heydens reports on the two EPA scientists that “will actually participate in the meeting,” and two other EPA representatives that will be attending as observers. He identifies the two observers as “Catherine [Eiden] is a Special Assistant in the Pesticide Re-evaluation Division, and we all know Jess.” (MONGLY00986901)

606. The phrase, “we all know Jess,” implies a high degree of familiarity among several Monsanto people.

607. In an April 27, 2015 email exchange between Dan Jenkins (registration, EPA interface) and William Heydens (toxicology, safety), Heydens asks Jenkins about approaching EPA and asking them directly “about what area they see as most problematic [in the IARC monograph] or just ask if there is anything that would help them [EPA] defend the situation?”

608. In effect, Heydens is asking Jenkins if there is anything Monsanto can do to support EPA in sticking by the agency’s current position that glyphosate is not oncogenic, despite the IARC determination. Jenkins responds: “I think you and I could get on the phone w Jess Rowland and discuss this openly. He’ll give us straight talk.” (MONGLY03929023)

609. The next day (April 28<sup>th</sup>), Jess Rowland called Dan Jenkins “out of the blue” and told Jenkins:

“We have enough to sustain our conclusions [that glyphosate is not oncogenic]. Don’t need gene tox or epi. The only thing is the cheminova [another registrant of glyphosate herbicides] study with the sarcoma in mice – we have that study now and its conclusions are irrelevant...I am chair of the CARC and my folks are running this process for glyphosate in reg review.” (MONGLY00987756)

610. But Rowland had another message to pass on to Jenkins that day. The Agency for Toxic Substances and Disease Registry (ATSDR), another U.S. government agency responsible for assessing the toxicity of chemicals, was planning to undertake a review of glyphosate. It was

well known in the toxicology community, and in Monsanto, that ATSDR historically reached conclusions similar to IARC. Monsanto was deeply concerned that an ATSDR determination similar to IARC's would raise serious doubts about the EPA's position that glyphosate does not pose cancer risk.

611. In this email, Rowland then asks Jenkins for a contact name at ATSDR, and reports that there is no coordination underway between EPA and ATSDR in terms of ATSDR's pending assessment of glyphosate. Then, according to Jenkins's email, Rowland said: "If I can kill this [the ATSDR review] I should get a medal."

612. I am not aware of another instance in which a senior scientist in the Office of Pesticide Programs made such a blatantly inappropriate statement to a pesticide registrant. In the government agencies for which I have tracked similar regulator-company interactions over the last few decades, an act so blatantly solicitous and inappropriate would have been grounds for dismissal, or worse.

613. Monsanto recognized Rowland's actions and eagerness to help in the company's efforts to downplay the risk of glyphosate-based herbicides. In a September 3, 2015 email to a large group of colleagues, Dan Jenkins wrote that:

"No questions but Jess Rowland at EPA is quite proud of their recent endocrine conclusions and is also on point regarding their IARC response. Jess will be retiring from EPA in ~5-6 mos and could be useful as we move forward with ongoing glyphosate defense." (MONGLY03351980)

614. Rowland was responsible for an October 2015 evaluation of glyphosate as head of the Cancer Assessment Review Committee (CARC). In conducting this review Rowland apparently violated EPA's own cancer assessment guidelines in concluding that glyphosate was "Not Likely to be Carcinogenic to Humans." In a May 2, 2016 email, Jim Jones, an Assistant Administrator at the EPA, informed Gina McCarthy, the Administrator of the EPA that the

CARC “assessment was not consistent with Agency’s guidelines.” (EELI\_0000037)

615. This Assessment was “inadvertently” released to the public despite its violation of guidelines and “Monsanto saw it and put out a release saying EPA had confirmed glyphosate is not carcinogenic.” (EELI\_0000037)

## **2. Jack Housenger**

616. As events unfolded in 2015 after the release of the IARC classification, Monsanto’s most commonly mentioned rebuttal was that the EPA’s Office of Pesticide Programs still classified glyphosate as not likely to pose a human cancer risk. Moreover, EPA had been working for years on its own re-registration of glyphosate. There was intense interest in whether the IARC classification would alter EPA’s judgement regarding glyphosate herbicide cancer risk.

617. If EPA did change its position, that would be an extremely grave development, almost sure to seriously curtail Monsanto’s “Freedom to Operate,” and it would also, in all likelihood, impact the causality phase of ongoing or future litigation.

618. If EPA stuck by its existing determination, it would be helpful to Monsanto in multiple venues, and likely reduce threats to the company’s FTO.

619. At the time, Jack Housenger was the Director of the Office of Pesticide Programs, and had been a senior OPP manager for many years.

620. The record (including some text message exchanges) shows a close, deferential, and supportive relationship in communications flowing from Housenger and Monsanto, as well as from Monsanto and Housenger. In short, the communications give rise to the sense that Housenger and Monsanto are on the same “team,” pursuing the same goals.

621. In one important sense, they did share a common goal – defending the EPA’s scientific judgement that glyphosate herbicides do not pose a risk of cancer to humans, a

judgement directly challenged by IARC's March 2015 classification of glyphosate as a probable human carcinogen. But this EPA-Monsanto comradery obviously depended on EPA sticking to its current judgement regarding glyphosate cancer risk.

622. So, priority number one in Monsanto's interactions with EPA was to assure they did not change their classification of glyphosate herbicide cancer risk, and priority number two was to encourage, if not compel via political pressure, the EPA to be vocal in defense of its position and criticism of IARC.

623. One example of Housenger taking the initiative to help Monsanto occurred in May, 2015, about two months after the release of the IARC report. Monsanto, Jess Rowland of EPA, and apparently Housenger were concerned that a review of glyphosate toxicity by ATSDR might align with IARC's, and undermine EPA's view of the science.

624. After asking Monsanto for help identifying contacts at ATSDR, and calling the ATSDR staff member assigned to carry out the review, Housenger sent a May 20, 2015 email to Patrick Breysse, head of the ATSDR program. Housenger introduced himself as the Director of the EPA Office of Pesticide Programs (OPP), and updated him on the near-complete, comprehensive OPP review. Then he wrote:

"However, given that our reviews [OPP's and ATSDR's] would be basically done very close in time to one another, there is a question of whether this is a good use of government resources. I'd like to talk to you about this and can be reached at the number below." (Public document).

625. Breysse responds nine minutes later: "Can we discuss today or tomorrow".

626. Housenger's email and call with Breysse, the ATSDR Director, was not the only contact he made. In an email sent June 24, 2015 to Dan Jenkins, Monsanto's top, D.C.-based registration official, Housenger writes:

"Dan, here is everyone I talked to

Henry [Abadin] was the one who ended up saying that they [ATSDR] would put glyphosate on hold holding the OPP risk assessment release [he actually meant “pending” rather than “holding” the OPP risk assessment release]

Hope this helps

Breyse, Patrick N...he’s the Director of HCEH/ATSDR  
Stephan, James W (aka Jimmy) he’s the acting director of the Division of Community Health Investigation  
Henry Abadin....he’s the branch chief  
Hannah Pohl.....is the person doing the work on glyphosate” MONGLY04028722)

627. This Housenger email to Jenkins reads like a status report from a junior staff person to his/her manager. It reflects a desire to be helpful to Monsanto that is fundamentally at odds with Housenger’s role as the senior manager of the EPA’s Office of Pesticide Programs.

628. On October 13, 2016, Jay Vroom of CropLife America (Monsanto’s lobbying organization) called and emailed Jack Housenger to discuss removing epidemiologist Peter Infante from the glyphosate SAP panel and to invite him to a retreat with Monsanto and other Industry executives at a West Virginia casino and resort. EPA-HQ-2017-000442-0000205.

629. On October 14, 2016, the OPP announces that it was postponing the SAP hearing on glyphosate scheduled for October 18, 2016. On October 19, 2016, the OPP announced that Peter Infante would no longer be on the SAP panel evaluating glyphosate.

630. Jack Housenger attended a CropLife retreat at a Casino and Resort with executives of Monsanto and other pesticide companies in November of 2016, one month before a key SAP Panel Hearing on glyphosate. These executives noted that, “[w]e had some quality time with EPA OPP Office Director Jack Housenger to dig into key issues and operational matters at that vital department of EPA.” MONGLY07063555.

920. For example, Heydens sharply disagreed with some panel-members, and ex-employee Acquavella over how sharply to be critical of IARC and its classification decision. Examples of such disagreements are evident throughout Heydens' track-changes comments and editing of Acquavella's edits to the draft of the summary panel report. (MONGLY01000680-01000709)

## **7. Political and Other Activities Post-IARC**

921. The breadth of Monsanto's activities in response to the IARC classification of glyphosate herbicide as a probable human carcinogen is striking. A June 5, 2015 update on "US Government Outreach – WHO IARC Classification on Glyphosate" outlines dozens of ongoing and proposed actions and goals. Under "**THE STRATEGY**", the document states:

"One strategy for addressing widespread confusion in the wake of the IARC classification has been to seek clarification from the World Health Organization (WHO) which would provide the proper context of the classification for governments and regulators around the world to have greater confidence defending their science based regulatory decisions." (MONGLY02953363)

922. The document reports on multiple briefings given to U.S. government agencies, including a Donna Farmer briefing of Dr. Mitchell Wolfe, the Deputy Assistant Secretary for Global Health, in the of Department of Health and Human Services (HHS), to which "we came prepared with a robust set of technical materials for the Secretary's background...".

923. In the briefing for the HHS Deputy Secretary Dr. Wolfe, he was told about ATSDR (Agency for Toxic Substances and Disease Registry), an agency under HHS of which he was reportedly unaware. Monsanto then told Wolfe about the ongoing ATSDR review of glyphosate, and made the case that such a review was unnecessary and that the EPA bears the primary responsibility for "determination of pesticide safety."

924. Then Monsanto briefed Wolfe on "A common element between IARC and

ATSDR...Christopher Portier Ph.D...[who] was Director of ATSDR and co-chair of the IARC Advisory Group.”

925. Dr. Portier’s views on glyphosate oncogenicity were no doubt discussed, as was the fact that Dr. Portier “was an invited specialist representing the Environmental Defense Fund.”

926. According to Monsanto’s recounting of the meeting “Dr. Wolfe said he would follow up on what was going on with ATSDR and he was encouraged to have discussions with the EPA staff, as well.”

927. Last, Monsanto asked for Wolfe’s and HHS’s “assistance in securing a WHO clarification. We emphasized that we were not seeking changes to IARC, the classification or the IARC process.”

928. In fact, Monsanto had already initiated, and is still carrying out campaigns to punish IARC for its classification through, among other things (details below):

- Lobbying members of Congress to challenge U.S. government funding for IARC, via U.S. government support for the WHO;
- Calling for Congress to hold hearings;
- Mounting a campaign to force IARC to release drafts of its glyphosate review document and notes from Working Group deliberations;
- Working with a Washington Post reporter purportedly doing a hit piece; and
- Mounting multi-faceted outreach and third-party expert criticisms of the IARC process, the people who participated in it, the conclusion it reached, and its accountability.

929. Accordingly, the statement in Monsanto’s account of the Wolfe-HHS briefing that “...we were not seeking changes to IARC, the classification or the IARC process” was clearly not truthful.

### **Blocking the ATSDR Review of Glyphosate**

930. Another important Monsanto action-item, post-IARC, was stopping an ongoing

ATSDR review of glyphosate safety. Monsanto regarded the ATSDR review as a clear threat because the agency is “IARC-like,” very conservative, and has often disagreed with EPA in the past.

931. An ATSDR review that supported IARC’s conclusions and classifications was to be avoided. (MONGLY03342947)

932. Since Monsanto suspected that ATSDR would agree with IARC on the science, the only way to avoid a huge setback in Monsanto’s ongoing campaign to isolate and marginalize IARC would be to stop ATSDR from issuing the results of its review.

933. In pursuit of their ATSDR goal, Monsanto:

- Sought and carried out meetings, briefings, and webinars with ATSDR to communicate its assessment of the issues, explain why it felt the ATSDR review was unneeded, and the scientific flaws in the IARC review;
- Received significant help from two senior OPP/EPA officials – Jess Rowland and the OPP Director, Jack Housenger;
- Sought assistance and support from the Deputy Assistant Secretary for Global Health in HHS (the agency home of ATSDR);
- Asked Monsanto’s home-state Senators to contact HHS and reinforce the urgency of quick HHS action to intercede with ATSDR, given information Monsanto had obtained suggesting the ATSDR report might be released in only a few weeks;
- Lobbied Congresswoman Lynn Jenkins to submit questions regarding the ATSDR glyphosate review to the Secretary of HHS at the conclusion of a hearing before the House Ways and Means Committee on health care reform (MONGLY03064699); and
- Recruited individuals to write letters to Congressmen complaining that the ATSDR review was duplicative and a waste of taxpayer money, so that the letter(s) could be used to trigger media coverage of the campaign to stop the ATSDR study. (MONGLY03342947)

## **E. Allied Organizations, Front Groups, and the Media**

934. Monsanto engages with a wide diversity of organizations in the course of promoting its business and industry objectives. These include pesticide industry trade associations, the most important of which is CropLife America, which is part of CropLife

International. (CropLife America was formerly called the National Agricultural Chemicals Association, or NACA).

935. Monsanto and other pesticide manufacturers use CropLife to align the industry on issues, organize and carry out initiatives that are responsive to industry-wide issues, lobby the U.S. Congress and federal agencies, and conduct a wide array of media and PR activities.

936. Monsanto also works with all major farm commodity groups (corn growers, cotton growers etc), and general farm organizations like the Farm Bureau and Future Farmers of America. It provides financial and content support to most agriculture and food-relevant scientific and professional society meetings.

937. The company is working simultaneously with several PR, communications, and issue management companies on specific projects.

938. In some cases, Monsanto's financial support is welcomed and acknowledged, while in other cases it is not. In the later case, Monsanto works out a scheme to route its funding through one or a few organizations, in order to hide the source of the funding (Monsanto) from the person or entity receiving the funding, as well as from the general public.

939. While comprehensive statistics are not publically available, I suspect that a substantial portion of Monsanto's funding for scientific organizations, science-related activities, and individual scientists is provided through circuitous channels that avoid the need for recipients to openly acknowledge the company's funding support.

940. Such practices are not unique to Monsanto, but I am not aware of another company in the pesticide industry that invests so heavily, creatively, and aggressively in its third-party network of scientists and the activities of scientific organizations.

## **1. CropLife America and CropLife International**

941. CropLife America routinely carries out special projects and activities, with funding provided by member companies, or sometimes one or a few company members. In some cases, such funding comes from routine membership dues, in other cases, CropLife requests and/or is offered targeted support for a special project. Many such projects are done under contract by consulting firms or academics with ties to the industry.

942. Such arrangements often assure that funding from a given company passes through at least two entities before reaching the person or entity carrying out an activity. As a result, it becomes difficult, if not impossible for members of the public to know exactly who actually paid for a given activity or project, nor the basic motivation leading to the project or activity.

943. A good example unfolded in the fall of 2015. Several pesticide manufacturers were concerned by the way OPP/EPA was using epidemiological studies done by scientists not working for, or representing the pesticide industry. Several such studies had been published in peer-reviewed journals, and had become a part of the science-base reviewed by EPA in the pesticide risk assessment process.

944. Three companies were acutely aware of the risk posed to one of their major products: Dow AgroSciences over epidemiological studies showing a link between chlorpyrifos insecticide use and neurodevelopment in infants and children; Syngenta over the link between atrazine exposures via drinking water and breast cancer; and, Monsanto over the cancer risks posed by glyphosate.

945. A decision was made by the companies to commission a scientific critique of how OPP/EPA had utilized the results of epidemiology studies. On behalf of the companies, CropLife America requested a proposal from a closely aligned consulting firm, Exponent. Exponent

provided a detailed proposal to CropLife outlining such a study, at a projected cost across three major tasks of \$70,000-\$100,000. (MONGLY02134326)

946. Task 1a in the proposal describes four case studies focused on glyphosate, organophosphate insecticides (and especially Dow's chlorpyrifos), and Syngenta's atrazine.

947. On January 4, 2016 Exponent released the 89-page report commissioned via the September contract. It was entitled "Human Epidemiology Data Incorporated Into Regulatory Risk Assessment: Retrospective Analysis." (MONGLY03409329-03409423)

948. After the release of the IARC classification, CropLife International developed and implemented a multi-prong response on behalf of the industry. Key activities included:

- "Generating influencer commentary on IARC...to challenge the credibility of IARC...working with the issue management consultancy v-Fluence to generate proactive news/commentary articles...all articles have been pushed widely on social media channels through a wide network of industry commentators";
- "High level outreach to WHO";
- "Building credible 3<sup>rd</sup> part support...(in particular toxicologists and academics)"; and
- "Coordinating industry alignment."

## **2. Engaging PR Firms**

949. Over the years, Monsanto used a variety of PR and communication firms to assist in the defense of glyphosate herbicides. These firms were typically tasked with actions that would be difficult and/or tainted if undertaken by Monsanto staff.

950. There is nothing unusual about pesticide manufacturers or other companies engaging such firms in support of outreach, policy, regulatory, and political goals. But the scope and nature of the activities pursued by Monsanto via such firms stands out as uniquely broad and aggressive.

951. Monsanto commissioned Potomac Communications to place not just one or a few supportive op-eds and letters to the editor in response to the IARC decision, but dozens.

952. In May 2015, Monsanto received a detailed document from the PR firm FleishmanHillard (FH). This firm had conducted multiple projects for Monsanto in the past. The current proposal focused on triggering expressions of support for the EPA's re-registration of glyphosate in the political, farm, academic, and gardening communities. (MONGLY03550020-24)

953. FH recommended targeting two audiences: "those who live and work in congressional districts with significant agricultural glyphosate use and whose elected representative sit on committees relevant to EPA"; and second, "those who live in suburbs that lean conservative politically." FH then adds:

"Please note that this general consumer approach is intended as a supplement to a stakeholder outreach campaign targeting farmers, agricultural trade associations and other agricultural audiences... Finally, please note that the below campaign elements represent efforts that FH would conduct above and beyond the scope of ongoing support for the [Monsanto-funded] Cultivating Trust campaign."

954. The scope of the newly proposed "Re-registration Campaign" is impressive. Seven "markets" would be included (suburban Dallas and/or Houston, Atlanta, Davenport/Iowa City, Detroit, Indianapolis, Memphis Minneapolis/St. Paul, St. Louis); a table describes each area, noting key politicians or reasons why the area was selected.

955. Within each area, a set of FH-paid "community organizers" (COs) would be assigned a specific set of tasks and goals. Each "would target 750-1,000 consumer signatures/comments or letters and 15-25 'high quality' letters ...per month of the [glyphosate re-registration] comment period (either 60-90 days)."

956. The proposal then spells out what FH would do to prepare/support the COs in achieving their target goals. In addition, FH "would manage a paid digital campaign on Facebook, using sponsored content targeted at a relevant audience...with the aim of driving them

to Monsanto's comment generation website."

957. The estimated budget for the proposed 3-4 months of activity was \$355,000-\$400,000.

### **3. Shaping the Agenda and Supporting Scientific Meetings**

958. There are several instances in the record of this case documenting why and how Monsanto played a role in shaping the focus of a scientific meeting to include discussion of glyphosate risk issues, as well as some instances where Monsanto also provided the funding needed for a meeting to occur.

959. In a March 10, 2016 email, Dan Goldstein, Monsanto's "Lead, Medical Sciences and Outreach," contacts a colleague, Allister Vale, a consulting clinical pharmacologists and Director of the National Poisons Information System (Birmingham Unit), in the U.K.

960. Dr. Vale is active in several organizations that convene meetings of medical toxicologists, a group that Monsanto is striving to engage in the ongoing reaction to IARC and debate over glyphosate safety.

961. In his "preliminary inquiry," Goldstein asks Vale if she would work with Sir Colin Berry to "reincarnate" an expert panel, this time composed of European medical toxicologists. (MONGLY0256574-75) He writes that: "Cost (including Honoria) will be picked up by Monsanto via an appropriate granting mechanism which allows for a proper degree of academic independence."

962. Vale and Goldstein meet briefly later in the month at a meeting of the Society of Toxicology (SOT). They discuss the idea raised by Goldstein in the March 10 email, and agree to get back in touch after the meeting.

963. Vale sends Goldstein a March 24, 2016 email apologizing for her limited time

during the SOT meeting and stating:

“The issues you raise in regard to glyphosate are of course of considerable professional interest to me...we have proposed a symposium for next year’s SOT which will include a discussion of the carcinogenicity of glyphosate.”

964. Goldstein responds the next day, and provides much more detail, and points out that “the situation around glyphosate continues to be, frankly, bizarre.” He goes on to note “serious process issues surrounding this IARC assessment. Then he writes:

“Our only goal at this point is to create a large number of medical toxicologists who know about glyphosate products. You have hit on the key problem of course – direct involvement of Monsanto is not going to be acceptable to experts in the EU.”

965. Goldstein then returns to the issue of funding for a meeting. He writes:

“I assume that the cost will be considerable....Funding can perhaps come from the Glyphosate Consortium which is conducting the EU re-registration or via ECETOX or CEFIC, for example, and be routed via SOT or one or more academic institutions. At that point, we can be ‘hands off’ altogether.”

966. So, under the Goldstein proposal, Monsanto would provide funding to the Glyphosate Consortium, the Consortium would contract with one or more academic institutions, and/or route funding to the SOT, which would then make invitations and cover the costs of participants and presenters. As Goldstein notes in his email, there would be an “appropriate degree” of separation between Monsanto funds and the people receiving them.

967. Vale responds two weeks later, in general agreeing that an indirect funding mechanism could be found. But she then reminds Goldstein, “However, to make this work, neither I nor they could be in receipt of direct funding from Monsanto or the [industry-funded] Glyphosate Consortium.”

968. This correspondence is important not because of the impact of one meeting, or even whether the meeting took place. It is important because it documents clearly the techniques Monsanto deploys to engineer meetings, papers, events, and other activities where the company

will have a well-controlled forum, or a mechanism to communicate its view of some set of issues to a possibly influential audience.

969. Goldstein ends his March 25<sup>th</sup> email to Vale with a statement referring to the government-employed medical toxicologists that Monsanto is trying to reach out to: “As important resources for their respective national agencies, we are of course hopeful that they can support *a balanced and scientific approach in the EU*.” (Emphasis added).

970. Of course, such an approach would have to be aligned with Monsanto’s positions on issues, and certainly not IARC’s on the issue of glyphosate oncogenicity.

## **VII. Protecting “Freedom to Operate” and Scientific Deceit Characterize Monsanto’s Assessments of and Response to Glyphosate-Related Risks**

971. Pesticide companies bear an obligation vested in various laws and regulations, and common corporate decency, to assure that the products they bring to market are safe and will reliably produce the benefits for which they are registered, i.e. control of weeds as in the case of glyphosate.

972. The term “product stewardship” is used within the industry and regulatory agencies to describe and encompass the actions pesticide manufacturers should take on an ongoing basis in the interest of product stewardship, before and after a new use of a pesticide is approved.

973. In the pesticide arena, the sciences supporting both human-health risk assessments and environmental-impact assessments are dynamics and imperfect, and heavily dependent on location- and even application-specific data, which is almost never available. So, in companies and regulatory agencies alike, many assumptions and a considerable degree of judgement is essential in deciding upon the science that must be conducted prior to seeking, and approving a new use of a pesticides.

974. Where to draw the line between presumably safe and possibly risky pesticide uses is also fraught with scientific, social, and political challenges, uncertainty and tension.

975. The same is true after approval, as companies and regulators strive to refine and agree on the nature and magnitude of risks after a pesticide is approved and has been applied for a period of time.

976. But in general, Monsanto claims that they base all their product development, testing, commercialization, and regulatory actions on the best available science. Such science is

1096. Over the last decade, scientists in Europe, South America, and the U.S. have reported steadily rising levels of glyphosate in drinking water resources. In heavily farmed areas where Roundup Ready crops are widely planted and Roundup is heavily used, glyphosate detections in drinking water are now common.

Charles Benbrook

12/21/17

# **EXHIBIT 14**

BEFORE THE WORKERS' COMPENSATION APPEALS BOARD  
OF THE STATE OF CALIFORNIA

DEWAYNE JOHNSON, )  
Applicant, )  
-vs- ) CASE NO.  
BENICIA UNIFIED SCHOOL ) ADJ10102319,  
DISTRICT, PSI AS A SELF-INSURED ) ADJ10094287  
GROUP, ADJUSTED BY NORTH BAY )  
SCHOOLS INSURANCE AUTHORITY, )  
Defendants. )  
\_\_\_\_\_ )

DEPOSITION OF  
DEWAYNE JOHNSON  
October 28, 2015

Reported by: VICTORIA L. PETERSON, CSR #6992

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601 University Avenue, Suite 213, Sacramento, CA 95825  
(916) 646-1891

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1 APPEARANCES:  
2  
3 FOR THE APPLICANT:  
4 LEVITZ LEGAL GROUP  
5 Attorneys at Law  
6 BY: BRUCE LEVITZ, Esq.  
7 2216 Laguna Vista Drive  
8 Novato, CA 94945  
9  
10 FOR THE DEFENDANT:  
11 LAW OFFICES OF CRYSTAL CUNNINGHAM  
12 Attorneys at Law  
13 BY: CRYSTAL CUNNINGHAM, Esq.  
14 2485 Natomas Park Drive, Suite 420  
15 Sacramento, CA 95833  
16  
17 ALSO PRESENT:  
18 Catherine Chyi, Esq.  
19  
20  
21  
22  
23  
24  
25

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1 BE IT REMEMBERED that on Wednesday,  
2 October 28, 2015, commencing at the hour of  
3 12:08 p.m., at the offices of LEVITZ LEGAL GROUP,  
4 Attorneys at Law, 2216 Laguna Vista Drive, Novato,  
5 California, before me, VICTORIA L. PETERSON, a  
6 Certified Shorthand Reporter, empowered to administer  
7 oaths and affirmations pursuant to Section 2093(b) of  
8 the Code of Civil Procedure, personally appeared  
9 DEWAYNE JOHNSON,  
10 an applicant in the within-entitled matter, called as  
11 a witness by the defendant, who, having been duly  
12 sworn by the Certified Shorthand Reporter to tell the  
13 truth, the whole truth, and nothing but the truth,  
14 testified as follows:

15 --oOo--  
16 EXAMINATION BY MS. CUNNINGHAM  
17 Q. Good afternoon, Mr. Johnson. My name is  
18 Crystal Cunningham, and I represent the School  
19 District on the workers' compensation claims that you  
20 filed.  
21 Please state your entire name for the record.  
22 A. **Dewayne Anthony Lee Johnson.**  
23 Q. What is your date of birth?  
24 A. **1/20/72.**  
25 Q. Have you ever gone by any other names?

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1 light, and try to wrap it up by 10:00 o'clock, 10:30  
2 at the latest. So at least no more than five hours,  
3 four to five hours a day.

4 Q. Would somebody be spraying it with you?

5 A. Not all the time.

6 Q. Did you use any type of mask?

7 A. Yes I used the required PPE.

12 Q. For the spraying, could you give me like a  
13 range of how many times that you sprayed in one year.  
14 So the minimum amount that you had sprayed to the  
15 maximum amount in one year.

16 A. The minimum amount would probably be -- I don't  
17 know -- maybe 20 applications. And at the most, maybe  
18 up to maybe like 40 applications.

19 Q. And when you say "applications," do you mean --  
20 well, what do you mean by that?

21 A. Applications to me -- as a pesticide guide or  
22 as an applicator, each application. So that means  
23 that if I was spraying that yard out there and I  
24 showed up today and I sprayed, that's an application.  
25 Even if I sprayed for 20 minutes. If I come back

17

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1 tomorrow, that's another application. Then the day  
2 after, that's another application. So each  
3 application that you apply chemicals, each time you  
4 apply, even if it's 24 hours, that's an application.

5 Q. And what about if you go -- you said there were  
6 five locations at the district that you would spray,  
7 correct?

8 A. Yes.

9 Q. So what if you sprayed at all five locations in  
10 one day, would that be one application or five?

11 A. You would never do that. But if you did that  
12 in one day, of course like I said, you would be  
13 applying to one site, that would be an application  
14 there. You would have to report that for that  
15 application. If you go to another school, be it Queen  
16 Bee down the street, and then you have to use that as  
17 another application. So it would be five separate  
18 applications in one day.

19 Q. Why wouldn't you do five in one day?

20 A. It's just not -- time-wise, you don't have the  
21 time. And it's just time. You don't have the time to  
22 do it.

23 Q. Would you do more than one in a day?

24 A. Usually, if it's something small. If it's a  
25 small area, you might be able to get it done in a day,

18

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1 or because of people milling, you can only get so much  
2 done, then you can only do that, that site. I mean,  
3 that much. You know what I mean? It's depending on  
4 people and depending on time.

11 Q. I have that you got the pest manager position  
12 on September 11, 2012.

13 Does that sound about accurate?

14 A. About. It's been a while. So, yeah, I don't  
15 remember the exact date or anywhere near exact. But,  
16 yeah, maybe. I don't know.

17 Q. That was about a year and three to  
18 three-and-a-half months after you started?

19 A. Like I said, you know, after about a year is  
20 when I went into full time. I moved pretty fast. So  
21 it was kind of not, you know, something I really  
22 remember. Because I was moving pretty fast, and time  
23 was moving pretty fast. That's about accurate.

24 Q. You needed certification for that position?

25 A. Yes.

19

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1 Q. So you weren't allowed to spray anything until  
2 you got that certification?

3 A. Not true.

4 Q. You were allowed to spray?

5 A. Yes.

6 Q. Were there certain things that you weren't  
7 supposed to spray without it?

8 A. Well, even now. But, yeah, there were certain  
9 things you're not supposed to spray without it.

10 Q. And what were those things?

11 A. There's several things without it. I don't  
12 know. You know, there's a list of things you're not  
13 supposed to spray without that license.

14 Q. Do you know when you got the license?

15 A. I can check my license in my pocket.

16 Q. Okay.

17 A. But, no, I don't know exactly.  
18 So it was issued 4/20/2015.

19 Q. And you don't know what the chemicals were that  
20 you did not use before you got the license?

21 A. That I did not use before I got the license?

22 Q. Correct.

23 A. I don't understand your question.

24 Q. Weren't there certain types of things that you  
25 weren't supposed to spray until you got the license?

20

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1 think I should bring that today. So I have a copy of  
2 roughly around the time, but I didn't bring that,  
3 because I didn't think we were really even discussing  
4 this part. But, yeah, I do have a record of, you  
5 know, right around the time when this happened. And  
6 when I brought it up to my supervisor, it was a little  
7 bit boring to my sickness, and it just -- it was --  
8 his response was not good, but I won't even go into  
9 that. But, yeah.

10 Q. So what year was it?

11 A. The exact year, I don't know. But it was not  
12 in the beginning. It was basically in the middle of  
13 my four or five-year -- four-year thing since I've  
14 been out there. I don't know exactly.

15 Q. Well, do you know about how long it happened  
16 before you were diagnosed with the lymphoma?

17 A. Not exactly.

18 Q. So if you have the log of when it happened, how  
19 would you know that that was the date that it  
20 happened?

21 A. Because I know when I was spraying Mary Farmer  
22 from that log, and I know right around the time that I  
23 think this happened.

24 And all the time -- you know, because the  
25 machine has no control because they built that, all

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1 fandangle that gun, because it was a fandangled  
2 machine. And I could feel all the time you get the  
3 mist, you get the stuff.

4 And even my own supervisor said, "You know, I'm  
5 seeing a lot of drift off of there." I told him,  
6 "There's no way for me to control the drift. There's  
7 no drift control on this machine." That's why we  
8 don't spray on certain windy days or whatever, because  
9 the machine had to be fandangled, yeah.

10 Q. When you're spraying the machine, are you fully  
11 covered?

12 A. PPE only covers -- I don't know if you've ever  
13 seen a Tyvek, T-y-v-e-k.

14 Q. No.

15 A. So a Tyvek suit is sort of like a throw-away  
16 paper jumpsuit. It's supposed to be chemical proof,  
17 right? So it comes up like a jumpsuit. You know, you  
18 wear boots, and you wear a Tyvek suit, and it comes up  
19 and is zips up to here (indicating). It's sort of how  
20 my shirt is. It's the opening down here (indicating)  
21 or whatever. It's not like a closed or a sealed suit.  
22 This is an open arm, open leg, open neck suit. And  
23 then you wear the mask and goggles.

24 Q. And when you say "up to here," you're pointing  
25 to like the bottom part of your neck in the front?

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1 the time I felt like you can feel what's called drift.  
2 Drift was always getting on my face. It was always  
3 getting on my hands, because I had no control over the  
4 drift. Like I said, this machine was built by the  
5 supervisor. He'd say, "Take this hose from that old  
6 machine. Take this reel from that old machine. Take  
7 that old Honda motor and let's just make a sprayer."  
8 This is what I heard. I wasn't there yet.

9 Now, after I got hired, I was introduced to the  
10 machine. "This is your spray machine. Go out and  
11 start spraying." You know what I mean?

12 So I went out and I started spraying. I  
13 figured out different things. Figured out why the  
14 pressure was low, why I couldn't get it to do this.  
15 But there's no pressure regulator on that machine.  
16 I'm pretty sure on the ones that Clark and whatever  
17 they had, they had a thing you could regulate your  
18 pressure. This didn't have that. All you can  
19 regulate is by the gun. Meaning "by the gun," is that  
20 you either squeeze the trigger hard or you squeeze the  
21 trigger not too hard, and you either get a stream or  
22 you get a mist. So you kind of fandangle the thing  
23 and try to make it work and keep it off the  
24 beneficials or the things that you want to keep. You  
25 try to hit the weeds only, with just trying to

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1 A. It's just like this (indicating). The zipper  
2 will come --

3 Q. But the court reporter can't record --

4 A. Okay. So the Tyvek suit would come up to  
5 your -- what is that? Is that the larynx? What is  
6 that thing?

7 Q. The Adam's apple?

8 A. Adam's apple. It comes up to about the bottom  
9 of your Adam's apple is where the opening that the  
10 zipper would be.

11 Q. And so your -- it would cover -- it's like a  
12 jumpsuit basically?

13 A. It is a jumpsuit.

14 Q. Okay.

15 A. It's basically like coveralls, yeah. Tyvek.

16 Q. And so when you say you're feeling the drift,  
17 where would you feel it? What do you mean?

18 A. All in my face. It's the only thing that's not  
19 totally covered, is your face. You know what I mean?  
20 You've got gloves on. You have glasses over your  
21 eyes. You have a mask over your this part  
22 (indicating). But then all of this (indicating) is  
23 exposed. This (indicating) is exposed. Your ears,  
24 your neck, all that is exposed.

25 Q. So when you say -- because remember the court

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4 November 5, 2015

5 DEWAYNE JOHNSON  
2851 REDWOOD, NUMBER 109  
6 VALLEJO, CA 94591

7 RE: JOHNSON v. BENICIA U.S.D.  
Date taken: October 28, 2015

Dear Deponent:

10 Your deposition taken in the above-entitled action is  
11 now available for your review. If you are represented  
12 by counsel, you may read your attorney's copy and  
13 advise us by letter of any changes you wish to make in  
your testimony, or elect to come into our office and  
read and sign the original transcript between the  
hours of 8:30 a.m. and 4:30 p.m., Monday through  
Friday, or approve the transcript in its printed form.

14 If you wish to read your transcript, please call our  
15 office between the hours of 8:30 a.m. and 4:30 p.m. to  
schedule an appointment.

16 If you have any questions regarding reading,  
17 correcting and signing your deposition, please consult  
your attorney.

18 If we do not hear from you within thirty days, we will  
19 assume you are waiving your signature, and the  
20 original transcript will be sealed and forwarded to  
the noticing attorney. It is our policy not to  
release the original transcript from our office.

24 Peterson Deposition Reporters

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That the witness named in the foregoing deposition was present at the time and place specified; was by me sworn to testify to the truth, the whole truth, and nothing but the truth;

That I am a disinterested person to the said  
action;

VICTORIA L. PETERSON  
Certified Shorthand Reporter  
California License # 6992

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11/05/2015 05:32:33 AM

# **EXHIBIT 15**

1 SUPERIOR COURT OF THE STATE OF CALIFORNIA  
2 FOR THE COUNTY OF SAN FRANCISCO  
3

4 DEWAYNE JOHNSON,  
5 Plaintiff,

6 vs.

No. CGC-16-550128

7 MONSANTO COMPANY,  
8 Defendant.

---

9  
10  
11  
12  
13  
14 DEPOSITION OF EDWIN MARTINEZ  
15 Vallejo, California  
16 Friday, January 19, 2018  
17 Volume 2  
18  
19  
20  
21

22 Reported by:

JODI L. BOSETTI

23 CSR No. 11316, RPR

24 JOB No. 2795475

25 PAGES 28 - 79

1 A Before going to spray?

2 Q Yes.

3 A In the yard?

4 Q Yes.

5 A Yes.

09:14

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

24 Q And when you say safety rule, who told you

25 that was the safety rule?

09:15

1 I, the undersigned, a Certified Shorthand  
2 Reporter of the State of California, do hereby  
3 certify:

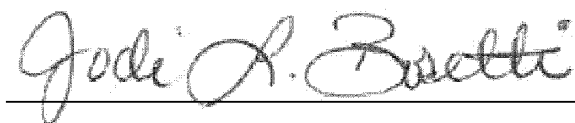
4 That the foregoing proceedings were taken  
5 before me at the time and place herein set forth; that  
6 any witnesses in the foregoing proceedings, prior to  
7 testifying, were administered an oath; that a record  
8 of the proceedings was made by me using machine  
9 shorthand which was thereafter transcribed under my  
10 direction; that the foregoing transcript is a true  
11 record of the testimony given.

12 Further, that if the foregoing pertains to  
13 the original transcript of a deposition in a Federal  
14 Case, before completion of the proceedings, review of  
15 the transcript [ ] was [ ] was not requested.

16 I further certify I am neither financially  
17 interested in the action nor a relative or employee  
18 of any attorney or any party to this action.

19 IN WITNESS WHEREOF, I have this date  
20 subscribed my name.

21 Dated: January 31, 2018

22  
23   
24

JODI L. BOSETTI

25 CSR No. 11316, RPR