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Attorneys for Defendant
MONSANTO COMPANY

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

vs.

MONSANTO COMPANY,

Defendant.

Case No. CGC-16-550128

EXHIBITS 31 THROUGH 45 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

EXHIBIT 31

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO, UNLIMITED JURISDICTION

--oOo--

DEWAYNE JOHNSON,

Plaintiff,

v. Case No. CGC-16-550128

MONSANTO COMPANY,

Defendants.

DEPOSITION OF DEWAYNE JOHNSON

Vallejo, California

VOLUME 3

Saturday, January 20, 2018

Reported by:

Alisa A. James

CSR No. 10901

Job #2795471

Pages 588 - 779

BY MR. LITZENBURG: 12:05:33

Q Okay. Mr. Johnson, just a couple more questions. 12:05:33 12:05:35

As we sit here today, how is your cancer? How is your health? 12:05:36 12:05:40

MR. COPLE: Objection, vague. 12:05:40

THE WITNESS: Uh -- 12:05:42

MR. COPLE: The medical records speak for themselves. 12:05:43 12:05:45

THE WITNESS: Um, my cancer at this point is -- is at a point where the pain from the treatments and the physical things that I have to go through from taking chemotherapy, and the cancer, itself, is still at a very difficult stage. 12:05:46 12:05:48 12:05:56 12:06:00 12:06:03 12:06:07

I'm in a lot of pain. In my feet, I have neuropathy. In my hands and feet, I have numbness and tingling. I can't run. I can walk pretty well, but the pain in my feet is pretty 12:06:08 12:06:11 12:06:14 12:06:18

bad. 12:06:22

Um, I have lesions on my skin that are open 12:06:22

that will not close. I have certain scars, or -- 12:06:25

there would be scars to the regular, you know, 12:06:28

human, but I guess the middle -- the medical name 12:06:30

or the name that I've been used to using is 12:06:34

nodules or lesions. And these things are very 12:06:36

hard to deal with. They're very painful, very 12:06:41

deep, nerve pain where it's very difficult 12:06:44

sometimes. 12:06:50

I also have mouth sores that looks like a 12:06:50

canker sore, but it's not because it's sort of 12:06:56

spread throughout my whole mouth where the inside 12:06:58

of my mouth is very sensitive to warm liquids or 12:07:02

hard liquids-(sic), like I couldn't east toast or 12:07:06

something crunchy, like a cookie or something 12:07:10

like that. I can't eat cookies, and things like 12:07:13

that. I have to eat soft things right now. 12:07:16

There is some sickness sometimes after I eat, or 12:07:21

whatever else. I can have some vomit, or some 12:07:24

other things that can happen, stomach pain. 12:07:27

I'm not allowed to be in the sun. I can't 12:07:30

use, like, public pools and things like that. 12:07:35

My immune system is broken right now from the 12:07:37

treatments, and just from the cancer itself. 12:07:40

It's still at a bad stage where I have things where I wouldn't want to be taking chances of getting infections and things inside. 12:07:42 12:07:45 12:07:46

Yeah, this cancer is very hard to deal with because, mentally, I feel strong, but I have these physical things that are stopping me from doing a lot of stuff. So, yeah, my cancer at this point, it's just difficult to deal with the pains, and the ups and downs of it. And I try to just do my best and push through the hard days, and take the good days with the bad days. 12:07:53 12:07:56 12:07:59 12:08:01 12:08:06 12:08:09 12:08:12 12:08:14

Q Have you lost any weight during the course of this disease? 12:08:17 12:08:19

MR. COPLE: Objection, asked and answered. 12:08:20

THE WITNESS: Yeah. I've lost up to 20 pounds. I'm down about five pounds right now, because I haven't been able to eat properly in the last two weeks, because I've had the mouth sores ever since the last treatment that I got from the Pralatrexate -- I think it's, yeah, Pralatrexate. 12:08:22 12:08:24 12:08:27 12:08:31 12:08:35 12:08:38 12:08:42

Whenever I get that treatment, I get really bad mouth sores, and it lasts a few weeks, or it could last a week or so. 12:08:45 12:08:47 12:08:50

BY MR. LITZENBURG: 12:08:52

Q And your wife testified, actually, 12:08:52

yesterday, that for a stretch of weeks at the end of 12:08:55

the turn of the year, you were basically bed-bound, and 12:08:59

unable to eat. 12:09:03

Is that pretty much true? 12:09:05

MR. COPLE: Objection. Lacks foundation. 12:09:06

THE WITNESS: Yeah, I was having a very 12:09:08

bad -- bad time getting coverage through Covered 12:09:09

California and getting my healthcare together. I 12:09:17

got kicked off the healthcare after I stopped 12:09:21

working for the Benicia Unified School District. 12:09:24

Eventually, my healthcare was no longer taken 12:09:28

care of, you know, by me, personally, paying for 12:09:31

my healthcare. 12:09:34

So, for a while, I had no healthcare. I had 12:09:35

no healthcare dealing with the cancer treatments, 12:09:37

and I was taking this -- this clinical trial drug 12:09:40

called brentuximab. 12:09:44

And, yeah, I was very, very sick. I had a 12:09:46

lot of -- like you saw in the pictures from one 12:09:50

of the exhibits, very serious skin nodules, 12:09:53

blistering, and it was very tough to get out of 12:09:57

bed and get out -- and get going. It was a very 12:10:03

painful stage, because I had no pain coverage at 12:10:06

all. I mean, no pain medication, no way to deal with it. No creams or anything. All I could get was over-the-counter stuff. 12:10:09 12:10:13 12:10:16

So, yeah, I was in a really bad state. 12:10:18

BY MR. LITZENBURG: 12:10:20

Q Okay. Now let me ask a little similar question. We had tried to take your deposition one day in early December, and you were unable to make it. Was this during that time when you were, basically, in bed because of the cancer? 12:10:20 12:10:23 12:10:26 12:10:30 12:10:33

MR. COPLE: Objection, asked and answered. 12:10:34

THE WITNESS: Yeah, it was. And I think -- yeah, we did talk about that. 12:10:35 12:10:36

Yeah. I was pretty -- it was pretty bad at that point, and it didn't get better. When I first started the treatments, it got worse first before it got better. 12:10:38 12:10:41 12:10:44 12:10:46

BY MR. LITZENBURG: 12:10:48

Q Okay. You've told us about a few things, but I want to give you the opportunity to tell the jury, is there anything additional that you haven't mentioned, that you used to be able to do before you got cancer, before you started the chemo, that you're unable to do today? 12:10:49 12:10:51 12:10:54 12:10:57 12:10:59 12:10:59

A Um, one of the main things I used to be 12:11:01

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 _____, 2018, at _____, (City) (State) _____.

_____

DEWAYNE ANTHONY LEE JOHNSON

REPORTER'S CERTIFICATE

I, ALISA A. JAMES, CSR No. 10901, Certified Shorthand Reporter, certify;

That the foregoing proceedings were taken before me at the time and place therein set forth, at which time the witness was put under oath by me;

That the testimony of the witness, the questions propounded, and all objections and statements made at the time of the examination were recorded stenographically by me and were thereafter transcribed;

That the foregoing is a true and correct transcript of my shorthand notes so taken.

I further certify that I am not a relative or employee of any attorney of the parties, nor financially interested in the action.

I declare under penalty of perjury under the laws of California that the foregoing is true and correct.

Dated this 26th day of January, 2018.

<%signature%>

ALISA A. JAMES, CSR No. 10901

EXHIBIT 32

EDSP: WEIGHT OF EVIDENCE ANALYSIS OF POTENTIAL INTERACTION WITH THE ESTROGEN, ANDROGEN OR THYROID PATHWAYS

CHEMICAL: GLYPHOSATE

OFFICE OF PESTICIDE PROGRAMS

OFFICE OF SCIENCE COORDINATION AND POLICY

U.S. ENVIRONMENTAL PROTECTION AGENCY

C. Androgen Pathway

There was no evidence of interaction of glyphosate with the androgen pathway in the Tier 1 *in vitro* (*i.e*, AR binding and steriodogenesis assays were negative) or Tier 1 *in vivo* FSTRA and mammalian assays (*i.e.*, Hershberger and male pubertal assays were negative in the absence of overt toxicity). In addition, glyphosate was negative in an AR transactivation assay (Kojima *et al.*, 2004). The only treatment-related effects observed in the Part 158 mammalian studies in the absence of overt toxicity were decreases in sperm count in the subchronic rat study (1678 mg/kg/day) and a delay PPS in the post 1998 2-generation reproduction study (1234 mg/kg/day) in the rat. Both effects were observed at a dose that was above the limit dose (1000 mg/kg/day) for those studies. No androgen-related effects were seen in the wildlife Part 158 studies (decreases in offspring body weight observed in one avian reproduction study).

D. Thyroid Pathway

There was no convincing evidence of potential interaction of glyphosate with the thyroid pathway. There were no treatment-related effects on thyroid hormones (T4 and TSH), thyroid weights or thyroid histopathology in the male pubertal assay in the absence of overt toxicity. There were no thyroid-related effects observed in the female pubertal assay. In the AMA, there were no developmental effects or alterations in thyroid histopathology. No thyroid-related effects were noted in any of the Part 158 studies.

E. Conclusions

The conclusion of the WoE evaluation is that glyphosate demonstrates no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals or wildlife.

V. EDSP Tier 2 Testing Recommendations

Based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for glyphosate since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

EXHIBIT 33

WHO/PCS/06.1

Pesticide residues in food - 2004

Joint FAO/WHO Meeting on Pesticide Residues

EVALUATIONS 2004

Part II—Toxicological

IPCS

International Programme on Chemical Safety

WORLD HEALTH ORGANIZATION

Pesticide residues in food—2004

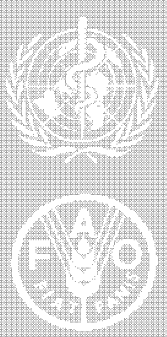
Toxicological evaluations

Sponsored jointly by FAO and WHO
With the support of the International Programme on Chemical Safety (IPCS)

Joint Meeting of the
FAO Panel of Experts on Pesticide Residues in Food and the Environment
and the
WHO Core Assessment Group

Rome, Italy, 20–29 September 2004

WHO/PCS/04.1



WORLD HEALTH ORGANIZATION

WHO Library Cataloguing-in-Publication Data

Joint Meeting of the FAO Panel of Experts on Pesticides Residues in Food and the Environment and the WHO Core Assessment Group (2004 : Rome, Italy) Pesticide residues in food : 2004 : toxicological evaluations : part II / Joint Meeting of the FAO Panel of Experts on Pesticides Residues in Food and the Environment and the WHO Core Assessment Group, Rome, Italy 20–29 September 2004.

1.Pesticide residues—toxicity. 2.Food contamination. 3.No-observed-adverse-effect level. I.FAO Panel of Experts on Pesticide Residues in Food and the Environment. II.WHO Core Assessment Group on Pesticide Residues. III.Title. IV.Pesticide residues in food : evaluations : 2004 : part II—toxicological.

ISBN 92 4 166520 3 (NLM classification: WA 240)
ISBN 978 92 4 166520 9

This report contains the collective views of two international groups of experts and does not necessarily represent the decisions nor the stated policy of the Food and Agriculture Organization of the United Nations or the World Health Organization.

The preparatory work for the toxicological evaluations of pesticide residues carried out by the WHO Expert Group on Pesticide Residues for consideration by the FAO/WHO Joint Meeting on Pesticide Residues in Food and the Environment is actively supported by the International Programme on Chemical Safety within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.
The **International Programme on Chemical Safety** (IPCS), established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessing the risk to human health and the environment to exposure from chemicals, through international peer-review processes as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.
The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 United Nations Conference on the Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

Typeset in Hong Kong
Printed in Malta

body-weight gain in F_1 animals, and an increased incidence of alterations of the parotid and submaxillary salivary glands in F_0 and F_1 animals at 10 000 ppm.

In studies of developmental toxicity in rats, the NOAEL for maternal and developmental toxicity was 300 mg/kg bw per day, on the basis of clinical signs and reduced body-weight gain in the dams and increased incidences of fetuses with delayed ossification and skeletal anomalies.

In studies of developmental toxicity in rabbits, the NOAEL for maternal toxicity was 100 mg/kg bw per day on the basis of clinical signs and reduced food consumption and body-weight gain. The NOAEL for developmental toxicity was 175 mg/kg bw per day on the basis of reduced fetal weight and delayed ossification, and an increased incidence of postimplantation loss. The Meeting concluded that glyphosate is not teratogenic.

The Meeting concluded that the existing database on glyphosate was adequate to characterize the potential hazards to fetuses, infants, and children.

Hypertrophy and cytoplasmic alterations of the salivary glands (parotid and/or mandibular) was a common and sensitive end-point in six studies: in three 90-day studies (one in mice, two in rats), a 1-year study in rats, a 2-year study in rats and a two-generation study of reproductive toxicity in rats. Mechanistic studies available to the Meeting hypothesized that the mechanism was adrenergic. However, the inability of a β-blocker to significantly inhibit these effects indicates that glyphosate does not act as a β-agonist. Other proposed mechanisms for the salivary gland alterations include oral irritation caused by dietary administration of glyphosate, a strong organic acid. Although the mechanism of the cytoplasmic alterations in the salivary glands was unclear, the Meeting concluded that this treatment-related effect is of unknown toxicological significance.

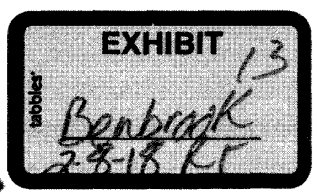
In a study of acute neurotoxicity in rats, the NOAEL for neurotoxicity was 2000 mg/kg bw, the highest dose tested. In a short-term study of neurotoxicity in rats, the NOAEL for neurotoxicity was 20 000 ppm, equal to 1547 mg/kg bw per day, the highest dose tested. In a study of acute delayed peripheral neuropathy in hens, clinical and histopathological examination found no evidence for acute delayed peripheral neuropathy at a dose of 2000 mg/kg bw.

New toxicological data on AMPA (the primary degradation product of glyphosate in plants, soil and water, and the only metabolite of glyphosate found in animals) was submitted to the present Joint Meeting for evaluation. AMPA was of low acute oral and dermal toxicity in rats (LD_{50}, >5000 and >2000 mg/kg bw, respectively), and was not a skin sensitizer in guinea pigs. In a 90-day study of toxicity in rats, the NOAEL was 1000 mg/kg bw per day, the highest dose tested. AMPA had no genotoxic potential in vitro or in vivo. In a study of developmental toxicity in rats, no evidence for embryo- or fetotoxicity was found and the NOAEL for maternal and developmental toxicity was 1000 mg/kg bw per day, the highest dose tested.

On the basis of the new toxicological data, the present Joint Meeting concluded that AMPA is of no greater toxicological concern than its parent compound, thus confirming the conclusion of the 1997 JMPR.

Routine medical surveillance of workers in production and formulation plants revealed no adverse health effects attributable to glyphosate. In operators applying

EXHIBIT 34



Glyphosate/Tox

Bill Dykstra (46)

releasable

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

FEB 24 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Transmittal of the Final FIFRA Scientific Advisory Panel Reports on the February 11-12, 1986 Meeting

TO: Steven Schatzow, Director
Office of Pesticide Programs (TS-766)

The above mentioned meeting of the FIFRA Scientific Advisory Panel (SAP) was an open meeting held in Arlington, Virginia to review the following topics:

(1) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Glyphosate;

(2) A set of scientific issues in connection with the Agency's proposed action on the non-wood uses of Pentachlorophenol as set forth in the Position Document 4;

(3) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Oryzalin;

(4) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Amitraz;

(5) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Acephate;

(6) A set of scientific issues being considered by the Agency in connection with Subdivision U of the Pesticide Assessment Guidelines.

Please find attached the SAP's final reports on the six issues discussed at the meeting.

Stephen L. Johnson, Executive Secretary
FIFRA Scientific Advisory Panel (TS-769)

Attachments

cc: Panel Members
John A. Moore
James Lamb
Al Heier
Susan Sherman
John Melone
Douglas Campt
EPA Participants

FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT

SCIENTIFIC ADVISORY PANEL

A Set of Scientific Issues Being Considered by the Agency in Connection with the Registration Standard for Glyphosate

---

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) has completed review of the data base supporting the Environmental Protection Agency's (EPA) decision to classify Glyphosate as a class C (possible human) carcinogen. The review was conducted in an open meeting held in Arlington, Virginia, on February 11, 1986. All Panel members, except Dr. Thomas W. Clarkson, were present for the review. In addition, Dr. David Gaylor, Director of the Biometry Staff at the National Center for Toxicological Research, served as an ad hoc member of the Panel.

Public notice of the meeting was published in the Federal Register on Friday, January 17, 1986 (Citation 51-FR2568).

Oral statements were received from staff of the Environmental Protection Agency and from Mr. Robert Harness and Dr. Timothy Long of Monsanto Company.

In consideration of all matters brought out during the meeting and careful review of all documents presented by the Agency, the Panel unanimously submits the following report.

REPORT OF SAP RECOMMENDATIONS

General Comments on Carcinogen Classification

The Panel concurs that it is necessary to categorize chemicals as to their apparent carcinogenic risk to man. The Panel is concerned that the categories outlined in the Agency's Cancer Guidelines are somewhat limited in scope. For only a small number of specific chemicals is there epidemiologic evidence of their carcinogenicity in man, either sufficient evidence (Group A) or limited evidence (Group B-1). Thus, most chemicals that are carcinogenic for animals have been placed in Groups B-2 and C. Category D has apparently not been used. The Panel urges the Agency to attempt to develop a more discriminatory classification scheme.

Glyphosate

The Agency requested the Panel to focus its attention upon a set of issues relating to the pesticide Glyphosate. There follows a list of the issues and the SAP's response to each question.

1. Based on the Agency's weight of the evidence assessment with emphasis on the mouse kidney tumors, the Agency has classified Glyphosate as a class C (possible human) carcinogen. The Agency specifically requests any comment that the Panel may wish to present with regard to its assessment of the weight of evidence and subsequent determination of carcinogenicity according to the Agency's Cancer Guidelines.

2. The Agency requests also that the Panel consider what weight should be given to this marginal increase in kidney tumors, the importance of this type of tumor in the assessment of the carcinogenicity of Glyphosate, and the weight placed on historical and concurrent controls for this type of evaluation.

Panel Response:

In the instance of Glyphosate, the Panel concurs that the data on renal tumors in male mice are equivocal. Only small numbers of tumors were found in any group, including those at the highest dose which appear to have exceeded the maximal tolerated dose. The vast majority of the pathologists, who examined the proliferative lesion in the male control animal, agreed that the lesion represented a renal adenoma. Therefore, statistical analysis of the data should utilize this datum. In addition, the statistical analysis shall be age-adjusted; when this is done, no oncogenic effect of Glyphosate is demonstrated using concurrent controls. Nevertheless, the occurrence of three neoplasms in high dose male mice is unusual and using historical controls is statistically highly significant. Furthermore, categorization of the oncogenic risk of Glyphosate is complicated by the fact that doses used in the rat study do not appear to have reached the maximal tolerated dose. Under these circumstances, the Panel does not believe that it is possible to categorize Glyphosate clearly into Group C (possible human carcinogen) or Group E (no evidence of carcinogenicity for humans). The Panel proposes that Glyphosate be categorized as Group D (not classified) and that there be a data call-in for further studies in rats and/or mice to clarify unresolved questions.

Regarding the issue of using historical or concurrent controls, the Panel believes that this has to be decided on a case-by-case basis. For Glyphosate, the historical control data support that there may be reason for concern. However, the level of concern raised by historical control data was not great enough to displace putting primary emphasis on the concurrent controls.

FOR THE CHAIRMAN

Certified as an accurate report of Findings:

Stephen L. Johnson
Executive Secretary
FIFRA Scientific Advisory Panel

Date: 2/24/86

EXHIBIT 35

TNO-rapport / TNO report

V 4478

In vitro percutaneous absorption study with [^{14}C]glyphosate using viable rat skin membranes

Nederlandse Organisatie voor toegepast-natuurwetenschappelijk onderzoek / Netherlands Organisation for Applied Scientific Research

TNO Nutrition and Food Research

Nederlandse Organisatie voor toegepast-natuurwetenschappelijk onderzoek / Netherlands Organisation for Applied Scientific Research

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TNO report

V 4478

In vitro percutaneous absorption study with [^{14}C]glyphosate using viable rat skin membranes

Date	29 July 2003
Authors	[redacted]
At request of	Monsanto Europe S.A. Tervuren Avenue 270-272 B-1150 Brussels Belgium
TNO Project number	010.45110
TNO Study number	4478
Sponsor Study code	-
Status report	Final report
Previous version	Draft report, 27 March 2003
Number of pages	41
Number of tables	4
Number of appendices	6

TN-2002-011

6. In conclusion, an 8-hour exposure resulted in a penetration of *ca.* 10 % (MON 35012 concentrate), *ca.* 2.6 % (MON 35012 field dilution), *ca.* 0.5 % (MON 0139 70% concentrate) and *ca.* 1.4 % (MON 0139 70% field dilution) over a period of 48 h in viable rat skin membranes. Due to the high variation in dermal penetration within the test groups and the poor recoveries, the data presented in this report are not acceptable for regulatory use and risk assessment. The study should be regarded as a sighting study rather than a definitive study.

EXHIBIT 36

STUDY TITLE

A Study of the Short-Term Effects of MON 35050 in Male CD-1 Mice

DATA REQUIREMENT

None

AUTHORS

Kathy J. Hotz

REPORT DATE

May 8, 2001

PERFORMING LABORATORIES

Metabolism and Safety Evaluation - Newstead (MSE-N)
645 South Newstead Avenue
St. Louis, Missouri 63110

Metabolism and Safety Evaluation - Creve Coeur (MSE-CC)
800 N. Lindbergh Blvd.
St. Louis, Missouri 63167

University of Illinois, Chicago
Medicinal Chemistry and Pharmacognosy (MC 781)
College of Pharmacy
833 S. Wood Street
Chicago, IL 60612

PROJECT NUMBER

Laboratory Project Number: MSE-N 99052
Monsanto Study Number: ML-99-170
Monsanto Report Number: MSL 16949

STATEMENT OF NO DATA CONFIDENTIALITY CLAIM

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA 10(d)(1)(A), (B), or (C).

"We submitted this material to the United States Environmental Protection Agency specifically under provisions contained in FIFRA as amended, and thereby consent to use and disclosure of this material by EPA according to FIFRA. Some pages of this report are stamped with the following: CONTAINS TRADE SECRET OR OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY. This claim of confidentiality is not meant to convey supplemental claims of confidentiality regarding data subject to disclosure under sections 10 (d) and 10 (e) of FIFRA. In submitting this material to the EPA according to method and format requirements contained in PR Notice 86-5, we do not waive any protection rights involving this material that would have been claimed by the company if this material had not been submitted to the EPA".

COMPANY: Monsanto Company

COMPANY AGENT: Stephen J Wratten (Stephen J Wratten)
Sponsor/Submitter

DATE: 25-Jul-2002

GLP COMPLIANCE STATEMENT

The study MSE-N 99052 (ML-99-170) was conducted in accordance with the principles of Good Laboratory Practice (GLP) Standards of the EPA (USA, FIFRA: 40 CFR, Part 160), and the GLP Principles of the OECD (1981) with the following exceptions:

1. Determination of 8-hydroxydeoxyquanosine, conducted in the laboratory of Dr. Richard van Breemen at the University of Illinois, Chicago, did not conform to the principles of GLP Standards of the EPA and OECD.

2. Heat shock protein 70 (hsp 70) mRNA and NADPH Menadione Oxidoreductase (NMO) mRNA analyses, conducted at Metabolism and Safety Evaluation - CC, did not conform to the principles of GLP Standards of the EPA and OECD.

3. Stability of the test material and the concentration, homogeneity and stability of the test material in carrier were not determined before or during the study.

4. The MON 35050 used in this study was obtained from the manufacturing plant and was not characterized according to GLP.

Kathy J. Hotz 5/8/01

Kathy J. Hotz, B.S. — Date
Study Director, MSE-Newstead

Merrill R. Osheroff 5/4/01

Merrill R. Osheroff, Ph.D., D.A.B.T. — Date
Director, MSE-Newstead

Stephen Wratt 25-Jul-2002

Sponsor/Submitter — Date
Monsanto Company

QUALITY ASSURANCE AUDIT STATEMENT

Study Number: 99052

Study Title: A Study of the Short-Term Effects of MON 35050 in Male CD-1 Mice

Phase Inspected/Audited	Date of Inspections and Audits	Dates of Communication to Study Director and Management
Protocol Review	June 16, 1999	June 16, 1999
Dosing	July 27, 1999	July 28 1999
Necropsy	July 28, 1999	July 30, 1999
Blood Collection	July 28, 1999	July 30, 1999
Blood Analysis	July 28, 1999	July 30, 1999
Protocol Amendment Review	July 30, 1999	July 30, 1999
Metabolism Analysis	August 31, 1999	August 31, 1999
Protocol Amendment Review	August 31, 1999	August 31, 1999
Histology	September 14, 1999	September 16, 1999
Protocol Amendment Review	November 16, 1999	November 16, 1999
Inlife Data Review	August 24, 2000	August 24, 2000
Metabolism Data Review	August 24, 2000	August 24, 2000
Histology Data Review	August 24, 2000	August 24, 2000
Gross Pathology Data Review	August 24, 2000	August 24, 2000
Clinical Chemistry Data Review	August 24, 2000	August 24, 2000
Formulation Data Review	August 24, 2000	August 24, 2000
Metabolism Data Review	September 12, 2000	September 12, 2000
Inlife Data Review	September 12, 2000	September 12, 2000
Formulations Data Review	September 12, 2000	September 12, 2000
Metabolism Data Review	November 7, 2000	November 7, 2000
Metabolism Data Review	November 15, 2000	November 15, 2000
Draft Report Review	March 23, 2001	March 23, 2001
Draft Report Review	May 3, 2001	May 3, 2001

Quality Assurance Review(s) Conducted by: S. Garrett, J. Kronewitter, M. Shawgo, and P. Price

This signed statement indicates the R & D Quality and Compliance, St. Louis Quality Assurance Unit has monitored this study and reviewed the data and final report.

Mary C. Shawgo
Quality Assurance Specialist

5-8-2001
Date

REPORT SIGNATURE PAGE

This report accurately represents the data developed during the study.

Kathy J. Holz 5/8/01

Kathy J. Holz, B.S. Date
Study Director, MSE-Newstead

Daryl C. Thake 5/04/01

Daryl C. Thake, D.V.M., D.A.C.V.P. Date
Pathologist, MSE-Newstead

Merrill R. Osheroff 5/4/01

Merrill R. Osheroff, Ph.D., D.A.B.T. Date
Director, MSE-Newstead

SUMMARY

The purpose of the present acute study was to evaluate the potential hepatic and renal toxicity of MON 35050 in male CD-1 mice following single intraperitoneal (IP) administration. This study was conducted to address suggested genotoxicity findings in studies with MON 35050, the results of which are reported in the literature.

MON 35050, suspended in a mixture of 1% dimethyl sulfoxide (DMSO) in olive oil, was intraperitoneally administered to male CD-1 mice at a target dose of 600 mg/kg body weight. Two control groups received single IP doses of either DMSO/olive oil or isotonic saline. All animals were euthanized 24 hours following dose administration. A white, pasty substance was found on tissues in the peritoneal cavity of the MON 35050 treated mice at sacrifice. To better understand the cause of this finding, an additional group of mice was administered MON 35050 dissolved in saline at a dose level of 600 mg/kg. A control group received only saline by IP administration. Serum obtained at sacrifice from all animals was analyzed for alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), sorbital dehydrogenase (SDH), blood urea nitrogen (BUN) and creatinine. The liver and kidneys were weighed and histological sections were prepared and examined microscopically. Histological sections of the liver were also evaluated for cell proliferation. The following endpoints were determined from frozen liver and kidney sections: reduced glutathione (GSH) and oxidized glutathione (GSSG) concentrations, 8-hydroxydeoxyquanosine (8-OHdG) levels, and mRNA expression of heat shock protein 70 (hsp 70) and NADPH menadione oxidoreductase (NMO).

Additional groups of mice were dosed intraperitoneally with MON 35050 in saline at 600 mg/kg or saline only, and sacrificed at 4 hours post dose. These animals were assigned to study number MSE-N 99075. Serum was obtained at sacrifice and analyzed for alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), sorbital dehydrogenase (SDH), blood urea nitrogen (BUN) and creatinine. The liver and kidneys were weighed and stored frozen. The following endpoints were determined from frozen liver and kidney sections: reduced glutathione (GSH) and oxidized glutathione (GSSG) concentrations, and expression of heat shock protein 70 (hsp 70) and NADPH menadione oxidoreductase (NMO) mRNA.

Terminal body weights at 24 hours following a single IP dose of MON 35050 (600 mg/kg) in saline were significantly decreased compared to vehicle controls. Absolute and relative liver and kidney weights were also significantly decreased in this treatment group at 24 hours.

The only treatment-associated histological changes were observed in the capsule and subcapsular tissue in the livers and kidneys primarily in the group given MON 35050 (600 mg/kg) in the DMSO/olive oil vehicle. Changes included deposition of fibrin and an amorphous material on the capsule of livers and kidneys. Inflammation and hemorrhage involving the renal capsule was observed in a small number of animals from this group. Necrosis of hepatocytes immediately subjacent to the capsule, along with acute

inflammation and vacuolization in subcapsular regions was apparent in the liver. Similar changes in the liver occurred only rarely in other groups. Lesions in the kidneys and livers were apparently responses to direct deposition of the vehicle(s) or a combination of vehicles and test substance on the organs in the peritoneal cavity, with no evidence that they were associated with systemic toxicity.

Treatment-related effects on blood chemistry parameters occurred primarily in the treatment group receiving MON 35050 in DMSO/olive oil. Significant increases were also seen after 4 hours in the group treated with MON 35050 in saline. Significant increases in ALT, AST, BUN and SDH were observed after 24 hours in the MON 35050/DMSO/olive oil treatment group in comparison to the DMSO/olive oil vehicle control group. Significant increases in all parameters, except creatinine, were observed 4 hours after dose administration in the MON 35050/saline group. SDH was the only parameter that was significantly increased in the MON 35050/saline group, sacrificed 24 hours post dose.

Hepatic cell proliferation was significantly decreased in the MON 35050 (in saline) treatment group, 24 hours after dose administration.

The only significant difference in reduced glutathione (GSH) concentration in the livers of mice in this study was at 4 hours after administration of MON 35050 in saline. Total GSH was decreased in the kidneys only in the MON 35050 (in saline) treatment group, 24 hours after administration. Oxidized GSSG concentrations were not significantly different in any of the treatment groups compared to their respective controls.

8-hydroxydeoxyquanosine (8-OHdG) levels were measured in the liver and kidneys of five mice each from the saline control and the MON 35050 in saline treatment group at the 24 hour time point. Levels of 8-OHdG in the liver or kidneys of the treated mice were not significantly different from the levels in control animals.

Mean values for heat shock protein 70 (hsp 70) mRNA and NMO reductase mRNA in the livers of treated groups of mice were not significantly different from their respective controls. Mean values for hsp 70 mRNA in the kidneys of the MON 35050 in saline and MON 35050 in DMSO/olive oil treated mice were significantly decreased from respective controls 24 hours after dose administration. Mean values for NMO reductase mRNA in the kidneys of the MON 35050 in DMSO/olive oil treated mice were significantly increased from respective controls 24 hours after dose administration.

Results from this study indicate that a single intraperitoneal dose of MON 35050 at a dose level of 600 mg/kg is toxic to the liver and kidneys of male mice. Intraperitoneal administration of 600 mg/kg MON 35050 in DMSO/olive oil was substantially more toxic to these organs. Signs of toxicity included marked increases in gross and microscopic lesions and large increases in serum enzymes. The nature of the lesions indicated that these responses were primarily due to direct deposition of the test material on the liver and kidneys rather than systemic toxicity. Such experimental conditions are not considered appropriate to assess the potential genotoxicity of a test material. Evidence of DNA

damage, including renal and hepatic 8-OHdG, have been reported in the literature after IP administration of MON 35050. However, intraperitoneal administration of MON 35050 did not affect 8-OHdG levels in the liver or kidneys of mice in this study. The occurrence of severe renal and hepatic toxicity under these conditions strongly indicates that effects on DNA, if they do occur, represent a secondary effect related to cytotoxicity rather than a primary genotoxic response. These findings further support the conclusion that glyphosate, and its formulations, do not represent a genotoxic risk to humans.

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INTRODUCTION

MON 35050 is a herbicide formulation containing the IPA salt of glyphosate. Single intraperitoneal (IP) administration of MON 35050 in mice has been reported to produce genotoxic responses (1, 2). Evidence of possible DNA adducts in the liver and kidney of mice after IP administration of a glyphosate herbicide prepared in dimethyl sulfoxide (DMSO)/olive oil has been reported in one published study. The other study reported DNA damage, including elevated 8-OHdG, in liver and kidneys of mice. The purpose of the present study was to determine the significance of these results.

In the present study, MON 35050 was administered to male CD-1 mice as a single dose intraperitoneally, at a dose level of 600 mg/kg body weight. MON 35050 was either suspended in DMSO/olive olive or dissolved in saline. Separate control groups received DMSO in olive oil or saline only. Eight to ten animals/group were euthanized 24 hours following dose administration. Blood was collected from all animals for serum chemistry analysis. The livers and kidneys were weighed and histological sections of the liver were retained and examined microscopically. Histological sections of the liver were also evaluated for cell proliferation. Frozen liver and kidney samples were analyzed for total reduced glutathione (GSH) and oxidized GSSG concentrations, 8-hydroxydeoxyquanosine levels, and expression of heat shock protein 70 (hsp 70) and NADPH menadione oxidoreductase (NMO) mRNA.

Additionally, a saline control and a MON 35050 (600 mg/kg; in saline) treatment group were dosed and sacrificed 4 hours later (study number MSE-N 99075). Blood was collected from ten animals/group and analyzed for serum enzymes. Frozen liver and kidney samples were analyzed for reduced glutathione (GSH) and oxidized GSSG concentrations and expression of heat shock protein 70 (hsp 70) and NADPH menadione oxidoreductase (NMO) mRNA.

Date protocol signed by study director: July 22, 1999
Date of first exposure: July 27, 1999
Date last animal sacrificed: September 22, 1999
Date study completed: May 8, 2001

MATERIALS AND METHODS

Test Material

Identification:	MON 35050
MSE-N Test Substance Identification Code:	T990057
Lot Number:	A9C3015201
Stated Purity of the Active Ingredient (Glyphosate IPA Salt):	484 g/l
Date Received:	June 18, 1999
Description at Receipt:	Light amber liquid

Storage of Neat Material:	Room temperature in a well-sealed container held within a plastic bag.
Source:	Monsanto Europe NV Agriculture Sector Haven 627 Scheldelaan 460 B-2040 Antwerp, Belgium

Absorption of Test Material

Measurement of the degree of absorption was not necessary for the objectives of the study and was not performed.

Dose Formulation

Vehicle: DMSO (Sigma, Lot No. 068H2338) in olive oil (Sigma, Lot No. 088H6055)

On the day that dosing occurred, DMSO (1%) was mixed with olive oil. The appropriate amount of test material (~0.6 g) was weighed into a volumetric flask and the DMSO/olive oil mixture was added to obtain a final volume of 10 mL. The contents were vortexed and sonicated for approximately 20 minutes. A stir bar was added and the mixture was stirred for approximately 20 minutes. The mixture appeared cloudy and was deemed a suspension. The test material suspension was placed on a stir plate in the animal room and stirred continually until dosing was complete. The vehicle control group (MV) received DMSO/olive oil only.

Vehicle: Saline (Phoenix Scientific, Inc., Lot No. 8020116)

On the days that dosing occurred, the appropriate amount of test material (~0.6 g) was weighed into a volumetric flask and saline (~7-9 mL) was added. The contents were vortexed and the pH of the solution was adjusted with NaOH to a pH of approximately 7. Saline was added to obtain a final volume of 10 mL and the solution was transferred to a scintillation vial. A stir bar was added and the solution was stirred until well mixed. The dose solution was then placed on a stir plate in the animal room and stirred continually until dosing was complete. The vehicle control groups (MN, MN2 and MSE-N 99075 MN) received isotonic saline only.

The stability of the primary formulation components has been verified in previous studies and was not conducted with this lot of test material for this study. The concentration, homogeneity and stability of the test material in carrier were not determined.

Group Designations and Treatment Levels

24-hours

99052 Group Id	Test material and/or vehicle	Dose level (mg/kg)	No. of animals
MV	DMSO/olive oil	0	10
MN	Isotonic saline	0	10
M1	MON 35050 in DMSO/olive oil	600	10
MN2	Isotonic saline	0	8
M2	MON 35050 in isotonic saline	600	8

4-hours

99075 Group Id	Test Material	Dose level (mg/kg)	No. of animals
MN	Isotonic saline	0	10
M1	MON 35050 in isotonic saline	600	10

All animals were treated by a single intraperitoneal injection. Eight or ten animals/group were euthanized at approximately 4 or 24 hours following dose administration.

Animals

Species:	Mouse
Strain:	Crl:CD-1®(ICR)BR
Sex:	Male
Source:	Charles River Laboratory, Raleigh, NC
Date of Arrival:	MSE-N 99052: July 6, 1999 MSE-N 99075: September 7, 1999
Acclimation Period:	All animals were acclimated for a minimum of ten days. Animals in groups MN, MV and M1 (99052) were dosed on 7/27/99 and those in groups MN2 and M2 (99052) were dosed on 8/2/99. Animals in groups MN and M1 (99075) were dosed on 9/22/99.
Number Used in Study:	66
Method of Assignment:	Computer randomization by body weight (within 20% of mean weight): 99052 MN, MV and M1 99075 MN and M1 Random number generator (Microsoft Excel, version 7.0): 99052 MN2 and M2 Only animals judged to be healthy were used.
Method of Identification:	Individual ear-tag and bar-coded cage card
Age at Study Start:	MSE-N 99052: 7-8 weeks old MSE-N 99075: 8 weeks old
Average Body Weight at Study Start:	MSE-N 99052: MN 31.3 grams, MV 31.2 grams, M1 31.9 grams, MN2 33.9 grams, M2 31.4 grams

MSE-N 99075: MN 31.6 grams M1 31.0 grams

Type of Housing:	Individual stainless steel cages with wire mesh bottoms. Animals were double-housed upon arrival and single-housed after assignment to study.
Water Availability:	ad libitum (St. Louis public water supply)
Food Availability:	ad libitum (Certified Rodent Diet #5002, PMI Feeds, Inc, St. Louis, MO). The rodent diet was assayed by the manufacturer and met established specifications. No contaminants were expected to be in the food (or water) at levels that would interfere with results or conclusions of the study.
Temperature and Humidity:	Animal room temperature and humidity were targeted to be within 64-74°F and 30-70%, respectively.
Light Cycle:	Lights were set to come on at 0630 (±30 minutes) and go off at 1830 (±30 minutes). Interruptions in the light cycle of 30 minutes or less were not considered a deviation.

Note: Animal housing and husbandry were in accordance with the provisions of 'Guide for the Care and Use of Laboratory Animals', National Research Council, 1996.

In-life Observations

Checks for Mortality:	Although not specified in the study protocol, mortality checks were conducted once or twice daily (AM and/or PM) during the study.
Cageside Animal Observations:	Animals were observed once daily 6-7 hours post dose and/or at time of sacrifice for overt signs of toxicity. Animals were not routinely removed from their cages during the examinations. The general health condition of the animals was documented.
Body Weights:	Non-fasted body weights taken prior to randomization, on the morning of dosing (Table 1, Appendix 5) and just prior to sacrifice.

Dosing Method

A single intraperitoneal dose was administered to each animal. All animals were dosed at a target dose volume of 10 mL/kg body weight. MON 35050 was administered as a suspension in DMSO/olive oil or as a solution in isotonic saline using 1 mL plastic syringes

and 25 gauge, 5/8 inch or 23 gauge, 1 inch hypodermic needles. The vehicle control groups received DMSO/olive oil or isotonic saline only.

Unscheduled Deaths

All mice that died spontaneously or were terminated (by carbon dioxide asphyxiation) in a moribund condition were to be necropsied. No blood was to be collected. The liver, kidney, and a small section of the duodenum were to be placed in 10% neutral buffered formalin fixative, but were not to be processed or used further unless deemed necessary by the study director. No terminal body weights were to be taken.

Scheduled Sacrifice

All study animals were sacrificed by carbon dioxide asphyxiation 4 hours (± 30 minutes) or 24 (± 2) hours after dosing. A slight deviation from the 24-hour time point occurred in one animal (99075M1 003), however this did not negatively impact the study. Blood was collected from the posterior vena cava using a syringe and needle and transferred to serum microvette clot tubes. All sacrificed animals were necropsied and the livers and kidneys were removed, rinsed in saline, blotted dry and weighed. A small section of the duodenum from each animal (24-hour time point only) was also taken but not 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 longitudinal section of the left kidney) were placed in cassettes along with a section of the duodenum and retained in 10% neutral buffered formalin for microscopic evaluation and cell proliferation. The remaining portions of the liver and kidneys were divided into three parts, snap frozen in liquid nitrogen and stored at -70°C (± 10°C). There were no gross lesions retained. A limited gross observation was conducted at each sacrifice period and any observations noted were documented manually.

Sample Analysis

Microscopic Pathology
Fixed livers were rinsed, dehydrated, embedded in paraffin, sectioned at approximately 5 microns and stained with hematoxylin and eosin and examined microscopically.

Clinical Pathology
Serum was separated from the cellular fraction by centrifugation and analyzed for lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), sorbitol dehydrogenase (SDH), blood urea nitrogen (BUN), and creatinine using a Hitachi 717 clinical analyzer.

Liver Cell Proliferation
Sections of formalin fixed liver and kidney tissue from all animals sacrificed at 24 hours were processed and embedded in paraffin and sectioned at approximately 4 microns. A small section of duodenum retained and fixed at necropsy was used as a positive control for

staining. Proliferating cell nuclear antigen (PCNA) was used to determine cell proliferation in the liver only.

Cell proliferation was detected on microscope slides using the monoclonal mouse PC10 antibody to PCNA followed by streptavidin-peroxidase reagents. Biotinyl tyramide in working solution was then applied followed by streptavidin-horseradish peroxidase diluted in TNB buffer. The staining reaction was detected with the chromogen substrate, diaminobenzidine on a background of hematoxylin counterstain. Tissue sections of human tonsil were used as positive and negative controls. Liver tissue from each dose group was also used as negative controls. The negative controls were processed in the same way as the test samples except that the primary PCNA antibody was replaced with normal mouse serum matched to the same protein concentration as the PCNA antibody. The negative controls were processed separately from the positive control slides to prevent cross contamination with PCNA antibody. The controls indicated that the staining was adequate.

Labeling for PCNA was determined in the liver from the control and treatment groups sacrificed 24 hours after dose administration without knowledge of the group from which they originated. Eight to ten animals from each group were analyzed. A standard pattern was used to count total cells and labeled cells (S phase cells only) which included 10 random fields for each lobe. Results were determined by using a square eyepiece graticule (0.2 mm x 0.2 mm) with a 40x objective. Results were expressed as the mean labeling index; mean number of labeled cells per total number of cells per field.

Glutathione concentration

Reduced glutathione (GSH + GSSG) and oxidized glutathione (GSSG) concentrations were determined in the liver and kidneys of 5-8 animals/group sacrificed at 24 hours post dose and from 10 animals/group sacrificed at 4 hours post dose. Sections of the liver and kidneys were removed at sacrifice and were quickly rinsed in cold saline (Dulbecco's PBS without Ca^{2+} and Mg^{2+}). The sections were then placed in cassettes and frozen in liquid nitrogen. The tissue sections were stored at -80°C (± 10°C) until analyzed. The tissues were weighed and minced in a volume of ice cold 5% sulfosalicylic acid (SSA) + 100 mM $NaPO_4$ + 1 mM EDTA equal to approximately 3-5 times the weight of the tissue sample. The samples were then homogenized using a Tissuemizer or other appropriate homogenization tool. The homogenates were extracted for 15-20 minutes (± 10 minutes) on ice and then centrifuged at 20,000 x g (or 11,500 rpm) for 10 minutes (± 2 minutes) at 4°C (± 2°C) to remove precipitated material. After centrifugation, the supernate was removed, aliquotted into cryovials, and stored at -80°C (± 10° C) until assayed. Total GSH + GSSG and GSSG levels were measured using an enzymatic recycling assay referenced in Baker, Cerniglia, and Zaman, 1990 (3). This assay measures the kinetics of reduction of colorless 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB) to the chromophore 5-thio-2-nitrobenzoic acid (TNB) in a 96 well plate format. The reaction was initiated by the addition of 100 µL of reaction buffer containing 2.8 mL of 1 mM 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB), 3.75 mL of 1 mM NADPH, 5.85 mL of 100 mM sodium phosphate buffer (containing 1 mM EDTA, pH 7.5), and 20 units of glutathione reductase (the 1 mM DTNB and 1 mM NADPH were made up in 100 mM sodium phosphate buffer) to 50 µL of tissue homogenate, standard

or blank. Standards were run with each set of samples to determine the glutathione concentration of the tissue homogenate samples. The samples (including standards and blanks) were run in triplicate in individual wells of a 96 well plate. Samples were read using a SpectraMax250 microtiter plate reader (Molecular Devices Corporation, Sunnyvale, CA). The plate reader protocol for this assay included a 5 second initial mixing of the 96 well plate, followed by kinetic measurements at 405 nm at 20 second intervals for two minutes at 37°C.

The oxidized form of glutathione (GSSG) concentration was determined using the enzymatic recycling assay as described above with one additional step. Separate aliquots of the tissue homogenates (including standards, controls and blanks) were incubated with 2-vinyl pyridine for the purpose of derivitizing or removing the reduced form of glutathione (GSH). The derivitization was performed by adding 0.029 mL of tissue homogenate (or blank), 0.0072 mL of 97% 2-vinyl pyridine and 0.96 mL of 100 mM sodium phosphate buffer (containing 1 mM EDTA, pH 7.5). The mixture was then vortexed vigorously for one minute, and incubated at room temperature for 15 minutes. Standards, controls and blanks were treated in the same manner. Following incubation, the samples (including standards, controls and blanks) were added to the 96 well plate followed by 100 µL of reaction buffer and the assay was continued as described in the paragraph above. The GSSG concentration was calculated by dividing the calculated value obtained from the standard curve (picomoles of GSSG in GSH equivalent picomoles per gram of wet tissue weight) by two, and was reported as picomoles GSSG per gram of wet tissue weight. The reduced glutathione concentration was calculated by subtracting the oxidized glutathione (in GSH equivalent picomoles per gram of wet tissue weight) from the total glutathione (GSH + GSSG) picomoles per gram of wet tissue weight and reported as picomoles glutathione (GSH) per gram of wet tissue weight.

8-Hydroxydeoxyguanosine

Analysis for 8-hydroxydeoxyguanosine in the liver and kidneys of five animals from the control (MN2) and five animals from the MON 35050 in saline treatment group (M2) (24-hour sacrifice) was conducted using a LC-MS-MS method. Frozen tissues were transferred on dry ice for analysis by the Medicinal Chemistry and Pharmacognosy group at the University of Illinois, Chicago. The methods used can be found in Appendix 3.

Heat Shock Protein 70 (hsp 70) mRNA

Analysis for hsp 70 mRNA expression in frozen liver and kidney samples was conducted by the Investigative Discovery Toxicology and Pathology (IDTP) group at MSE-Creve Coeur. Frozen livers and kidneys from all animals (8-10 animals/group) were transferred on dry ice for analysis. Analysis and results can be found in the sub-report in Appendix 4.

NADPH Menadione Oxidoreductase (NMO) mRNA

Analysis for NMO mRNA expression in frozen liver and kidney samples was conducted by the IDTP group at MSE-Creve Coeur. Frozen livers and kidneys from all animals (8-10 animals/group) were transferred on dry ice for analysis. Analysis and results can be found in the sub-report in Appendix 4.

Statistical Analysis

The data were assembled, stored and processed by MSE-N computer programs (EHL decision-tree) or with an IBM personal computer (Microsoft Excel, version 7.0; GSH, cell proliferation and mRNA analyses). Results are presented as the mean ± 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 (two-tailed, $p \leq 0.01$ or $p \leq 0.05$) (4, 5). These were used to evaluate cell proliferation, reduced and oxidized glutathione concentrations, hsp 70 and NMO mRNA expression, 8-hydroxydeoxyquanosine levels and body weights. Fisher's Exact test (two-tailed, $p \leq 0.01$ or $p \leq 0.05$) (6) 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 EHL decision-tree statistical analysis which, depending on the results of tests for normality and homogeneity of variances (Bartlett-Box test) (7), utilized either parametric (Dunnett's test and linear regression) (8) or non-parametric (Kruskal-Wallis (9), Jonckheere's (10) and/or Mann-Whitney tests (11)) routines to detect group differences and analyze for trend (two-tailed, $p \leq 0.01$ or $p \leq 0.05$. Where appropriate for the 24-hour time point, the DMSO/olive oil control group (MV) was statistically compared to the MON 35050/DMSO/olive oil treatment group (M1). The saline control group (99052MN) was not used for statistical comparisons. Grubbs' test (12, 13) was used to identify outliers for cell proliferation and 8-hydroxydeoxyquanosine. Due to assay variability, Grubbs' test was not run on results from other analyses (i.e. GSH, hsp 70 and NMO reductase mRNA).

RESULTS

In-life Observations

In-life observations noted 6-7 hours after dosing or just prior to sacrifice are summarized in Appendix 5, Table 2.

Mortality

One animal (99075M1 003) was misdosed and died shortly after dosing. No necropsy was performed. Another lot number animal was chosen and assigned to replace the misdosed animal. There were no other mortalities in this study.

Gross Pathology

Terminal body, liver and kidney weights (absolute and relative to body weight) are presented in Table 1. Individual animal data are presented in Appendix 8, Table 1.

Terminal body weights of the MON 35050 in saline treated animals were statistically significantly decreased compared to the controls at 24 hours post dose. Statistically significant decreases in absolute and relative (normalized to body weight) liver and kidney weights occurred in this treatment group, 24 hours post dose.

No gross lesions were observed at time of sacrifice. A white, pasty material was observed on the surface of the tissues in the peritoneal cavity in 6 of the 10 animals which received MON 35050 in DMSO/olive oil (Appendix 5, Table 3).

Microscopic Pathology

All microscopic alterations are summarized in Appendix 5, Table 3. Lesions considered related to administration of the test material, or otherwise noteworthy, are described here.

The only treatment-associated changes occurred in the capsule or subcapsular tissue in both livers and kidneys. Changes were primarily limited to tissues from animals in the group given MON 35050 (600 mg/kg) in the DMSO/olive oil vehicle. Changes included deposition of fibrin and an amorphous material on the capsule of livers and kidneys. Inflammation and hemorrhage involving the renal capsule were also present in 3 of the 10 animals from this dose group. In addition, small depositions of fibrin/amorphous material occurred on the capsule of the kidney in one mouse from the saline control group and in three mice from the group given MON 35050 in saline.

The deposition of 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. Likewise, there was vacuolization of hepatocytes in most subcapsular regions. Similar changes in the liver occurred only rarely in other groups. They included capsular hemorrhage in a single animal from the saline control group and deposition of fibrin/amorphous material in one animal from the DMSO/olive oil, control group.

Fibrin/amorphous material was also present in the peritoneal cavity or omentum in single animals from the group given DMSO/olive oil.

Clinical Pathology

Blood chemistry results are summarized in Table 2. Individual animal data can be found in Table 1 of Appendix 7. Treatment-related effects on blood chemistry parameters occurred primarily in the treatment group receiving MON 35050 in DMSO/olive oil. Statistically significant increases in ALT, AST, BUN and SDH were observed 24 hours post dose in this treatment group. Statisitically significant increases in all parameters, except creatinine, were observed in the MON 35050 (in saline) treatment group, 4 hours post dose. SDH was the only parameter which was significantly increased 24 hours post dose in animals administered MON 35050 in saline.

Cell Proliferation

Cell proliferation was determined in the liver of all the control and treated animals, sacrificed 24 hours post dose. The only statistically significant difference between control and treated animals was a decrease in the treatment group receiving MON 35050 in saline and sacrificed 24 hours post dose. Since the effect was in the opposite direction from that expected, the reason for the change was not apparent. Results are summarized in Table 3. Individual animal data is shown in Appendix 1.

Glutathione (GSH) and GSSG concentrations

Reduced glutathione and oxidized GSSG liver and kidneys results are summarized in Table 4. Individual animal data are shown in Appendix 2, Tables 1 and 2. There was a

statistically significant increase in GSH levels in the liver of mice 4 hours after administration of MON 35050 in saline. A statistically significant decrease in GSH was observed in the kidneys 24 hours after administration of MON 35050 in saline. Total GSSG in the liver and kidneys was not significantly different in any treatment group compared to their respective controls at either the 4 or 24 hour time point.

8-Hydroxydeoxyguanosine

8-hydroxydeoxyguanosine results are summarized in Table 5. Individual animal data are shown in Appendix 3. The degree of oxidation in the liver and kidneys of mice dosed with MON 35050 in saline and sacrificed 24 hours post dose was not significantly different from controls.

Heat Shock Protein 70 (hsp 70) mRNA

Heat shock protein 70 mRNA results are shown in Table 6. The sub-report along with mean and individual animal data are located in Appendix 4. Expression levels of liver hsp 70 mRNA in the treated groups of mice were not significantly different from controls. Mean values in the kidneys of the MON 35050 in saline and in the MON 35050 in DMSO/olive oil treated mice were statistically significantly decreased compared to their respective control group 24 hours after dose administration. The biological significance of this finding, if any, is unknown.

NADPH Menadione Oxidoreductase (NMO) mRNA

NMO reductase mRNA results are shown in Table 6. The sub-report along with mean and individual animal data are located in Appendix 4. The only statistically significant difference in NMO reductase mRNA was an increase in the kidneys of MON 35050 in DMSO/olive oil treated mice 24 hours after dose administration.

DISCUSSION AND CONCLUSIONS

Several parameters have been evaluated to determine the effects of MON 35050 on the liver and kidneys of male mice following single intraperitoneal administration at a dose level of 600 mg/kg, 4 and 24 hours after dose administration. This work was done to assess the significance of genotoxic effects reported in the literature (1, 2).

Results from the present study indicate that single IP administration of MON 35050 causes hepatic and renal injury at the 600 mg/kg dose level, and MON 35050 is substantially more toxic to these organs when administrated in DMSO/olive oil. The hepatic and renal toxicity was evidenced by significant increases in serum enzymes along with the production of microscopic liver and kidney lesions.

The lesions observed in the kidneys and livers were apparently associated with the deposition of the test substance or the combination of vehicles and test material on the surface of these organs following intraperitoneal injection. These changes were largely confined to the group that received the test agent in a vehicle of DMSO and olive oil, and occurred at substantially higher incidence and severity in this group. These experimental

conditions are not considered appropriate to assess the potential genotoxicity of the test material.

The literature studies referenced above have reported evidence of DNA damage, including increased 8-hydroxydeoxyguanosine, in the liver and kidneys of mice. However, increased levels of 8-OHdG were not observed in the liver or kidneys of mice in this study. Because of the robust nature of the present investigation, the previous literature report is not considered sufficient to conclude that a high intraperitoneal dose of MON 35050 causes oxidative damage to DNA.

Increased mRNA expression of NMO reductase (an indicator of oxidative stress) was observed in the kidneys of mice from the MON 35050/DMSO/olive oil treatment group. This finding, along with the clinical chemistry and histopathology results described above, suggest that the changes to the liver and kidneys of mice reported in the literature are not primary genotoxic responses but rather represent secondary effects due to toxicity. This study provides additional support to the extensive database which clearly demonstrates that neither glyphosate, nor its formulations, pose a genotoxic risk to humans.

REFERENCES

1) Bolognesi, C. et. al. (1997). Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup. J. Agric. Food Chem. 45: 1957-1962.

2) Peluso, M. et. al. (1998). ^{32}P-Postlabeling Detection of DNA Adducts in Mice Treated with the Herbicide Roundup. Environmental and Molecular Mutagenesis 31: 55-59.

3) Baker, M.A., Cerniglia, G.J. and Zaman, A. (1990). Microtiter plate assay for measurement of glutathione and glutathione disulfide in large numbers of biological samples. Analytical Biochemistry 190: 360-365.

4) Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. Journal Am. Stat. Assoc. 50: 1096-1121.

5) Dunnett, C.W. (1964). New tables for multiple comparisons with a control. Biometrics 20: 482-491.

6) Fisher, R.A. (1946). Statistical Methods for Research Workers. Oliver and Boyd, and Edinburgh, U.K.

7) Bartlett, M.S. (1937). Supplement to the Journal of the Royal Statistical Society, 4: 137.

8) Draper, N.R. and Smith, H. (1966). Applied Regression Analysis, Wiley, NY.

9) Breslow, N. (1970). A generalized Kruskal-Wallis test for comparing K-Samples subject to unequal patterns of censorship.

10) Hollander, M. and Wolfe, D.A. (1973). Nonparametric Statistical Methods. Wiley, NY.

11) Mann, H.B. and Whitney, D.R. (1947). On a test of whether one of two variables is stochastically larger than the other. Ann. Math. Stat. 18:50.

12) Grubbs, F.E. (1969). Procedure for detecting outlying observations in samples. Technometrics 11: 1-21.

13) Grubbs, F.E. and Beck, G. (1972). Extension of sample sizes and percentage points for significance tests of outlying observations. Technometrics 14(4): 847-854.

SUPPLEMENTAL STUDY INFORMATION

Study Director:	Kathy J. Hotz, B.S.
Director, Metabolism and Safety Evaluation-Newstead	Merrill R. Osheroff, Ph.D., D.A.B.T.
Study Personnel and (Group Supervisor):	
Clinical Pathology (MSE-N)	(Marie T. Rock, Ph.D.)
Formulations	(Michael R. Baldwin)
Investigative Discovery Metabolism and PK	(Alan G.E. Wilson, Ph.D.) Constance A. Wagner, B.S, M.T. (ASCP) Lori J. Kraus, A.A.S., H.T.
Investigative Discovery Toxicology and Pathology	(Dale Morris, Ph.D.) Sandra W. Curtiss, Ph.D. Elsa M. Blomquist, B.S.
Pathology	(Daryl C. Thake, D.V.M, D.A.C.V.P.) Johnna G. Napier, H.S., H.T. (ASCP) Debra S. Garner, H.T.
Toxicology Services	(Francis L. Speck, B.S., A.A.S., V.T.)
University of Illinois-Chicago	(Richard B. van Breemen, Associate Professor of Medicinal Chemistry and Pharmacognosy)

Location of Study Material:

Raw Data, Protocol and Amendments	MSE-N Archives
Tissue Blocks and Slides	MSE-N Archives
Final Report	MSE-N Archives

EXHIBIT 37

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IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF CALIFORNIA

NATIONAL ASSOCIATION OF WHEAT GROWERS ET AL., Plaintiffs, **v.** **LAUREN ZEISE, IN HER OFFICIAL CAPACITY AS DIRECTOR OF THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT; AND XAVIER BECERRA, IN HIS OFFICIAL CAPACITY AS ATTORNEY GENERAL OF THE STATE OF CALIFORNIA,** Defendants.	Civil Action No. 2:17-CV-02041-WBS-EFB **ANSWER OF DR. LAUREN ZEISE, DIRECTOR OF THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT AND XAVIER BECERRA, ATTORNEY GENERAL OF THE STATE OF CALIFORNIA TO FIRST AMENDED COMPLAINT** Courtroom: 5 Judge: The Honorable William B. Shubb Trial Date: None set. Action Filed: November 15, 2017

Defendants Dr. Lauren Zeise, Director of Office of Environmental Health Hazard Assessment and Xavier Becerra, Attorney General of the State of California (jointly the "State Parties") hereby respond to the First Amended Complaint filed by Monsanto Company, and the

National Association of Wheat Growers et al. (jointly "Plaintiffs").

1. The State Parties deny that any warning under Proposition 65 is false, misleading and highly controversial. The State Parties lack information or belief sufficient to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

2. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph concerning glyphosate and, on that basis, deny them. The remainder of the allegations are Plaintiffs' characterizations of law and require no response. To the extent a response is deemed required, OEHHA denies the allegations.

3. The allegations of this paragraph are Plaintiffs' characterizations of the conclusions of other entities, which speak for themselves and require no response. To the extent that a response is required, the State Parties admit that a program within the Office of Health Hazard Assessment ("OEHHA") that establishes non-regulatory goals for contaminants in drinking water concluded in 1997 and 2007, based on the evidence they reviewed at those times, that glyphosate "is unlikely to pose a cancer hazard to humans," and established a public health goal for the chemical based on non-cancer health effects. OEHHA denies that the discussion in the public health goal document has any relevance to the issues before this Court. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

4. The State Parties admit that OEHHA listed glyphosate as a carcinogen under Proposition 65 on July 7, 2017 under the Labor Code Listing mechanism of Proposition 65 based on a determination by IARC that there is sufficient evidence from scientific studies in animals of glyphosate's carcinogenicity, strong mechanistic evidence, and limited evidence in scientific studies in humans that glyphosate is "probably carcinogenic to humans." The remainder of the allegations of this paragraph are the Plaintiffs' characterization of the law and require no response. To the extent that a response is deemed required, OEHHA denies the allegations of this paragraph.

5. Denied.

6. The State Parties admit that OEHHA does not independently review the scientific validity of the IARC determination and that the listing is "ministerial" as long as the IARC

determination meets the requirements of California Health and Safety Code section 25249.8(a) and California Code of Regulations, title 27, section 25904. ("27 CCR".) The State Parties admit that private enforcers are entitle to 25% of any penalty assessed under Proposition 65. Except as expressly admitted herein, OEHHA denies the remainder of the allegations of this paragraph.

7. Denied.

8. Denied.

9. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

10. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

11. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

12. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

13. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

14. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

15. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

16. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

17. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

18. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

19. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

20. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

21. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

22. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

23. The State Parties admit that Dr. Lauren Zeise, the Director of OEHHA and the highest ranking administrative officer, is sued in her official capacity, and that OEHHA has offices in Sacramento and Oakland. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

24. Admitted.

25. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

26. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent that a response is deemed required, the State Parties admit that Defendants are located within this District. Except as expressly admitted herein, the State Parties deny the remaining allegations of this paragraph.

27. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent that a response is deemed required, the State Parties admit that federal law regulates the sale and use of pesticides and the labeling of food products to some extent. Except as expressly admitted herein, the State Parties deny the allegations of this paragraph.

28. This paragraph is Plaintiffs' statement of the law and of the content of particular documents, which speak for themselves, and requires no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

29. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

30. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

31. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

32. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

33. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

34. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

35. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

36. The State Parties deny that glyphosate has been recognized as a "safe" herbicide by OEHHA. The State Parties lack information or belief sufficient to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

37. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from an EPA document, that document speaks for itself, and requires no response.

38. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from an EPA document, that document speaks for itself and requires no response.

39. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

40. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

41. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

42. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

43. The State Parties deny that OEHHA has concluded that glyphosate is non-carcinogenic for purposes of Proposition 65. OEHHA admits that one of its programs unrelated to Proposition 65 reviewed the health effects of glyphosate based on the scientific information available at that time, including some of the same studies relied on by IARC, and stated that, for purposes of establishing a non-regulatory public health goal for glyphosate, the program determined there was insufficient evidence of carcinogenicity to use as a basis for the public health goal.

44. The State Parties admit that IARC is an agency of the United Nations World Health Organization and is based in Lyon, France; that it convenes Working Groups of international scientific experts who review the scientific evidence and reach conclusions and prepare Monographs concerning the cancer hazard posed by different substances; and that it is not a regulator. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

45. Denied.

46. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

47. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

48. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph characterizes the content of another document, that document speaks for itself and requires no response.

49. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document, that document speaks for itself and requires no response.

50. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them. To the extent that this paragraph contains quotations from a document and characterizes the content of a document, that document speaks for itself and requires no response.

51. Denied.

52. This paragraph is Plaintiffs' characterization of media articles concerning glyphosate, which speak for themselves and require no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

53. This paragraph is Plaintiffs' characterization of a media article concerning glyphosate, which speaks for itself and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

54. The State Parties admit that OEHHA personnel wrote the statement quoted in a letter in 2002, but deny that the characterization of that statement by Plaintiffs' is accurate. The State Parties lack information or belief sufficient to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

55. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

56. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

57. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

58. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

59. The State Parties admit that OEHHA has described its process for listing chemicals pursuant to the Labor Code Listing mechanism (Health & Saf. Code, § 25249.8, subd. (a)), as

"ministerial." The remainder of the allegations of this paragraph are Plaintiffs' statement of the law and require no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

60. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

61. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

62. This paragraph is Plaintiffs' statement of the law and requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

63. The allegations of this paragraph are Plaintiffs' statement of the law, which require no response. To the extent that a response is deemed required the State Parties admit that the Attorney General of California has a history of enforcing Proposition 65's warning requirement. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

64. The allegations of this paragraph are Plaintiffs' statements of the law, which require no response. To the extent a response is deemed required the State Parties deny the allegations of this paragraph.

65. The allegations of this paragraph are Plaintiffs' statements of the law, which require no response and Plaintiffs' characterization of a media article, which requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

66. The allegations of this paragraph are Plaintiffs' statements of the law, which requires no response. To the extent a response is deemed required, defendants deny the allegations of this paragraph.

67. The allegations of this paragraph are Plaintiffs' quotations from a dissenting opinion in a court of appeal decision, which requires no response. To the extent a response is deemed required, the State Parties deny the allegations of this paragraph.

68. The allegations of this paragraph are Plaintiffs' characterization of statements made in media articles, which speak for themselves and require no response. To the extent a response is deemed required, defendants deny the allegations of this paragraph.

69. The State Parties admit that a number of Proposition 65 lawsuits have been filed and that parties have sometimes provided sixty-day notices shortly after the warning requirement goes into effect. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

70. The State Parties admit that on July 7, 2017 glyphosate was listed under Proposition 65 as a chemical known to the state to cause cancer based on IARC's determination that there was sufficient evidence of carcinogenicity in animal studies and limited evidence of carcinogenicity in human studies. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

71. The State Parties admit the approximately 9,183 comments were filed in response to the NOIL, both for an against listing the chemical, and that the language quoted by Plaintiffs from the NOIL is accurate. To the extent that the allegations characterize the NOIL, that document speaks for itself, and requires no response. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

72. The State Parties lack information or belief sufficient to admit or deny the allegations of this paragraph and, on that basis, deny them.

73. Denied.

74. The State Parties admit that certain foods are permitted to contain glyphosate residues under federal law and that businesses that expose individuals to glyphosate must either provide a warning or be prepared to demonstrate that the exposure does not cause a significant risk of cancer as defined by the regulations. Except as expressly admitted herein, the State Parties deny the remaining allegations of this paragraph.

75. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

76. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

77. Denied.

78. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

79. The State Parties deny that any Proposition 65 warning for exposure to glyphosate that may be provided by a particular business is false and highly controversial. The State Parties lack information or belief to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

80. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

81. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

82. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

83. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

84. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

85. The State Parties lack information or belief to admit or deny the allegations of this paragraph and, on that basis, deny them.

86. The State Parties deny that any Proposition 65 warning for exposures to glyphosate that may be provided by a particular business is false and highly controversial or that Plaintiffs will be injured. The State Parties lack information or belief to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

87. The State Parties deny that Proposition 65 creates "unreasonable litigation risk." The State Parties lack information or belief to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

88. Denied

89. Denied.

90. The State Parties deny that a Proposition 65 warning for exposures to glyphosate that may be provided by a particular business would be "false speech" or "false warnings." The State Parties lack information or belief to admit or deny the remaining allegations of this paragraph and, on that basis, deny them.

91. Denied.

92. The foregoing paragraphs are incorporated by reference as if set forth in full herein.

93. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

94. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

95. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

96. Denied.

97. Denied.

98. Denied.

99. Denied.

100. Denied.

101. Denied.

102. Denied.

103. Denied.

104. Denied.

105. The foregoing paragraphs are incorporated by reference as if set forth in full herein.

106. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

107. Denied

108. Denied.

109. Denied.

110. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

111. Denied.

112. The State Parties lack information or belief to respond to the allegations of this paragraph and, on that basis, deny them.

113. Denied.

114. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

115. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

116. Denied.

117. Denied.

118. The foregoing Paragraphs are incorporated by reference as if set forth in full herein.

119. The allegations of this paragraph are the Plaintiffs' statement of law and require no response. To the extent that a response is deemed required, the State Parties deny the allegations of this paragraph.

120. Denied.

121. The State Parties admit that glyphosate was listed as a carcinogen under Proposition 65 because it met the requirements for listing pursuant to Health and Safety Code, section

25249.8(a) and California Code of Regulations, title 27, section 25904, based on IARC's determination in the March 2015 Monograph that there was sufficient evidence in animals that IARC causes cancer and glyphosate is "probably carcinogenic to humans." The State Parties admit that OEHHA did not conduct an independent assessment of the studies concerning glyphosate for purposes of the listing. Except as expressly admitted herein, the State Parties deny the remainder of the allegations of this paragraph.

122. Denied.

123. Denied.

124. Denied.

125. Denied.

AFFIRMATIVE DEFENSES

1. As and for a first affirmative defense, the State Parties state that the claims against some or all of the State Parties are barred by the Eleventh Amendment.

2. As and for a second affirmative defense, the State Parties state that glyphosate was listed by OEHHA on July 7, 2017, and any challenge to the listing is therefore moot.

3. As and for a third affirmative defense, the State Parties allege that OEHHA's listing of glyphosate as a chemical known to the State to cause cancer is in all respects in accordance with law.

4. As and for a fourth affirmative defense, the State Parties allege that the complaint fails to state a cause of action upon which relief can be granted.

5. As and for a fifth affirmative defense, the State Parties allege that the matter is not ripe, that there is therefore no case or controversy as required by Article III of the United States Constitution, and that the Court therefore has no jurisdiction over the matter.

6. As and for a sixth affirmative defense, the State Parties allege that the Plaintiffs cannot meet the standard for a preliminary or permanent injunction.

7. As and for a seventh affirmative defense, the State Parties allege that this Court should exercise its discretion not to take jurisdiction of this matter under the Declaratory Judgment Act.

8. As and for an seventh affirmative defense, the State Parties allege that this Court should abstain, based on considerations of comity and federalism, from deciding this matter until the State Courts have ruled.

9. As and for a ninth affirmative defense, Title 42 United States Code section 1988 does not apply to this matter.

PRAYER FOR RELIEF

1. That the Court enter judgment in favor of the State Parties, and dismiss Plaintiffs' action with prejudice and that Plaintiffs take nothing by this action;

2. That the Court deny Plaintiffs' request for a preliminary or permanent injunction and decline to issue any provisional or permanent relief of any kind against the State Parties;

3. That the Court deny the declaration sought by the Plaintiffs;

4. That the State Parties be awarded their costs of suit, including reasonable attorney's fees; and

5. For such other and further relief as the Court deems just and proper.

Dated: January 9, 2018

Respectfully Submitted,

XAVIER BECERRA
Attorney General of California
LAURA J. ZUCKERMAN
DENNIS A. RAGEN
HEATHER LESLIE
Deputy Attorneys General

/s/ Susan S. Fiering
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Supervising Deputy Attorney General
Attorneys for Dr. Lauren Zeise, Director, Office of Environmental Health Hazard Assessment and Xavier Becerra, Attorney General of the State of California

OK2017950064

EXHIBIT 38

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

vs. Case No. CGC-16-550128

MONSANTO COMPANY,

Defendant.

_____/

Reporter's Transcript of Proceedings

San Francisco, California

Thursday, May 10, 2018

Reported by:

SHEILA PHAM

CSR NO. 13293

PAGES 1 - 79

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

vs. Case No. CGC-16-550128

MONSANTO COMPANY,

Defendant.

_____/

Reporter's Transcript of Proceedings, taken at SAN FRANCISCO SUPERIOR COURT, 400 McAllister Street, Department 304, San Francisco, CA 94102, beginning at 9:10 a.m. and ending at 11:00 a.m., on Thursday, May 10, 2018, before Sheila Pham, Certified Shorthand Reporter No. 13293.

APPEARANCES OF COUNSEL

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that this state, California, embraced it and now declares --

THE COURT: We embraced it for regulatory purposes?

MR. MILLER: For the Proposition 65.

THE COURT: Yeah.

MR. MILLER: That glyphosate is a known cause of non-Hodgkin lymphoma.

THE COURT: But you're not suggesting, are you, that everything on the Prop 65 list is, by definition, something which you could present to a jury as, therefore, a potential cause, or a reasonable cause, or a cause with assurance of 2.0 for a disease; right?

MR. MILLER: No, Your Honor. I'm not making such a proffer. That's not my job and I wouldn't make that proposition.

THE COURT: It doesn't strike me that Prop 65 lists -- or things that meets criteria to be on the Prop 65 list are something that's going to be useful in a jury trial. Do you think I'm wrong about that?

MR. MILLER: I think it's admissible in a jury trial.

THE COURT: Really?

MR. MILLER: And I think it's a piece of evidence that the jury can consider.

from Wayne Johnson.

And during that deposition, we handed him a document from 2004, which we find to be a very important document in this case. I don't want to say what the document is in open court. But what happened is: After about ten questions, I took a break, counsel and witness left the room, they came back and claimed that it was prepared at the request of attorneys, and therefore, they weren't going to talk about it anymore and they wanted to claw him back.

We're waiting for them to do the proper procedures, but we're running out of time. Our argument is: There's nothing in there about lawyers. The metadata shows nothing --

THE COURT: We don't have to go into the details. You have a disagreement about this issue?

MR. MILLER: Yes, we have a disagreement and we'd like to have a few minutes. Yes, Your Honor.

THE COURT: So why don't we go off the record and pick a date that works for everybody's calendar.

MR. MILLER: Sure.

THE COURT: Off the record.

(Off the record.)

THE COURT: The informal conference will be at 9:00 on the 16th of May.

Off the record.

(Proceedings concluded at 11:00 a.m.)

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

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

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

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

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

Dated: May 14, 2018

<%signature%>
Sheila Pham
CSR No. 13293

EXHIBIT 39

Timothy Litzenburg (appearance *pro hac vice*)
Curtis G. Hoke (State Bar No. 282465)
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Attorneys for Plaintiff
DEWAYNE JOHNSON

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

DEWAYNE JOHNSON,

Plaintiff,

v.

MONSANTO COMPANY

Defendant.

Case No. CGC-16-550128

PLAINTIFF'S RESPONSES TO DEFENDANT'S FIRST SPECIAL INTERROGATORIES

RESPONSE TO SPECIAL INTEROGATORIES

No. 1:

Mr. Johnson was employed by the Benicia Unified School District in the maintenance/groundskeeping department from June 2011 until 2017; his title and rates of pay varied over this period. Mr. Johnson's duties included pesticide application, pest control by other means (such as trapping animals), chalk-lining athletic fields, and repairing/maintaining irrigation systems for school grounds and athletic fields. His supervisor was Roy Owens, Head of Maintentance and Operation. Benicia Unified School District, 350 East K St Benicia, CA 94510. Mr. Johnson worked full-time beginning in 2005 and periodically as late as 2012 for Adecco Staffing, 575 Lincoln Ave Suite 208, Napa, California, 94558. His duties consisted of "palleting" wine: moving bottled, boxed wine onto pallets for shipping. His pay ranged from $8.50 to $11.00 per hour. For approximately three years in the early 2000s, Mr. Johnson was employed by Urban Waterproofing seasonally, where his duties consisted of applying waterproofing sealant to the edges of commercial building windows. His pay was approximately $9.00 per hour. From 1996 to 1997, Mr. Johnson was employed by the Vallejo Unified School District, 665 Walnut Ave., Vallejo, California, 94592. He served as a custodian and "campus supervisor," which entailed working security at athletic events.

No. 2:

In addition to those primary duties set forth above, Mr. Johnson served at times as a custodian, lunch delivery person, and mail carrier in his first year of employment at Benicia. In his pest control position, he also cut trees and shrubs and restored gutters.

No. 3:

Mr. Johnson in 2016 filed Workers' Compensation claim numbers 15-000734-1 and 16-001046-1 relating to his development of non-Hodgkin lymphoma from applying glyphosate-based pesticides at

Mr. Johnson's non-Hodgkyin lymphoma was first diagnosed by pathologist Laura Pincus, M.D. and John Geisse, M.D. in August 2014.

No. 13:

See medical records, previously provided in their entirety.

No. 14:

See the relatives listed in No. 8. Mr. Johnson generally attended medical appointments alone, but these family members can testify as lay witnesses to damages. See health care providers as identified in the medical records and elsewhere in these Answers.

No. 15:.

Plaintiff objects to this interrogatory as unduly burdensome and overly broad in scope. Without waiving, he answers in full below.

See medical records, previously provided in their entirety. In addition to the providers listed in the medical records, Mr. Johnson recalls visiting La Clinica Vallejo (an urgent care center formerly known as Clinic Ole, for the worsening nodule on his right knee in early 2014. Mr. Johnson has chiefly been a patient of the Kaiser Permanente system since before his diagnosis of any type of cancer, through 2017. His primary care physician is Jennifer Mackinam, M.D. His primary dermatologist has been Onaopemipo Ofodile, M.D. and his primary medical oncologist at this time is Thach-Giao, M.D.; he was previously a patient of Youn H. Kim, M.D. (medical oncology), Richard Hoppe, M.D. (radiation oncology) and their department at Stanford University, and has had pathology services performed by the pathology department at UCSF medical center.

No. 16:

Mr. Johnson suffers from active, recurrent, metastatic non Hodgkin lymphoma, Mycoses Fungoides, which is the subject of this lawsuit and was first diagnosed in 2014. He has received extensive chemotherapy which is detailed in the records, previously provided.

No. 17:

Plaintiff is in the process of gathering medical bills and tabulating special damages claimed in this lawsuit and will supplement.

No. 18:

In addition to medical bills, Mr. Johnson incurred travel expenses associated with driving 3 to 4 hours round trip for each Stanford University medical visit. Mr. Johnson has also suffered lost wages as a result of his inability to work and will suffer future lost wages. Mr. Johnson is still tabulating damages for lost wages and will supplement.

No. 19:

Mr. Johnson has sought and received a partial disability rating for his shoulder, SSDI XXX-XX-7844A, for which he receives benefits of $1314.10 per month.

No. 20. None.

No. 21. Mr. Johnson has been insured by Kaiser Permanente, through the Self-Insured Schools of California plan, Subscriber # 110005612536 during his employment at Vallejo Unified School District and Benicia Unified School District.

No. 22:

Mr. Johnson's MediCAL application was rejected for lack of employment information in September 2017 and he is in the process of supplementing that application.

No. 23:

Mr. Johnson's employer purchased Roundup and RangerPro pesticides from Horizon Distributors, which he used from 2011 through 2016. At times throughout that period Mr. Johnson himself would pick up the chemical at Horizon's retail location; at other times Horizon delivered 50 gallon drums of the chemicals to his workplace. He occasionally purchased small amounts of Roundup from Ace Hardware.

Mr. Johnson received a one-day training in or around 2011 from Horizon Distributors' Leanne Schroeder. He placed the telephone calls described in No. 29.

No. 31.

Mr. Johnson is unable to recall with specificity which advertisements he viewed for these products, but does recall having seen advertisements.

No. 32.

Mr. Johnson used Monsanto's website in 2014 to look up a contact telephone number. In addition, he has visited a Mayo Clinic public website with information about glyphosate and its potential carcinogenicity.

No. 33.

Mr. Johnson placed the telephone calls described in No. 29.

No. 34.

None.

No. 35.

Plaintiff objects to this interrogatory on the grounds of attorney client privilege and attorney work product. Expert witnesses will be identified in accordance with California's rules and the applicable scheduling order. Without waiving, Stuart Shear, M.D. has previously rendered a report/opinion that Mr. Johnson's Roundup and RangerPro exposure was a cause of his non Hodgkin lymphoma.

DATED: October 5, 2017 By:/s/ Timothy Litzenburg

Timothy Litzenburg (appearance *pro hac vice*)
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Attorneys for Plaintiff,
DEWAYNE JOHNSON

PROOF OF SERVICE

Johnson v. Monsanto Company, CGC-16-550128

On this date, I served via email and first class mail, these Plaintiff Responses to Monsanto's First Special Interrogatories to Defendant, on:

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Attorneys for Defendants
MONSANTO COMPANY

October 5, 2017

____/s/ Timothy Litzenburg

EXHIBIT 40

HOW KAISER PERMANENTE PROVIDERS ARE PAID

Kaiser Permanente is made up of three legal entities that work closely together to provide your health care. In the Northern California region of Kaiser Permanente, the three entities are:

- Kaiser Foundation Health Plan, Inc. (Health Plan),
- Kaiser Foundation Hospitals (Hospitals), and
- The Permanente Medical Group, Inc. (Medical Group)

In the Southern California region of Kaiser Permanente, the three entities are:

- Kaiser Foundation Health Plan, Inc. (Health Plan),
- Kaiser Foundation Hospitals (Hospitals), and
- Southern California Permanente Medicare Group (Medical Group)

Each of these three entities serves a different function. The Health Plan offers you benefits, enrolls you, and collects your premiums. To provide your medical care, Health Plan then contracts with the other two entities. It contracts with the Medical Group to provide the physicians in charge of your medical care, and it contracts with Hospitals to provide facility care to you (for example, hospital and skilled nursing care). In addition, in some parts of our Service Areas, Hospitals and Medical Group may contract with non-Kaiser Permanente physicians, hospitals, or other health care providers and medical organizations for services to members. (Look in *The Guidebook to Kaiser Permanente Services* to see specific instances.)

Every month, the Health Plan prepays the Medical Group a set dollar amount for each member enrolled. This payment method is called "capitation." The Medical Group receives this payment for each enrolled member whether or not the member seeks or receives services during that month. In addition, every month the Health Plan reimburses the Medical Group for certain expenses. The capitation payments and other payments pay for physician services provided or arranged by the Medical Group.

Medical Group physicians are rewarded for doing what's right for you, rather than being paid based on the number of services they provide or on their use of referral services. The Medical Group pays physicians a market-based salary, supplemented by small incentives. These

incentives are based on several things, including: quick and easy access to appointments, patient satisfaction, and high quality care. These small incentives do not require Health Plan to provide stop-loss protection to its physicians. Medical Group physicians are rewarded for delivering care that helps keep you healthy and productive – the right care at the right time. For more information about how health care resources are managed and used, refer to *Your Guidebook to Kaiser Permanente Services.*

Non-Permanente physicians associated with our Medical Groups are paid a predetermined amount for each service that they provide, commonly called fee-for-service payments or by capitation. Other providers of medical and hospital services may be paid in a number of ways. The most common forms of payment include fee-for-service payments, percent discount from charges, per diem or daily rates, and case rates.

We hope this information is helpful. If you have further questions, please call our Member Services Call Center at appropriate number.

1-800-464-4000 (English)
1-800-777-1370 (toll-free TTY for the hearing/speech impaired)
1-800-788-0616 (Spanish)
1-800-757-7585 (Chinese dialects)

Medicare members
1-800-443-0815 (toll free)
1-800-777-1370 (toll-free TTY for the hearing/speech impaired)

Thank you for your inquiry.

August 6, 2014

EXHIBIT 41

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

-vs- Case No. CGC-16-550128

MONSANTO COMPANY,

Defendant.

CONFIDENTIAL VIDEOTAPED DEPOSITION OF

DR. CHARLES M. BENBROOK

9:04 a.m. to 7:45 p.m.

February 8, 2018

Orange, Virginia

Job No. 137478

REPORTED BY: Rhonda D. Tuck, RPR, CRR

the slides.

As we're going to get to, the final position of EPA in this reregistration standard was to follow the advice of the scientific advisory panel and require Monsanto to do a new mouse study and a new rat study. And then, of course, as I testified earlier, OPP provided Monsanto with a very detailed explanation of a rigorous protocol for a new male mouse feeding study designed to specifically resolve the apparent tentative, equivocal issues related to whether the statistically increased incidence of renal tubular adenomas in this study were treatment related.

That's the -- that was the underlying controversy, and the identification of this -- what I call it, a magic tumor in the Male Mouse Number 1028 was -- if that had not occurred and if we -- there wouldn't have been a reassessment of this study.

It was really Monsanto's ability to interject Dr. Kuschner's assessment of the slides that kept the debate opened, kept requiring the EPA to spend staff and scientific resources in responding to Monsanto's ongoing submissions, arguments, information data on the question.

So that's -- that would have -- that was the appropriate and proper way for this underlying uncertainty to be resolved. It's what EPA put in the registration standard document, which is the appropriate place for such a request or requirement to be imposed on the registrant.

In my opinion, a responsible company, a company that really wanted to be sure that the most heavily used and widely sold herbicide in the world surely did not contribute to increased cancer risk, they would have done the study as EPA had requested and required.

Q. And EPA has resolved the uncertainty today by concluding that glyphosate is not a human carcinogen, correct?

MR. LITZENBURG: I object to form.

THE WITNESS: The EPA changed the classification of glyphosate because they -- they didn't -- were unable to convince Monsanto to do the requested additional studies, and the agency felt that it was time to move on to other things. And it just -- they didn't -- they didn't want to continue the assessment of that particular cancer study.

I -- it is my opinion that some of the

07:45 A. Correct.

MR. COPLE: We can adjourn until tomorrow morning.

THE VIDEOGRAPHER: The time is now 7:45. We are off the record.

(Deposition adjourned at 7:45 p.m.)

(Signature reserved)

* * * * *

COMMONWEALTH OF VIRGINIA AT LARGE, to wit:

I, Rhonda D. Tuck, RPR, CRR, Notary Public in and for the Commonwealth of Virginia at Large, and whose commission expires on May 31, 2020, do certify that the aforementioned appeared before me, was sworn by me, and was thereupon examined by counsel; and that the foregoing is a true, correct, and full transcript of the testimony adduced.

I further certify that I am neither related to nor associated with any counsel or party to this proceeding, nor otherwise interested in the event thereof.

Given under my hand and notarial seal at Charlottesville, Virginia, this 12th day of February, 2018.

_____

Rhonda D. Tuck, RPR, CRR

Notary Public Registration No. 224847

Commonwealth of Virginia at Large

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

-vs- Case No. CGC-16-550128

MONSANTO COMPANY,

Defendant.

CONFIDENTIAL VIDEOTAPED DEPOSITION OF

DR. CHARLES M. BENBROOK

9:04 a.m. to 7:45 p.m.

February 8, 2018

Orange, Virginia

Job No. 137478

REPORTED BY: Rhonda D. Tuck, RPR, CRR

A. Okay.

Q. And that includes the tumor that was identified in the control group, right?

A. The additional magic tumor in Control Mouse 1028, yes.

Q. You used the term "magic tumor," not only in your testimony today, but in a number of places in your report. Is that a term that EPA has used to describe the control group tumor?

A. No.

Q. Is that a term that is used in the scientific evaluation of pathology slides, "magic tumor"?

A. I haven't encountered it.

Q. So you came up with that phrase?

A. Yeah. I came up with it.

Q. It has no scientific significance or relevance, right?

A. I think the -- my discussion of the -- the process that led to the identification of an additional tumor in this control animal is spelled out in considerable detail in my report, and my opinions about it are also spelled out.

In short, and basically, the EPA pathologists that looked at the same slides as the

07:45 A. Correct.

MR. COPLE: We can adjourn until tomorrow morning.

THE VIDEOGRAPHER: The time is now 7:45. We are off the record.

(Deposition adjourned at 7:45 p.m.)

(Signature reserved)

* * * * *

COMMONWEALTH OF VIRGINIA AT LARGE, to wit:

I, Rhonda D. Tuck, RPR, CRR, Notary Public in and for the Commonwealth of Virginia at Large, and whose commission expires on May 31, 2020, do certify that the aforementioned appeared before me, was sworn by me, and was thereupon examined by counsel; and that the foregoing is a true, correct, and full transcript of the testimony adduced.

I further certify that I am neither related to nor associated with any counsel or party to this proceeding, nor otherwise interested in the event thereof.

Given under my hand and notarial seal at Charlottesville, Virginia, this 12th day of February, 2018.

_____

Rhonda D. Tuck, RPR, CRR

Notary Public Registration No. 224847

Commonwealth of Virginia at Large

EXHIBIT 42

IN THE CIRCUIT COURT OF THE CITY OF ST. LOUIS

STATE OF MISSOURI

----------x

TIMOTHY KANE, et al., :

Plaintiffs, : Case No.

v. : 1622-CC10172

MONSANTO COMPANY, :

Defendant. :

----------x

DEPOSITION OF CHRISTOPHER PORTIER, Ph.D.

Tuesday, April 17th 2018

AT: 8.03 a.m.

Volume 2

Taken at:

Marriott Park Lane Hotel

140 Park Lane, Mayfair

London W1K 7AA

United Kingdom

Job ref: 184936

Pages: 385 - 600

reporter: Alan J. Bell, MBIVR

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Also present:

Alan Bell - Court Reporter
Wendy Viner - Videographer

BY MR. KALAS: 12:41:23

Q. And am I also correct that in the 12:41:24
context of the animal data, no one prior to 2015 12:41:26
was talking about glyphosate causing cancer? 12:41:31

A. No, that is not true. 12:41:33

Q. Okay, who was? 12:41:35

A. Séralini. 12:41:36

Q. Okay, and you have stated before, I 12:41:37
think yesterday, that Séralini was in your opinion 12:41:39
an unreliable study; right? 12:41:42

MS. GREENWALD: Objection, form. 12:41:45

THE WITNESS: A study that 12:41:45
I couldn't use. 12:41:46

BY MR. KALAS: 12:41:47

Q. Because it was unreliable? 12:41:47

A. That's a legal term. I'm using a 12:41:49
scientific term. The study was underpowered, it 12:41:51
was poorly presented and poorly analysed. 12:41:56

Q. Okay. And the IARC working group 12:41:58
rejected use of the Séralini study as well? 12:42:00

A. That is correct. 12:42:05

Q. And I think you stated in the 12:42:05
context of Exhibit 46 that the Ramazzini Institute 12:42:19
had all of the data on aspartame and so you would 12:42:27
defer to them over FDA? 12:42:30

CERTIFICATE OF COURT REPORTER

I, Alan Bell (Accredited Court Reporter, Member of the British Institute of Verbatim Reporters) do hereby certify that CHRISTOPHER PORTIER, Ph.D. was duly sworn, that I took the Stenograph Notes of the foregoing statement under oath and that the transcript thereof is a true and accurate record transcribed to the best of my skill and ability.

I further certify that I am neither counsel for, related to, nor employed by any of the parties to the action in which the deposition was taken, and that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of the action.

.....

Alan Bell

EXHIBIT 43

GLYPHOSATE

1. Exposure Data

1.1 Identification of the agent

1.1.1 Nomenclature

Chem. Abstr. Serv. Reg. No.: 1071-83-6 (acid); also relevant:
38641-94-0 (glyphosate-isopropylamine salt)
40465-66-5 (monoammonium salt)
69254-40-6 (diammonium salt)
34494-03-6 (glyphosate-sodium)
81591-81-3 (glyphosate-trimesium)

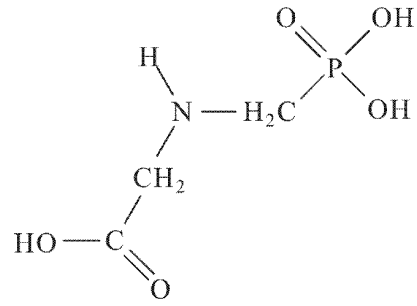
Chem. Abstr. Serv. Name: *N*-(phosphonomethyl)glycine

Preferred IUPAC Name: *N*-(phosphonomethyl)glycine

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

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

1.1.2 Structural and molecular formulae and relative molecular mass



Molecular formula: $C_3H_8NO_5P$
Relative molecular mass: 169.07

Additional information on chemical structure is also available in the PubChem Compound database (NCBI, 2015).

1.1.3 Chemical and physical properties of the pure substance

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

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

mice [age at start not reported] were given diets containing glyphosate (purity, 94–96%) at a concentration of 0, 1600, 8000, or 40 000 ppm for 18 months. The increase in the incidence of bronchiolo-alveolar adenoma and carcinoma, and of lymphoma, was reported to be not statistically significant in males and females receiving glyphosate. [The Working Group was unable to evaluate this study because of the limited experimental data provided in the review article and supplemental information.]

In the second study (identified as Study 13, 2001), groups of 50 male and 50 female Swiss albino mice [age at start not reported] were given diets containing glyphosate (purity, > 95%) at a concentration of 0 (control), 100, 1000, or 10 000 ppm for 18 months. The authors reported a statistically significant increase in the incidence of malignant lymphoma (not otherwise specified, NOS) in males at the highest dose: 10/50 (20%), 15/50 (30%), 16/50 (32%), 19/50 (38%; $P < 0.05$; pairwise test); and in females at the highest dose: 18/50 (36%), 20/50 (40%), 19/50 (38%), 25/50 (50%; $P < 0.05$; pairwise test). [The Working Group was unable to evaluate this study because of the limited experimental data provided in the review article and supplemental information.]

In the third study (identified as Study 14, 2009a), groups of 51 male and 51 female CD-1 mice [age at start not reported] were given diets containing glyphosate (purity, 94.6–97.6%) at a concentration of 0, 500, 1500, or 5000 ppm for 18 months. Incidences for bronchiolo-alveolar adenoma and carcinoma, malignant lymphoma (NOS), and hepatocellular adenoma and carcinoma in males, and for bronchiolo-alveolar adenoma and carcinoma, malignant lymphoma (NOS) and pituitary adenoma in females, were included in the article. In males, the authors reported that there was a significant positive trend [statistical test not specified] in the incidence of bronchiolo-alveolar carcinoma (5/51, 5/51, 7/51, 11/51) and of malignant lymphoma (0/51, 1/51, 2/51, 5/51). [The Working Group was unable to evaluate this study because of the limited experimental data provided in the review article and supplemental information.]

3.2 Rat

See Table 3.2

3.2.1 Drinking-water

Groups of 10 male and 10 female Sprague-Dawley rats (age, 5 weeks) were given drinking-water containing a glyphosate-based formulation at a dose of 0 (control), 1.1×10^{-8}% (5.0×10^{-5} mg/L), 0.09% (400 mg/L) or 0.5% (2.25×10^{3} mg/L), ad libitum, for 24 months (Séralini *et al.*, 2014). [The study reported is a life-long toxicology study on a glyphosate-based formulation and on genetically modified NK603 maize, which the authors stated was designed as a full study of long-term toxicity and not a study of carcinogenicity. No information was provided on the identity or concentration of other chemicals contained in this formulation.] Survival was similar in treated and control rats. [No data on body weight were provided.] In female rats, there was an almost twofold increase in the incidence of tumours of the mammary gland (mainly fibroadenoma and adenocarcinoma) in animals exposed to the glyphosate-based formulation only versus control animals: control, 5/10 (50%); lowest dose, 9/10 (90%); intermediate dose, 10/10 (100%) [$P < 0.05$; Fisher exact test]; highest dose, 9/10 (90%). [The Working Group concluded that this study conducted on a glyphosate-based formulation was inadequate for evaluation because the number of animals per group was small, the histopathological description of tumours was poor, and incidences of tumours for individual animals were not provided.]

In another study with drinking-water, Chruscielska *et al.* (2000) gave groups of 55 male and 55 female Wistar rats (age, 6–7 weeks) drinking-water containing an ammonium salt

EXHIBIT 44

Croat Med J. 2013;54:91-6
doi: 10.3325/cmj.2013.54.91

Science, safety, and trust: the case of transgenic food

Lucia Martinelli[1], Małgorzata Karbarz[2], Helena Siipi[3]

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[3]University of Turku, Department of Behavioural Sciences and Philosophy, Turku, Finland

Abstract Genetically modified (GM) food is discussed as an example of the controversial relation between the intrinsic uncertainty of the scientific approach and the demand of citizen-consumers to use products of science innovation that are known to be safe. On the whole, peer-reviewed studies on GM food safety do not note significant health risks, with a few exceptions, like the most renowned "Pusztai affair" and the recent "Seralini case." These latter studies have been disregarded by the scientific community, based on incorrect experimental designs and statistic analysis. Such contradictory results show the complexity of risk evaluation, and raise concerns in the citizen-consumers against the GM food. A thoughtful consideration by scientific community and decision makers of the moral values that are present in risk evaluation and risk management should be the most trustable answer to citizen-consumers to their claim for clear and definitive answers concerning safety/un-safety of GM food.

In this essay in the series of articles from "Bio-Objects" research network supported by the Cooperation in Science and Technology (COST) program (1), we focus on genetically modified (GM) plants for food production as a remarkable example of a biotechnology innovation fitting the "bio-object" classification. GM plants are defined as organisms whose genomes have been modified applying recombinant techniques (rDNA) by transferring extra genes or modulating (knockdown or knockout) genes already present in the species, with the aims of acquiring knowledge on gene functions, obtaining genetic improvement, and yielding selected compounds (2).

GM plant generation dates back already 30 years when at the Miami Winter Symposia of January 1983, three independent groups announced successful transfer of bacterial genes into plants, producing tobacco and petunia resistant to antibiotics (3-5). A few months there followed an insertion of a plant gene from one species into another species, generating a sunflower expressing the bean phaseolin gene (6). Thereafter, gene transfer technology increased dramatically while expectations on applications in agro-food genetic improvement were progressively rising. Besides overcoming conventional breeding constraints, solutions of crucial worldwide human questions were foreseen, such as adequacy of food resources to be available to the increasing world population and in particular to the hungry countries; generation of healthier food with enhanced nutritional values; development of an agricultural practice more respectful to environmental issues, based on crops constructed to be intrinsically resistant to the most relevant pests and diseases, thus free from chemical protection.

As extensively reported in literature, molecular tool applications in agriculture, human health, and food offer today remarkable opportunities even though more promises than concrete achievements on the market have been accomplished. The further achievements are continually expected based on the information accumulated through genetic research advancements (7).

GM PLANTS AS "BIO-OBJECTS"

From 2000, while use of GM plants in agriculture was increasingly becoming a consolidated practice and novel GM foods were entering into the market with a globally upward trend reaching nowadays 160 million hectares cultivated with biotech crops, concerns and passionate social and political controversies replaced enthusiastic expectations from the biotech era (7). Biotech-

nology application in agriculture soon became – and still is – a problematic issue and various countries all over the world gradually adopted own regulations for production, cultivation, import, and traceability of GM crops and their derivates to meet public demand of safety and to manage (perceived/true) technical risks, while biotech public research suffered from funding cut off.

This new course, which we regard as a significant step of a "bio-objectification" process, well portraits the controversial interactions occurring when science innovations break into society. GM plants, accordingly, as other "biological creatures" of agriculture and medicine research, bear some crucial features of "bio-objects." They are constructed and manipulated biologies on the fine line between "natural" and "non-natural"/"artificial" that have hybridity (thus evoking the language of the "unnatural") and are potentially useful for enhancing human life quality, resulting in the challenge of conventional natural, cultural, scientific and institutional orderings (8,9). Moreover, they have potential to move between domains, shifting from agriculture (the "first-generation GM plants," whose modifications are aimed at solving agronomic constraints), nutrition (the "second-generation" GM plants, whose modifications are aimed at enhancing nutritional values) and health and industry (the "third generation" GM plants, whose modifications are aimed at farming specific compounds to be adopted in pharmaceutical and health care).

Bio-social impacts of GM plants have been extensively reported in literature (10) and at the Web sites of various associations and no-profit organizations involved in social issues and environment protection, while perceived risks related to hybridity and "crawling" across genetic barriers (11), as well as the significance of human intervention in Nature (12), have been already considered.

Here, focusing on human health risk, as evaluated by scientific community and institutional organs, we aim to discuss GM food as an example of "bio-object," which enlightens the controversial relation between the intrinsic uncertainty of the scientific approach and the demand of citizen-consumers to use the products of science innovation that are known to be safe.

RISK EVALUATION

Release of GM crops in open field and on the market is authorized all over the world according to various regulations and policies of different countries, and in Europe according to Reg. 1829/2003/EC. Moreover, "the European Union guarantees the traceability and labelling of GMOs and products produced from these organisms throughout the food chain. Traceability allows the monitoring and checking of information given on labels, the monitoring of effects on the environment and the withdrawal of products from the market in cases where new scientific data demonstrate that the GMOs used in the product present an environmental or health risk" (Reg. 1830/2003/EC). Within this regulatory framework, specific recommendations were formulated by EFSA (13). Accordingly, the evaluation of GM plants' potential effects on the environment are based on a case-by-case basis, following a step-by-step assessment approach, which takes into account crucial aspects of hazards and risks such as their persistence, invasiveness, and interactions with other organisms, the production systems, the receiving environment, and the biogeochemical processes, as well as their effects on human and animal health. This evaluation is meant to be supported by independent experts and based on the most accredited and updated scientific knowledge on the topic.

After 1995, assessment of health impact of GM plants has been the subject of extensive peer reviewed scientific literature, which has been mostly focused on maize, soybean (the primary transgenic crops distributed on the market), rice, and potato. Together with in vitro analysis, long-term and multigenerational feeding studies were mainly performed on rats as model system, besides mice, cows, and fish, by assessing body and organ weight, hematological values, enzyme activities, organ and tissue histopathological examination and transgenic DNA detection. According to comprehensive studies (14), in which the most accredited scientific papers on feeding trials have been analyzed on the basis of certified experimental and statistical parameters (15,16), no significant health risks were found, and possible differences detected between transgenic feedings and their isogenic counterparts were considered of no biological or toxicological significance. Worth stressing, in the few studies where indications of no nutritional equivalence or altered parameters were reported, thus supporting health hazard, severe incorrect experimental designs with detrimental effects on statistical analysis have been advocated within the scientific community, hence rejecting these results (14).

CONTROVERSIAL CASES

Among the first animal feeding studies on GM diet to be independently peer reviewed, the most renowned is the

one conducted at the Rowett Research Institute, Scotland, also known as "Pusztai affair" (17), which resulted for the researcher in suspension and banning from speaking publicly, and ended up with the not renewing his annual contract. Also co-author reported on suffering from mobbing, while *The Lancet*, which published this work as a letter was object of criticism. This study aimed at evaluating the effects of short-term rat feeding with GM potatoes expressing the lectin *Galanthus nivalis* agglutinin (GNA) gene developed to increase nematode and insect resistance. Histological observations of the stomach, jejunum, ileum, cecum, and colon showed that the presence of GNA in the diets, irrespective of whether originating from transgenic potatoes or from control potato diets supplemented with GNA, was associated with significantly greater mucosal thickness of the stomach when compared with controls. By contrast, a potent proliferative effect on the jejunum was observed in GM potato-based diet, an outcome not observed in controls or in rats fed with control potatoes but added with GNA. This latter result was interpreted as the effect of the gene transfer technique, such as the plant vector used for transferring the exogene or some form of positioning effect in the potato genome caused by the exogene insertion. Two official audits (respectively by Rowett Institute and the Royal Society) stated that the data did not support conclusions and severe experimental drawbacks were remarked, such as poorly designed experiments, presence of uncertainties in the composition of diets, inadequate rat number, incorrect statistical methods, and lacking consistency within experiments. On the other hand, this study has been the banner of anti-GMO movement for attributing interference by biotech companies on GM safety evaluation.

The "Seralini case" (18) is the most recent example of controversy associated with scientific publications on GM food evaluation. Authors aimed at assessing the long-term toxicity of the commercial formulation of Roundup herbicide and the maize line NK603 (Monsanto Corp., USA) harboring the gene encoding a glyphosate tolerant form of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) and developed to allow the use of the herbicide glyphosate as a weed control option in corn (19). As compared with its nearest isogenic non transgenic counterpart, rat feeding for two years with maize NK603 with or without supplements of the herbicide, resulted in severe kidney nephropathies and a significant sex-dependent increased mortality, development of large mammary tumors in females and liver congestions and necrosis in males. These outcomes were explained as a non linear endocrine-disrupting effects of herbicide as well as the overexpression of the transgene in the GM maize and its metabolic consequences. Together with the data originated from the study, doubts on the reliability of official risk evaluation methods were raised, in particular concerning duration of the long-term evaluation (15,16). Moreover, in the concluding remarks, further studies were forecasted concerning the assessment of "other mutagenic and metabolic effects of the edible GMO, which, according to Authors, 'cannot be excluded'" (18).

These alarming results and related pictures of rats bearing tumors resonated in the media and on the internet, opening a renewed concern in citizen-consumers against the use of biotech applications in food and feed, and motivating criticism by various actors involved in biotech matters (20). As for governments, the French and Russian launched investigations into the safety of NK603, and Russia and Kazakhstan placed temporary bans on its imports. Scientific community – with few exceptions (21) – replied with a quantity of opinions and response letters from top scientists, where the Seralini study was dismissed and a more solid peer review system in scientific journals was claimed for (22). As for institutions deputed to safety evaluation, EFSA delivered its final statement (also in agreement with the independent assessments by organizations of Belgium, Denmark, France, Germany, Italy, and the Netherlands) (23), which recommended rejection of this paper as scientifically unsound and stated a no need to re-examine its previous safety evaluations of maize NK603. Weaknesses in the methodology and experimental design, leading to misleading conclusions, were the basic faults assessed in this paper in particular deriving from the use of inappropriate animal line bearing a natural tumor formation rate of more than 50% and the minimal size of animal sample which was in contrast with the internationally recommended standards for a proper nutritional or toxicological assessment of a GM line. Controversial results concerning the dose-dependency between mortality or cancerogenesis of either the herbicide supplemented- or the maize NK603-diets were also pointed out.

SCIENCE, SAFETY, AND TRUST

A proper scientific risk evaluation requires specific scientific knowledge, and, as above described, controversies regarding risk evaluation are still common within the scientific community. This makes lay people, in their safety considerations, dependent on interpretations and explanations provided by scientists and the media. Ac-

cordingly, the question of trust is inherently embedded in the safety discussion. Because of the progressive collection of data and uncertainties presented above, GM food may be regarded as a "bio-object" that crosses back and forward the boundaries of "safe/unsafe" and "well known/still to be known." Thus, it is worth asking, how should the controversial relation between the intrinsic uncertainty of the science and citizen-consumers' desire to eat food that is known to be safe be understood and managed?

It should be pointed out that citizen-consumers are quite well aware of uncertainty features of scientific knowledge and are not demanding or expecting a "zero risk:" they rather complain that uncertainties are not taken seriously enough in decision-making concerning GMOs and in risk communication with the public (24). This may be a part of the reason for their unwillingness to consume GM food, as long as no specific benefits from choosing GM products are perceived (25,26). Besides, the unwillingness to eat GM food cannot be explained merely by referring to consumers' lack of knowledge regarding the risk evaluation. The deficit model type of thinking (the paradigm "more knowledge – more acceptance") has been criticized on theoretical and empirical grounds for overemphasizing the role of scientific ignorance in attitude formation (11,27-29). Nonetheless, it should be remarked that this assumption is still a common mindset in the scientific community, and shapes science communication, public engagement initiatives, and policymaking (29-31). Thus, it has been suggested that scientists and decision-makers should concentrate in being trustworthy, instead of focusing merely on providing information about scientific and values issues (32). But how to be trustworthy?

MORAL VALUES AND VALUE EVALUATIONS

Risk evaluation and risk management are usually presented as fundamentally and primarily scientific undertaking. In the "Pusztai affair" and "Seralini case," for example, the public and academic discussion was related merely to scientific issues, or at least issues that have been presented as a matter of science. However, moral value questions –evaluations on what is morally right and wrong, desirable and undesirable – are necessarily present in risk evaluation and risk management. These include: How big risks are acceptable? Which risks should we take? How safe is safe enough? Which of the identified possible consequences are risks (undesirable) and which benefits (desirable)? How severe are the identified risks? To whom may the risks fall? Which are the suitable objects of comparison (33-35)? The aim of science (truth) and risk analysis (safety) are not the same, and risk analysis is intimately connected to the following question: Which should be a sufficient amount of evidence for safety or unsafety claims? In the "Pusztai affair" and "Seralini case," the critics necessarily took a stand in this question when stating that these studies did not provide sufficient evidence for unsafety of a GM crop. We suggest that the controversy as well as the problem of trust may at least partly lie in a mistaken assumption that views concerning these moral value questions are commonly shared in the academia as well as in public sphere, as already pointed out: "what is typically called 'public rejection of science' is properly described as public rejection of commitments based on value commitment that are misunderstood and misrepresented by scientists and policy experts as solely scientifically determined" (36). Thus, building trust, as well as understanding and solving the controversy, requires making the moral values visible for all parties concerned and accepting them as topic of both public and academic discussion.

If we are right about the presence of value questions and disagreements concerning values in risk evaluation and management, being trustworthy may require acknowledging them and spelling them out in science communication. However, it has been noted that "being trustworthy cannot be limited to increasing transparency and providing information to consumers;" it further requires acting in a predictable manner, taking one's responsibilities seriously (32), and maybe also "including citizen-consumers into decision-making" (37). The requirement for engaging the public in the decision-making concerning GM plants is also pointed out by European Union (Reg. 2001/18/EC), according to which *"member states shall [. . .] consult the public and, where appropriate, groups on the proposed deliberate release."* The European practice, however, has been criticized as being too concentrated on purely scientific points and less concerned about the value questions, which seem to be left without notice. Since most citizen-consumers are unable to carry out scientific risks evaluations, the consultation practice leaves them a very limited (if not absent) possibility to really affect the decisions made (38). Thus, if building trustworthiness requires real (not just apparent) possibilities to affect decision, the current European practice seems unlikely to contribute to being trustworthy.

UNCERTAINTY AND DEMAND FOR SAFETY

Finally, we would like to ask whether the question "Are GM crops safe/dangerous to human health?" is sensible and

should it be the topic of public discussion. It is certainly true that GM techniques could be used to develop plants that are dangerous to human health (for example poisonous variants of common crop plants). That possibility, however, does not imply that the way the GM technique is used today is likely to lead into dangerous outcomes. Thus, the question intended in a literal form is left without a definitive answer, as science innovations are on the same time "results of science knowledge" and "carriers of new questions to be investigated." This question, therefore, may even be considered too broad and thus unanswerable. For these reasons, giving a simple yes/no answer to the query concerning safety of GMOs is impossible. Rather, we should concentrate on more definite answerable questions and in so doing emphasize the "case-by-case" evaluation of GM plants, where each individual product of biotech innovation – instead of the technique in its whole – is thoroughly assessed.

In conclusion, the most suitable answer to the "big question" raised by the consumers, "Can science give clear and definitive answers concerning safety/un-safety of certain GM plants?", according to our understanding, would require spelling out the values and assumptions (regarding, for example, the sufficient evidence for safety) behind risk assessment. This would greatly contribute to building trust and solving the controversy between uncertainty and demand for safety, at least when it is accompanied by predictability in decision-making, taking responsibilities, and conferring some possibility to citizen-consumers to really affect the decision-making.

References

1 Metzler I, Webster A. Bio-objects and their boundaries: governing matters at the intersection of society, politics, and science. Croat Med J. 2011;52:648-50. Medline:21990084 doi:10.3325/cmj.2011.52.648

2 Martinelli L. Recombinant DNA (rDNA) [Entry]. In: Priest SH, ed. Encyclopedia of Science and Technology Communication. Thousand Oaks (CA): Sage Publications; 2010. p. 623-6.

3 Fraley RT, Rogers SB, Horsch RB. Use of a chimeric gene to confer antibiotic resistance to plant cells. In: Downey K, ed. Advances in gene technology: molecular genetics of plants and animals: proceedings of the Miami Winter Symposium, January 1983. Academic Press; 1983. p. 211-21.

4 Framond AJ, Bevan MW, Barton KA, Flavell F, Chilton MD. Mini-Ti plasmid and a chimeric gene construct: new approaches to plant gene vector construction. In: Downey K, ed. Advances in gene technology: molecular genetics of plants and animals: proceedings of the Miami Winter Symposium, January 1983. Academic Press; 1983. p. 159-70.

5 Schell J, van Montagu M, Holsters M, Zambryski P, Joos H, Inze D, et al. Ti plasmids as experimental gene vectors for plants. In: Downey K, ed. Advances in gene technology: molecular genetics of plants and animals: proceedings of the Miami Winter Symposium, January 1983. Academic Press; 1983. p. 191-209.

6 Murai N, Sutton DW, Murray MG, Slightom JL, Merlo DJ, Reichert NA, et al. Phaseolin gene from bean is expressed after transfer to sunflower via tumor-inducing plasmid vectors. Science. 1983;222:476-82. Medline:17746179 doi:10.1126/science.222.4623.476

7 Martinelli L, Karbarz M, Gribaudo I. Gene transfer and modulation for the production of food with enhanced quali-quantitative values: potentials, promises and achievements. Food Technol Biotechnol. Forthcoming 2013.

8 Holmberg T, Schwennesen N, Webster A. Bio-objects and the bioobjectification process. Croat Med J. 2011;52:740-2. Medline:22180274 doi:10.3325/cmj.2011.52.740

9 Chrupek M, Siipi H, Martinelli L. Bio-objects as 'boundary crawlers': the case of microRNAs. Croat Med J. 2012;53:285-8. Medline:22661143 doi:10.3325/cmj.2012.53.285

10 Ferretti MP, Pavone V. What do civil society organisations expect from participation in science? Lessons from Germany and Spain on the issue of GMOs. Sci Public Policy. 2009;36:287-99. doi:10.3152/030234209X436527

11 Martinelli L. Gene transfer: technical visions and emotional perceptions. In: Lavino JG, Neumann RB, eds. Psychology of risk perception. Hauppauge (NY): Nova Science Publishers, Inc.; pp. 47-70.

12 Dhanda RK. Guiding Icarus. Merging bioethics with corporate interests. Hoboken (NJ): Willey & Sons; 2002.

13 European Food Safety Authority. Panel on Genetically Modified Organisms (GMO). Scientific opinion. Guidance on the environmental risk assessment of genetically modified plants. EFSA J. 2010;8:1879. doi:10.2903/j.efsa.2010.1879

14 Snell C, Bernheim A, Bergé J-B, Kuntz M, Pascal G, Paris A, et al. Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: a literature review. Food Chem Toxicol. 2012;50:1134-48. Medline:22155268 doi:10.1016/j.fct.2011.11.048

15 Organisation for Economic Co-operation and Development. Health Effects: repeated dose 90-day oral toxicity study in rodents, guideline for the testing of chemicals. Paris: OECD; 1998. section 4, part 408.

16 European Food Safety Authority. Safety and nutritional assessment of GM plants and derived food and feed: the role of animal feeding trials. Food Chem Toxicol. 2008;46:S2-70. Medline:18328408 doi:10.1016/j.fct.2008.02.008

17 Ewen SWB, Pusztai A. Effects of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on

rat small intestine. Lancet. 1999;354:1353-4 Medline:10533866. doi:10.1016/S0140-6736(98)05860-7

18 Seralini GE, Clair E, Mesnage R, Gress S, Defarge N, Malatesta M, et al. Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chem Toxicol. 2012;50:4221-31. Medline:22999595 doi:10.1016/j.fct.2012.08.005

19 International Life Science Institute. GM Crop Database. ILSI Research Foundation 2013. Available from: http://www.cera-gmc.org/?action=gm_crop_database&mode=ShowProd&data=NK603. Accessed: February 25, 2013.

20 Entine J. Genetic Literacy Project. Available from: http://www.geneticliteracyproject.org/2012/11/19/anti-gm-corn-study-reconsidered-seralini-finally-responds-to-torrent-of-criticism/. Accessed: February 25, 2013.

21 ENSSER Statement on Séralini et al. (2012) publication and reactions evoked. Available from: http://www.ensser.org/fileadmin/files/ENSSER-Comments-Seralini-etal2012-en.pdf. Accessed: February 25, 2013.

22 Hirt H. Science first in GM debate. The European Plant Science Organisation (EPSO). Available from: http://www.epsoweb.org/file/1094. Accessed: February 25, 2013.

23 European Food Safety Authority. Statement of EFSA: Final review of the Séralini et al. (2012a) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA J. 2012;10:2986. doi:10.2903/j.efsa.2012.2986

24 Marris C, Wynne B, Simmons P, Weldon S. Public perceptions of agricultural biotechnologies in Europe: final report of the PABE research project. Available from: http://csec.lancs.ac.uk/archive/pabe/docs/pabe_finalreport.pdf. Accessed: February 25, 2013.

25 Bonny S. Why are most Europeans opposed to GMOs? Factors explaining rejection in France and Europe. Electronic J Biotechnol. 2003;6:50-71. Available from: http://www.ejbiotechnology.info/content/vol6/issue1/full/4. Accessed: February 25, 2013.

26 Knight JG, Mather DW, Holdsworth DK, Ermen D. Acceptance of GM food – an experiment in six countries. Nat Biotechnol. 2007;25:507-8. Medline:17483829 doi:10.1038/nbt0507-507

27 Evans G, Durant J. The relationship between knowledge and attitudes in the public understanding of science in Britain. Public Underst Sci. 1995;4:57-74. doi:10.1088/0963-6625/4/1/004

28 Sturgis P, Cooper H, Fife-Shaw C. Attitudes to biotechnology: estimating the opinions of a better informed public. New Genet Soc. 2005;24:31-56. Medline:16552916 doi:10.1080/14636770500037693

29 Sturgis P, Allum N. Science in society: re-evaluating the deficit model of public attitudes. Public Underst Sci. 2004;13:55-74. doi:10.1177/0963662504042690

30 Hails R, Kinderlerer J. The GM public debate: context and communication strategies. Nat Rev Genet. 2003;4:819-25. Medline:14526377 doi:10.1038/nrg1182

31 Bubela T, Nisbet MN, Borchelt R, Brunger F, Critchley C, Einsiedel E, et al. Science communication reconsidered. Nat Biotechnol. 2009;27:514-8. Medline:19513051 doi:10.1038/nbt0609-514

32 Meijboom LB, Visak T, Brom FWA. From trust to trustworthiness: why information is not enough in the food sector. J Agric Environ Ethics. 2006;19:427-42. doi:10.1007/s10806-006-9000-2

33 Ahteensuu M. The precautionary principle and the risks of modern agri-biotechnology. In: Launis, V., Räikkä, J, eds. Genetic democracy: philosophical perspectives. Springer; 2008. p. 75-92.

34 Hansson SO. Risk and ethics: three approaches. In: Lewens T, ed. Risk: philosophical perspectives. London: Routledge; 2007. p. 21-35.

35 Siipi H, Ahteensuu M. The deficit model and the forgotten values. Nordicum-Mediterraneum. 2011;6:1-12.

36 Wynne B. Public engagement as means of restoring public trust in science – hitting the notes, but missing the music. Community Genet. 2006;9:211-20. Medline:16741352 doi:10.1159/000092659

37 Sterckx S, Macmillan T. Taking citizens seriously. J Agric Environ Ethics. 2006;19:219-23. doi:10.1007/s10806-005-6168-9

38 Ahteensuu M, Siipi H. A critical assessment of public consultations on GMOs in the European Union. Environ Values. 2009;18:129-52. doi:10.3197/096327109X438035

EXHIBIT 45

STATEMENT OF EFSA

Final review of the Séralini *et al.* (2012a) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology [1]

European Food Safety Authority[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

On 19 September 2012, Séralini *et al.* published online in the scientific journal Food and Chemical Toxicology a publication describing a 2-year feeding study in rats investigating the health effects of genetically modified maize NK603 with and without Roundup WeatherMAX® and Roundup® GT Plus alone (both are glyphosate-containing plant protection products). As requested by the European Commission, EFSA reviewed this publication taking into consideration assessments conducted by Member States and any clarification given by the authors. The assessments of Member States and EFSA revealed an overall agreement. The study as reported by Séralini *et al.* was found to be inadequately designed, analysed and reported. The authors of Séralini *et al.* provided a limited amount of relevant additional information in their answer to critics published in the journal Food and Chemical Toxicology. Taking into consideration Member States' assessments and the authors' answer to critics, EFSA reaches similar conclusions as in its first Statement (EFSA 2012). The study as described by Séralini *et al.* does not allow giving weight to their results and conclusions as published. Conclusions cannot be drawn on the difference in tumour incidence between treatment groups on the basis of the design, the analysis and the results as reported. Taking into consideration Member States' assessments and the authors' answer to critics, EFSA finds that the study as reported by Séralini *et al.* is of insufficient scientific quality for safety assessments. EFSA concludes that the currently available evidence does not impact on the ongoing re-evaluation of glyphosate and does not call for the reopening of the safety evaluations of maize NK603 and its related stacks. EFSA's evaluation of the Séralini *et al.* article is in keeping with its role to review relevant scientific literature for risk assessment on an ongoing basis to ensure that the advice it provides is up-to-date.

Key words

Maize NK603, Roundup, glyphosate, experimental design, rat/rodent feeding study, toxicity, carcinogenicity

[1] On request from European Commission Question No EFSA-Q-2012-00842, approved on 23 November 2012.

[2] Correspondence: sas@efsa.europa.eu

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

On 19 September 2012, an article was published online in the scientific journal Food and Chemical Toxicology that described a 2-year rat feeding study investigating the health effects of genetically modified (GM) maize NK603 sprayed during growth with or without a Roundup® (glyphosate-containing plant protection product) and of Roundup® alone. The authors of the study conclude that low levels of glyphosate herbicide formulations, at concentrations well below officially set safe limits, induce severe hormone-dependent mammary, hepatic and kidney disturbances in rats. Similarly, they report disruption of biosynthetic pathways that may result from over expression of the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) transgene from *Agrobacterium sp.* strain CP4 in the maize NK603. The authors suggest that such disruptions may have given rise to comparable pathologies that may be linked to abnormal or unbalanced phenolic acid metabolites or related compounds.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

EFSA received a mandate from DG SANCO on 26/09/2012 requesting to address the following terms of reference (ToR) as a matter of urgency.

(A) Review the scientific publication

(B) Ask any clarification needed to the authors

(C) Advise whether the publication contains new scientific elements that could lead EFSA to reconsider the outcome of its opinion on maize NK603 and its related stacks

(D) Take into consideration the assessment of Member States

(E) Take into consideration the assessment of the German authorities responsible for the evaluation of glyphosate

EFSA'S APPROACH TO ADDRESS THE TERMS OF REFERENCE

Following the publication of Séralini *et al.* (2012a), EFSA set up an internal task force chaired by the Director of Regulated Products (REPRO) and composed of staff scientists with expertise in biostatistics, experimental design, mammalian toxicology, biotechnology, biochemistry, pesticide safety assessments and GMO safety assessments.

EFSA decided to address the terms of reference in phases. The first EFSA Statement (EFSA, 2012) addressed ToR A, B and C solely based on the study information available through the Séralini *et al.* (2012a) publication.

The first Statement published by ESFA (EFSA, 2012) identified a number of issues that required clarification. This Statement was forwarded to Professor Séralini on the 4th October[4], and subsequently again on the 18th October[5] requesting these clarifications.

The task force was mandated to draft this final EFSA Statement which covers all the ToRs and is intended to take into account any information received from the authors, in addition to the assessment activities from the Member States (MSs) and the assessment of the German authorities responsible for the evaluation of glyphosate.

[4] http://www.efsa.europa.eu/en/press/news/121004a.htm
[5] http://www.efsa.europa.eu/en/press/news/121018a.htm

1. Introduction

In EFSA's first Statement (EFSA, 2012), the Séralini *et al.* (2012a) publication was reviewed taking into account good scientific practices such as internationally accepted reporting guidelines (Kilkenny 2010) and internationally agreed study guidelines (e.g. OECD guidelines for testing of chemicals[6]).

This final Statement takes into consideration assessments by MS institutions of Séralini *et al.* (2012a) that had been made available to EFSA and/or published prior to the finalisation of this EFSA Statement, namely Belgium, Denmark, France, Germany, Italy and The Netherlands.

The intention was to take into consideration and include the responses from the authors (i.e. study documentation and procedures followed, including the original study protocol, along with documentation on any planned or unplanned changes to it, the statistical analysis plan, the statistical report/analyses and the final full study report). At the time of publication no such reply from the authors had reached EFSA. A response from Séralini *et al.* (2012b) to criticisms of their publication was however published on-line in the journal Food and Chemical Toxicology on 9th November 2012 which has been taken into account in this final EFSA Statement.

2. Member States Reviews of the Séralini *et al.* (2012a) publication

In this section EFSA provides an overview of the assessments of the MS institutions (hereafter referred to as MSs) of the Séralini *et al.* (2012a) publication. This overview will only focus on the MSs scientific review of the Séralini *et al.* (2012a) publication. All MSs agreed to include their assessments in an Annex to this Final Statement (see Annex 1 for the full text versions and, where available, the respective mandates). Some MS mandates had included additional aspects, which are outside the remit of the EFSA mandate and therefore are not addressed in this Statement.

In line with EFSA's first Statement (EFSA, 2012), an overview of different topics is provided taking into account good scientific practices such as internationally accepted reporting guidelines (Kilkenny 2010). For each topic addressed in EFSA's first Statement (EFSA, 2012), the MSs and EFSA assessment are discussed. Where the MSs addressed scientific aspects other than those raised by EFSA in the first Statement (EFSA, 2012) this is described in section "2.6 Other issues raised by the MSs". The following assessments are considered in this final Statement:

- BE BAC Belgian Biosafety Advisory Council (BAC), 2012. Advice of the Belgian Biosafety Advisory Council on the article by Séralini *et al* 2012 on toxicity of GM maize NK603 (WIV-ISP/41/BAC/2012_0898). Available from: http://www.bio-council.be/bac_advices.html Accessed on 20/11/2012.

- DE Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL), 2012. Stellungnahme des Bundesamtes für Verbraucherschutz und Lebensmittelsicherheit (BVL) zu der Veröffentlichung "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" von Séralini et al. 2012.

    - DE Bundesinstitut für Risikobewertung (BfR), 2012. Feeding study in rats with genetically modified NK603 maize and with a glyphosate containing formulation (Roundup) published by Séralini et al. (2012). BfR-Opinion 037/2012. Available from: http://www.bfr.bund.de/cm/349/feeding-study-in-rats-with-genetically-modified-nk603-maize-and-with-a-glyphosate-containing-formulation-roundup-published-bei-seralini-et-al-2012.pdf

- DK Danish Technical University (DTU), 2012. DTU Fødevareinstituttets vurdering af nyt langtidsstudie med gensplejset majs NK603 og med sprøjtemidlet Roundup. Available from: http://www.dtu.dk/upload/institutter/food/publikationer/2012/vurdering_gmostudieseralini_okt12.pdf

[6] Listed at http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788

- FR ANSES French Agency for Food, Environmental and Occupational Health & Safety (ANSES), 2012. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety concerning an analysis of the study by Séralini *et al.* (2012) "Long term toxicity of a ROUNDUP herbicide and a ROUNDUP-tolerant genetically modified maize". Available from: http://www.anses.fr/Documents/BIOT2012sa0227EN.pdf
- FR HCB High Council For Biotechnology Scientific Committee (HCB), 2012. High Council For Biotechnology Scientific Committee. Opinion on the paper by Séralini *et al.* (Food and Chemical Toxicology, 2012). Available from: http://www.hautconseildesbiotechnologies.fr/IMG/pdf/HCB_scientific_opinion_Seralini_121019.pdf
- IT ISS Istituto Superiore di Sanità (ISS), 2012. National Institute of Health (ISS) assessment on the Gilles-Eric Séralini et al study: "Long term toxicity of Roundup Herbicide and Roundup-tolerant Genetically Modified maize".
    - IT IZSLT Istituto Zooprofilattico Sperimentale delle Regioni Lazio e Toscana (IZSLT), 2012. Technical advice concerning the study conducted by Gilles-Eric Séralini et al. "Long term toxicity of a Round-up herbicide and a Roundup-tolerant genetically modified maize".
- NL NVWA, Nederlandese Voedsel-en Warenautoriteit (NVWA), 2012. Opinion of the director of the Office for Risk Assessment & Research (BuRO) concerning the assessment of the article of Séralini *et al.* (2012). Available from: http://www.vwa.nl/actueel/bestanden/bestand/2202699

Where English translations were not available (DK DTU and DE BVL/BfR) from the originating institution, translations were obtained through the Translation Centre for the Bodies of the European Union.

EFSA was requested by BE BAC not to explicitly refer to any of their findings in this final Statement. In the interest of openness and transparency and in agreement with BE BAC their assessment has been included in Annex 1.

2.1. Study objectives

In its first Statement (EFSA, 2012), EFSA stated that the study objectives are unclear in the Séralini *et al.* (2012a) publication. A lack of clarity in the study objectives was also mentioned by FR HCB and IT ISS & IZSLT.

2.2. Study Design

EFSA noted in its first Statement (EFSA, 2012) that Séralini *et al.* (2012a) did not follow the internationally accepted protocols for sub-chronic, chronic toxicity and carcinogenicity studies; furthermore, the strain of rats chosen is known to be prone to development of tumours over their life. The study design includes only one control group which is not suitable to serve as control for all the treatment groups. Further, it was noted that for carcinogenicity testing 10 rats per treatment group per sex is not sufficient. Apparently, no measures were taken to reduce the risk of bias such as blinding.

Overall, EFSA and MS institutions raised the same issues. Member States DE BVL/BfR, DK DTU, FR ANSES, FR HCB, IT ISS & IZSLT and NL NVWA criticised the use of such a small number of rats to draw conclusions on tumour incidence especially on a strain of rats that is highly prone to spontaneously develop tumours in their lifespan. The use of one control group for nine treated groups was considered to be inadequate by DK DTU, FR ANSES, FR HCB, IT ISS & IZSLT and NL NVWA.

2.3. Feed and Treatment Formulation

EFSA noted in its first Statement (EFSA, 2012) that details on the feed composition, the storage conditions and the presence of harmful substances (such as mycotoxins) or chemical contaminants (such as residues from glyphosate or other pesticides) were not provided. In addition, the actual exposure to GMO and/or Roundup® GT Plus (R) could not be evaluated since no food and water intakes were reported for the various treatment groups.

Member States also highlighted the lack of detail on the feed composition (DE BVL/BfR, DK DTU, FR HCB, IT ISS & IZSLT, NL NVWA), the lack of information on the presence of contaminants (FR HCB, IT ISS & IZSLT), specifically mycotoxins (DE BVL, DK DTU, IT ISS & IZSLT) and the lack of information on the actual intake of food and water (DE BVL/BfR, FR ANSES, FR HCB, NL NVWA).

Member State DE BVL/BfR highlighted that the daily applied doses of Roundup have not been determined. Member States DE BVL/BfR, IT ISS & IZSLT and NL NVWA also mentioned that further details on the composition of the applied formulations are lacking.

2.4. Statistical Methods

In its Statement (EFSA, 2012) EFSA reported that the statistical methods lacked key information, in particular, summary statistics, the unbiased treatment effect from an appropriate model and a summary of drop outs. In addition, the statistical methods used to analyse the biochemical parameters were considered to be unconventional and it was not clear if these were pre-planned.

Overall, EFSA and MS institutions raised the same issues. Member States DE BVL/BfR, FR ANSES, FR HCB, NL NVWA in addition raised the issue of the fact that multiplicity was not shown to be taken into account.

2.5. Endpoint Reporting

EFSA noted in its first Statement (EFSA, 2012) that an incomplete set of measurement endpoints was reported compared to the set of endpoints collected as reported in Séralini *et al.* (2012a). For example, the reporting of biochemical parameters, tumours and other clinical observations is incomplete.

Member States also generally highlighted the incomplete, fragmentary and selective presentation of data (DE BVL/BfR, FR ANSES, FR HCB, NL NVWA).

The attention of several MSs focused on the assessment of the tumours occurring in the experimental animals. The presentation of the data was considered by MSs DE BVL/BfR, DK DTU, FR ANSES, FR HCB, IT ISS & IZSLT and NL NVWA as being unclear. In particular the following aspects were considered to be unclear/lacking: supporting data (DE BVL/BfR), characterisation from a differential diagnostic standpoint and assessing the grade of severity (DE BVL/BfR), definitions of the groups of pathologies (DK DTU and FR ANSES, FR HCB) and histopathological characterisation of the neoplasia/animal (NL NVWA). The use of non-conventional nomenclature was addressed (FR HCB).

2.6. Other issues raised by Member States

In their Statements/opinions some MSs reported on aspects that were not mentioned in the first EFSA Statement. Those issues are reflected below.

2.6.1. Study design: choice of dose levels

Member States DE BVL/BfR and FR ANSES reflected on the lowest dose of Roundup GT Plus tested in the study and pointed out that the likelihood of finding the tested quantities in groundwater/drinking water is negligible. In addition the second dose level tested is not representative of the level to which European consumers are exposed which is far lower. The third dose level of glyphosate tested is in

line with the doses applied in practice on the field. Member State DE BVL/BfR pointed out that workers are exposed to lower dose levels and only in the short term through skin and inhalation.

2.6.2. Statistical analysis

Member States (DE BVL/BfR, FR ANSES and FR HCB) conducted statistical analyses on the tumour and mortality data that could be derived from the Séralini *et al.* (2012a) publication. They concluded that the results of their independent analyses did not support the conclusions drawn by Séralini *et al.* 2012a).

2.6.3. Interpretation of results

Member State DE BVL/BfR reported that glyphosate has been comprehensively tested and no carcinogenic effect was observed (see Section 3). The absence of carcinogenic potential of glyphosate was also mentioned by MS NL NVWA.

Member States FR HCB and NL NVWA discussed the absence of a comparison of the study results with historical control data for the chosen strain of rats. Member states DE BVL/BfR, DK DTU and FR HCB reported that mortality and tumour incidence data fall within the historical control data for the Sprague-Dawley strain of rats.

Member State DK DTU highlighted the lack of any dose-response relationship for the parameters reported as well as the "lack of a balanced scientific discussion". Member State FR HCB, questioned the authors' interpretation of biochemical parameters as indicators of kidney and liver failure. FR ANSES and FR HCB noted that the reported biochemical data do not establish the existence of endocrine-disrupting effects, and that the mechanistic assumptions related to modification of secondary metabolism are not supported by the results. Member States NL NVWA and DE BVL/BfR questioned the proposed endocrine mode of action for occurrence of tumours.

2.7. Member States' conclusions

Member States DE BVL/BfR, DK DTU, FR-ANSES, FR HCB, IT ISS & IZSLT, NL NVWA highlighted that the data presented in Séralini *et al.* (2012a) do not support the conclusions drawn by the authors.

Member States DE BVL/BfR, DK DTU, FR ANSES, NL NVWA stated that the publication by Séralini *et al.* (2012) does not provide information that would indicate the necessity to reopen the risk assessment of NK603 and glyphosate while MSs FR HCB and IT ISS & IZSLT did not discuss this specific issue.

3. German authorities evaluation of glyphosate

Currently, the rapporteur MS Germany is in the process of carrying out an assessment in the context of the approval renewal of glyphosate based on Regulation (EU) No 1141/2010.

The German authority (DE BVL/BfR) reviewed the Séralini *et al.* (2012a) publication and concludes with respect to glyphosate that:

> *"Glyphosate has been comprehensively tested. Numerous long-term studies in rats and mice showed no indications of either a carcinogenic potential or increased mortality or any effects on the endocrine system [...]. While the performance of a long-term study in the case of the glyphosate containing formulation is in principle appreciated, it needs to be mentioned that the published study shows significant shortcomings in the study design and further shortcomings due to incomplete and unclear presentation of the collected data. Furthermore, the main statements were not supported by the experimental data. [...] it is therefore impossible to comprehend the main conclusions of the authors."*

4. Séralini *et al.* (2012b): Answers to critics

On the 9th November 2012 an accepted manuscript titled : "Answers to critics: why there is a long term toxicity due to NK603 Roundup tolerant genetically modified maize and to a Roundup herbicide" by Séralini *et al.* (2012b) has been made available on-line in which the authors provide further information about their study. In this publication no reference is made to MS assessments nor to EFSA's first Statement (EFSA, 2012).

Below, Séralini *et al.* (2012b) is discussed in the light of all the open issues identified in the first EFSA Statement.

4.1. Study Objectives

Séralini *et al.* (2012b) state that they replicated and improved the study by Hammond *et al.* (2004) and "in order to know if the statistical findings (in 90 days) were biologically relevant or not on the long term".

This is not reflected in the analysis and reporting in Séralini *et al.* (2012a).

4.2. Study Design

Séralini *et al.* (2012b) acknowledge that the study design is not suitable to assess long term carcinogenicity. The authors mention that the assessment of long term carcinogenicity needs to follow OECD 453 guideline with at least 50 rats per group. The authors clarify that all treatment groups contained 33% maize and give details of blinding that they implemented for some aspects of their study.

It is still unclear if there was a sample size (power) analysis conducted prior to the start of the study.

4.3. Feed and Treatment Formulation

Séralini *et al.* (2012b) state that diets were nutritionally "equilibrated" from substantially equivalent maize, and that mycotoxins were below recommended limits for food/feed. Furthermore, they refer to an assessment of diet composition, storage and diet contaminants by approved laboratories.

The feed and water consumption, and the amount of glyphosate and other used pesticides residues were however not provided.

4.4. Statistical Methods

Séralini *et al.* (2012b) do not address any of the open issues for the statistical methods as raised in EFSA's first Statement (EFSA 2012). They state that statistical methods for the analysis of tumours endpoints cannot allow to conclude on a mortality linked or not to the treatment groups.

EFSA notes that this is inconsistent with the conclusions with respect to the tumours and mortality as drawn by Séralini *et al.* (2012a).

4.5. Endpoint Reporting

Séralini *et al.* (2012b) mention that a scientific publication is limited with respect to space and can therefore only show the data necessary to understand and discuss the conclusions, and refer to future publications that will provide more data.

It is unclear how the authors have selected the endpoints for reporting and why, for reported endpoints, the complete analysis was not provided (e.g. biochemical data were reported only for selected treatment groups, and only at one time point).

CONCLUSIONS

The review of MS and EFSA assessments revealed an overall agreement. Séralini *et al.* (2012b) in their answer to critics provided a limited amount of relevant additional information which does not address the majority of the open issues raised in the first EFSA Statement (EFSA 2012). In particular, issues such as statistical methods and endpoint reporting remain unresolved. Moreover, with regard to long term carcinogenicity and mortality, Séralini *et al.* (2012b) acknowledge that the sample size is too small to draw conclusions.

Taking all of the above into account, EFSA reaches similar conclusions, for its final review of the Séralini *et al.* (2012a) publication as in its first Statement (EFSA 2012):

> Taking into consideration Member State assessments, EFSA notes that the study as described in Séralini *et al.* (2012a, 2012b) does not allow to give weight to the results and conclusions as published.
>
> Conclusions cannot be drawn on the difference in tumour incidence between the treatment groups on the basis of the design, the analysis and the results as reported in the Séralini *et al.* (2012a, 2012b) publications. In particular, Séralini *et al.* (2012a, 2012b) draw conclusions on the incidence of tumours based on 10 rats per treatment per sex. This falls short of the 50 rats per treatment per sex as recommended in the relevant international guidelines on carcinogenicity testing (i.e. OECD 451 and OECD 453). Given the spontaneous occurrence of tumours in Sprague-Dawley rats, the low number of rats reported in the Séralini *et al.* (2012a, 2012b) publications is insufficient to distinguish between specific treatment effects and chance occurrences of tumours in rats.
>
> Considering that the study as reported in the Séralini *et al.* (2012a, 2012b) publications is inadequately designed, analysed and reported and taking into consideration MS assessments, EFSA finds that it is of insufficient scientific quality for safety assessments. Therefore, EFSA concludes that the Séralini *et al.* study as reported in their publications (2012a, 2012b) does not impact the ongoing re-evaluation of glyphosate. Based on the currently available evidence EFSA does not see a need to reopen the existing safety evaluation of maize NK603 and its related stacks.

REFERENCES

Gilles-Eric Séralini, Emilie Clair, Robin Mesnage, Steeve Gress, Nicolas Defarge, Manuela Malatesta, Didier Hennequin, Joël Spiroux de Vendômois (2012a) Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food and Chemical Toxicology http://dx.doi.org/10.1016/j.fct.2012.08.005 – Pre-release version dated 19th September 2012.

Gilles-Eric Séralini, Robin Mesnage, Nicolas Defarge, Steeve Gress, Didier Hennequin, Emilie Clair, Manuela Malatesta, Joël Spiroux de Vendômois (2012b), Answers to critics: Why there is a long term toxicity due to NK603 Roundup-tolerant genetically modified maize and to a Roundup herbicide, Food and Chemical Toxicology, Available online 9 November 2012, http://dx.doi.org/10.1016/j.fct.2012.11.007

EFSA (European Food Safety Authority), 2012. Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA Journal 2012;10(10):2910 [9 pp.]. doi:10.2903/j.efsa.2012.2910

Hammond, B., Dudek, R., Lemen, J., Nemeth, M., 2004. Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food Chem. Toxicol. 42, 1003–1014.

Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. PLoS Biol 8(6): e1000412. doi:10.1371/journal.pbio.1000412.

ANNEX 1