













Not the first lawsuit:

Storions		IN THE COURT OF COMMON PLEAS OF CIVIL ACT KEITH DEANGELIS VS. E.I. DU PONT DE NEMOURS & COMPANY, INC. and MONSANTO COMPANY and DOW CHEMICAL COMPANY and ELANCO PRODUCTS COMPANY DIVISION OF ELI LILLY COMPANY	F MONTGOMERY COUNTY, PENNSYLVANIA TION - LAW No. 95-01922 : : : :	
TO: Overve are Address of Desindang		COMP	LAINT	
MONSANTO COMPANY 800 N. Lindbergh Blvd. 8t. Louis, MO 800 N. Louis, MO	Fuller Avenue		anna an	
Helena, MT 59601		SUPERIOR COURT OF	F THE STATE OF CALIFORNIA	
UNITED STATES DISTRICT COURT SOUTHERN DISTRICT OF CALIFORNIA			FOR THE COUNTY OF SAN FRANCISCO	
MANUEL RICHARD GIGLIO, Plaintiff ONSANTO COMPANY and JOHN DOES 1-50. Civil Action COMPLA JURY TR		STEVEN BIDEGAIN and YVETTE BIDEGAIN, Plaintiffs,	CASE NO. C. 05445155 COMPLAINT FOR TOXIC INJURIES ASSERTING CAUSES OF ACTION FOR:	
UNITED STATES DISTRICT COUDT		UNITED ST	TATES DISTRICT COURT	
UNITED STATES DISTRICT COURT EASTERN DISTRICT OF NEW YORK		CENTRAL DISTRICT OF CALIFORNIA		
JUDI FITZGERALD, Plaintiff, v. MONSANTO COMPANY, Defendant.	COMPLAINT Civil Action No. JURY TRIAL DEMANDED	CHRISTINE SHEPPARD Plaintiff, vs. MONSANTO COMPANY, Defendants.	Case No.: 2:15-CV-8632 JURY TRIAL DEMANDED	

How the trial works:

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

























Dr. Donna Farmer Product Protection Lead



Dr. Daniel Goldstein Medical Sciences and Outreach

Dr. William Heydens Product Safety Assessment Strategy Lead



































Dr. Mark Martens Toxicology Director (former)



Dr. David Saltmiras Toxicology Manager



Dr. John Acquavella Epidemiologist (former)





























Daniel Jenkins Manager for Regulatory Affairs





David Heering Strategy, Compliance, Operations Lead































Steve Gould National Accounts Manager (includes California)















Opening Statement Roadmap:

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

Opening Statement Roadmap:

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





ACTIVE INGREDIENT:	
*Glvphosate, N-(phosphonomethyl)glycine,	
in the form of its potassium salt	.7%
OTHER INGREDIENTS:	.3%
100).0%

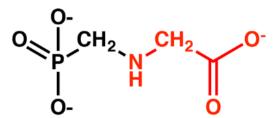


ACTIVE INGREDIENT:
*Glyphosate, N-(phosphonomethyl)glycine,
in the form of its isopropylamine salt
OTHER INGREDIENTS (including surfactant):
100.0%

Glyphosate

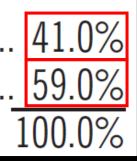


glyphosate



Surfactant

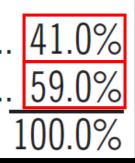
ACTIVE INGREDIENT: *Glyphosate, N-(phosphonomethyl)glycine, in the form of its isopropylamine salt...... OTHER INGREDIENTS (including surfactant): ...



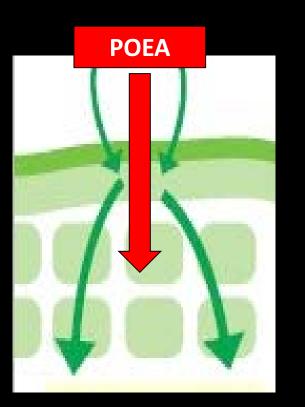
<u>POlyE</u>thoxylated tallow <u>A</u>mine

Surfactant

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

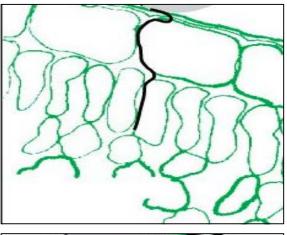


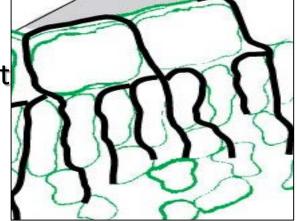




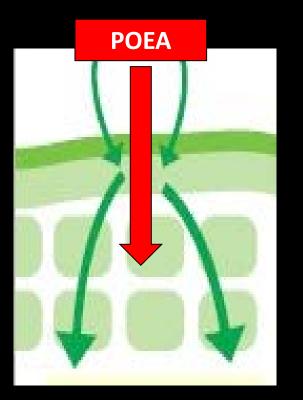
Without Surfactant

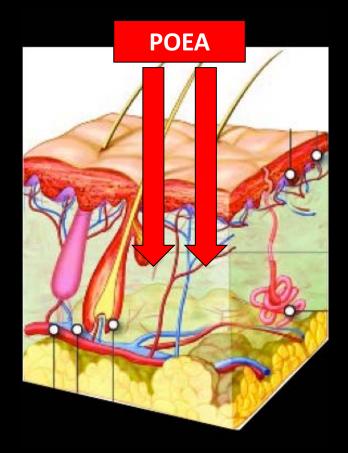
With Surfactant





Penetrates the surface of a leaf, but also human skin





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

Ashley,

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

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

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

Hi Donna/Bill,

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

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







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

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

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

What do you think?



From: HEYDENS, WILLIAM F [AG/1000] Sent: Thursday, August 06, 2015 9:55 AM

To: 'Ashley Roberts Intertek'; FARMER, DONNA R [AG/1000]

Subject: RE: Keith



Ashley,

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

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

Original	Message

From: Ashley Roberts Intertek

@intertek.com]

Sent: Thursday, August 06, 2015 09:47 AM Central Standard Time To: FARMER, DONNA R [AG/1000]; HEYDENS, WILLIAM F [AG/1000] Subject: Keith



Hi Donna/Bill,



ACTIVE INGREDIENT:	
*Glvphosate, N-(phosphonomethyl)glycine,	
in the form of its potassium salt	.7%
OTHER INGREDIENTS:	.3%
100).0%



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

Opening Statement Roadmap:

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

Opening Statement Roadmap:

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

Three Pillars of Cancer Science

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

Plaintiff's Experts

Christopher Portier, PhD.





THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

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

Plaintiff's Experts

Alfred Neugut, M.D., PhD.



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



Three Pillars of Cancer Science

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

2. Can Roundup cause cancer?

Three Pillars of Cancer Science

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

2. Can Roundup cause cancer?

1. Animal Carcinogenicity Studies





Glyphosate only

Long term – typically, 2 years

Control	Low Dose	Mid Dose	High Dose

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

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

Admission No. 7 Monsanto admits that it did not conduct any further long-term carcinogenicity animal studies after 1991.

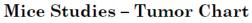
- Significant increases in tumors
- Replication
- Dose response
- Cross-species
- Rare tumors

1. Animal Carcinogenicity Studies

Mice Studies - Tumor Chart

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





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



1. Animal Carcinogenicity Studies

Mice Studies - Tumor Chart

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



1. Animal Carcinogenicity Studies

Mice Studies - Tumor Chart

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



1. Animal Carcinogenicity Studies



George Study (2010)

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



Evidence that glyphosate is a tumor promoter

1. Animal Carcinogenicity Studies



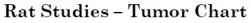


Glyphosate only

Long term – typically, 2 years

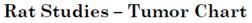
Control	Low Dose	Mid Dose	High Dose

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



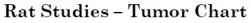
Lankas (1981)	Stout & Ruecker (1990)	Atkinson (1993)	Enemoto (1997)	Suresh (1996)	Brammer (2001)	Wood (2009)
Testicular interstitial cell tumors	Thyroid C-Cell carcinomas or adenomas	Thyroid follicular carcinomas or adenomas	Kidney carcinomas or adenomas		Hepatocellular carcinomas or adenomas	Skin kera-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





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





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



1. Animal Carcinogenicity Studies



nat studie	s = 1 union x					
Lankas (1981)	Stout & Ruecker (1990)	Atkinson (1993)	Enemoto (1997)	Suresh (1996)	Brammer (2001)	Wood (2009)
Testicular interstitial cell tumors	Thyroid C-Cell carcinomas or adenomas	Thyroid follicular carcinomas or adenomas	Kidney carcinomas or adenomas		Hepatocellular carcinomas or adenomas	Skin kera- toacanthoma
Thyroid C-Cell carcinomas or adenomas	Pancreatic islet cell tumors	Skin kera- toacanthoma	Skin kera- toacanthoma			Mammary gland carcinomas or adenomas
Pancreatic islet cell tumors	Hepatocellular carcinomas or adenomas		Basal cell tumors			Pituitary adenomas
	Adrenal cortical carcinomas					

Rat Studies – Tumor Chart

Skin keratoacanthoma

Three Pillars of Cancer Science

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

Three Pillars of Cancer Science

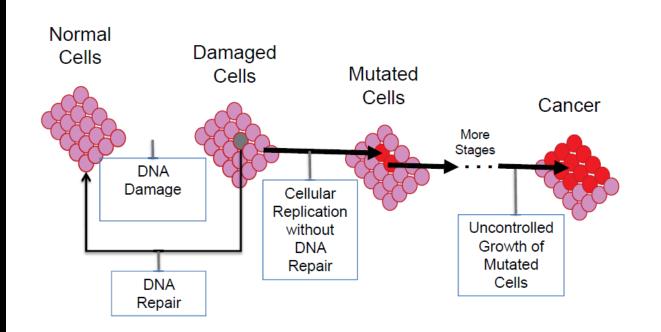
- 1. Animal Carcinogenicity Studies
- 2. Mechanistic Data
- 3. Epidemiology



2. Mechanistic Data

Mechanistic Data:

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



2. Mechanistic Data

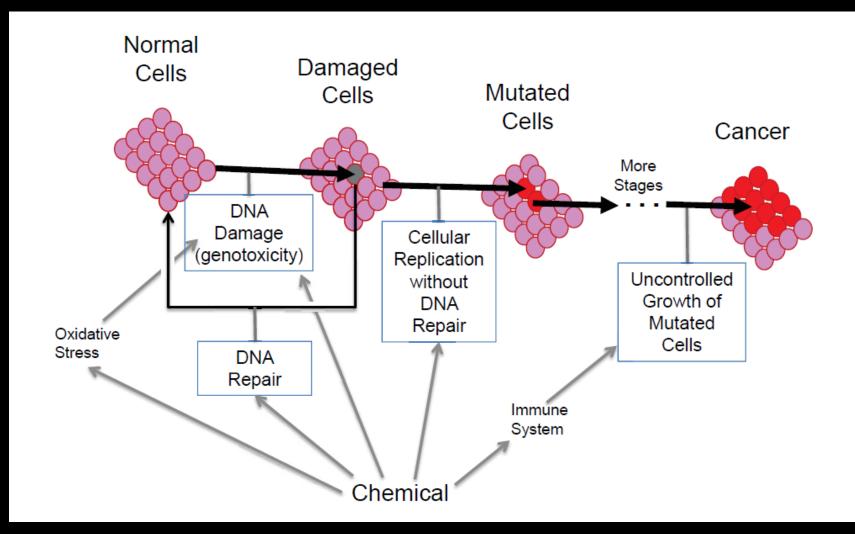
Genotoxicity:

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

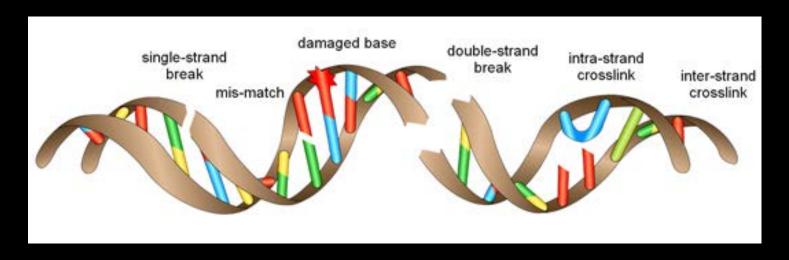
Oxidative Stress:

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

2. Mechanistic Data



2. Mechanistic Data



Different methods of testing DNA damage Over 100 different studies

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

In vivo: In a living organism.

In vitro: In glass, as in a test tube.

2. Mechanistic Data

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

Jan 1992

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

Mature Scarol, 20 (2010) 21-28 d 1990 Elevier Science Publishes B.V. All rights second (200-1231/93/9348)

MORNEY

Genotoxicity testing of the herbicide Roundup and its active ingredient glyphoante isopropylamine using the mouse bone marrow micronucleus test, Salmonella mutagenicity test, and Allium anaphase-telophase test

J. Rank, A.-G. Jennen, B. Skow, L.H. Pedernen and K. Jennen Spanner framman framming on Solid Index, Statist Banna, Danuel Bannard Statistics PTC: Danuel Streamer 1920 Danuel Streamer 1920

Kennels: Haustap, Opplevas lagrappinsies, Generating, Miccassina, Allon, Solomath

Summery

The generation protocol of the broken boundary and an active space, applyond recomputations are similared in two different straps. No objective effects were boundary to be the straps of the straps were broken as the strap objects are broken as the broken as the strap objects are broken as the broken as the strap objects are broken as the broken as the strap objects are broken as the broke

Roundap is a relatively new horticide first nucleared in the USA in 20%. The active agent is tracked as in globologic OS/photphonometric lycinel, which is considered almost numerical numeric (LL) _{pp} , rat coll = 4.2 g/L2 (Atkinon, 193). The horiboide Roundap is commonly used anglobales. Formation and avery the spin- sterily set of the set of the set of the spin- sterily set of the set of the set of the set of the spin- sterily set of the set of	the factor, when utility planes with revisitance abspherite are introduced on the movies. Spe- ing with Rouckup or glyphorano-aristant on with make a possible to efficience all other waterd planes on the field. The generativity of Rouchup and ghyphoi has been investigated in different assure
raid and is expected to be used even more in	1972. Vigfusion and Vyse, 1980. Li and Le 2988. Nagi and Gopolan, 1991; Dr Marco et a 1992. The neuda from these studies are could as could be studies and could be studies.
sempendance Anto Nack, Experiment of Environment, industing and food Mades, London University, Box 201, and applied in the Content of Contents, Box 201,	ing, and note of the investigators have be both Boundup and glpphcaste in the same an In the present study we have examined

And short or added by the state of the s

An other is a strategy of the str

W Yang, Ching, and Li, Xi, Conduct (PR): Merganizes was been all because control in the control of the control of control performance in the control of the control of control performance in the control performance of parameters. In the control performance of the control of control performance in the control performance of performance in the control performance of the control of performance in the control performance of the control performance in the control performance of the period of the control performance of the control performance of the period of the control performance of the period of the control period of the control period of the control period of the period of the control period of



Jan 1992

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

J Agriz, Fool Own	1987, 45, 1987-1942	ESST Organisatio System
Genotoxic Activity of Glyphosate a Roundap	and Its Technical Formulation	Table 2. Norm
Clauta Balagnesi, * Stefania Sonatti, Pa-	do Degan, Eliona Gallierani, Marro Prikan. 1911, anii Anarely Abhendaralish	feel or
Centre Nameale per le Studie des Tumert di Orge	ne Andrestale, Stitute Naronae per la Elevita na an 18, 18132 Geneva, Daly	E nationation EA1102, DA EA1103 2, 1910 2, 1910
anatus actio to plasts. The prototic patential autilable in the open literature reveal a weak at the formulated connectual conduct. Nanadon, at	ettros harbicido arting on the specthenis of armanitic of this horbicide has been scatted, the results porty of the technical formulations. In this study, of this article agost, gripplenate, were trained in the	patienteita Exception Exception Suppose Suppo
statute battery of analysis for the induction of TMA million. Syndro CEU million water treated intruportition	domage and chromosomal offsets in rise and in welly with test solutions, and the DNA damage	E
was realizated by alkalitat shattan exhibition and h	by the property of the property of the second secon	£. out W7
all title at home makelow of many an energometric fire	quercy and courts in human prophecyle outcare a DNA single-arrival breaks and 8 COMC and a	Channel house
	new-observed with both substances in one and in	D. metangara
Keywords: Poststate; in one protostate; in a	tregeneoustry SCI; estimation test alkalate	
etution; EPLA analytice demage		and have reader
NUMERCUE	The property of the property o	ne of model in the second seco
ortically bladded (FAG) 2016. No address of these size representations in radius there is not non-address on representations in radius buildnesses. TRUE. Children and the second size of the start of the second time. California Experiments of The second Type in Advances Two-california Experiments of The second Type in Advances in Second Industry and 1911 ED000215. Sec 303:010.2002/ED.	MATERIALS AND METRICS Creating of the start part of phonon CAM Regar- perturbation of the start phonon CAM Regar- Regard has been been been been been been been Regard based based based based based based based balance. Main: Provide the start of the start phonon of the SH Regard based based based based based based based balance based. Based base	dent. A low of the second seco
ik roard (inkplanar 30 012 1006215; fax 30 515 55573).	In First SCE: Hyperinted senses bland samples abusined level two buildy Broakt deart. While blan 8 100 America Chemica Yoony	

the second s				NUR DA		
fact of generations.	-	interpretation (without sugression surfaceaute allocateaute	with respected	444	-
		Gani Mate	fields.			
S. Inputtion-Plane T.M.M. TAXIM, EALL/25, TAXIDIT, EX11/28, TAXIDIT, EX11/28		ghyshocata port-questilizet)			194	Morrow, et al. (1982)
A DEGREGATION THE TAKE	INCOME.	strobulate but specified		- to have	20	Witteman and Nacar (1962)
R replementary THM, TANK, SAIDE, TAIDEL, SAIDE, TAIDEL, SAIDER,	Annal State	(holocate (MPI)			2506	Thired Long (2580)
2. Optimizant 1239	anima ha	(Investigation)			100	Name of all COVER-
R. optimeurous TALIN	Projulate organization	Which water DPts Microsofter			340	Easth et al. (1987).
E out WIT in		altufaceate sifts			2000	This one of all (1982)
£. out: NPT	Building .	and questions			700	Is and Long dillets
	atomic and a					
Classes have overy sills	And the owner of the owner of the owner	distances of the			22.1	\$1.1ml long (1188)
D.meteogener	SVR CARLINE ENCHANCE Instrume	Nuclear per sected				Capital and Noigh 028-2
		-Chrystewoodal 5	Automatical Con-			
A. 1954	chromosomel			15	1440	Rook et al. (1963)
ent hore marrow (in 1946)	phone allows	Bilyshease 1995 Bilyshease (SPh)			1000	Li and Long (1986)
Ineman pregnanal bland.	36.2	illuster (at specified)		10	25496	Vigiania and Type (1980)
home propheral blood	801	Backler (http://www.in.Fill		9	300	nym byfan.
Instangerginend tited	307	photosan 199.954			1000	tips below
Y fabricost tipe.	MATERIA Part	Interior Pres			13007	To Marcaral.
ment per nerme (a stel	And Print Print	ghotourr per spectral		3	396	Freek et al. (1983).
cooke here entropy in a set	BETTON INS	Stratkey Studies and			209	Room of all CONTR.
taking joine structure 54 march	Bill and	those and		8	104	apprication.
INCOMPANY AND AND AND AND	MATERIAL PART	Hornbar Witho			330	oper balles.
6. submits	10.000	10% Inc.	-		14000	As and Long times.
n autorphy	125	2000a	12.1		100	To and Long (1988)
		009102				
panior (de unio)	Segle Crist	Wathout a grant wat			300	and below
mana (in cond	TNA Ungle strend	Stareiter Wystendu 20.8%			370	oper latter.
rainor (pr ninit	B-CH-IBC	grodinate	+*		300	this paper
Income Life office	a chiat	Bits Mul Decembra	1.		270	this pager
*+ publics septime it a reflective dose "Expressed on ideary orde	nat taskal 1 for a raje of sol, 17ps	ighphenets 20.81) rise tosts, agend, and dire creative have bee	ini tonis, Aug a difedent in	by at his 1212. Date calls. "Po	kranst efter	um dom, 2020, bight Same break obtained

or waits use of this hertmake for aga-

We thank Patrena Laps, Garmen Lapergelo

ity testing of the herbicide Roandap and its active ingredient e isopropylamine using the mouse bone marrow micronocleus onella mutagenicity test, and Allium anaphase-telophase test

J. Rank, A.-G. Jensen, B. Skov, L.H. Pederson and K. Jensen (Resided Flockwhor 192) Robies assisted (Misengler 192)

Roundary is a relatively new hashielde first nederstel in the USA in 1794. The notive agains in incoding in globalous (Argonykonomettel) by the sensitive of a sensitive of the sensitive number (LD ₂), at cost of 4.0 graph (Arkinov, HE). The herbicide Roundary is consistently used in activitizes. Formus and neuronism all over the reliabant for the sensitive for more the reliabant.	the future, when utility plans with resistance to physicase are introduced on the matrix. Spear- ing with Rescaled on algobarceristance copy will make it possible to elisionet all other on- search planses of the field. The geneticides of Rescalage and physicase from here to resolutions of algobarts assess fields: 1973, Vallance and Vars. 1980, 14 and Leng.
	2988. Naui and Gopelan, 1981; De Marco et al., 1982). The results less these studies are coeffici-
errapordence: Jone Karls, Expositence of Environment, infesting and Social Bades, Exatility Dimensity, Box 261, 57 (19) Rockiek, Donarch,	ing, and aone of the investigators have tested both Boundup and glpphcaste in the same many. In the general study we have examined the

Mar 1997



Bolognesi study shows that Roundup formulation causes genetic damage in human cells.

Plaintiff Exhibit 0852

Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup

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

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

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

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

INTRODUCTION

Roundup, an extremely effective nonselective postemergence herbicide, is a combination of an active ingredient, the isopropylamine salt of glyphosate, and a surface-active agent that enhances the spreading of 1985), but Roundup has been identified as a cau irritation phenomenon or contact dermatitis, repo in occupationally exposed agricultural workers (1 1986).

The formulated commercial product, Roundup, se

Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup

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

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

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

vitro. A weak increment of the genotoxic activity was evident using the technical formulation.

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

INTRODUCTION

Roundup, an extremely effective nonselective postemergence herbicide, is a combination of an active ingredient, the isopropylamine salt of glyphosate, and a surface-active agent that enhances the spreading of 1985), but Roundup has been identified as a cau irritation phenomenon or contact dermatitis, repo in occupationally exposed agricultural workers (1 1986).

The formulated commercial product, Roundup, se

Jan 1992

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

J April: Pool Own	1987, 45, 1987-1942	687	Orginaute Serversity	
Genotoxic Activity of Glyphosate a	and Its Technical Formulation		Table 2. Summer of EeuD	to an Ear
Roundap				-
Claudia Bolognesi," Stefania Sonatti, Pas Enterta Rahhusi, Pasia Rossi			ini station.	
Centre Nammale per le Studie des Europe Canyo, Large Rounnis Ber	ar Andrewiale, Mittade Narionale per la Riceria nal sti 10, 10132 Genero, Daly		 Spectroscovicus Table, TABLE, Ex11/25, TAURE, Ex11/26, TAURE, Ex11/28 	1
		24.0	A DESERVICE THE TARE	-
Cipphenate (Nphosphereonethylgistice) is an effe	ctive herbicide acting us the synthesis of arranatic of this beclinitle has been scalard, the results		R replaced as THM, TABM, SAUDI, DAUDEL, TAUDE	-
available to the open literature reveal a weak ac-	porty of the technical fermidation. In this study,		2. Optime/sam1139	-
the Britishted conservation product, Biasidogs, an name hortery of analysis for the industries of DNA.	al its active agent, glyphesate, wore tested in the		8. optimizana TX180	1.00
name. Swato CD1 miles were treated astroperitors	colly with test solutiones, and the DNA damage		E with MPT law	-
was evaluated by alkaline statum ochnique and b in lover and kidney. The chromosomal damage of t	by drony decay guarantee (B-CE-GC) quantification		£. out/1072	-
all vivo as how makeney of mary as meritonacies from	purry and in ratio in hamail temphonyle manare		Danna hanathe every sills	-
as SCE frequency: A DNA damaging activity a significant increase in the processial alterations in	a DNA single-strand brasks and 8 CBBG and a			
ration. A small increment of this growtings activity	r was evident using the belies of formulation		ty understands.	PD 1
Keywords: Protester, in other protestative, in or evenes, 271A conductor director	trageneously SCE astronation test, alkalaw		A. 1994	chrome
			and here reasons (in cost)	show
EDUCTION	1985, but Routidap has been identified as a case irritation phenomenon or contact demantitis, rep-	ow of	Inexat preptanal blast	447
and an extremely effective number the peak- perce herbication is a combination of an extre-	in occupationally exposed agricultural workers (TAD,	intrafes bounds pergheral blood atrates	
effect, the inspropriations sait of glophosate and rface-active agent thus exhauses the spreading of cy dropiets when they contact inlage. Glophesate 1976, N-dependencembringlations, is subscribely	The formulated conserved product, Reserving, who be nather more took than the parent comport chiratal reports citing cases of acute polyaning too	sund. Buate	Inaman pergitienal titled attractory T. Data (not tape)	
a to plaints and celulively montrate to uniously. The	that the long could be caveldored the target org Riservice trainity. The pulmovery testicity of Rose		insurines never deviati	
handom of action of this heybnide is a competitive lation of the endpersoryl shikimute plenplant sen- er (ESP spectrose), an ensyster about to antiside.	has been demonstrated in min, ofter a direct tra- administration (Martinez et al., 1990; Martinez	thead to be a set of the set of t		-
ndlad to the synthesis of acomatic antitic acids in-	strown, 1997. This effect has been atombated to wa active ingredients: Canada et al. 1999; prevents	etice -	taxent para thereas for and	
ets (Acerbaim et al., 1980; Hollander and Acerbain, D. Growthard and Advance, 1985; Jowarski, 1972). hydrosete Ran teen reported to have a low acute	a study on the interactive between glyphonate worker-sents severabelises antagenistic affect (halo a 1989).	and .	Incorporation and one and	
Bty Le Billerent antiesd species with an oral LD _{ab}	The property of globlogate and my tech	interest and a second sec	S. admin	10.0
ping from 0.7 to 11.0 g/kg of body weight (Worthnig Harws, 1994, 1216, 1082, FAG, 1086). The results	formulations has been studied to different test syst The results disideed inducer or geneticity attrict	Induits.	and appeticipies	. 1.1
monther of tests on a variety of species have shown i ghydowate him, at the range of concontration mally used in agriculture, nu chronic er neuritoxic	glyphosate and a week effort for technical formula The aim of our kneet/gaton in the evaluation or grounous, peterstal of Han herbickle, writing	disor.	paraisian (also solitant)	sega
rts (Atkiroen, 1983). Sysse: lending studies did out exidence a cartini- ic activity of this herhitide in rate and dogs (FAC).	Minuthap and ghyphesate in the same battery of an Fire data have been reported on the DNA-dama	natria.	mean (in could	-
0, IPCS, 1994). In three soulies the active argenda-	artiety of this herbacide in otos. We have really the DNA damage to trents of single-strand brocks	satud	encode (ar nind)	2-0
glypfamate-documentratisd an organizegostificity for the sary system, industring in technolog in prostolal mead do howepfilling-toppertringity and in hyperplastic of the	8 Systemy descriptionerate (3 (343C). MATTERALS AND METHODS	0.0000	texione (de útroit	*0
ary Mabler (FAO, 2008), is adverse effects on reproduction or listal develop-			4.4 pentrus -, septros 8.	rat Inclu
 adverse ethers on reproduction or total develop- st have been observed in these generation studies nots and in a developmental lockity study on calibits kiewen, 128(1). 	Connicals. Analytical grade gluphonair CAMRogen 1971-02-00 was anarbaned from Securit Italiana Chi- Bana Judy Pority declared by the producer max 9 Randhag formulate (2) CP gluphonatol was from Mor-	denicit. Historie	perfective dose "Experiend on Addary orde	
arren, 1983). Syptemate in a mild skin and eye irritant (Mathach, 6. Calificate Department of Tool and Agriculture.	Indiana, Milas, Jacky, Medioj mechanicallynamic (MDE). Registery, Nr. 88, 19, 19 and hear lightering (Denoid Car. 86, Nr. 19, 27 H wave databased from Sagan (Denoid Car. 86, Nr. 19, 27 H wave databased from Sagan (Denoid Car. 86, MC). 47, 55 Enginetry, Nr. www.preschildrich.the and and the Same Same Same Same Same Same Same Same	(CAS) ganny meta	The tagter activity of tech ing time oral generous due tal systems suggests a role	the stars
*Author to whom consequences about the ad- road (inkplaces 20.012.000212; fax 20.010.055572).	20 Vitro SCE. Hoper inited senses blast samples, character from the baselity fitnesh shares. While these	- Annota	ant/or columnularies in the the active ingentation. Considering the web an	
50011-8H19600M14 CCC 214.00	8 192 America Chemica Scorey		cultural and senagranitur	al uses

			1.0	No.		
fast organization	profit affert	instgeword (partic)	without engression end.studie species	anta rangement particular particular	444	abaagaa
I References Title Table		Carel Mate	1919		194	Marray of al 1782
EALUS, SALDI. EXILOR	month and	post-question)				
5 DESERVITION TARE	or other has	distant and		- 100 (1997)	25	Widowski ord
Companyation Title Table.	Brook and	Deal specified)			2506	Narue (2002) 13 and Long (2000)
EASTER, TAYON, SALESS	Pulping	04.0				to take and have
1. Openador y sum 1 intel	and the second	iteratulasi			191	Roome and all CONTR.
0.1117 exercised to 1	(selection)	Which water DPts -			340	Englant of COUL
C	and the second second	algohoost arts			2006	
C. sald WE'L Bee	Training and	greet quelled)			1300	This see or al. (796)
6. outrWFT	official.				7100	12 and Long d1905
Classes have overy with	and a second	(MER)			22.1	ALLord Long (1788)
	012100.010	(1870)				
g websites.	SPE CARLINE ENCHARTER Instructor	Telectron Bet spectrol	- C.			Coperat and Yorks
		-Chrystewoodal 5	Hutebard 1			
1.059	chromosomal abortations	Sheekd Bits		15	1.440	Rook et al. (2007)
tel bore realizes (in cha)	(Aranasana)	algohanan ana			1000	Lived long (1986)
inenan preightenal bland.	developm 36.2	illuctor (at sevided			25490	Vigiants and Type (1983)
being pergheral blend	801	(Insistant			300	tion paper
Intrates Instangeorgianal Med	301	(http://www.it.Fill photosis/			1000	tion pages
Strepps Tobs cost thes	and the local	202.9%J			1000	To Marco et al.
Construction right	the state	introducement 7 PEa				2160
mane bene merrors (in total	ADDRESS OF THE OWNER OWNE OWNER OWNE OWNER OWNE	ghokouar pari spejenti		2	306	Freek et al. (1963)
NAME AND ADDRESS OF A ROLL	IS A Price Park				200	ROOM of ALL CONTR.
	and the second	aboliouse 1995	1.2		100	this pager
	818	190.5%				
NEAR AND ADDRESS AND ADDRESS ADDRE	BREEDWARDS Mrst	Moneyber Unterstate 70.8%			330	on type.
L submits		10% Inc.	-		14000	Is and Long (1986)
	10.0343	0010				
of appropriate	1.0%	afterdamous and			176	To and Long (1988)
maine sta wheel	INA segle costi	Wathanan .			300	the paper
mean (in end	UTNIKI TNA	Unreity			370	the paper
	unde mond .	Westwards 20.852				
manute (at a link)	ECHOC	Stational Control of C	**		300	this paper.
mine (dr. 1916)	8.0161	Brentup Strentup (gl-plenutu 20.8%)	*		270	Shin pager
4.4 pentitus -, negative 8.4 effective dans "Experiment on dany unlik	nat taskel 131-1 right of sell."(To	stor tinds, pained ; may	rim tenis, aug n-diteitard in	by of her 1975 Deep coller. "Po	hund effet	tan don 110. high
The taggler activity of tool ing look on the generation of the al services suggests a rain ration collectionalizes in the	of the sections	active agents	start prore	as al contence dervi of price	cial for hat-	un die risk asse of fermidations h ann

his berlinsie fie ags bas berlinsie fie ags bas berlinsie fie ags bas berlinsie fie ags

ty testing of the herbicide Roandap and its active ingredient isopropylamine using the mouse bene marrow micronucleus nella mutagenicity test, and Allium anaphase-telophase test

J. Rank, A.-G. Jonson, B. Skov, L.H. Pedemon and K. Jonson (Recited I Sockeller 19C) Robie patient (Nicepter 19C)

Roundap is a relatively new herbicide first	the famore, when utility plants with revistance to
authories in the USA in 27%. The active agent in	phythomer are introduced on the matter. Stream
condap is glophozate (VA) phytophozonectric	ing with Rescales on applications evaluate copy
letisch, which is overählened almost assumatic	will under it possible to elisistant all other on-
annumle (LD) _{in} rate cost = 0.2 µ/cl (Arkänon,	warder places or the field.
183). The herbicide Roundap is commonly used	The grandwarder of Rescales areas (failure
anglophone. Remates and assured and over the	to be an investment of Rescales areas (failure
old and is expected to be used even more in	1977, Vigluence and Vyae, 1980, Li and Long, 1988, Nauji and Gopolan, 1981; De Marco et al., 1982). The results from these studies are coeffici-
erropendence Arts Hack, Expanses of Environment,	ing, and anne of the investigators have tested
infesting and feed States, Knithle University, Bio Sci.	both Boundup and gliphcaste in the same many.
5, 410 Backles, Deservic	In the generat study we have examined the

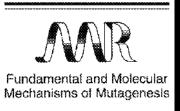
Mar 1997



Bolognesi study shows that Roundup formulation causes genetic damage in human cells.

Plaintiff Exhibit 0852

Jul 1998



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



Dec 1998



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

Jul 1998



Fundamental and Molecular Mechanisms of Mutagenesis

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



Dec 1998

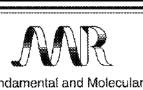


Dec

1998

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

Jul 1998



Fundamental and Molecular Mechanisms of Mutagenesis

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



Monsanto's Reaction:

Need to hire an expert to refute these studies, so Monsanto reaches out to Dr. James Parry.



Sets: 12/21/18 1.32 PM	
When SECTO - glupple come - Mile SLAL (Deally an West) and Tarves 20	
Wok 2021/ - physicians - revolution and interfault to	
 and c all contact the lab, pri presently, repart test satural ere. 	
 We will be put the start the end-two end two ends. But recommends an and other the startacted or and startacted as morely of grown indextors of stargers for; 	
 B) igned in further statues and excelse "Metargert schools" (saling process) 	
and arrive the measures, there after the recent of the proof section. These for a first section fact defining for the following days he can always receil the mething of as ince- rest heart path.	
an	
2.000 2.0000 2.00000 2.00000 2.0000 2.00000000	
() spinel as extend giving interval $\sigma_{\rm s}$ before effects effects between μ in the spin μ	
is the bar or result to send and the a set from some can be an spread that the the performance of the two y and perform of some with the the performance is the spread of the trans- plagement team ""forther at an off performance.	
affine control contact, of do, herey to specific the second state of the second state	
for an elements - the second project and the second project and the project and the provided by agreed to the second project and the seco	
 conference of point time rate and for present and coupled a little article longer and thermal the present. 	
 We dots are very stated and satural () as the tend'to ten- reflect to articles of some processory or even both to tenderthese in some prices but not be achieved at Whin's to refute based whethy as the reflects of the some. 	
a de la constance de la constan anticipar de la constance de la constance de la constance de la	
 Its reaction of the forum lipschedges test by the set agree with the set step and after to the take lipschedges many sets and by apriles as within. 	
Becceneralizations.	
maining the authors, seen a forther and thus managing truly of provides and porter semitting about	
 The data discut's agree with tribut data as have - the aprillage shally throwfore as an interview law interview law manipulation the manipulation of the aprillation and and they taked the manipulation. 	

Really Sources -

not neard yet).

AM of:

	Reply Separator
Subject:	Actions from12/17 Meeting on Mutagenicity
Author:	
Date:	12/27/98 1:31 PM

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

As EU has an immediate need and is a critical area now it was agreed that would contact Dr. Parry next week to discuss with him his participation in the support of glyphosate, glyphosate-based ***formulation*** gentox issues.

> After initial contact, if Dr. Parry is agreeable than will be included in discussion to outline issue/needs etc.



For North America - will be here in early February as part of the CANTOX project. as graciously agreed to join in those discussions.

2) Unfortunately our time rain out but and and stayed a
1ittle while longer and dicussed the papers:

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

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

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

Dec 1998

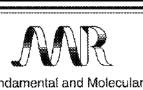


Dec

1998

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

Jul 1998



Fundamental and Molecular Mechanisms of Mutagenesis

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



Monsanto's Reaction:

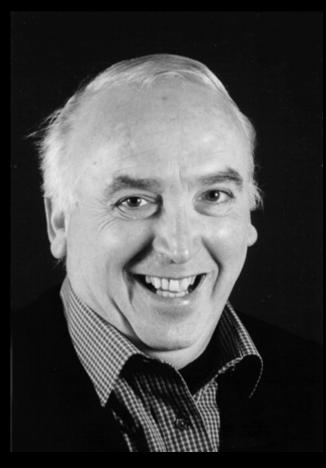
Need to hire an expert to refute these studies, so Monsanto reaches out to Dr. James Parry.



Sets: 12/21/18 1.32 PM	
When SECTO - glupple come - Mile SLAL (Deally an West) and Tarves 20	
Wok 2021/ - physicians - revolution and interfault to	
 and c all contact the lab, pet presently, repart test satural ere. 	
 We will be put the start the end-two end two ends. But recommends an and other the startacted or and startacted as morely of grown startacted or analyzed provide morely of grown startacted or analyzed provide the startacted of t	
 B) igned in further statues and excelse "Metargert schools" (saling process) 	
and arrive the transverse, there after the recent of the proof section. These for a first section fact defining for the following days he can always receil the waiting if as ince- rest heart path.	
an	
2.000 2.0000 2.00000 2.0000 2.0000 2.0000 2.000000 2.00000 2.00000000	
() spinel as extend giving interval $\sigma_{\rm eff}$ interval $\sigma_{\rm eff}$ between entering means in the methods of	
is the bar or result to send and the a set from some can be an spread that the the performance of the two y and perform of some with the the performance is the spread of the trans- plagement team ""forther at an off performance.	
affine control contact, of do, herey to specific the second state of the second state	
for an elements - the second project and the second project and the project and the provided by agreed to the second project and the seco	
 conference of point time rate and for present and coupled a little article longer and thermal the present. 	
 We dots are very stated and satural () as the tend'to ten- reflect to articles of some processory or even both to tenderthese in some prices but not be achieved at Whin's to refute based whethy as the reflects of the some. 	
a de la constance de la constan anticipar de la constance de la constance de la constance de la	
 It is reach to all the description that by the set agree with the set step and after to the taken behaviours many security to approximate an effect. 	
Beccessed at the second	
maining the authors, seen a forther and thus managing truly of provides and porter semitting about	
 The data discut's agree with tribut data as have - the aprillage shally throwfore as an intervented to threadyparting the manipulating - the owner tribut product of data. How provide the manipulation 	

Really Sources -

Dr. James Parry



1940 - 2010

Swansea University Prifysgol Abertawe

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

Dr. James Parry

Monsanto Unsure About Dr. Parry





External global network of genotox experts:

- EU

- NA

 While Dr. Parry is a recognized genotox expert what is not known is how he views some of the "non-standard endpoints" (such as SCE, DNA P-32 postlabling, Comet assays etc) evaluated in the genotox articles by Rank, Bolognesi etc.

- Therefore it was recommended that before we ask him to get more deeply involved (reviewing all the literature, glyphosate data; represent us as a consultant with regulators, etc) we would ask him to review a subset of the articles.

- It was proposed that would contact Dr. Parry and ask him for a written review the articles by Rank, Bolognesi, Peluso & Lioi

- Based on his critique of the the genotox papers a decision would be made as to expanding or terminating his involvement.

Regarding , no further contact will be made at this time. When a clear role has been identified for Alan will contact him.
 Money for this initial consultation will come from budget. A bigger initiative will require additional funds to be located.

 Expanded discussions with Dr. Gary Williams on genotox issues will occur as part of the CANTOX meetings (2/5,647). Dr. Williams is recognized internationally as a genotox expert and might be used in Europe on a contingency basis.

- LA/SEA - no action at this time

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

- Larry Kier will finalize his rebuttal
- Include the Lioi papers in the articles to be reviewed by Dr. Parry
- Bill/Donna will draft for Larry a letter to the editor or a short publication to be submitted to the journal upon receipt of Parry's evaluation
- While there is \$90K in the glyphosate toxicology testing budget for mutagenicity testing, this may not be enough. Further

External global network of genotox experts:

- EU



 While Dr. Parry is a recognized genotox expert what is not known is how he views some of the "non-standard endpoints" (such as SCE, DNA P-32 postlabling, Comet assays etc) evaluated in the genotox articles by Rank, Bolognesi etc.

- Therefore it was recommended that before we ask him to get more deeply involved (reviewing all the literature, glyphosate data; represent us as a consultant with regulators, etc) we would ask him to review a subset of the articles.

- It was proposed that would contact Dr. Parry and ask him for a written review the articles by Rank, Bolognesi, Peluso & Lioi

 Based on his critique of the the genotox papers a decision would be made as to expanding or terminating his involvement.

Regarding , no further contact will be made at this time. When a clear role has been identified for Alan will contact him.
Money for this initial consultation will come from budget. A bigger initiative will require additional funds to be located.

- NA

 Expanded discussions with Dr. Gary Williams on genotox issues will occur as part of the CANTOX meetings (2/5,6&7). Dr. Williams is recognized internationally as a genotox expert and might be used in Europe on a contingency basis. endpoints" (such as SCE, DNA P-32 postlabling, Comet assays etc) evaluated in the genotox articles by Rank, Bolognesi etc.

- Therefore it was recommended that before we ask him to get more deeply involved (reviewing all the literature, glyphosate data; represent us as a consultant with regulators, etc) we would ask him to review a subset of the articles.

- It was proposed that would contact Dr. Parry and ask him for a written review the articles by Rank, Bolognesi, Peluso & Lioi

 Based on his critique of the the genotox papers a decision would be made as to expanding or terminating his involvement.

Regarding , no further contact will be made at this time. When a clear role has been identified for Alan will contact him.
 Money for this initial consultation will come from budget. A bigger initiative will require

additional funds to be located.

- NA

111

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

- LA/SEA - no action at this time

7). There is a concern that the papers by Lioi et al, may present an even bigger problem because the studies are with glyphosate and are on a more standard endpoints. The results of the human

Dr. James Parry

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

DRAFT DRAFT DRAFT DRAFT

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

Dec 1998

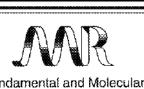


Dec

1998

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

Jul 1998



Fundamental and Molecular Mechanisms of Mutagenesis

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



Monsanto's Reaction:

Need to hire an expert to refute these studies, so Monsanto reaches out to Dr. James Parry.



Autor: Salar	10/21/W 1.12 Pe	
	When SIZER - ghaplesester + Mill SIZE (Indigen Will) and Tareet 20	
	work 2005/ - physicileme - increase the section and	
	all all sectars the lak, proprietally, require term	
	 W will be part to start the starter of beauty. By starter is as an effective the starter are not been been been an entry of prior and another or target for the starter. 	
	ignee is further statues on exclus "Advegant schools" testing - propriet	
	will arrange this integrates, 'taking after the receipt of the period memory, 'these line in term new periodiality per- site full budge dopt line ten charge rescal. He meeting if we have not new yeek.'	
	an (7)	
	578 245 245 248 248 248 248 248 248	
0	agines) an external giving' interva of penetro externa tenes to in-	
	In this way trend do near and to a stilling area and it and spread that the second part is interfact to favor and and to choose and the the second particulation in the same to the same to the spread area the second seco	
	after termal contact, of in, tary to openatio the will be included to dramatic to believe toost/costs who	
	for an of exercise - and the second of the form of any formation and the formation of the formation of provided to grant to these differences of	
- P.	inflationship or the rais as for provide an organic and the state of the second state	
21	fo Bala are very analogi and salassi (1.a. Die readius rep fort on artificat of some another of environment of the terminations in ring) but has been and ready of Thick's to refute based simply on controls of the last.	
5	i i col ana in ana contra contra da da	
	to results of the April Typicayle test by the interaction of the test of t	
	Served all total	
15	the actions. Next a forther mark than managing low's or coats and copies semiciting abays;	
	The data depict 1 space of the other, data are loss - the apticipe shalp three her are an effectively in the entropy of the providency. In other the active of the three states of the data and	

Dec 1998 **Plaintiff Exhibit**

Dec

1998

0842

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

Jul 1998



Mechanisms of Mutagenesis

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



Monsanto's Reaction:

Need to hire an expert to refute these studies, so Monsanto reaches out to Dr. James Parry.



We have	- Charlester - Mill 1111, 2019/144 (012)) and Tarret 21
	physicists a tabulantin and intifusi iti
and a state of the	tant de lak, pripresents, regenin tent
	a start the studies and tensors. But receptor or the studies well or test teterative tensor or prise teachers or test percent.
Ri Aprile In Rucher a	statuse and enables "Metargent selling" or "balting
	ge bits strangereds. Thereig affect for storage of provident. refuses has an investigation of the for- ing days like the strange second the metting of as ince- pands.
44.15	
COLUMN STREET	
methane.	given interval particular experts taken to to take and and for a string part and to be and and and to be the second string to be transmission for the second string taken to the second
1000 CT	nal seators, of in. Narry is special tops to factored to dragan to in Sattline Scamplands
for both service service service of the control of	
l) colorisately or listle artis longer a	The rate and the second statements
	entad and estanti ().e. the team'ts tep 7 more processory of anyon botton terminities in directly of Phica's to refute based starty on MMT.
and the second second	t Car attac papers my result as too bigget
- bin reality of the tool the test strain and down	hanger lyngbergin tool by and in nor agree with In the former lyngensyst trans semicrist by
Recommendations.	
matters the actions. Brought and particle and	many a firth, and the meaning tra's of employing sheet;
- The Ball Basis's ap-	ree all 0 siles data as have - the aprilies shalp terrated to microfigative the startigenty

Feb 1999

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



security land The security and security devices of the security of th a constant a constant a la service de latacion d'in bigan e d'COM met in A serie of a subset of the lique of 20% (was) + Hand, and a statistic may be of calculated may be of the (M)



Plaintiff Exhibit 0264

a constraint the function of the source of the constraint the source of t

Grydwade Bartele | aurospeciel is topic of Salaansia make periodely with Roaning toisons. 2 (anomené a logie of Manasia, mala periodo) wati kandige nasawa. I ornej in opisal c Bank Marger on Andre, malante la Simo. **Compania** Il manasari en a nive mitatologies ando poliado la balan logitapora. Al nasariar a los mortes di Balanzante la de possaria del por referenza di Simo. An enej wati tabam sinde Galanza sinte la posterizza di Anno ence eneretti

a opinize constantor o ta b famile, label o loose after. The do

Monsanto Europe Parc Scientifique Fleming Rue Laid Burniat 5 B-1348 Louvain-La-Neuve Belgium

11 February 1999

Dear

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

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

I have enclosed my invoice for the evaluation.

Yours sincerely

Feb 1999

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



security land The security and security devices of the security of th a constant a constant a la service de latacion d'in bigan e d'COM met in A serie of a subset of the lique of 20% (was) + Hand, and a station Hand, and a station Hand, and a station Hand, and a station is an experiment of the station of the Hand, and a station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the Hand, and an experiment of the station of the Hand, and an experiment of the station of the stat (M)



Plaintiff Exhibit 0264

a constraint the function of the source of the constraint the source of t

Organisati Bantola | Bantagani i topar of Salaansia malas periodorly with Roundy toisons. 2 (anonymi i hypor of Mannish mini periodicy with Nandige Nanon, I verity in optical C Bank Marger on Andrew Market Mannish Companyation Companyation Companyation of the Andrew Mannish Strategy and Andrew Mannish Mannish Companyation of the Andrew Mannish Strategy and Andrew Andrew Mannish And anony want to know Mathematica Andrew Andrew Mannish Thin.

a opinize constantor o ta b famile, label o loose after. The do

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

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

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

Questions raised by the studies

, ÷.

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

Recommendations for further work to clarify the potential genotoxic activity of

7

The second second

based upon oxidative damage then hazard and risk assessment could be based upon a non-

linear model with a threshold of activity at low doses.

Questions raised by the studies

Role of components of mixture which leads to high levels of activity of Roundup?

Is the genotoxic activity observed due to oxidative damage?

3) Can the genotoxic activity be reduced by anti-oxidants?

Recommendations for further work to clarify the potential genotoxic activity of Glyphosate

Bacteria

I recommend a repeat of Salmonella studies particularly with Roundup mixtures. I would be surprised if these data are not already available in-house.

Cytogenetics

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

Feb 1999

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



security land The security and security devices of the security of th a constant a constant a la service de latacion d'in bigan e d'COM met in A serie of a subset of the lique of 20% (was) + Hand, and a station Hand, and a station Hand, and a station Hand, and a station is an experiment of the station of the Hand, and a station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the station of the station of the station of the Hand, and a station of the Hand, and an experiment of the station of the Hand, and an experiment of the station of the stat (M)



Plaintiff Exhibit 0264

a constraint the function of the source of the constraint the source of t

Organisati Bantola | Bantagani i topar of Salaansia malas periodorly with Roundy toisons. 2 (anomené a logie of Manasia, mala periodo) wati kandige nasawa. I ornej le opisal d'Anna kan ya se dwala, waisire la tom. **Compania** I manasari en a sire mitatorian sudo pelandro la bish logitopor, al nasariari siri en artista di Sanzando le de periodo di Anna Anna Anna anti-dare maja sudo tabuta di Anna andro la pelantegia di Anna ensu manari An maja sudo tabuta sidebo Gjalana bisha padempari di Anna ensu manari

a opinize constantor o ta b famile, label o loose after. The do

or numerical damage.

ر و

The in vitro micronucleus assay would allow both:-

- The assessment of the potential influence of anti-oxidants upon the genotoxic potential a) of Glyphosate - Note the measurement of the effect of anti-oxidant as a genetic endpoint is a critical deficiency in the Loi et al (1998) study.
- Assessment of the individual components of the Roundup Mixture to determine Ъ) whether there is any component(s) which act synergistically to increase the potential genotoxicity of Glyphosate. Such studies could be designed to investigate a panel of mixtures leaving out one component of the mix for each individual experiment.

In vivo studies

In view of the limitations of the Bolgnesi et al (1977) study i.e.

limited number of animals

single dose of compound

low spontaneous micronucleus frequency

20 south april it would be worth repeating the study to a more comprehensive design.

repeat both the DNA strand breaks and adduct work would require very large

Feb 1999

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



security land The security and security devices of the security of th a constant a constant a la service de latacion d'in bigan e d'COM met in A serie of a subset of the lique of 20% (was) + Hand, and a station Hand, and a station Hand, and a station Hand, and a station of the station of the station Hand, and a station of the station of the station of the station Hand, and and a station of the station of the station of the station Hand, which are in the station of the station of the station of the station Hand, which are in the station of the station o (M)



Plaintiff Exhibit 0264

a constraint the function of the source of the constraint the source of t

Grydwade Bartele | aurospeciel is topic of Salaansia make periodely with Roaning tricums. 2 (anomené a logie of Manasia, mala periodo) wati kandige nasawa. I ornej le opisal d'Anna kan ya se dwala, waisire la tom. **Compania** I manasari en a sire mitatorian sudo pelandro la bish logitopor, al nasariari siri en artista di Sanzando le de periodo di Anna Anna Anna anti-dare maja sudo tabuta di Anna andro la pelantegia di Anna ensu manari An maja sudo tabuta sidebo Gjalana bisha padempari di Anna ensu manari

a opinize constantor o ta b famile, label o loose after. The do

Feb 1999

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

Apr 1999

Monsanto Reaction:

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



NOTE IN Allow which because we were a second to the second second

To present our compare of the Eard out. The constant present of the Eard out. The constant present of the Eard out out, the eard out of the Sector Se

Los pareces comp consultate a context tempe?
 Los pareces activity to solve (1) use values?
 Los pareces activity to solve(1) use values?
 Los pareces activity of
 Logication
 Los activity (1) loss of Solvenity mate pareces and the loss of
 Logication

weight be separated if there also are not also by second in the term. (Sequencing (assumed on its other sequences only periodicy is being implements. Determined contrasts with empirical the second secon







A set of the set of th

particular of all the area including the part function straffic. In a difficult with with restartion is more, it was not not be another and a supervised and and but to not be another full particult, with with other and/ore the constraint of the constraint full strain proved in horizon a supervised for an for them been of them.

Letter as well as some with the approximate of the second state o

() the full man an analysis of which was bound to the tipi status and meand important. Neuroise it was accommoded that was after in a first contrast tipi and the in and a get a sample of what Way and it is four the setting tipi and the in the set a sample of what Way and it.

Plaintiff Exhibit 0264 Donna will arrange for further meetings to discuss/design this program

4)	Globa	l experts Review Dr. Parry's analyis - what is our next step? Dr. Parry concluded on his evaluation of the four articles that glyphosate is capable of producing genotoxicity both in vivo and in vitro by a mechanism based upon the production of oxidative damage.
		The data that Dr. Parry evaluated is limited and is not consistant with other better conducted studies. In order to move Dr. Parry from his position we will need to provide him with the additional information as well as asking him to critically evalute the quality of all the data including the open literature studies.
		As a followup Mark will contact Dr. Parry, discuss with him the existance of additional data and ask him to evaluate the full package. Mark will also explore his interest (if we can turn his opinion around) in being a spokesperson for us for these type of issues.
		Larry as well as others will be available to discuss the data with Parry as needed by e-mail, phone or in person or all the above.
		Dr. Williams - discuss the outcome of the Cantox meeting
		The panel concluded that glyphosate and Roundup were not mutagenic. That in the evaluation of these types of studies criteria should be set up front in the evaluation process as to what makes an acceptable study and what does not - this is t be included in the manuscript as well as a weight of evidence

5) Lioi followup

approach.

Feb 1999

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

Apr 1999

Monsanto Reaction:

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



NOTE IN Allow which because we were a second to the second second

To present our compare of the Eard out. The constant present of the Eard out. The constant present of the Eard out out, the eard out of the Sector Se

Los pareces comp consultate a context tempe?
 Los pareces activity to solve (1) use values?
 Los pareces activity to solve(1) use values?
 Los pareces activity of
 Logication
 Los activity (1) loss of Solvenity mate pareces and the loss of
 Logication

weight be separated if there also are not also by second in the term. (Sequencing (assumed on its other sequences only periodicy is being implements. Determined contrasts with empirical the second secon







A set of the set of th

particular of all the area including the part function straffic. In a difficult with with restartion is more, it was not not be another and a supervised and and but to not be another full particult, with with other and/ore the constraint of the constraint full strain proved in horizon a supervised for an for them been of them.

Letter as well as some with the approximate of the second state o

() the full man an analysis of which was bound to the tipi status and meand important. Neuroise it was accommoded that was after in a first contrast tipi and the in and a get a sample of what Way and it is four the setting tipi and the in the set a sample of what Way and it.

Plaintiff Exhibit 0264

Feb 1999

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

Apr 1999

Monsanto Reaction:

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



A DEFEND OF A ADDRESS SECTION OF ADDRESS ADDRE

Line and an end of the strengt and the maximum work is based open a werk that a strengt and the strength open a transmission work is based open a werk that a strength of the strength open and the

annexembles for further wat to durity the patients annexed websity hydroxy in annexemble is topic of future in many particularly with focusion incommunitive balance of future into a model watching to block.

Opegannian E prosessed as a view restriction unity periodicy is future (registerym. 37 customer with early unit? Me statusation for prosess and despect of suprameria. Diffs. Me may well to have related a Opelana taken protospant' discusses errored





Bit characterizes and the second of the seco

C. Setting of the set of the "Property of the set of the setting of the set of the se

(1) of real for Proton methods to instruction the transit of any entry. In the proton of the entry is to be a set of the transit of the proton of the entry is to be a set of the transit of the proton of the proton of the entry is the transit of the entry of the proton of the entry is the transit to entry of the proton of the entry is the entry. The entry of the proton of the entry is the entry of the e

The set of the second s

Lettra as well as others will be acceledine to accelerate the device of the second to exactly, plane to be person or 2010 or along. The period of the second the second to the second to the period of the second the second to the second term of the period of the second term of these spaces and the second term of the second term of these spaces of the term of the second term of te

(a) where we have a second of the start start as a second seco

Plaintiff Exhibit 0264



Dr. Parry submits second comprehensive report.

Dr. Parry submits second comprehensive report.

Clastogen:

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

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

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

- 18) There are no adequate data to evaluate the in vitro clastogenic activity of surfactants.
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus

inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the analy of LLI *et al.* (1998a and 1998b) i conclude that gluboux is a potential chargenic in vitro. The mady of Bolgmeit *et al.* (1997) indicates that this chargenic activity may be reproduced in vivo in somatic ettil. However, the dominant lethal assay (of limited sensitivity) indicates that this generative activity is not reproduced in gener ettils. The vork of Bolgmeit *et al.* (1997) and LLi *et al.* (1998a and 1998b) seggeen that the generativity intervent may be derived from the generation of oxidative damager in the presence of glybount.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of abequate data not evaluation of the clustegmic potential in view of glyphonten microares is possible. In the absence of an aniconaction and 9 to the protocol of that used by Bologanesi et al (1997) no adequate assencement of the potential activity of glyphonten microares in bone manyow in possible. The available madies do not provide any evidence of the structure in the manyow in possible. The available madies do not Demoghida to suggest that glyphonsten mixtures may have some germs cell society.

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

Specific evaluation of surfactants

Plaintiff Exhibit **0220**

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

James M. Parry

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

Key Questions

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

inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

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

Specific evaluation of genotoxicity of glyphosate mixtures

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

The studies of Bolognesi et al (1997) suggests that glyphosate mixtures may be

presence of glyphosate.

Specific evaluation of genotoxicity of glyphosate mixtures

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

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

Specific evaluation of surfactants

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



same to uncername whether there are exposed individuals and groups within the numan lation. If such individuals can be identified then the extent of exposure should be mined and their lymphocytes analysed for the ny-sence of chromosome aberrations. In

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

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

- 18) There are no adequate data to evaluate the in vitro clastogenic activity of surfactants.
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus

inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the analy of LLI *et al.* (1998a and 1998b) i conclude that gluboux is a potential chargenic in vitro. The mady of Bolgmeit *et al.* (1997) indicates that this chargenic activity may be reproduced in vivo in somatic ettil. However, the dominant lethal assay (of limited sensitivity) indicates that this generative activity is not reproduced in gener ettils. The vork of Bolgmeit *et al.* (1997) and LLi *et al.* (1998a and 1998b) seggeen that the generativity intervent may be derived from the generation of oxidative damager in the presence of glybount.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of abequate data not evaluation of the clustegmic potential in view of glyphonten microares is possible. In the absence of an aniconaction and 9 to the protocol of that used by Bologanesi et al (1997) no adequate assencement of the potential activity of glyphonten microares in bone manyow in possible. The available madies do not provide any evidence of the structure in the manyow in possible. The available madies do not Demoghida to suggest that glyphonsten mixtures may have some germs cell society.

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

Specific evaluation of surfactants

Plaintiff Exhibit **0220**

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

James M. Parry

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

Key Questions

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

does the mechanism lead to other types of genotoxic activity in vivo such as point mutation induction?

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

formulations?

that the genotoxicity observed may be derived from the generation of oxidative damage in the presence of glyphosate. Sociefie evaluation of erenotoxicity of rhythosate mixtures

In view of the absence of abequare data no evaluation of the clustogenic potential is vitro of physhosten encinences in pensible. In the absence of an international study to the protocol of the two of by Bologanei et al (1997) no adequate assessment of the potential activity of ghyshosten incitants in hote marrow in possible. The available studies do not provide any ovidences of genomologily include byten ansators. There is successful are observed abused of the approximation of the potential incidence and the potential of the potential and the study of the potential incidence and the potential incidence abused and the potential incidence and the study of the potential incidence abused and the potential incidence and the potential incidence and abused abused and abused abused and the potential incidence and the potential incidence abused abused

The stadies of Bolognesi et al (1997) suggests that glyphosate mixtures may be capable of inducing oxidative damage in vivo. Succific evaluation of surfacturate

41 Martin Contraction Contraction (1997) 1997 Instance on the Instantian Martine Contraction (Instance)

Plaintiff Exhibit **0220**

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

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

- 18) There are no adequate data to evaluate the in vitro clastogenic activity of surfactants.
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus

inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the analy of LLI *et al.* (1998a and 1998b) i conclude that gluboux is a potential chargenic in vitro. The mady of Bolgmeit *et al.* (1997) indicates that this chargenic activity may be reproduced in vivo in somatic ettil. However, the dominant lethal assay (of limited sensitivity) indicates that this generative activity is not reproduced in gener ettils. The vork of Bolgmeit *et al.* (1997) and LLi *et al.* (1998a and 1998b) seggeen that the generativity intervent may be derived from the generation of oxidative damager in the presence of glybount.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of abequate data not evaluation of the clustegmic potential in view of glyphonten microares is possible. In the absence of an aniconaction and 9 to the protocol of that used by Bologanesi et al (1997) no adequate assencement of the potential activity of glyphonten microares in bone manyow in possible. The available madies do not provide any evidence of the structure in the manyow in possible. The available madies do not Demoghida to suggest that glyphonsten mixtures may have some germs cell socivity.

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

Specific evaluation of surfactants

Plaintiff Exhibit **0220**

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

James M. Parry

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

Key Questions

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

Dr. Parry submits second comprehensive report.

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

a potential classogenic in vitro. The mody of Bologenie et al (1997) indicates that this clastogenic activity may be reproduced levivo in somatic cettle. However, the dominant ledual association of the sensitivity of indicates that this genotoxic activity is not reproduced in gene cells. The work of Bologenei et al (1997) and Lisie et al (1998a and 1998b) suggeons that the genomicativity observed may be derived from the generation of oxidative damage in the presence of glyphonate.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of abequare data no evaluation of the clustegmic potential is view of physionete microares is pensible. In the absence of an anicoraculous and/9 to the protocol of the toused by Bologanei et al (1997) no adequate assencement of the potential activity of ghyphosten microares in botte marrow in possible. The available matines do not provide any evidence or genomically in order measures. There is usere electron from *Devolophila* to suggest that ghyphosten microares may have some germ cell activity.

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

Plaintiff Exhibit **0220**

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

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

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

- 18) There are no adequate data to evaluate the in vitro clastogenic activity of surfactants.
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus

inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the analy of LLI *et al.* (1998a and 1998b) i conclude that gluboux is a potential chargenic in vitro. The mady of Bolgmeit *et al.* (1997) indicates that this chargenic activity may be reproduced in vivo in somatic ettil. However, the dominant lethal assay (of limited sensitivity) indicates that this generative activity is not reproduced in gener ettils. The vork of Bolgmeit *et al.* (1997) and LLi *et al.* (1998a and 1998b) seggeen that the generativity intervent may be derived from the generation of oxidative damager in the presence of glybount.

Specific evaluation of genotoxicity of glyphosate mixtures

In view of the absence of abequate data not evaluation of the clustegmic potential in view of glyphonten microares is possible. In the absence of an aniconaction and 9 to the protocol of that used by Bologanesi et al (1997) no adequate assencement of the potential activity of glyphonten microares in bone manyow in possible. The available madies do not provide any evidence of the structure in the manyow in possible. The available madies do not Demoghida to suggest that glyphonsten mixtures may have some germs cell socivity.

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

Specific evaluation of surfactants

Plaintiff Exhibit **0220**

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

James M. Parry

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

Key Questions

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

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

Monsanto Reaction:

"We simply are not going to do the studies Parry suggests."

17) None of the surfactants demonstrated any mutagenic activity in bacteri

- There are no adequate data to evaluate the in vitro clastogenic activity of surfactant 18)
- 19) One limited bone marrow micronucleus assay failed to detect any micro

inducing activity with the surfactant MON0818.

Specific evaluation of the prmotoxicity of phyphosate

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

Sneeific evaluation of genotoxicity of glyphosate mixtures

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

The studies of Bolognesi et al (1997) suggests that glyphosate mixtures may be canable of inducing exidative damage in vivo

Specific evaluation of surfactants

Plaintiff Exhibit 0220

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

James M. Parry

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

Key Ouestions

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

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

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

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

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



Message

From

Sent

To:

CC

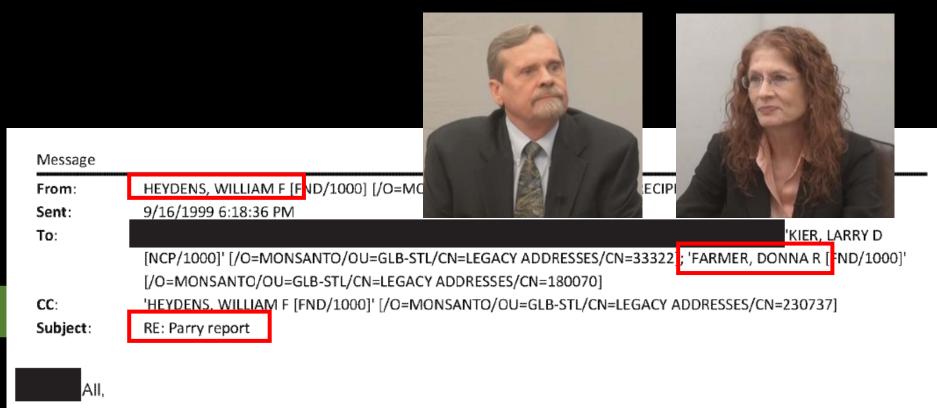
Sept

1999





'KIER, LARRY D



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

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

Bill



divisable to determine whether there are exposed individuals and groups within the human opulation. If such individuals can be identified then the extent of exposure should be letermined and their lymphocytes analysed for the presence of chromosome aberrations. In

Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

Monsanto Reaction:

"We simply are not going to do the studies Parry suggests."

17) None of the surfactants demonstrated any mutagenic activity in bacteri

- There are no adequate data to evaluate the in vitro clastogenic activity of surfactant 18)
- 19) One limited bone marrow micronucleus assay failed to detect any micro

inducing activity with the surfactant MON0818.

Specific evaluation of the prmotoxicity of phyphosate

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

Sneeific evaluation of genotoxicity of glyphosate mixtures

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

The studies of Bolognesi et al (1997) suggests that glyphosate mixtures may be canable of inducing exidative damage in vivo

Specific evaluation of surfactants

Plaintiff Exhibit 0220

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

James M. Parry

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

Key Ouestions

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

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

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

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

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



Message

From

Sent

To:

CC

Sept

1999





'KIER, LARRY D

Dr. Parry submits second comprehensive report.

SeptMonsanto Reaction:
"We simply are not going to do
the studies Parry suggests."

Admission No. 26 Monsanto admits that it has no record of submitting Dr. Parry's Reports to the EPA.

improve the report. develop someone who is gulators and Scientific a person, and it would take

protocol of that used by Biologansi of all (1997) no adequate assessment of the potential attivity of glyphoste micrares in bose marrow is possible. The available studies do not provide any evidence of gasotuncicity in rodent beas marrow. There is some evidence from Descophila to suggest that glyphoste mixtures may have some germ cell activity.

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

Plaintiff Exhibit 0220

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

If the genotoxic activity of glyphosate and its formulations is confirmed it would be advisable to determine whether there are exposed individuals and groups within the human population. If such individuals can be identified then the extent of exposure should be determined and their lymphocytes analysed for the presence of chromosome aberrations. In quite some time and spandules to get nim time. We simply aren't going to do the sudde Parry suggests. The do yo think Parry can become a strong advocate without doing this work Parry? If not, we should <u>serious</u>ly start looking to one or more other individuals to work with. Even if we think we can eventually bring Parry around closer to where we need him, we should be currently looking for a second/back-up genetox, supporter. We have not made much progress and are currently very vulnerable in this area. We have time to fix that, but only if we make this a high priority now.







Dr. Parry submits second comprehensive report.

Dr. Parry concludes glyphosate is clastogenic.

Monsanto Reaction:

"We simply are not going to do the studies Parry suggests."

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

- 18) There are no adequate data to evaluate the in vitro clastogenic activity of surfactant
- 19) One limited bone marrow micronucleus assay failed to detect any micronucleus
- inducing activity with the surfactant MON0818.

Specific evaluation of the genotoxicity of glyphosate

On the basis of the mady of Like *et al* (1998a and 1998b) i conclude that glyphome is a potential charagenic in vitro. The mady of Bolypane *et al* (1997) indicates that this charagenic activity **may** be reproduced at vivo in somatic etth. However, the dominant lethal assay (of limited sensitivity) indicates that this generative activity is not reproduced in gene ethat. The work of Bologenei *et al* (1997a and Like *et al* (1998b) rangents that the generativity observer be derived from the generation of oxidative damage in the presence of glyphonen.

Specific evaluation of genotoxicity of glyphosate mixtures

In low of the absence of alonguese data no evaluation of the characteristic potential vitro of phythonate micratures in possible. In the absence of a micromatclean study to the protocol of thus used by Bulkgapeni et al. (1979) no adoptuse assessment of the potential activity of phythosete micratures in home marrow it possible. The mixilable matlers due to provide any evidence of genetocidary in rodem home marrow. There is notes evidence from Domophilds to suggest the thythosete micromatory how some general evidence.

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

Specific evaluation of surfactants

Plaintiff Exhibit **0220**

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

James M. Parry

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

Key Questions

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

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

Message From HEYDENS, WILLIAM F [FND/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737] Sent 9/16/1999 6:18:36 PM To: 'KIER, LARRY D [NCP/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=33322]; 'FARMER, DONNA R [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=180070] CC 'HEYDENS, WILLIAM F [FND/1000]' [/O=MONSANTO/OU=GLB-STL/CN=LEGACY ADDRESSES/CN=230737] RE: Parry report I have read the report and agree with the comments - there are various things that can be done to improve the report. However, let's step back and look at what we are really trying to achieve here. We want to find/develop someone who is comfortable with the genetox profile of glyphosate/Roundup and who can be influential with regulators and Scientific Outreach operations when genetox, issues arise. My read is that Parry is not currently such a person, and it would take quite some time and \$\$\$/studies to get him there. We simply aren't going to do the studies Parry suggests. do vou think Parry can become a strong advocate without doing this work Parry? If not, we should seriously start looking for one or more other individuals to work with. Even if we think we can eventually bring Parry around closer to where we need him, we should be currently looking for a second/back-up genetox, supporter. We have not made much progress and are currently very vulnerable in this area. We have time to fix that, but only if we make this a high priority now.



Sept

1999





Ghostwriting: Dr. Heydens ghostwrites Williams paper.

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

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

*Department of Pathology, New York Medical Callage, Valluella, New York 10595, 1877DX, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yahiann 2, The Netherlands and Teamou Health Sciences InternetRead, 2023 Argentin Read, State 2004, Missianago, Oramin Lin XFT, Causate

Received December 6, 1999

From: HEYDENS, WILLIAM F [AG/1000] Sent: Thursday, February 19, 2015 7:53 AM To: FARMER, DONNA R [AG/1000] Co: ROOM, MICHAEL S [AG/1000]; SALTMIRAS, DAVID A [AG/1000]; HODGE-BELL, KIMBERLY C [AG/1000] Studject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Ep. 1 sa, Genetox, MOA, Exposure - no size who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more patiable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we post-write the Exposure Tox & Genetox sections. An option would be to add the and Kier or to the transmost on the publication, but we would be keeping the cost down By us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.





Ghostwriting: Dr. Heydens ghostwrites Williams paper.

Ghostwriting:

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

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

Gary M. Williams,* Robert Kroes,1 and Ian C. Munrot*

*Department of Pathology: New York Medical Callege: Valhaila. New York 10595. tRITON, Universited Urecht, P.D. Box 40175. NL-3568 TD Direcht Pathain 2, The Netherlands and Cassiae Institu Sciences Internetilical. 2233 Agentia Rauk, Studi GB, Missianga Omaria UAP XFC Cassate

Received December 6, 1999

From: HEVDERS, WILLIAM F (AG1000) Sent: Thurnday, February 19, 2015 7:53 AM To: FARMER, DONNAR (AG1000) CC: KOOH, MICHAEL: 5 (AG1000); SALTMIRAS, DAVID A (AG1000); HODGE-BELL, KIMBERLY C (AG1000) Subject: RE: IAAC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Ep). Los, Genetox, MOA, Exposure - not sure who we'd get], we could be pushing \$250K or maybe even more. A less expensive/more patatable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we ghost-write the Exposure Tox & Genetox, sections. An option would be to add the and kier or to have their names on the publication, but we would be keeping the cost down by us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.



Ghostwriting: Dr. Heydens ghostwrites

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

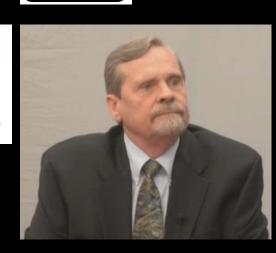
Gary M. Williams,* Robert Kroes,† and Ian C. Munro‡2

*Department of Pathology, New York Medical College, Valhalla, New York 10595, tRITOX, Universiteit Utrecht, P.O. Box 80176, NL-3508 TD Utrecht Yalelaan 2, The Netherlands; and ‡Cantox Health Sciences International, 2233 Argentia Road, Suite 308, Mississauga, Ontario L5N 2X7, Canada

Received December 6, 1999

From: HEYDENS, WILLIAM F [AG(1000] Sent: Thursday, February 19, 2015 7:53 AM To: FANNER, DONNA R [AG(1000) CC: KOCH, MICHAEL S [AG(1000)]; SALTMIRAS, DAVID A [AG/1000]; HODGE-BELL, KIMBERLY C [AG/1000] Subject: RE: TARC Flanning Subject: RE: TARC Flanning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Ep). Los, Genetox, MOA, Exposure - not sure who we'd get], we could be pushing \$250K or maybe even more. A less expensive/more patatable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we ghost-write the Exposure Tox & Genetox, sections. An option would be to add the and kier or to have their names on the publication, but we would be keeping the cost down by us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.



Ghostwriting: Dr. Heydens ghostwrites Williams paper.

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

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

*Department of Pathology, New York Medical Callage, Vallaulia, New York 10595, 18770X, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yahiann 2, The Netherlands and Teamor Health Sciences Internet/Read, 2023 Argentin Read, State 2004, Missianago, Oramin Lin XFT, Causate

Received December 6, 1999

From: HEYDENS, WILLIAM F [AG/1000] Sent: Thursday, February 19, 2015 7:53 AM To: FARMER, DONNA R [AG/1000] Co: ROOM, MICHAEL S [AG/1000]; SALTMIRAS, DAVID A [AG/1000]; HODGE-BELL, KIMBERLY C [AG/1000] Studject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Ep. 1 sa, Genetox, MOA, Exposure - no size who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more patiable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we post-write the Exposure Tox & Genetox sections. An option would be to add the and Kier or to the transmost on the publication, but we would be keeping the cost down By us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.





Ghostwriting:

From: HEYDENS, WILLIAM F [AG/1000] Sent: Thursday, February 19, 2015 7:53 AM To: FARMER, DONNA R [AG/1000] Cc: KOCH, MICHAEL S [AG/1000]; SALTMIRAS, DAVID Subject: RE: IARC Planning



G/1000]

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Epi, Tox, Genetox, MOA, Exposure - not sure who we'd get), we could be pushing \$250K or maybe even more. <u>A less expensive/more palatable approach</u> might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we ghost-write the Exposure Tox & Genetox sections. An option would be to add **and** and Kier or **and** to have their names on the publication, but we would be keeping the <u>cost down by us doing the writing and they would just edit & sign their names so to speak</u>. Recall that is how we handled <u>Williams Kroes & Munro, 2000</u>.

Ghostwriting: Dr. Heydens ghostwrites Williams paper.

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

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

*Department of Pathology, New York Medical Callage, Vallaulia, New York 10595, 18770X, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yahiann 2, The Netherlands and Teamor Health Sciences Internet/Read, 2023 Argentin Read, State 2004, Missianago, Oramin Lin XFT, Causate

Received December 6, 1999

From: HEYDENS, WILLIAM F [AG/1000] Sent: Thursday, February 19, 2015 7:53 AM To: FARMER, DONNA R [AG/1000] Co: ROOM, MICHAEL S [AG/1000]; SALTMIRAS, DAVID A [AG/1000]; HODGE-BELL, KIMBERLY C [AG/1000] Studject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Ep. 1 sa, Genetox, MOA, Exposure - no size who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more patiable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we post-write the Exposure Tox & Genetox sections. An option would be to add the and Kier or to the transmost on the publication, but we would be keeping the cost down By us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.





Ghostwriting: Dr. Heydens ghostwrites Williams paper.

Apr 2010

Ghostwriting:

The Williams paper "has served us well over the last decade."

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

Gary M. Williams,* Robert Kroes,1 and Ian C. Munro1*

*Department of Pathology, New York Medical Callage, Valhalla, New York 10593, 1RITOX, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yabidain Z, The Netherlandte and "Canatos Health Sciences Internet/Read, 2233 Argentin Read, State 2004, Mississaugo, Onzarie Lin VET, Canasta

Received December 6, 1999

From: HEYDENS, WILLIAM F (AG(1000) Sent: Thursday, February 19, 2015 7:3 AM To: FARMER, DONNA R (AG(1000) Cc: KOOH, MICHAE, S (AG(1000); SALTMIRAS, DAVID A (AG/1000); HODGE-BELL, KIMEERLY C (AG/1000) Subject: RE: TARC Planning Subject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Epi, Los, Genetox, MOA, Exposure - not sure who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more palatable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we phost-write the Exposure Tox & Genetox sections. An option would be to add the and Kier or the troub of the Archae the publication, but we would be keeping the cost down by us doing the writing and they would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munro, 2000.







From: SALTMIRAS, DAVID A (AG:1000) Sent: Viecnessky, December (0, 2010) 11:17 AM To: HETCHES, WILLAM F (AG(1000) Subject: Updated glyphosate activities presentation for Priday's CPTLT meeting

Updated and attached for your comment

Thanks,

David Saltmiras, Ph.D., D.A.R.T. Toxicology Manager Regulatory Product Safety Corter Mecsanto



re facing regulatory reviews with increased focus on reviewed increase. Interpretent of the quality of the science it including activits researchers ron outcomes - e.g. pOIAs in Germany e we in general a) has served us well in tonicology over the last docade areand of robust scientific papers to support the safe use of area the increase is of chemistry regularization reviews encouse the fiber set of chemistry regularization reviews encoused area the increase reviews the

siness interests in South America, a local network credible rucial to facilitate scientifically robust and objective ms of ot



From: SALTMIRAS, DAVID A [AG/1000]

Sent: Wednesday, December 08, 2010 11:17 AM

To: HEYDENS, WILLIAM F [AG/1000]

Subject: Updated glyphosate activities presentation for Friday's CPTLT meeting

Bill,

Updated and attached for your comment.

Safety Eva ai

20

Thanks,

From: Hi Sent: Th To: FARM C: KOCH Subject: For the ov I'm still hs from all ti pushing { experts or out of the be to add the cost d that is ho

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







icreased focus on the quality of the science

over the last decade to support the safe use of tration reviews across the a local network credible sust and objective



Ghostwriting: Dr. Heydens ghostwrites Williams paper.

Apr 2000

Ghostwriting:

The Williams paper "has served us well over the last decade."

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

Gary M. Williams,* Robert Kroes,1 and Ian C. Munro1*

*Department of Pathology, New York Medical Callage, Valhalla, New York 10593, 1RITOX, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yabidain Z, The Netherlandte and "Canatos Health Sciences Internet/Read, 2233 Argentin Read, State 2004, Mississaugo, Onzarie Lin VET, Canasta

Received December 6, 1999

From: HEYDENS, WILLIAM F (AG(1000) Sent: Thursday, February 19, 2015 7:3 AM To: FARMER, DONNA R (AG(1000) Cc: KOOH, MICHAE, S (AG(1000); SALTMIRAS, DAVID A (AG/1000); HODGE-BELL, KIMEERLY C (AG/1000) Subject: RE: TARC Planning Subject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Epi, Los, Genetox, MOA, Exposure - not sure who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more palatable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we ghost-write the Exposure Tox & Genetox, sections. An option would be to add the and Kier or to the trouble would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.







From: SALTMIRAS, DAVID A (AS;1000) Sett: WechesBay, December 00, 2010 11:17 AN To: HETCHS, WILLANF F (AG(1000) Subject: Updated glyphosate activities preservation for Friday's CPTLT meeting

Updated and attached for your comment

Thanks,

David Saltmiras, Ph.D., D.A.R.T. Tonology Manager Regulatory Product Balety Corter Montanto



re facing regulatory reviews with increased focus on previewed literature, interpreter of the quality of the science t including activist researchers in outscores - e.g. POPAs in Germany e.uw: in general 0. has served us well in toxicology over the last decade arsenal of robust acientific papers to support the safe use of ace the next set of chemistry registration reviews across the

siness interests in South America, a local network credible rucial to facilitate scientifically robust and objective ms of ot



Glyphosate Toxicology Activities Supporting Registration Reviews

David Saltmiras, PhD, DABT CPTLT December 10, 2010



Publications

- Williams et al. (2000) an invaluable asset
 - Monsanto responses to agencies
 - Scientific Affairs rebuttals
 - Regulator reviews



- More current external expert publications are now needed to support our FTO and Registration Reviews
 - EU Annex 1 Renewal requires extensive lit. review
 - Will <u>weight</u> of evidence be measured by <u>number</u> of publications or quality of the science???

Political Science

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



Apr 2000

Ghostwriting: Dr. Heydens ghostwrites Williams paper.

Apr 2000

Ghostwriting:

The Williams paper "has served us well over the last decade."

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

Gary M. Williams,* Robert Kroes,1 and Ian C. Munro1*

*Department of Pathology, New York Medical Callage, Valhalla, New York 10593, 1RITOX, Universited Utrecht, P.O. Bas 80176, NL-3508 TD Direcht Yabidain Z, The Netherlandte and "Canator Health Sciences Internet/Read, 2233 Argentin Read, State 2004, Mississaugo, Onzarie Lin VET, Canasta

Received December 6, 1999

From: HEYDENS, WILLIAM F (AG(1000) Sent: Thursday, February 19, 2015 753 AM To: FARMER, DONNA R (AG(1000) Cc: KOOH, MICHAE, S (AG(1000); SALTMIRAS, DAVID A (AG/1000); HODGE-BELL, KIMEERLY C (AG/1000) Subject: RE: TARC Planning Subject: RE: TARC Planning

For the overall plausibility paper that we discussed with John (where he gave the butadiene example), I'm still having a little trouble wrapping my mind around that. If we went full-bore, involving experts from all the major areas (Epi, Los, Genetox, MOA, Exposure - not sure who we'd get), we could be pushing \$250K or maybe even more. A less expensive/more palatable approach might be to involve experts only for the areas of contention, epidemiology and possibly MOA (depending on what comes out of the IARC meeting), and we ghost-write the Exposure Tox & Genetox, sections. An option would be to add the and Kier or to the trouble would just edit & sign their names so to speak. Recall that is how we handled Williams Kroes & Munno, 2000.







From: SALTMIRAS, DAVID A (AS;1000) Sett: WechesBay, December 00, 2010 11:17 AN To: HETCHS, WILLANF F (AG(1000) Subject: Updated glyphosate activities preservation for Friday's CPTLT meeting

Updated and attached for your comment

Thanks,

David Saltmiras, Ph.D., D.A.R.T. Tonology Manager Regulatory Product Balety Corter Montanto



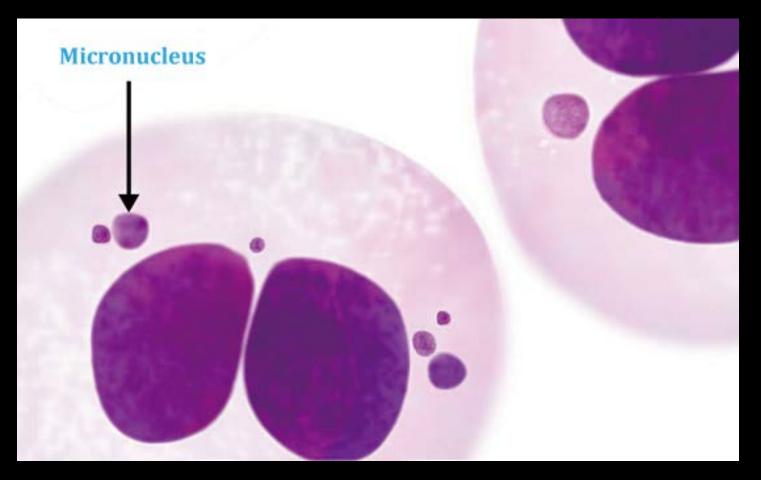
re facing regulatory reviews with increased focus on previewed literature, interpreter of the quality of the science t including activist researchers in outscores - e.g. POPAs in Germany e.uw: in general 0. has served us well in toxicology over the last decade arsenal of robust acientific papers to support the safe use of ace the next set of chemistry registration reviews across the

siness interests in South America, a local network credible rucial to facilitate scientifically robust and objective us of ot



- 2. Can Roundup cause cancer?
 - 2. Mechanistic Data

Recent Data Findings:

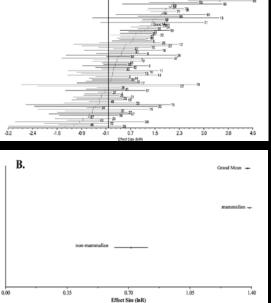


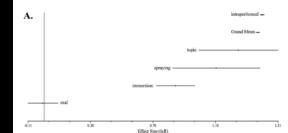
2. Mechanistic Data

Recent Data Findings: Ghisi (2016)



laintiff Exhil





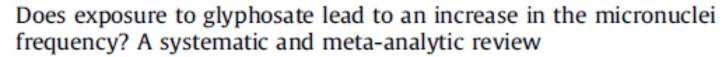


Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Review





Chemosphere

5

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

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

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

HIGHLIGHTS

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

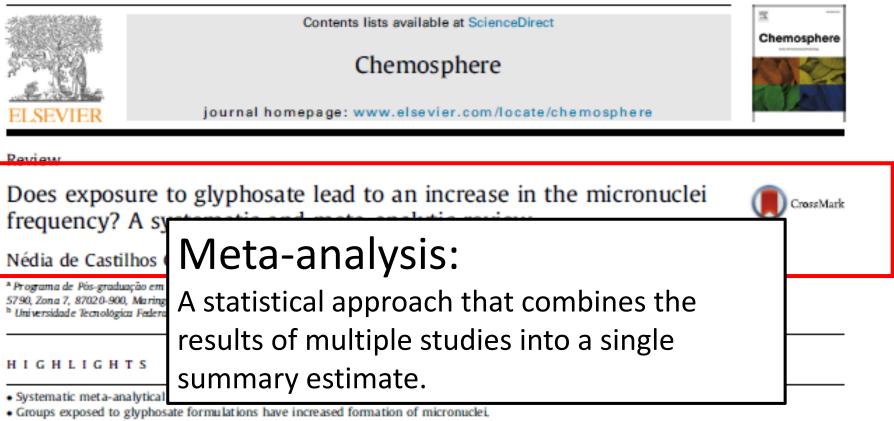
ARTICLE INFO

Article history: Received 11 March 2015 Received in revised form 6 August 2015 Accepted 15 November 2015 Available online 10 December 2015

Handling Editor; Frederic Leusch

ABSTRACT

Glyphosate-based herbicides are among the most used pesticides worldwide. Reviews on the safety of glyphosate have been conducted by several regulatory agencies and researches centers, many times with contradictory results. This study is a systematic meta-analytical review of experimental studies on the relationship between exposure to the glyphosate (GLY) and its formulations with the formation of micronuclei (MN) to establish a quantitative estimate of the environmental risks. The natural logarithm (ln) of the estimated response ratio was calculated from 81 experiments. A meta-analysis was performed on the complete data set, and individual meta-analyses were conducted after stratification by test system, class of vertebrate, exposure route, gender, endpoints, type of literature, formulation, GLY dose and



- Significant difference among glyphosate (GLY) and its commercial formulations.
- Difference in MN formation among different exposure routes of GLY.
- Difference in MN formation among different groups of vertebrates.

ARTICLE INFO

Article history: Received 11 March 2015 Received in revised form 6 August 2015 Accepted 15 November 2015 Available online 10 December 2015

Handling Editor; Frederic Leusch

ABSTRACT

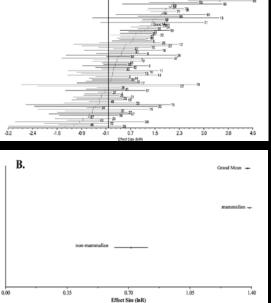
Glyphosate-based herbicides are among the most used pesticides worldwide. Reviews on the safety of glyphosate have been conducted by several regulatory agencies and researches centers, many times with contradictory results. This study is a systematic meta-analytical review of experimental studies on the relationship between exposure to the glyphosate (GLY) and its formulations with the formation of micronuclei (MN) to establish a quantitative estimate of the environmental risks. The natural logarithm (ln) of the estimated response ratio was calculated from 81 experiments. A meta-analysis was performed on the complete data set, and individual meta-analyses were conducted after stratification by test system, class of vertebrate, exposure route, gender, endpoints, type of literature, formulation, GLY dose and

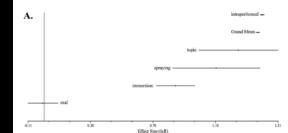
2. Mechanistic Data

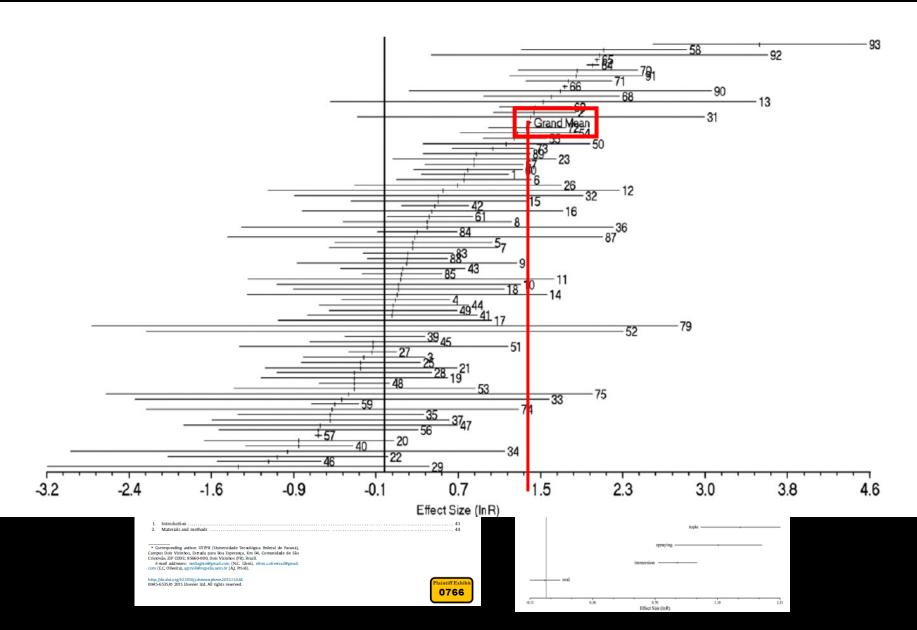
Recent Data Findings: Ghisi (2016)



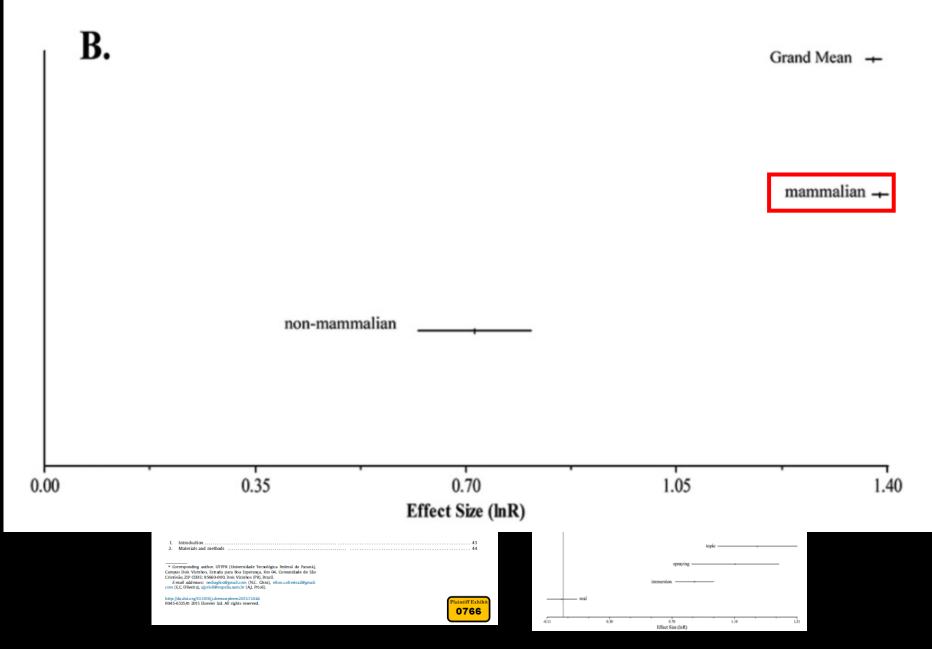
laintiff Exhil

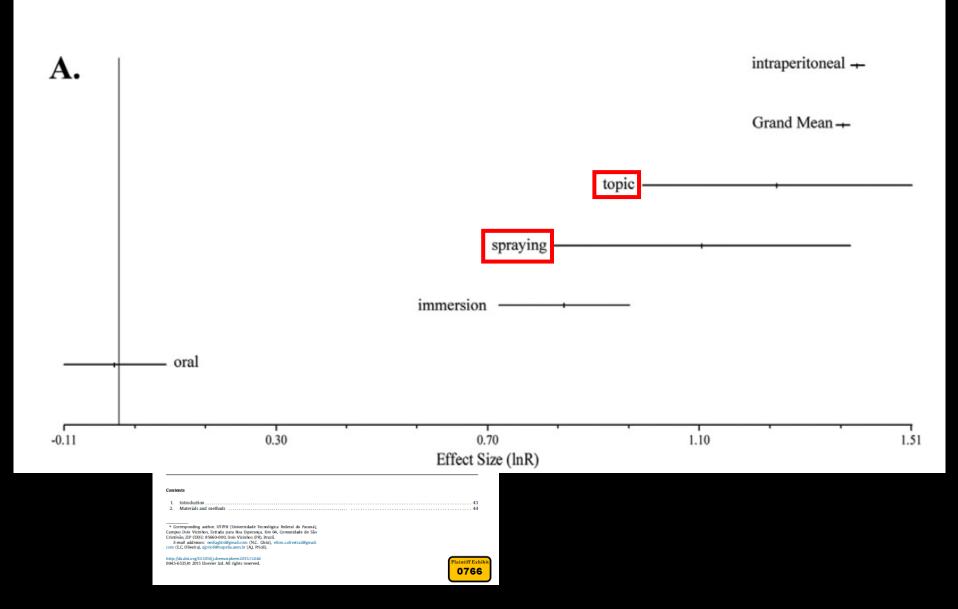












Three Pillars of Cancer Science

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



Three Pillars of Cancer Science

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



3. Epidemiology

Epidemiology:

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

Non-Hodgkin Lymphoma-specific

3. Epidemiology

Non-Hodgkin Lymphoma:

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

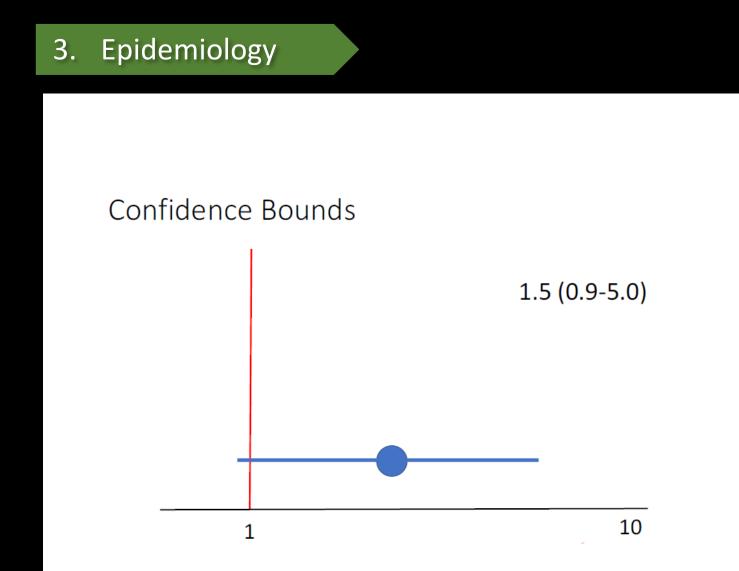
Two types:

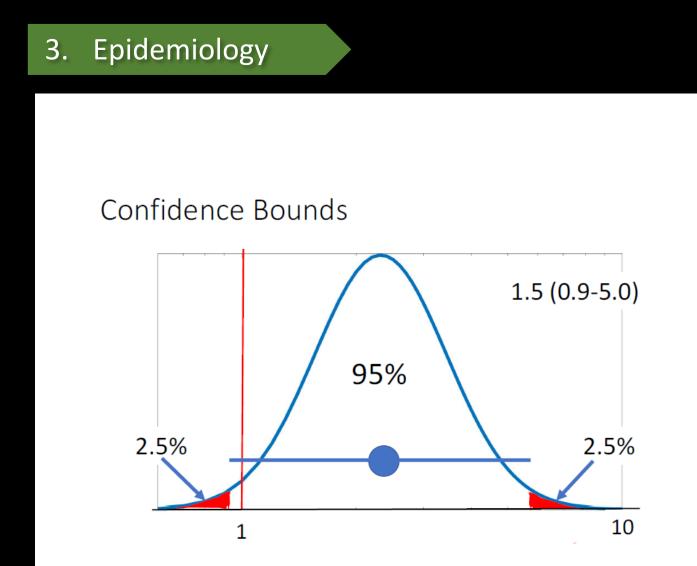
- B-Cell (most common)
- T-Cell (less common)

3. Epidemiology

Confidence Bound:

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





3. Epidemiology

NHL – Never / Ever

Study	RR	Lower	Upper
McDuffie et al. (2001)			
no pesticide adjustment	1.20	0.83	1.74
Hardell et al. (2002)			
no pesticide adjustment	3.04	1.08	8.52
adjusted for pesticides	1.85	0.55	6.20
De Roos et al. (2003)			
adjusted for pesticides	2.10	1.10	4.00
Bayesian modeling	1.60	0.90	2.80
De Roos et al. (2005)			
no pesticide adjustment	1.20	0.70	1.90
adjusted for pesticides	1.10	0.70	1.90
Eriksson et al., (2008)			
no pesticide adjustment	2.02	1.10	3.71
adjusted for pesticides	1.51	0.77	2.94
Orsi et al. (2009)			
no pesticide adjustment	1.00	0.50	2.20
Meta-Analysis: Model 1			
most adjusted analysis	1.30	1.01	1.60
Andreotti et al. (2018)			
not provided			

2.

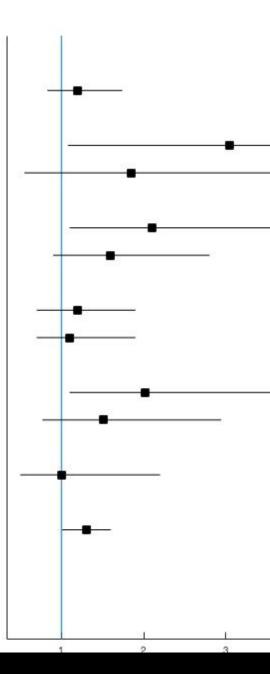
NH

Study

McDuffie et al. (2001) no pesticide adjustment Hardell et al. (2002) no pesticide adjustment adjusted for pesticides De Roos et al. (2003) adjusted for pesticides Bayesian modeling De Roos et al. (2005) no pesticide adjustment adjusted for pesticides Eriksson et al., (2008) no pesticide adjustment adjusted for pesticides Orsi et al. (2009) no pesticide adjustment Meta-Analysis: Model 1 most adjusted analysis

Andreotti et al. (2018) not provided

RR	Lower	Upper		
1.20	0.83	1.74		
	1.08 0.55			
	1.10 0.90			
1.20	0.70	1.90		
	0.70			
	1.10 0.77			
1.00	0.50	2.20		
1.30	1.01	1.60		



2.

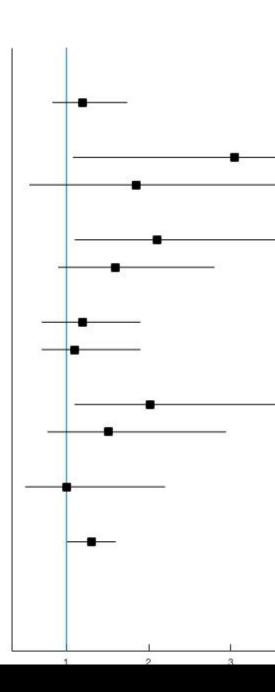
NH

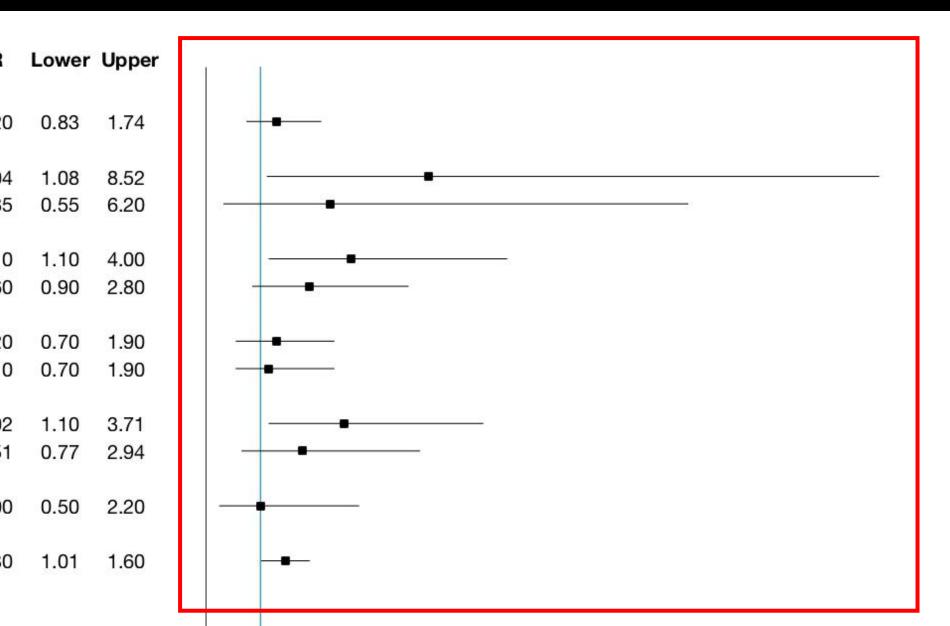
Study

McDuffie et al. (2001) no pesticide adjustment Hardell et al. (2002) no pesticide adjustment adjusted for pesticides De Roos et al. (2003) adjusted for pesticides Bayesian modeling De Roos et al. (2005) no pesticide adjustment adjusted for pesticides Eriksson et al., (2008) no pesticide adjustment adjusted for pesticides Orsi et al. (2009) no pesticide adjustment Meta-Analysis: Model 1 most adjusted analysis

Andreotti et al. (2018) not provided

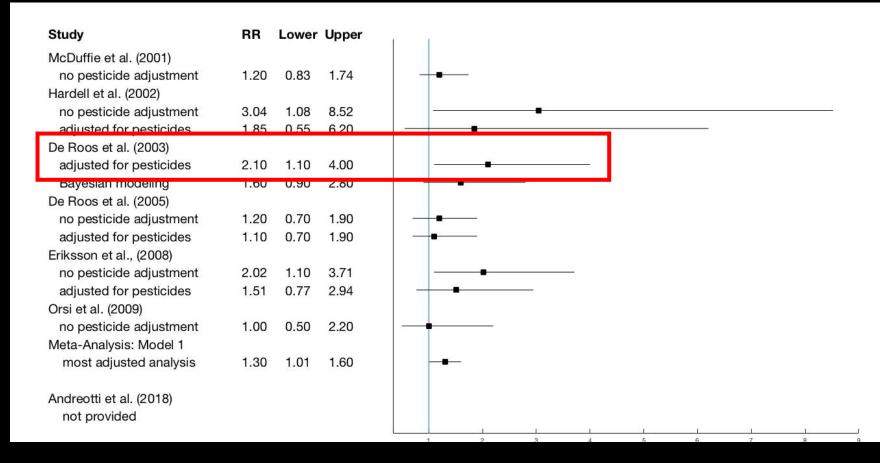
RR	Lower	Upper
1.20	0.83	1.74
	1.08 0.55	
	1.10 0.90	- 2832-23
	0.70 0.70	
	1.10 0.77	200 AUX 100 100 100 100
1.00	0.50	2.20
1.30	1.01	1.60





3. Epidemiology

NHL – Never / Ever



3. Epidemiology

NHL – Never / Ever

Study	RR	Lower	Upper
McDuffie et al. (2001)			
no pesticide adjustment	1.20	0.83	1.74
Hardell et al. (2002)			
no pesticide adjustment	3.04	1.08	8.52
adjusted for pesticides	1.85	0.55	6.20
De Roos et al. (2003)			
adjusted for pesticides	2.10	1.10	4.00
Bavesian modeling	1.60	0.90	2.80
De Roos et al. (2005)			
no pesticide adjustment	1.20	0.70	1.90
adjusted for pesticides	1.10	0.70	1.90
Eriksson et al., (2008)			
no pesticide adjustment	2.02	1.10	3.71
adjusted for pesticides	1.51	0.77	2.94
Orsi et al. (2009)			
no pesticide adjustment	1.00	0.50	2.20
Meta-Analysis: Model 1			
most adjusted analysis	1.30	1.01	1.60
Andreotti et al. (2018)	Δα	rici	ultu
not provided	78		ancu

3. Epidemiology

The Agricultural Health Study

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

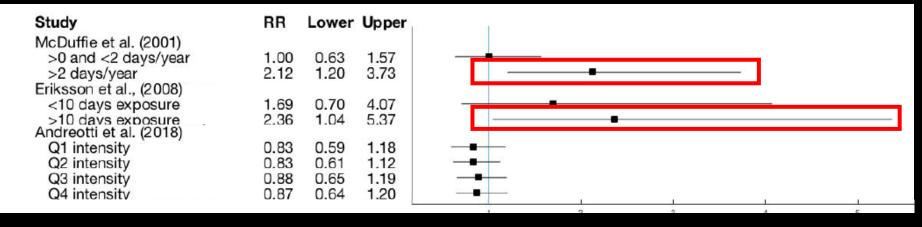
3. Epidemiology

The Agricultural Health Study

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

3. Epidemiology

NHL – Exposure Duration



3. Epidemiology

NHL – Exposure Duration

Study R	R	Lower	Upper	
McDuffie et al. (2001)	Takon 10			
>0 and <2 days/year 1.	.00	0.63	1.57	
>2 days/year 2.	.12	1.20	3.73	
Eriksson et al., (2008)				
	.69	0.70	4.07	
10 dave exposure 2	26	1 04	5 37	
Andreotti et al. (2018)				
Q1 intensity 0.	.83	0.59	1.18	
	.83	0.61	1.12	
	.88	0.65	1.19	
	.87	0.64	1.20	

Mar 1999 Epidemiology: Hardell study shows 230% increased risk of NHL for glyphosate formulation. Mar 1999 Epidemiology: Hardell study shows 230% increased risk of NHL for glyphosate formulation.







Apr 1999

Haddl L, Erikson M. A Case-centrel Sudy of non-Heighin Lymphona and Exposure to Pericides. *Career* 1999; 15:1353–1363.

Hardell and Erbloson conducted a case eventrel mady to look fire anociations between reported nicide two and rene-blockint's benchman (MHL). The mudy included 404 MHL cases and 741 music. The measure of amoretaxion in this mady was the adde mais (UR), a stratistic that estimates of ratio of closure rates (in this case NHL nature) for capared and uncepted appendixtors.

To address reported institution, specificant exercisions for RML with capabilities of the physical structure of the structure of the structure of the structure of the physical structure of the structure of the structure of the structure of the physical structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the str

The address also reported a moderately desired OR of 2.3 for glophonat. The toRs was not notificately deployed and was been and been "expected" means and their "expected" controls. This meaning or dimension of the incursive in glophone been plotped on the on-entropy or addression sections of the one of the incursive in glophone been plotped on the on-entropy or addression sections are not expected by controls of the other plotped on the one-topped on the section of the other section of the control been glophone to the section of the other plotped on the section of the other section of the control been globalants for the fields product for glophone to the section of the other section of the control been globalants for the fields product for glophone to the section of the other section of the control been globalants for the fields product for globalants in the fields product of the section of the control been globalants for the fields product for globalants in the field section of the control been globalants for the fields product for globalants in the field section of the control been globalants for the field section of the field section of the field been the section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the section of the control been globalants in the field section of the control been globalants in the section of the section of the control been globalants in the section of the control been globalan

Succession or an architecture on the lower large equilation for the findings reported for glyphonese Hord and Television (monitors) are explored by the second sec

The present study presents new data about phonormatics acids and other commonly used posicides. Havein, FE review the methods and results of this revent study.

Herdel and Entanen onployed a case control decaps for their vacanch. In case control readers whipers are schemed on the basis of their disease status. These which the disease of investors in this case how whith NFL2 are the crosse. Bosone free study participants are the controls. Information about reasonaprive addingte factors are collected from cases and controls on gundar subhaldings.

The controls in a case control study provide an estimate of the exposure prevalence (in th or of self-aported porticide study in the base population that gave rise to the states and on ourse odds for the cases in these compands to the exposure odds for the costeclis. The sess

John Acquirvella, PiD, and Donna Farmer, PhD Manuani: Commany, Anni 18, 1999

Executive Summary

Sud- doion

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

ablease's acidity; exilipate was not exclupence in this source when the pH was adjusted to a hysicological lock? " Also, EPA characterised if is adfance resource contemposition couly?" as heaving? ... moving and cardinogenicity ... at the device tents?" and classified without as at appre 1. - or couldracter for cardinogenicity in human."

To one galaxies wearing ends due 7 and 7 areas of any positive fielding for since derivative endspire is herein physics in site. The model has been fielding in herein sector specific endspire is herein the completed reset by the first physics. The comparison of the physics of the sector specific endspire is the sector so endspire endspire is the sector so endspire endspire. The physics is the sector so endspire endspire is the sector so endspire endspire is the sector so endspire endspire is the sector so endspire endspire. The physics is the sector so endspire e

space is a marging program (see a marging instantion) is made and in the same of the same

.

- Hanlel L, Erkosen M. A Case-sourcel Bashy of neu-Hodgkin Lymphone and Exposury to Particides. Cancer 1999;85:1351-1364.
- Handell L, Midgmant lyinghnous of the histocytic type and exposure to phonesynctric acids or chloropheroits. Easter 1979;1:35-36.
 - Handel L, Erlesen M, Lawser P, Landpun E. Malguare benchmera and creases to chemicals, expectably organic solvane, chicospherelis, and phenory acide: a case control endy: West J. Cance 1981;02:109–175.
 - Hoar SK, Blair A, Holmas FF, et al. Agricultural hobicide use and risk of lymphoma and soft times accessa. JAMA (1996;256:1141-117).
- Huar Zahor S, Weisenbarger DD, Babbi PA, et al. A true control study of non-blodgia's lymphoma and the hubblede 2.4-field-througheneopactic acid 12.4-Dr in cantean Nebraha Epidemiology (2012) 200-256.
- Devicemental Ponettion Agency, An SA'B Report: Assessment of potential 2.4-D random generation, Review of the epidemiclogical and other data on ponetrial carcinegenisty of 2.4-D (b). the SAB'SAP just contained. E78-654-DER6-44-09, Washington, DC 18 D'A, 1974.
- 7. Mictiana OS. Theoretical Epidemiology. John Wiky & Sons, New York, 1985.
- Bothman KJ, Grazeland S. Mislam Epidemiology: Sound Edition. Lippincate-Raven, Philadelphia, 1991.

Review of:

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

By:

Mar

1999

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



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

Pla

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

sulfosate's acidity: sulfacete was not mutagenic in this access when the nH was adjusted to a



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

References

- Hardell L, Eriksson M. A Case-control Study of non-Hodgkin Lymphoma and Exposure to Pesticides. Cancer 1999;85:1353-1360.
- Hardell L, Malignant lymphomas of the histiocytic type and exposure to phenoxyacetic acids or chlorophenols. Lancet 1979;I:55-56.
- 3. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphpoma and exousre to chemicals,

Mar 1999 Epidemiology: Hardell study shows 230% increased risk of NHL for glyphosate formulation.







Apr 1999

Haddl L, Erikson M. A Case-centrel Sudy of non-Heighin Lymphona and Exposure to Pericides. *Career* 1999; 15:1353–1363.

Hardell and Erbloson conducted a case eventrel mady to look fire anociations between reported nicide two and rene-blockint's benchman (MHL). The mudy included 404 MHL cases and 741 music. The measure of amoretaxion in this mady was the adde mais (UR), a stratistic that estimates of ratio of closure rates (in this case NHL nature) for capared and uncepted appendixtors.

To address reported institution, specificant exercisions for RML with capabilities of the physical structure of the structure of the structure of the structure of the physical structure of the structure of the structure of the structure of the physical structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the structure of the structure of the specificant of the structure of the str

The address also reported a moderately desired OR of 2.3 for glophonat. The toRs was not notificately deployed and was been and been "expected" means and their "expected" controls. This meaning or dimension of the incursive in glophone been plotped on the on-entropy or addression sections of the one of the incursive in glophone been plotped on the on-entropy or addression sections are not expected by controls of the other plotped on the one-topped on the section of the other section of the control been glophone to the section of the other plotped on the section of the other section of the control been globalants for the fields product for glophone to the section of the other section of the control been globalants for the fields product for glophone to the section of the other section of the control been globalants for the fields product for globalants in the fields product of the section of the control been globalants for the fields product for globalants in the field section of the control been globalants for the fields product for globalants in the field section of the control been globalants for the field section of the field section of the field been the section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the field section of the control been globalants in the section of the control been globalants in the field section of the control been globalants in the section of the section of the control been globalants in the section of the control been globalan

Succession or an architecture on the lower large equilation for the findings reported for glyphonese Hord and Television (monitors) are explored by the second sec

The present study presents new data about phonormatics acids and other commonly used posicides. Havein, FE review the methods and results of this revent study.

Herdel and Entanen onployed a case control decaps for their vacanch. In case control readers whipers are schemed on the basis of their disease status. These which the disease of investors in this case how whith NFL2 are the crosse. Bosone free study participants are the controls. Information about reasonaprive addingte factors are collected from cases and controls on gundar subhaldings.

The controls in a case control study provide an estimate of the exposure prevalence (in th or of self-aported porticide study in the base population that gave rise to the states and on ourse odds for the cases in these compands to the exposure odds for the costeclis. The sess

John Acquirvella, PiD, and Donna Farmer, PhD Manuani: Commany, Anni 18, 1999

Executive Summary

Sud- doion

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

ablease's acidity; exilipate was not exclupence in this source when the pH was adjusted to a hysicological lock? " Also, EPA characterised if is adfance resource contemposition couly?" as heaving? ... moving and cardinogenicity ... at the device tents?" and classified without as at appre 1. - or couldracter for cardinogenicity in human."

To one galaxies wearing ends due 7 and 7 areas of any positive fielding for since derivative endspire is herein physics in site. The model has been fielding in herein sector specific endspire is herein the completed reset by the first physics. The comparison of the physics of the sector specific endspire is the sector so endspire endspire is the sector so endspire endspire. The physics is the sector so endspire endspire is the sector so endspire endspire is the sector so endspire endspire is the sector so endspire endspire. The physics is the sector so endspire e

space is a marging program (see a marging instantion) is made and in the same of the same

.

- Hanlel L, Erkosen M. A Case-sourcel Bashy of neu-Hodgkin Lymphone and Exposury to Particides. Cancer 1999;85:1351-1364.
- Handell L, Midgmant lyinghnous of the histocytic type and exposure to phonesynctric acids or chloropheroits. Easter 1979;1:35-36.
 - Handel L, Erlesen M, Lawser P, Landpun E. Malguare benchmera and creases to chemicals, expectably organic solvane, chicospherelis, and phenory acide: a case control endy: West J. Cance 1981;02:109–175.
 - Hoar SK, Blair A, Holmas FF, et al. Agricultural hobicide use and risk of lymphoma and soft times accessa. JAMA (1996;256:1141-117).
- Huar Zahor S, Weisenbarger DD, Babbi PA, et al. A true control study of non-blodgia's lymphoma and the hubblede 2.4-field-througheneopactic acid 12.4-Dr in cantean Nebraha Epidemiology (2012) 200-256.
- Devicemental Ponettion Agency, An SA'B Report: Assessment of potential 2.4-D random generation, Review of the epidemiclogical and other data on ponetrial carcinegenisty of 2.4-D (b). the SAB'SAP just contained. E78-654-DER6-44-09, Washington, DC 18 D'A, 1974.
- 7. Mictiana OS. Theoretical Epidemiology. John Wiky & Sons, New York, 1985.
- Bothman KJ, Grazeland S. Mislam Epidemiology: Sound Edition. Lippincate-Raven, Philadelphia, 1991.

Mar 1999

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

Aug 2001

Monsanto:

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







Apr 1999

Hardell L. Eriksson M. A Case-control Study of non-Hedgkin Lymphona and Exp Researcher. Concern 1999; 85:1353–1363.

Hardell and Erideons conducted a case control study to look for associations between rep-tected one and rear-blogdain's loggebras (MHL). The study included 404 MHL cases and 741 into: The measure of associations in this study wend head in ratio (DE), a stratistic that evinat ratio of diseases onto: (in this case NHL rates) for capaced and unsequeed populations.

and the model with the significant measures for the Min. with responsed use of new CA reported one of the Hapitchic CM = 3.7 and a second one of 4.6 keVech-2-method (M = 2.7). The major hereins of 4.6 keVech M = 0.0 the major distribution of 4.6 keVech M

ant and was based on only four "expensel" cares and firee "expensel" controls evoluted in light of the invitations of the study, mentioned abeve, and the we tim that has resulted in glyphones being judged to be new-mutiganic and new US. Environmental Protection Agency and the World Health Organization.

ell and Eriloson¹ conducted an epidemiologic study to look for an Interface one and non-Hodgkin's hyrryborna (horeafter ME3). The rationale 1 is war providen studies by the flort author?² and by investigators at the U.S. Na and the studies of the studies and the studies of pleasary acceleration of the e studies were determined to be inconclu-its 1993a by the U.S. Eaviersmental Pro-

to present study presents new data about phone-subaric acids ar Bencis, FT review the methods and results of this recent study

John Acquirvella, PilD, and Donna Farmer, PhD Montante Communy, April 14, 1999

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

c one phythesate testimology study clied? showed weak positive finds that beprocess on the own points a results for glyphonts." success data have not shown points a result of the U.S. Erein VI. and the work black Organisation." These agrees owned is or cancicogenic - 1974 elsselfor glyphonte as eatogety E.²⁰⁷⁴ lignal planshilly of the findings reported by Hack II and E.W.

non, the study by Hashell and Erikanon found a receiver association between possibility on more receasily for MCPA, and the ordinative groups of fungicity mediana securities for glyphones can not stratistically significant and for confidenting him. It is clear, however, that the widependence of gr-tocicle extrated builts effects for tensors and those functions of music to be selected with the starts for tensors and those functions of music to the start of tensors.

- Haslell L. Erikosco M. A Case-control Study of non-Hodgkin Ly Particides. Cancer 1999;35:1353–1364
- Iandell L, Malegnant hyrophonias of the histocytic type and exposure to phonesyncetic acids theoryphenois. Lancet 1979:235-36.
 - (in M, Lawser P, Landgren E. Malignarch bengligana and evening to so-versions, eksembarch, and phonog acids: a case control study. Better and the source of the source
 - Joar SK, Bair A, Holman FF, et al. Agricultural bobicide use and risk of lymphorna and soft time presses. JAMA (2006) 266 (1017) 1173
- - Review of the spokenick-giral and other data on presented cancing-printity of 2,4-D by the SABSAI was consulted. IPA-SAB-EBC-94-005, Washington, DC US IPA, 1994.
 - deman OS. Theoretical Epidemiology, John Wiley & Som, New York, 1987 Rofman KJ, Greenland S, Mokers Tpideniology: Second Edition. Lippinext+Reven. 8

Additional analyses found significant relationships for more than 2 days use/year for glyphomate todds ratio 2.1, 955 CI 1.2-3.7 and mecaprop (odds ratio 2.1, 955 CI 1.2-3.6). The full range of confounding factors was not considered in the analyses, but one presumes that egain only mecoprop would ssociated with NHL in a multivariate organizars of the ISPE meeting asked no to ci

risk of MIL including secoprop. salathion. DOT, osthery), addrin, add Lindson, Alten the subtors controlled for personal factors including satecedent cancer, family history of cancer, personal history of mealise, add altery significantly related to BKL was secoprop (a.k.a. MCPP 2-(4-choro-2-methy)phonoxy proposite add).

Plaintiff Exhibi

0144



Hod ces" the

0144

chloro-2-methylphenoxy) propanoic acid).

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

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

etc.). I gave b told her of ou She was extrem informed of the to establish a research progra years. The FFE equitable shar

It remains to l eventual public up selectively finding that we we need to be information. I



Thosate review and re Study (FFES). Ind asked to be kept We obviously need lee because her is for the next few sis for an

ated in the ether anyone picks led glyphosate stract. Obviously, limited

information. I mention some specific forlow-up plans below.

Mar 1999

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

Aug 2001

Monsanto:

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







Apr 1999

Hardell L. Eriksson M. A Case-control Study of non-Hedgkin Lymphona and Exp Researcher. Concern 1999; 85:1353–1363.

Hardell and Erideons conducted a case control study to look for associations between rep-tected one and rear-blogdain's loggebras (MHL). The study included 404 MHL cases and 741 into: The measure of associations in this study wend head in ratio (DE), a stratistic that evinat ratio of diseases onto: (in this case NHL rates) for capaced and unsequeed populations.

and the model with the significant measures for the Min. with responsed use of new CA reported one of the Hapitchic CM = 3.7 and a second one of 4.6 keVech-2-method (M = 2.7). The major hereins of 4.6 keVech M = 0.0 the major distribution of 4.6 keVech M

ant and was based on only four "expensel" cares and firee "expensel" controls evoluted in light of the invitations of the study, mentioned abeve, and the we tim that has resulted in glyphones being judged to be new-mutiganic and new US. Environmental Protection Agency and the World Health Organization.

ell and Eriloson¹ conducted an epidemiologic study to look for an Interface one and non-Hodgkin's hyrryborna (horeafter ME3). The rationale 1 is war providen studies by the flort author?² and by investigators at the U.S. Na and the studies of the studies and the studies of pleasary acceleration of the e studies were determined to be inconclu-its 1993s by the U.S. Eaviersmental Pro-

to present study presents new data about phone-subaric acids ar Bencis, FT review the methods and results of this recent study

John Acquirvella, PilD, and Donna Farmer, PhD Montante Communy, April 14, 1999

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

c one phythesate testimology study clied? showed weak positive finds that beprocess on the own points a results for glyphonts." success data have not shown points a result of the U.S. Erein VI. and the work black Organisation." These agrees owned is or cancicogenic - 1924 elsselfor glyphonte as eatogety E.²⁰² lignal planshilly of the findings reported by Hack II and E.W.

non, the study by Hashell and Erikanon found a receiver association between possibility on more receasily for MCPA, and the ordinative groups of fungicity mediana securities for glyphones can not stratistically significant and for confidenting him. It is clear, however, that the widependence of gr-tocicle extrated builts effects for tensors and those functions of music to be selected with the starts for tensors and those functions of music to the start of tensors.

- Haslell L. Erikosco M. A Case-control Study of non-Hodgkin Ly Particides. Cancer 1999;35:1353–1364
- Iandell L, Malegnant hyrophonias of the histocytic type and exposure to phonesyncetic acids theoryphenois. Lancet 1979:235-36.
 - (in M, Lawser P, Landgren E. Malignarch bengligana and evening to so-versions, eksembarch, and phonog acids: a case control study. Better and the source of the source
 - Joar SK, Bair A, Holman FF, et al. Agricultural bobicide use and risk of lymphorna and soft time presses. JAMA (2006) 266 (1017) 1173
- - Review of the spokenick-giral and other data on presented cancing-printity of 2,4-D by the SABSAI was consulted. IPA-SAB-EBC-94-005, Washington, DC US IPA, 1994.
 - deman OS. Theoretical Epidemiology, John Wiley & Som, New York, 1987 Rofman KJ, Greenland S, Mokers Tpideniology: Second Edition. Lippinext+Reven. 8

Additional analyses found significant relationships for more than 2 days use/year for glyphomate todds ratio 2.1, 955 CI 1.2-3.7 and mecaprop (odds ratio 2.1, 955 CI 1.2-3.6). The full range of confounding factors was not considered in the analyses, but one presumes that egain only mecoprop would ssociated with NHL in a multivariate organizars of the ISPE meeting asked no to ci

risk of MIL including secoprop. salathion. DOT, osthery), addrin, add Lindson, Alten the subtors controlled for personal factors including satecedent cancer, family history of cancer, personal history of mealise, add altery significantly related to BKL was secoprop (a.k.a. MCPP 2-(4-choro-2-methy)phonoxy proposite add).

Plaintiff Exhibi

0144



Hod ces" the

0144

Mar 1999

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

Aug 2001

Monsanto:

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







Apr 1999

Hardell L. Eriksson M. A Case-control Study of non-Heighin Lymphona and Exp Researcher. Concern 1999; 83:1353–1363.

Hardell and Erlödsors conducted a case control study to leek for anocciations between recict use and reor-Hodgkin's hopphena (NHL). The mudy included #04 MHL cases and 74for. The measure of stansectation in this mudy was the defin min (OE), a stratest that contra aire of closure rates (in this case; NHL rates) for capaced and surveyeed populations.

> period use of any finguide (OR = 3.7), and sepond use of 4-th = 2.7). The major lampide (OR = 3.7), and sepond use of 4-th second sepond lampide investigation of this study were the relations on varied seponds) information, the small number of subjects who vanishing of real lists, the relations

it and was based on only four "expendel" cases and three "expendel" covaluated in light of the limitations of the study, mentioned above, and to on that has resulted in glyphosate being judged to be non-mutagonic an

al Erlossen¹ conducted an cyldeniologie study to look for associatio use and non-Hodgkin's hypeboracherosites NHLs. The entomate lisican studies by the first and/or¹¹ and by investigators at the U.S. Nations studies by the first and/or¹¹ and by investigators at the U.S. Na-

studies were determined to be incendial 1999s by the U.S. Eavinemental Pro-

John Acquirvella, PilD, and Donna Farmer, PhD Montante Communy, April 14, 1999

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

To use physicae variation may club "does not not potter things for our downside charges in terms spherosises in its: In Standard Standard

In continuous, the study by likely? and for its first an order at smooth which be been as the study of the st

. .

- Handell L, Erkneen M. A Case-control Realy of non-Hodgkin Lyrephones and Expresser to Postwides. Cancor 1999;85:1383–1344.
- Handell L, Malganet lymphonus of the hericeytic type and exposure to phonesynetric acids editorophenois. Lancet 1979;3:55-56.
 - Hardell L, Enforcen M, Lanner P, Landgran E. Malignarch replyons and evolution to chemically expectably organic universe, ehiemphenelis, and phenory acrile: a case control study. Birt J. Cancer 1081;42:3484-175.
 - Hoar SK, Bfair A, Holman JF, et al. Agricultural horbicide use and risk of hymphorna and soft time acrossing. JAMM, 1996;259:1141–1147.
- Prazi zako B, Honoreninger DD, Fachel PD, et al. A conclusion and a movie hypothesis and the holidade 2.4-diable-repletive-practic acids (2.4-00 in cartion N lipskinesistagy 1050).1509-156.
 - Brivinemental Powerlan Agency, An SA'B Report Assessment of potential 2.4-D carringgoidly, Review of the spatemidiguid and often data on promotif carcing pointy of 2,4-D by the SABSAI post committee. UPA-640-DHD 0-4-00; Washington, DC US UPA, 1974.
 - Maxtuen OS. Theoretical Epidemiology. John Wiley & Sons, New York, 1987.
 Bothman KJ, Grazaliand S. Mosken Epidemiology: Socied Edition. Ligginust-Flavor, Ph
- Robinser KJ, Greanland S. Misdam Epidemookigs: Soci prevalence on this case the 1258.
 Boltman KJ, Greanland S. Misdam Epidemookigs: Soci free manual controls.

risk of NBL indusing securop, salashion, DOT, salasy), sidti, sä lindae. Wen the author contolled for personal factors including antecedent cance, fasily history of desensilistich traintensi. The only period to the salas significantly related to NBL was securop (a.k.a. MCPP 2-(4mhore-2-methyphenoxy) promotion and).

Additional analyses found simificant relationships for more than 2 days use/year for glyphonete told scattor 2.1. 55 cft fault range of confounding factors was not considered in these analyses, but one presumes that equin coly mecoprop would remain associated with NKL in a multivariate analysis.

Since the organizers of the ISBE meeting asked me to chair the perticide account which included this paper. I had the opportunity to spend some time with the author. One atruck me as a reasonable person. I was expecting a

desarf a sem to lave any preconceived notions about ajphostes. Bue spreed to akase her paper with me when it is ready for submation for publication. The slave here to each, i gave her a copy of the cantox alphostes review and taid her of our copying farm family Exposure Staty (FFS). He was astrenely interested in the FFS and asked to be kept informed of the regults from this program. We obviously need to be an expression will be deverails for themes for the next for research normal will be deverails for themes for the next for

0144

Plaintiff Exhibi



relationships between pesticide showed variable findings by proauthors reported a significant

thoss reported a signitation. Titlah Columbia, but not elegenere in Canada (see table). Note - As is typical with epidemiologists, only the Britist Dumbia finding was included in the meeting abstract.) British Journal of Cancer (1998) 77(11), 2048–2052 © 1998 Cancer Research Campaign



Nov 2001

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



Nov 2001

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

Nov 2001





Monsanto's Reaction:

11/27/2002 20:03 PM GRUMERLA, JANE F MACLOROL U-MONSARIO (VL-RA-2000 GL/CH-RECHENTS/CH-10-46) GRUMERLA, MARTIN (UM-2000) (UM-MONSARIO (VL-RA-2000 GL/CH-RECHENTS/CH-372-HL, AMATTER MACLOROL (VL-RA-2006) (VL-RA-2000 GL/CH-RECHENTS/CH-372-HL, AMATTER (UM-2000) (VL-MONSARIT-QU-MA-3000 GL/CH-RECHENTS/CH-372-HL), HYDENS, WILLIAM F (F) MUNDAME STATER, Supers- GL/MONSARI CH-MONSARIT-SCH-372-HL), HYDENS, WILLIAM F (F) MUNDAME STATER, Supers- GL/MONSARI CH-MONSARIT-SCH-372-HL), HYDENS, WILLIAM F

ACQUARELLA, JOHN F (MQ1000) Thursday, November 29, 2005 7:54 Al MAIHER, DONNE R (NQ1000) GDL05TEIN, DAMIEL A (NQ1000); AR

11 know yet what is says in the "small print" - but the fact that glyphosate is no longer mentioned in the tuge step forward - it removes it from being picked up by abstract searches?

Celebrate the fact that glyphosate is not mentioned in the abstract.

laintiff Exhibi

0312

Original	Message
From:	ACQUAVELLA, JOHN F [AG/1000]
Sent:	Inursday November 29 Zuti Z154 AM
To: Cc:	FARMER, DONNA R [AG/1000]
Cc:	GOLDSTEIN, DANIEL A [AG/1000]; ARMSTRONG, JANICE M [AG/1000]; HEYDENS, WILLIAM F [AG/1000]
Subject:	the McDuffee article appears - glyphosate not mentioned in the abstract
Importance	: High

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



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



Message	
From:	FARMER, DONNA R [, G/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]
Sent:	11/29/2001 2:07:23 PM
To:	ACQUAVELLA, JOHN F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=145465]
CC:	GOLDSTEIN, DANIEL A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=527246]; ARMSTRONG,
	JANICE M [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=597137]; HEYDENS, WILLIAM F
	[AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]
Subject:	RE: the McDuffee article appears - glyphosate not mentioned in the abstract

John,

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

Donna

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



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



Nov 2001

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

Nov 2001





Monsanto's Reaction:

11/27/2002 20:03 PM GRUMERLA, JANE F MACLOROL U-MONSARIO (VL-RA-2000 GL/CH-RECHENTS/CH-10-46) GRUMERLA, MARTIN (UM-2000) (UM-MONSARIO (VL-RA-2000 GL/CH-RECHENTS/CH-372-HL, AMATTER MACLOROL (VL-RA-2006) (VL-RA-2000 GL/CH-RECHENTS/CH-372-HL, AMATTER (UM-2000) (VL-MONSARIT-QU-MA-3000 GL/CH-RECHENTS/CH-372-HL), HYDENS, WILLIAM F (F) MUNDAME STATER, Supers- GL/MONSARI CH-MONSARIT-SCH-372-HL), HYDENS, WILLIAM F (F) MUNDAME STATER, Supers- GL/MONSARI CH-MONSARIT-SCH-372-HL), HYDENS, WILLIAM F

ACQUARELLA, JOHN F (MQ1000) Thursday, November 29, 2005 7:54 Al MAIHER, DONNE R (NQ1000) GDL05TEIN, DAMIEL A (NQ1000); AR

11 know yet what is says in the "small print" - but the fact that glyphosate is no longer mentioned in the tuge step forward - it removes it from being picked up by abstract searches?

Celebrate the fact that glyphosate is not mentioned in the abstract.

laintiff Exhibi

0312

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



Nov 2001

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

May 2002 Epidemiology: Another Hardell study shows 306% increased risk of NHL for Roundup.

Nov 2001





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



LEUKEMIA & LYMPHOMA

> Autore Police Kopi Ves Ben Jose Strate

> > Plaintiff Exhibit

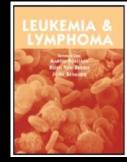
British Journal of Cancer (1998) 77(11), 2048–2052 © 1998 Cancer Research Campaign



Nov 2001

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

May 2002 Epidemiology: Another Hardell study shows 306% increased risk of NHL for Roundup. Plaintiff Exhibit 0777



Nov 2001





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

aintiff Exhi

0312

Mar 2003 Epidemiology: shows 210% increased risk of NHL for glyphosate formulation. Controlled for <u>60</u> other pesticides.

Plaintiff Exhibit 0710 for knowledge about how pestion to the risk of NHL. Both ds ratios with the number of icides used, but the relative e substantially different—25.9 a cytogenetic mechanism.¹⁴ However, there is only very limited evidence for genotoxicity of atrazine, although there are no studies in humans.⁴⁸ A small number of studies of atrazine on immune function in rodents and in vitro suggest a decreased lymphocyte count and cytokine production following expo-



e

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

tial comounting of pesticide Nevertheless, some previous e due to confounding by correrticular, a previously reported vl¹³ was not replicated in the sis here revealed that carbaryl sociated (p < 0.001), and pref different carbaryl measures y adjustment for diazinon, handling of carbaryl, and use vious analysis, estimates were ides, including a group for but adjustment for specific results. Similarly, previous isk associated with use of the tetrachlorvinphos¹² were neg-P insecticides in the model. mportance of considering cor-

risk associated with the use of ng coumaphos, diazinon, and

Glyphosate, commercially sold as Roundup, is a commonly used herbicide in the United States, both on crops and on non-cropland areas.⁵⁰ An association of glyphosate with NHL was observed in another case-control study, but the estimate was based on only four exposed cases.⁵¹ A recent study across a large region of Canada found an increased risk of NHL associated with glyphosate use that increased by the number of days used per year.⁸ These few suggestive findings provide some impetus for further investigation into the potential health effects of glyphosate, even though one review concluded that the active ingredient is non-carcinogenic and non-genotoxic.⁵⁰

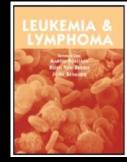
Much attention in NHL research has focused on the herbicide 2,4-D as a potential risk factor, and several studies have observed positive associations with 2,4-D exposure.^{6 8 9} Whereas an indicated effect of 2,4-D exposure on NHL was reported in NCI's Nebraska and Kansas studie: of the pooled data found no association with h 2,4-D. The null association does not result from other pesticides, missing data, or from the internet of the internet of the pooled data found no association with h British Journal of Cancer (1998) 77(11), 2048–2052 © 1998 Cancer Research Campaign



Nov 2001

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

May 2002 Epidemiology: Another Hardell study shows 306% increased risk of NHL for Roundup. Plaintiff Exhibit 0777



Nov 2001





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

aintiff Exhi

0312

Mar 2003 Epidemiology: shows 210% increased risk of NHL for glyphosate formulation. Controlled for <u>60</u> other pesticides.

Plaintiff Exhibit 0710 British Journal of Cancer (1998) 77(11), 2048–2052 © 1998 Cancer Research Campaign

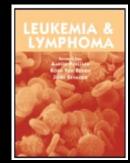


Nov 2001

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

May 2002 Epidemiology: Another Hardell study shows 306% increased risk of NHL for Roundup.





Nov 2001





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





Epidemiology: shows 210% increased risk of NHL for glyphosate formulation. Controlled for <u>60</u> other pesticides.



Monsanto's Reaction:

Dr. Acquavella warns that the De Roos study could add fuel to the fire.





WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523];

[/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=2802771]; DANHAUS, ROY G [AG/1000] (/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=218231] RE: Article re: NHL and #2vhosate. alaolior

The authors spent an entire paragraph in the discussion on glyphosate, specifically mentioning the Hardell and McDuffie studies:

status controls. Obsphonts, commercially soid as Romdup, is a commonly used harbiside in the United States, both on crops and non-croptand areas. An association of glyphonts with MRL was observed in another care-control study, but the estimate was board or only from exposed only according to a specific of the study of the morecond risk of MRL associated with glyphonts are that increased from explosine study of the reserve concluded but the active singulation is non-caretoring in the integration into the potential builts effects of glyphonat, even though one reserve concluded built the active singulation is non-caretoring in the integration in the potential builts effects of glyphonat, even though one private more than the active singulation is non-caretoring in the integration in the free study of the st

I'm afraid this could add more fuel to the fire for Hardell et al.

I'm going to see one of the authors of this paper this weekend at the American College of Epidemiology meeting. I'll ask him about some of these issues.

It looks like NHL and other lymphopoietic cancers continue to be the main cancer epidemiology issues both for glyphosate and alachlor. We're assembling a panel of experts to work on this.

Regards, John

Subject



Message	
From: Sent:	ACQUAVELLA, JOHN F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=145465] 9/2/2003 2:29:00 PM
To:	Constructive State (1000) (0=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=43435 ; GOLDSTEIN, DANIEL
	A =NA-1000-01/CN=RECIPIENTS/CN=527246; FARMER, DONNA R [AG/1000] [/ /CN=RECIPIENTS/CN=180070];
	[/ KRONENBERG, JOEL M [AG/1000] [/ /CN=RECIPIENTS/CN=501517]
CC:	V /O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523];
	HEYDENS, WILLIAM F [AG/1000]
	[ADDIVIDINS ANTO/ODDIVID CONSTRUCT/CN=RECIPIENTS/CN=218231]
Subject:	RE: Article re: NHL and glyphosate, alachlor

The authors spent an entire paragraph in the discussion on glyphosate, specifically mentioning the Hardell and McDuffie studies:

Olyphosate, commercially sold as Roundup, is a commonly used herbicide in the United States, both on crops and non-cropland areas.³⁰An association of glyphosate with NHL was observed in another case-control study, but the estimate was based on only four exposed cases.³⁰A recent study across large region of Canada found an increased risk of NHL associated with glyphosate use that increased by the number days used per year.³These few suggestive findings provide some impetus for further investigation into the potential health effects of glyphosate, even though one review concluded that the active ingredient is non-carcinogenic and non-genotoxic.³⁰

I'm afraid this could add more fuel to the fire for Hardell et al.

I'm going to see one of the authors of this paper this weekend at the American College of Epidemiology meeting. I'll ask him about some of these issues.

It looks like NHL and other lymphopoietic cancers continue to be the main cancer epidemiology issues both for glyphosate and alachlor. We're assembling a panel of experts to work on this.

Regards,

John

Se 20

Monsanto's Reaction:

Dr. Acquavella warns that the De Roos study could add fuel to the fire.





WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523];

[/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=2802771]; DANHAUS, ROY G [AG/1000] (/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=218231] RE: Article re: NHL and #2vhosate. alaolior

The authors spent an entire paragraph in the discussion on glyphosate, specifically mentioning the Hardell and McDuffie studies:

status controls. Obsphonts, commercially soid as Romdup, is a commonly used harbiside in the United States, both on crops and non-croptand areas. An association of glyphonts with MRL was observed in another care-control study, but the estimate was board or only from exposed only according to a specific of the study of the morecond risk of MRL associated with glyphonts are that increased from explosine study of the reserve concluded but the active singulation is non-caretoring in the integration into the potential builts effects of glyphonat, even though one reserve concluded built the active singulation is non-caretoring in the integration in the potential builts effects of glyphonat, even though one private more than the active singulation is non-caretoring in the integration in the free study of the st

I'm afraid this could add more fuel to the fire for Hardell et al.

I'm going to see one of the authors of this paper this weekend at the American College of Epidemiology meeting. I'll ask him about some of these issues.

It looks like NHL and other lymphopoietic cancers continue to be the main cancer epidemiology issues both for glyphosate and alachlor. We're assembling a panel of experts to work on this.

Regards, John

Subject



Monsanto's Reaction:

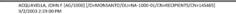
Dr. Acquavella warns that the De Roos study could add fuel to the fire.

Jan 2005

Epidemiology:

De Roos publishes first iteration of the AHS, showing no association between Roundup and NHL.





CARR, KATHERINE H [AG/1000] [/0=MONSANTO/CU=NA-1000-01/CN=RECIPIENTS/CN=3435]; GOLDSTEIN, DANIEL A [AG/1000] [/0=MONDNSANTO/CU=NA-1000-01/CN=RECIPIENTS/CN=327236]; FARMER, DONNA R [AG/1000] [/0=MONSANTO/CU=Ha:000-01/CN=FEE[PIMTS/CH=36070]]

KRONENBERG, JDEL M [AG/10] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=501517]

WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523];

(/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]; DAHNAUS, ROY G [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=218231] RE: Article re: NHL and Elvahosate, alachior

The authors spent an entire paragraph in the discussion on glyphosate, specifically mentioning the Hardell and McDuffie studies:

status controls. Obsphonts, commercially soid as Romdup, is a commonly used harbiside in the United States, both on crops and non-croptand areas. An association of glyphonts with MRL was observed in another care-control study, but the estimate was board or only from exposed only according to a specific of the study of the morecond risk of MRL associated with glyphonts are that increased from explosine study of the reserve concluded but the active singulation is non-caretoring in the integration into the potential builts effects of glyphonat, even though one reserve concluded built the active singulation is non-caretoring in the integration in the potential builts effects of glyphonat, even though one private more than the active singulation is non-caretoring in the integration in the free study of the st

I'm afraid this could add more fuel to the fire for Hardell et al.

I'm going to see one of the authors of this paper this weekend at the American College of Epidemiology meeting. I'll ask him about some of these issues.

It looks like NHL and other lymphopoietic cancers continue to be the main cancer epidemiology issues both for glyphosate and alachlor. We're assembling a panel of experts to work on this.

Regards,

From

Sent:

cc



Monsanto's Reaction:

Dr. Acquavella warns that the De Roos study could add fuel to the fire.

Jan 2005

Epidemiology:

De Roos publishes first iteration of the AHS, showing no association between Roundup and NHL.



From: ACQUAVELLA, JOHN F [AG/1000] [/G=MONSANTO/DU=NA-1000-01/CN=RECIPIENTS/CN=145465] Sent: 9/2/2003 2:29:00 PM

CARR, KATHERINE H [AG/1000][/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=43435]; GOLDSTEIN, DANIEL A [AG/1000][/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=327246]; FARMER, DONNA R [AG/1000] /(Ø=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=36070);

KRONENBERG, JOEL M [AG/1000 [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=501517]

WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523];

(/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]; DMHAUS, ROY G [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=218231] RE: Article re: NHL and alvahosate, alachior

The authors spent an entire paragraph in the discussion on glyphosate, specifically mentioning the Hardell and McDuffie studies:

Annot service. Objectuate, commercially sold an Romday, is a commonly used herbicide in the United States, both on creps and nen-eroptand areas. An association of glyphostare with NHL was observed an another case-control study, but the estimate was based or only four exposed cases. An entrol and a study of the more of the NHL is associated with glyphostare to the interested by the annoher days used per year. These few suggestive findings provide some impacts for further investigation into the potential health. effects of glyphostar, even though one review concluded that the active implication is non-activation; and into negationitie.

I'm afraid this could add more fuel to the fire for Hardell et al.

I'm going to see one of the authors of this paper this weekend at the American College of Epidemiology meeting. I'll ask him about some of these issues.

It looks like NHL and other lymphopoietic cancers continue to be the main cancer epidemiology issues both for glyphosate and alachlor. We're assembling a panel of experts to work on this.

Regards,

cc

Subject



Jul 2008

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

Jul 2008

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

Oct 2008

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

FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070 Sent 10/14/2008 6:31:44 PM To: Nasser Dean [; Scott Kohne [bayercropscience.com); Karen Cair opscience.com]; GOUGH, GEORGE N [AG/1230] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=556077]; 24d.org cc McAllister, Ray [rica.org]; MITCHELL, BRADLEY C [AG/1000] [/O=M/ONSANTO/OU=NA-1000 01/CN=RECIPIENTS/CN=BCMITC1) RE: Study Shows Herbicides Increase Risk of Non-Hodgkin's Lymphoma - Beyond Pesticides, October 14 Subject Nassar Thank you for fowarding this. We have been aware of this paper for awhile and knew it would only be a matter of time before the activists pick it up. I have some epi experts reviewing it. As soon as I have that review we will pull together a backgrounder to use in response. Here is their bottom line...how do we combat this? **Plaintiff Exhibit** Avoid carcinogenic herbicides in foods by supporting organic agriculta strategies that rely on soil health, not toxic herbicides.

0513



Regards Donna

Message

Plaintiff Exhibit Epide

Epidemiology:

Message		
From:	FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]	
Sent:	10/14/2008 6:31:44 PM	
To:	Nasser Dean [] Nasser Dean [] Note that the second s	
	bayercropscience.com]; GOUGH, GEORGE N [AG/1230] [/O=MONSANTO/OU=NA-1000-	
	01/CN=RECIPIENTS/CN=556077]; 24d.org	
CC:	McAllister, Ray [control of the croplifeamerica.org]; MITCHELL, BRADLEY C [AG/1000] [/O=MONSANTO/C	
	01/CN=RECIPIENTS/CN=BCMITC1]	
Subject:	RE: Study Shows Herbicides Increase Risk of Non-Hodgkin's Lymphoma - Beyond Pesticides, October 14	
		ANS A



Thank you for fowarding this. We have been aware of this paper for awhile and knew it would only be a matter of time before the activists pick it up. I have some epi experts reviewing it. As soon as I have that review we will pull together a backgrounder to use in response.

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

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

Regards,

Donna



Jul 2008

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

Oct 2008

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

FARMER, DONNA R [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070 Sent 10/14/2008 6:31:44 PM To: Nasser Dean [; Scott Kohne [bayercropscience.com); Karen Cair opscience.com]; GOUGH, GEORGE N [AG/1230] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=556077]; 24d.org cc McAllister, Ray [rica.org]; MITCHELL, BRADLEY C [AG/1000] [/O=M/ONSANTO/OU=NA-1000 01/CN=RECIPIENTS/CN=BCMITC1) RE: Study Shows Herbicides Increase Risk of Non-Hodgkin's Lymphoma - Beyond Pesticides, October 14 Subject Nassar Thank you for fowarding this. We have been aware of this paper for awhile and knew it would only be a matter of time before the activists pick it up. I have some epi experts reviewing it. As soon as I have that review we will pull together a backgrounder to use in response. Here is their bottom line...how do we combat this? **Plaintiff Exhibit** Avoid carcinogenic herbicides in foods by supporting organic agriculta strategies that rely on soil health, not toxic herbicides.

0513



Regards Donna

Message

Jul 2008

Epidemiology:

Eriksson study shows 202% increased risk of NHL for Roundup. Also shows 236% increased risk of NHL when used for more than 10 days a year. International Journal of Environmental Research and Public Health



Apr 2014

Epidemiology:

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

Oct 2008

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





Jul 2008

Epidemiology:

Eriksson study shows 202% increased risk of NHL for Roundup. Also shows 236% increased risk of NHL when used for more than 10 days a year. International Journal of Environmental Research and Public Health



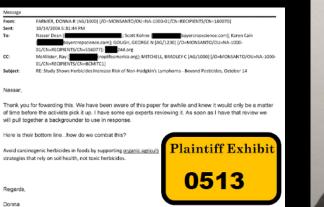
Apr 2014

Epidemiology:

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

Oct 2008

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





Oct 2016

Epidemiology: Monsanto-sponsored metaanalysis shows a 130% increased risk of NHL from Roundup use.



Oct 2016

Epidemiology: Monsanto-sponsored metaanalysis shows a 130% increased risk of NHL from Roundup use. Nov 2017

000

ARTI

Glyp Agri

Gabrie Jay H. Christ Laura Materia Adatas Ad

Epidemiology:

Latest version of the AHS is published using unreliable imputed data. Shows no overall NHL risk.



Access on the second	Table & Josef	rord				Table 3 (percent	und in		
(ACC) Head Camari Head (2008) 131(1) 4(ja210	Gamerale"	Clyphocase wert	-	Mark Cr.	1.1	Generalit'	Cipheau set	-	BARK CIT
Art 10.1495/bc.070a/0.0	Lilling		1.00	Second Contra	19000	Action			
20 Minut		- Normal	54	1.101 (minuted)			Trip free		LittleAssault.
		-Sh		1,124,024.001.712			Q3 Q2		(43 (H42 10 4 H)
		02		0.01.0539.59 to 1.431 0.070558 to 1.311			0		1.70(04) 104.72
	S	CN .	- 12	1.124546 10 1.412			G4		2.44 (0.04 to 0.32)
	Lympholence	Acces				Charles Appendi			
LE		CI	100	1.0504444464			NO	- 2	1.00(whereact) 4.30(path to \$.4.5
And the card of the other statement was represented as the other was an interest water part of the statement of the		GZ		101010-00112			MO.		0.0210122.00
hosate Use and Cancer Incidence in the		63		8154071 10 1.23		-			
	No.5811 Terro	C)A	244	100/0741/126	. 40	Total Annual States and Annual Conditioned States and Annual State	there and press	1 C a test	iar of Germanians, Ap Mean Drieve U.R.+
cultural Health Study	and a second	Autom .		L'Université					
		441	. *	615-02116-2.27		5-800 (-0,71,000.)	5-260 A TT 134	na n bhefh	a last, to plasted, last plasma in and could decount in
lla Andreotti, Stella Koutros, Jonathan N. Hofmann, Dale P. Sandler,	The Party of the	MJ	11	0304253x154		7 million and all	training a state of a		without in the first
Lubin, Charles F. Lynch, Catherine C. Lerro, Anneclaire J. De Roos,	and standard	And a local division of the local division o	100	1.00 (1					to entiting them,
		0	RET.	635pitht to 110					
ine G. Parks, Michael C. Alavanja, Debra T. Silverman,		0		R854543 10 1.12		Discussion			
E. Beane Freeman		C3 G6		8-38(0.45 to 1.10) 8-37(0.44 to 1.30)					
	The Reader	the family board		en alter er ritel					ate use and cargo
achiec being device and home means in patronning based (2), 98, 101, 2011 (200). National Based (201), and homenly of incorporate and the based of based for the part of the principal system of the based for an interval. Marked for the based of		Norm	434	100 paterness		table property	reaction dealer	es 50 de 1	optiones, we also and menall cars
venia (policensing) lacente (arte), fermana el cance (policensing peut clanario finanzia (cance transme, finanzia como el lacente (policensi al como fortes), lechende, UN, Epissonana el cance (policensi el cancera de lacente (cancera de lacente), lacente (cance traverse, lacente) (mange trad, mil calcente), policiense el cancera de lacente (cancera de lacente), lacente (cancera de lacente), la calcente (cancer		-01		679(03) 1115					rs, including 144.
mus levers, knowlik "magin bak, HC DPLCDI, Department of Systemizing, University of Sec, Learchy, B (PL) has block bagany if Sec, DPL repetition of sectors are not exceptions: Marty, inter transmission Research and Research and Research and P		CT CA		0.16(0.06 to 1.01)		pie reprisenta 1	However, they	-	or robbers of an
ne is Lase Reser Presses, R.D. 10744 deal locus Rev. As 1010, MILTER, DOLLAR, MILTER (Locus, MILTER) (Locus, MIL		-01		11 PE #1-52 10 L.1.P		risk of Abd, Ta	r applications, p	arieshe	p in the Mahast (
	Quarter Year	orytic benchmar	innal.	prophospile inclu	elula -				root users of glaph tries. Ald, in thes
		Norm Co.		1.00 (referenced) 0.75 (0.00 to 1.61)		will from an	altain presents	and a	elementer fai fa
2.1.1 · · · · · · · · · · · · · · · · · ·				6768641 10141		Occupational I	farming and p	etarral pe	u ticida esponare.
di Clyphonato is the meet commonly used herbiside worldwide, with both moldanitid and a priviltural uses. In		63		0.004538 10.142					a mena-aradysis -
stereational Agency for Research on Cover classified glyphosate as "probably carries getic to humain," noting	1000-010-02	08	- 22	0.07464810.1.51	. 12				density significa-
charactic weblence and positive associations for ron-Holgkin (prophena (DHL) in some epidemiologic studies. A valuation in the Agricultural (web): Study (AUS) with follow-up through 2001 (word no statistically significant	lifere april	And bring being	120	1.00 (millioned)					o posta lis - 115 conta a sere col-
reaction in the Agriculture means and young with booty of through that which in the bricking agriculture the with glyphosite case and cancer at any disk	22	42	- 22	1.11.4040-10.2.07					d glipphonate une
The Arts is a prospective colliant of domaed peeticide application that herts Larolina and ions, new, we updated		0	-83	10110-02-02 10 1-021		evidence of an	southering w	4th Secile	nut avenue have
on evaluation of gloph-mark with cancer is index or from registry listages through 2012 (North Carolina, 2012) (inves).		03		1120620-0127					THE AME (THE TO
ays and in turn ally weighted lifetime days of glyphonets we were lased on self reported information from excel	Marginiana	Q4	=	81745110145					ter preschafem te
1-200 % and follow-up question naives (1996-2005). We estimated incidence interactive (RRs) and WS combile nor		here		1.00 patronecci					s, and AML use: By in the first to
Cie) saing Poissen regression, controlling for potential confiscedere, including use of other posticides. All statistical two-oided		MI		0.75(0.0) [41]		possible spin-	ution between	L'YEROT	de the and AML
mmg14 251 application, 44 203 (82 PA) used grgbonate. including \$179 incident cancer cance(79.3% of all cancel	1244544	MT		0.000.0111	40	tiak estim	ARE WHEN I	mlar is	magnitude bet
d an ayses, glyphoses was not statistically algorithatily associated with nanow at any site. However, among	Patiendar (pro	Noise		1.00 redeement					not for all silves
n in the highest supresse guertile, there was an increased tak of soure reprint/Deckenda (MRL) compared with		11	22	0.3540.37 to 1 17					the highling copie bookerling signals
n (M 3. 44, MN, Ch., 1914) to 3.2. P _{ments} = 10, through this sumetator two our startestrally algolithmic famility erroinfiller with a free-point (M ₁₀₀₀₀₀₀ == 1.31, 92% Cl =0.31 to 5.51, P _{ment} = .07) and 20-year encounts lag		- 10	- 11	$6.11(0.25) \approx 1.40$					gern The Island
419 EXELLET WELL & BOOPPER (OCCUMENT OF LLL, 2019) CL WEI 2012 S. S.L. Pound W. D.Y. RED 20-PERFECTIONERS DR #3.09, 925 Cl = 1.05 to 3.37, 7 ₁₀₀₀₁ v. 50.	the state of the	15		KIND B 10 2 CT		times relevant	A espeniule an	A NAME OF	speciale in territory
as in this large, prospective inhert study, to association was apparent between glophouse and any solid turnors	a sector and to	Notes		1.00 (milescent)		every many lay is	ipe of oppinion	6.664.241	subation character
id malgrandee owns1, including Nill, and its actrypes. There was some evidence of increased risk of AML among		-01	18	0.75 (CW ++ 1.76)		Most studies a	d established	748, 119	federa such as
e explosed group the troupasse conductation.	_		_	B to 170 B to 150		Title an director	downy sheet to then of thermo-	cied on	erical (Seea than 6 8 Abril: (See to be)
				BULLET		D.A. Long terr	n studies of 1	o daties	expand p quby
						reported elons	and make of Ale	6.10121	System after expo
was introducied al a totad-spectrum tedatate in explosered. I yaidig bicance our of the most kennig und babi: anarastadi				Research.					trong evidences of
I stady become one of the model basely work have a sevential Analyses. Plaintiff		. i h.		12 10 2 6 14					n glyphonata eng
	C X	110	LL	11 10 10.00	Indust	negative states	they suggested to	and same	al spraying the
						1000 C 10		· · · · ·	
	-	-							
06									
			-						

	None	161	1.00 (reference)	
	Q1	136	0.87 (0.64 to 1.19)	
	Q2	126	0.88 (0.66 to 1.17)	
	Q3	137	0.93 (0.71 to 1.23)	
	Q4	144	1.00 (0.74 to 1.34)	.43
	Hodgkin lymphoma			
	None	7	1.00 (reference)	
Oct	M1	7	0.59 (0.17 to 2.11)	
	M2	11	0.90 (0.25 to 3.24)	.94
	Non-Hodgkin lymphoma			
201	None	135	1.00 (reference)	
	Q1	113	0.83 (0.59 to 1.18)	
	Q2	104	0.83 (0.61 to 1.12)	
	Q3	112	0.88 (0.65 to 1.19)	
	Q4	111	0.87 (0.64 to 1.20)	.95
	Non-Hodgkin lymphoma B cell			•
	None	128	1.00 (reference)	
	Q1	102	0.79 (0.55 to 1.13)	
	Q2	93	0.76 (0.56 to 1.05)	
Jagraf of Date	Q3	106	0.88 (0.64 to 1.21)	
A	Q4	103	0.86 (0.62 to 1.19)	.86
	Chronic lymphocytic lymphoma			nia
& Agric	None	36	1.00 (reference)	
3.0	Q1	28	0.75 (0.40 to 1.41)	
Æ	Q2	26	0.76 (0.41 to 1.41)	
	Q3	26	0.90 (0.50 to 1.62)	
<u> 100</u>	Q4	27	0.87 (0.48 to 1.58)	.71
	Diffuse large B cell lymphoma			
	None	27	1.00 (reference)	
Plai	Q1	28	1.11 (0.60 to 2.07)	
	Q2	23		
ľ	Q3	30	1.13 (0.59 to 2.17)	
	Q4	22	0.97 (0.51 to 1.85)	.83
	Marginal-zone lymphoma			
	None		1.00 (reference)	
	M1	6		
	M2	5	0.44 (0.09 to 2.17)	.67
	Follicular lymphoma			
	Mana	10	1.00 (

 None
 7
 1.00 (reference)

 M1
 5
 0.36 (0.09 to 1.43)

 M2
 11
 0.82 (0.23 to 2.98)

*Cancer sites are based and presented in order of Surveillance, Epide and End Results Site Recode ICD-O-3. CI = confidence interval; RR = rate †Quartiles: Q1: 1–598.9; Q2: 599–1649.9; Q3: 1650–4339.9; Q4: ≥4340.0. Te 1–866.24; T2: 866.25–2963.9; T3: ≥2964.0. Median: M1: 1–1649.9; M2: ≥169 ‡Poisson regression was used to model rate ratios and confidence inter P values were calculated using a two-sided Wald test. All models adj age, state of recruitment, education, cigarette smoking status, all month, family history of cancer, atrazine, alachlor, metolachlor, trifluralit

Discussion

In this updated evaluation of glyphosate use and cancer relarge prospective study of pesticide applicators, we observ associations between glyphosate use and overall cancer with total lymphohematopoietic cancers, including NHL and ple myeloma. However, there was some evidence of an inrisk of AML for applicators, particularly in the highest categlyphosate exposure compared with never users of glyphos

Like other hematological malignancies, AML is though sult from multiple genetic and environmental factor Occupational farming and general pesticide exposure has been linked to leukemia (13). In 2007, a meta-analysis of tional pesticide exposure found a statistically significant AML when restricting to cohort studies (meta RR = 1.55, 9 1.02 to 2.34) (14), although specific chemicals were not eva One case-control study that evaluated glyphosate use for evidence of an association with leukemia overall based of posed cases and did not report results for AML (15). Simi the previous AHS analysis, there was no association with mia overall based on 32 exposed cases, and AML was no ated (5). To our knowledge, our study is the first to r possible association between glyphosate use and AML.

Risk estimates were similar in magnitude betwee unlagged and lagged exposure analyses for all sites eva

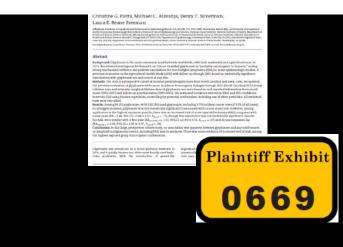
Q2	23	0.94 (0.49 to 1.80)	
Q3	30	1.13 (0.59 to 2.17)	
Q4	22	0.97 (0.51 to 1.85)	.83
Marginal-zone lymp	homa		
Nor	ne 4	1.00 (reference)	
M1	6	0.39 (0.06 to 2.45)	
M2	5	0.44 (0.09 to 2.17)	.67
Follicular lymphoma	ì		
Nor	ne 16	1.00 (reference)	
T1	21	0.89 (0.37 to 2.15)	
T2	11	0.61 (0.23 to 1.60)	
T3	20	0.85 (0.36 to 2.03)	.95
Multiple myeloma			
Nor	ne 30	1.00 (reference)	
Q1	19	0.70 (0.36 to 1.36)	
Q2	26	0.94 (0.50 to 1.76)	
Q3	19	0.78 (0.39 to 1.56)	
04	24	0.87 (0.45 to 1.69)	.84
Non-Hodgkin lymph	oma T cell	120/	
Nor	ne 2	102(ref)ronOe)	
M1	14	4.25 (0.73 to 24.64)	
M2	6	1.53 (0.23 to 10.38)	.31
		(0	onunuea

0701

evidence of an association with leukemia overall based of posed cases and did not report results for AML (15). Simil the previous AHS analysis, there was no association with mia overall based on 32 exposed cases, and AML was no ated (5). To our knowledge, our study is the first to r possible association between glyphosate use and AML.

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

The IARC Working Group noted strong evidence of g icity and oxidative stress effects from glyphosate expose In particular, they highlighted two studies in communi posed to glyphosate through aerial spraying that



Oct 2016

Epidemiology: Monsanto-sponsored metaanalysis shows a 130% increased risk of NHL from Roundup use. Nov 2017

000

ARTI

Glyp Agri

Gabrie Jay H. Christ Laura Materia Adatas Ad

Epidemiology:

Latest version of the AHS is published using unreliable imputed data. Shows no overall NHL risk.



Access on the second	Table & Josef	rord				Table 3 (percent	und in		
(ACC) Head Camari Head (2008) 131(1) 4(ja210	Gamerale"	Clyphocase wert	-	Mark Cr.	1.1	Generalit'	Cipheau set	-	BARK CIT
Art 10.1495/bc.070a/0.0	Lilling		1.00	Second Contra	19000	Action			
20 Minut		- Normal	54	1.101 (minuted)			Trip free		LittleAssault.
		-Sh		1,124,024.001.712			Q3 Q2		(43 (H42 10 4 H)
		02		0.01.0539.59 to 1.43 0.070558 to 1.26			0		1.70(04) 104.72
	S	CN .	- 12	1.124546 10 1.412			G4		2.44 (0.04 to 0.32)
	Lympholence	Acces				Charles Appendi			
LE		CI	100	1.0504444464			NO	- 2	1.00(whereact) 4.30(path to \$.4.5)
And the card of the other statement was represented as the other was an interest water part of the statement of the		GZ		101010-00112			MO.		0.0210122.00
hosate Use and Cancer Incidence in the		63		8154071 10 1.23		-			
	No.5811 Terro	C)A	244	100/0741/126	. 40	Total Annual States and Annual Conditioned States and Annual State	there and press	1 C a test	iar of Germanians, Ap Mean Drieve U.R.+
cultural Health Study	and a second	Autom .		L'Université					
		441	. *	615-02116-2.27		5-800 (-0,71,000.)	5-260 A TT 134	na n bhefh	a last, to plasted, last plasma in and could decount in
lla Andreotti, Stella Koutros, Jonathan N. Hofmann, Dale P. Sandler,	The Party of the	MJ	11	03048253x124		7 million and all	training a straining a s		without in the first
Lubin, Charles F. Lynch, Catherine C. Lerro, Anneclaire J. De Roos,	and standard	And a local division of the local division o	100	1.00 (1					to entiting them,
		0	RET.	635pitht to 110					
ine G. Parks, Michael C. Alavanja, Debra T. Silverman,		0		R854543 10 1.12		Discussion			
E. Beane Freeman		C3 G6		8-38(0.45 to 1.10) 8-37(0.44 to 1.30)					
	The Reader	the family board		en alter er ritel					ate use and cargo
achiec being device and home means in patronning based (2), 98, 101, 2011 (200). National Based (201), and homenly of incorporate and the based of based for the part of the principal system of the based for an interval. Marked for the based of		Norm	434	100 paterness		table property	reaction dealer	es 50 de 1	optiones, we also and menall cars
venia (policensing) lacente (arte), fermana el cance (policensing peut clanario finanzia (cance transme, finanzia como el lacente (policensi al como fortes), lechende, UN, Epissonana el cance (policensi el cancera de lacente (cancera de lacente), lacente (cance traverse, lacente) (mange trad, mil calcente), policiense el cancera de lacente (cancera de lacente), lacente (cancera de lacente), la calcente (cancer		-01		679(03) 1115					rs, including 144.
mus levers, knowlik "magin bak, HC DPLCDI, Department of Systemizing, University of Sec, Learchy, B (PL) has block bagany if Sec, DPL repetition of sectors are not exceptions: Marty, inter transmission Research and Research and Research and P		CT CA		0.16(0.06 to 1.01)		pie repriseras.	However, they	-	or robbers of an
ne is Lase Reser Presses, R.D. 10744 deal locus Rev. As 1010, MILTER, DOLLAR, MILTER (Locus, MILTER) (Locus, MIL		-01		11 PE #1-52 10 L.1.P		risk of Abd, Ta	r applications, p	arieshe	p in the Mahast (
	Quarter Years	orytic benchmar	innal.	prophospile inclu	elula -				root users of glaph tries. Ald, in thes
		Notes .		1.00 (referenced) 0.75 (0.00 to 1.61)		will from an	altain presents	and a	elementer fai fa
2.1.1 · · · · · · · · · · · · · · · · · ·				6768641 10141		Occupational I	farming and p	etarral pe	u ticida esponare.
di Clyphonato is the meet commonly used herbiside worldwide, with both moldanitid and a priviltural uses. In		63		0.004538 10.142					a mena-aradysis -
stereational Agency for Research on Cover classified glyphosate as "probably carries getic to humain," noting	1000-010-02	08	- 27	0.07464810.1.51	. 12				density significa-
charactic weblence and positive associations for ron-Holgkin (prophena (DHL) in some epidemiologic studies. A valuation in the Agricultural (web): Study (AUS) with follow-up through 2001 (word no statistically significant	lifere april	and broghons.	120	1.00 (millioned)					o posta lis - 115 conta a sere col-
reaction in the Agriculture means and young with booty of through that which in the bricking agriculture the with glyphosite case and cancer at any disk	225	42	- 22	1.11.4040-10.2.07					d glipphonate une
The Arts is a prospective colliant of domaed peeticide application that herts Larolina and ions, new, we updated		0	-83	10110-02-02 10 1-021		evidence of an	southering w	4th Secile	nut avenue have
on evaluation of gloph-mark with cancer is index or from registry listages through 2012 (North Carolina, 2012) (inves).		03		1120620-0127					THE AME (THE TO
ays and in turn ally weighted lifetime days of glyphonets we were lased on self reported information from excel	Marginiana	Q4	=	81745110145					ter preschafem te
1-200 % and follow-up question naives (1996-2005). We estimated incidence interactive (RRs) and WS combile nor		here		1.00 patronecci					s, and AML use: By in the first to
Cie) saing Poissen regression, controlling for potential confiscedere, including use of other posticides. All statistical two-oided		MI		0.75(0.0) [41]		possible spin-	ution between	L'YEROT	de the and AML
mmg14 251 application, 44 203 (82 PA) used grgbonate. including \$179 incident cancer cance(79.3% of all cancel	1244544	MT		0.000.0111	40	tiak estim	ARE WHEN I	mlar is	magnitude bet
d an ayses, glyphoses was not statistically algorithatily associated with nanow at any site. However, among	Patiendar (pro	Noise		1.00 redeement					not for all silves
n in the highest supresse guertile, there was an increased tak of soure reprint/Deckenda (MRL) compared with		11	22	0.3540.37 to 1 17					the highling copie bookerling signals
n (M 3. 44, MN, Ch., 1914) to 3.2. P _{ments} = 10, through this sumetator two our startestrally algolithmic famility erroinfiller with a free-point (M ₁₀₀₀₀₀₀ == 1.31, 92% Cl =0.31 to 5.51, P _{ment} = .07) and 20-year encounts lag		- 10	- 11	$6.11(0.25) \approx 1.40$					gern The Island
419 EXELLET WELL & BOOPPER (OCCUMENT OF LLL, 2019) CL WEI 2012 S. S.L. Pound W. D.Y. RED 20-PERFECTIONERS DR #3.09, 925 Cl = 1.05 to 3.37, 7 ₁₀₀₀₁ v. 50.	the state of the	15		KIND NO. 201		times relevant	A espeniule an	A NAME OF	speciale in territory
as in this large, prospective inhert study, to association was apparent between glophouse and any solid turnors	a sector and to	Notes		1.00 (milescent)		every many lay is	ipe of oppinion	6.664.241	subation character
id malgrandee owns1, including Nill, and its actrypes. There was some evidence of increased risk of AML among		-01	18	0.754LW-11.76		Most studies a	d established	748, 119	federa such as
e explosed group the troupasse conductation.	_		_	B to 170 B to 150		Title an director	downy sheet to chan of therein	cied on	erical (Seea than 6 8 Abril: (See to be)
				BULLET		D.A. Long terr	n studies of 1	o daties	expand p quby
						reported elons	and make of Ale	6.10121	System after expo
was introducied al a totad-spectrum tedatate in explosered. I yaidig bicance our of the most kennig und babi: anarastadi				Research.					trong evidences of
I stady become one of the model basely work have a sevential Analyses. Plaintiff		. i h.		12 10 2 6 14					n glyphoests and hollow in somer-
	C X	110	LL	11 10 10.00	Indust	negative states	they suggested to	and same	al spraying the
						1000 m 10		· · · · ·	
	-	-							
06									
			-						

Three Pillars of Cancer Science

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

International Agency Research on Cancer











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

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

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

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

Thanks.

Bill





It is my recollection that you notified the EU-GTF of this IARC evaluat of approaching the GTF about providing funding to fight this because I renewal. If so, is this really the case? I thought the EU evaluation c an adverse IARC evaluation have the real potential to impact the res ו any talk וg Annex wouldn't

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

And while we have vulnerability in the area of epidemiology, we also have potential vulnerabilities in the other areas that IARC will consider, namely, exposure, genetox, and mode of action (David has the animal onco studies under control). If there is a force working against glyphosate, there is ample fodder to string together to help the cause even though it is not scientifically justified in its purest form. Putting all this in the proper perspective will be quite resource

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

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

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

Thanks.

Bill



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

Participants

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

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: C₃H, Relative molecular mass Additional information ture is also available in the P database (NCBI, 2015).

1.1.3 Chemical and physica pure substance

> Description: Glyphosate actu is a coourless, 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

> Plaintiff Exhibit 0784

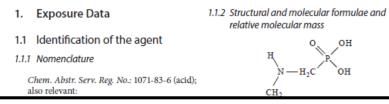
Three Pillars of Cancer Science

- 1. Animal Carcinogenicity Studies
- 2. Mechanistis Daticient

6.2 Cancer in experimental animals

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

GLYPHOSATE



Three Pillars of Cancer Science

- 1. Animal Carcinogenicity Studies
- 2. Mechanisti Softicient

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

Yerbimat (Farm Chemic 2015). 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



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 methyl)glycine
 - Synonyms: Gliphosate; glyphosat sate hydrochloride; glyphosat copper (2+), dilithium, disodiu sium, monoammonium, mon monosodium, sodium, or zinc] s Trade names: Glyphosate produc
 - sold worldwide under numeroust including: Abundit Extra; Cree Glifonox; Glyphogan; Ground-Roundup; Touchdown; Tragli; Yerbimat (<u>Farm Chemicals Ir</u> 2015).

Relative molecular molecular c_3ra_iNO5^{cP} Relative molecular mass: 169.07 Additional information on chemical structure is also available in the PubChem Compound

Three Pillars of Cancer Science

- 1. Animal Carcinogenicity Studies
- 2. Mechanisti Softicient
- 3. Epidemiology Strong

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

ethanol, and xylene; the alkali-metal and



GLYPHOSATE

1. Exposure Data

1.1 Identification of the agent

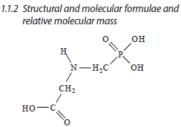
1.1.1 Nomenclature

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,



 $\begin{array}{l} Molecular \mbox{ 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). \end{array}$

1.1.3 Chemical and physical properties of the pure substance

Description: Glyphosate acid is a colour-

Three Pillars of Cancer Science

- 1. Animal Carcinogenicity Studies
- 2. Mechanisti Sofficient
- 3. Epidemiology Strong

Limited

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

0784

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

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

laintiff Exhil

Monsanto's Response to IARC

STRATEGIES/TACTICS

PRE-IARC

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

2. Inform / Inoculate / Engage Industry Partners

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

3. Address New Allegations

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

POST-IARC

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

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

5. Engage Regulatory Agencies

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



request time party experts to sing) op/ea) these units of hing reposed setteed etc.

POST-IARC

- 4. Orchestrate Outcry with IARC Decision ~ March 10, 2015
 - Industry conducts robust media / social media outreach on process and outcome
 - [Sense About Science?] leads industry response and provides platform for IARC observers and industry spokesperson
 - CLI and other associations issue press releases

February 23, 2015

Plaintiff Exhibit

0292

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

5. Engage Regulatory Agencies

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

Monsanto's Response to IARC

STRATEGIES/TACTICS

PRE-IARC

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

2. Inform / Inoculate / Engage Industry Partners

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

3. Address New Allegations

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

POST-IARC

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

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

5. Engage Regulatory Agencies

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



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

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

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

12 months ending in an eight-day meeting. The WG evaluates all of the

publicly available scientific information on each substance and, through a transparent

and rigorous process,1 decides on the

ientific evidence

v Health Month 2016

iced by BMJ Pi

The International Agency for Research on agents that cause cancer in humans and Cancer (IARC) Monographs Programme has evaluated about 1000 agents since identifies chemicals, drugs, mixtures, 1971. Monographs are written by ad hoc occupational exposures, lifestyles and personal habits, and physical and biological scientific experts over a period of about

For numbered affiliations see end of article.

Correspondence to Dr Christopher J Portier, Environmental Health Consultant: Thus: CH-3600 Switzerland; cportier@n

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

For Monograph 112,2 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate.3 The WG concluded that the data for glyphosate meet the criteria for classification as a probable human carcinogen. The European Food Safety Authority (EFSA) is the primary agency of the European Union for risk assessments regarding food safety. In October 2015, EFSA reported⁴ on their evaluation of the Renewal Assessment Report⁵ (RAR) for glyphosate that was prepared by the Rapporteur Member State, the German Federal Institute for Risk Assessment (BfR), EFSA concluded that 'glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential'. Addendum 1 (the BfR Addendum) of the RAR⁵ discusses the scientific rationale for differing from the IARC WG conclusion.

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

THE HUMAN EVIDENCE

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

The finding of *limited evidence* by the IARC WG was for NHL, based on highquality case-control studies, which are overeighted valuable for determining the



2.

Nearl the w asses

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

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

supports that a cause or not cause For Monograp

tists evaluated th four insecticides sate.³ The WG for glyphosate m fication as a prob

The European (EFSA) is the European Unio regarding food EFSA reported* Renewal Assess glyphosate that Rapporteur Mer Federal Institut (BfR), EFSA con unlikely to pose humans and t support classific carcinogenic pot BfR Addendum) scientific rational IARC WG concl

Serious flaws it in the RAR inc potential for a c exposure to glyp the basis for th Agency (EFSA)

iviolianieu Aquel Daivie, Devia Davis, Taul A Deniels, Anneclaire J De Roos,²⁶ Jamie DeWitt,²⁷ Francesco Forastiere,²⁸ Jonathan H Freedman, 29 Lin Fritschi, 30 Caroline Gaus, 31 Julia M Gohlke, 32 Marcel Goldberg, 33 Eberhard Greiser, 34 Johnni Hansen, 35 Lennart Hardell, 36 Michael Hauptmann, 37 Wei Huang, 38 James Huff, 39 Margaret O James, 40 C W Jameson, 41 Andreas Kortenkamp, 42 Annette Kopp-Schneider, 43 Hans Kromhout, 44 Marcelo L Larramendy, 45 Philip J Landrigan, 46 Lawrence H Lash, 47 Dariusz Leszczynski, 48 Charles F Lynch, 49 Corrado Magnani, 50 Daniele Mandrioli,⁵¹ Francis L Martin,⁵² Enzo Merler,⁵³ Paola Michelozzi,54 Lucia Miligi,55 Anthony B Miller,56 Dario Mirabelli, 57 Franklin E Mirer, 58 Saloshni Naidoo, 59 Melissa J Perry, 60 Maria Grazia Petronio, 61 Roberta Pirastu, 62 Ralph J Portier, 63 Kenneth S Ramos, 64 Larry W Robertson, 65 Theresa Rodriguez,66 Martin Röösli,67 Matt K Ross,68 Deodutta Roy,69 Ivan Rusyn, 70 Paulo Saldiva, 71 Jennifer Sass, 72 Kai Savolainen, 73 Paul T J Scheepers, 74 Consolato Sergi, 75 Ellen K Silbergeld, 76 Martyn T Smith, 77 Bernard W Stewart, 78 Patrice Sutton, 79 Fabio Tateo,⁸⁰ Benedetto Terracini,⁸¹ Heinz W Thielmann,⁸² David B Thomas,⁸³ Harri Vainio,⁸⁴ John E Vena,⁸⁵ Paolo Vineis,⁸⁶ Elisabete Weiderpass, 87 Dennis D Weisenburger, 88 Tracey J Woodruff,⁸⁹ Takashi Yorifuji,⁹⁰ II Je Yu,⁹¹ Paola Zambon,⁹² Hajo Zeeb, 93 Shu-Feng Zhou 94

The International Agency for Research on agents that cause cancer in humans and

2.

Nearl

the w

asses

carcinogenic pot BfR Addendum) scientific rational IARC WG concl Serious flaws i in the RAR inc potential for a c exposure to glyp the basis for th

Agency (EFSA) that these shorto

THE HUMAN EV EFSA concluded evidence for a glyphosate-based non-Hodgkin ly inconclusive for tive relationship cancer in hun Addendum (p. explains that 'no ciation was ob powerful study IARC WG cond dence of carcino means "A positi observed betwee and cancer for a ation is consider to be credible, I founding could 1

sonable confiden

Nearly 100 scientists from all over the world endorse IARC's assessment of glyphosate Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)

Christopher J Portier, ¹ Bruce K Armstrong,² Bruce C Baguley,³ Xaver Baur,⁴ Igor Belyaev,⁵ Robert Bellé,⁶ Fiorella Belpoggi,⁷ Annibale Biggeri,⁸ Maarten C Bosland,⁹ Paolo Bruzzi,¹⁰ Lygia Therese Budnik,¹¹ Merete D Bugge,¹² Kathleen Burns,¹³ Gloria M Calaf,¹⁴ David O Carpenter,¹⁵ Hillary M Carpenter,¹⁶ Lizbeth López-Carrillo,¹⁷ Richard Clapp,¹⁸ Pierluigi Cocco,¹⁹ Dario Consonni,²⁰ Pietro Comba,²¹ Elena Craft,²²

The most appropriate and scientifically based evaluation of the cancers reported omhout.44 in humans and laboratory animals as well as supportive mechanistic data is that glylutta Roy.⁶⁹ phosate is a probable human carcinogen. On the basis of this conclusion and in the $\frac{1}{1-\frac{1}{2}}$ ambon.⁹² absence of evidence to the contrary, it is n humans and reasonable to conclude that glyphosate 0 agents since tten by ad hoc international eriod of about an eight-day formulations should also be considered ates all of the information on h a transparent ecides on the ntific evidence likely carcinogens. human Health Month 2016 ed by BMJ P

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

For Monograph 112,2 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate.3 The WG concluded that the data for glyphosate meet the criteria for classification as a probable human carcinogen. The European Food Safety Authority (EFSA) is the primary agency of the European Union for risk assessments regarding food safety. In October 2015, EFSA reported⁴ on their evaluation of the Renewal Assessment Report⁵ (RAR) for glyphosate that was prepared by the Rapporteur Member State, the German Federal Institute for Risk Assessment (BfR). EFSA concluded that 'glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential'. Addendum 1 (the BfR Addendum) of the RAR⁵ discusses the scientific rationale for differing from the IARC WG conclusion.

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

THE HUMAN EVIDENCE

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

The finding of *limited evidence* by the IARC WG was for NHL, based on highquality case-control studies, which are everyouted well-which for determining the



11C PESTICIDE INFORMATION

American Cancer Society®

Known and Probable Human Carcinogens

0306

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



Glyphosate v. Roundup No one tests "Roundup"

Charles Benbrook, PhD.



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



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

Opening Statement Roadmap:

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

Yes.

Opening Statement Roadmap:

- 1. What is Roundup?
- 2. Can Roundup cause cancer?



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

Chadi Nabhan, M.D.



THE UNIVERSITY OF CHICAGO

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

William Sawyer, PhD.



 Ph.D. in toxicology from Indiana University School of Medicine (1983).



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

2012 – New Job at Benicia School District



Pest Management







The Label:

ATTENTION:

This specimen label is provided for general information only. This pesticide product may not yet be available or approved for sale or use in your area.

 It is your responsibility to follow all Federal, state and local laws and regulations regarding the use of pesticides. · Before using any pesticide, be sure the intended use is approved in your state or locality.

Your state or locality may require additional precautions and instructions for use of this product that are not included here

· Monsanto does not guarantee the completeness or accuracy of this specimen label. The information found in this label may differ from the information found on the product label. You must have the EPA approved labeling with you at the time of use and must read and follow all label directions. You should not base any use of a similar product on the precautions, instructions for use or other information you find here.

2007-1

41.0%

· Always follow the precautions and instructions for use on the label of the pesticide you are using.

21225G1-13



Complete Directions for Use

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

EPA Reg. No. 524-517

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

Read the entire label before using this product.

Use only according to label instructions

It is a violation of Federal law to use this product in any manner inconsistent with its labeling.

Not all products recommended on this label are registered for use in California. Check the registration status of each product in California before using.

Read the "LIMIT OF WARRANTY AND LIABILITY" statement at the end of the label before buying or using. If terms are not acceptable, return at once unopened

THIS IS AN END-USE PRODUCT, MONSANTO DOES NOT INTEND AND HAS NOT REGISTERED IT FOR REFORMULATION. SEE INDIVIDUAL CONTAINER LABEL FOR REPACKACING LIMITATIONS

1.0 INGREDIENTS

ACTIVE INCREDIENT Glyphosate, N-(phosphonomethyl)glycine, in the form of its isopropylamine salt. OTHER INGREDIENTS (including surfactant):

. <u>59.0%</u> 100.0% *Contains 480 grams per liter or 4 pounds per U.S. gallon of the active ingredient glyphosate, in the form of its isopropylamine salt. Equivalent to 356 grams per liter or 3 pounds per U.S. gallon of the acid, glyphosate.

This product is protected by U.S. Patent Nos. 5,683,958; 5,703,015; 6,063,733; 6,121,199; 6,121,200. No license granted under any non-U.S. patent(s).

2.0 IMPORTANT PHONE NUMBERS

FOR PRODUCT INFORMATION OR ASSISTANCE IN USING THIS PRODUCT, CALL TOLL-FREE 1-800-332-3111. IN CASE OF AN EMERGENCY INVOLVING THIS PRODUCT. OR FOR MEDICAL ASSISTANCE, CALL COLLECT, DAY OR NIGHT, (314)-694-4000.

3.0 PRECAUTIONARY STATEMENTS

3.1 Hazards to Humans and Domestic Animals

Keep out of reach of children.

CAUTION! CAUSES FYE IRRITATION

Avoid contact with eyes or clothing FIRST AID: Call a poison control center or doctor for treatment advice.

IF IN FACE a Held are seen and since shock, and worth with vertex for 17 - 20

IF IN EIE3	 nou eye oper and mise sowny and genuy with water for 15 - 20 minutes. Remove contact lenses if present after the first 5 minutes then continue rinsing eye.
	roduct container or label with you when calling a poison control center r going for treatment.
 You may all treatment i 	so contact (314) 694-4000, collect day or night, for emergency medical information.
 This produces No. 524-53 	uct is identified as Ranger PRO® herbicide, EPA Registration 17.

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

plus socks. Follow manufacturer's instructions for cleaning/maintaining Personal Protective Equipment (PPE). If there are no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

When handlers use closed systems, enclosed cabs or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240 (d) (4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations

lisers shore · Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. · Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

3.2 Environmental Hazards

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

3.3 Physical or Chemical Hazards

Spray solutions of this product should be mixed, stored and applied using only stainless steel, aluminum, fiberglass, plastic or plastic-lined steel containers.

DO NOT MIX. STORE OR APPLY THIS PRODUCT OR SPRAY SOLUTIONS OF THIS PRODUCT IN GALVANIZED STEEL OR UNLINED STEEL (EXCEPT STAINLESS STEEL) CONTAINERS OR SPRAY TANKS. This product or spray solutions of this product react with such containers and tanks to produce hydrogen gas which may form a highly combustible gas mixture This gas mixture could flash or explode, causing serious personal injury, if ignited by open flame, spark, welder's torch, lighted cigarette or other ignition source.

DIRECTIONS FOR USE

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

The Label:

Keep out of reach of children.

CAUSES EYE IRRITATION.

Avoid contact with eyes or clothing.

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

- Hold eye open and rinse slowly and gently with water for 15 20 minutes.
 - Remove contact lenses if present after the first 5 minutes then continue rinsing eye.
- Have the product container or label with you when calling a poison control center or doctor, or going for treatment.
- You may also contact (314) 694-4000, collect day or night, for emergency medical treatment information.
- \bullet This product is identified as Ranger PRO $^{\circledast}$ herbicide, EPA Registration No. 524-517.

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

Personal Protective Equipment (PPE)

Applicators and other handlers must wear: long-sleeved shirt and long pants, shoes plus socks. Follow manufacturer's instructions for cleaning/maintaining Personal Protective Equipment (PPE). If there are no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

When handlers use closed systems, enclosed cabs or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240 (d) (4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

3. Did Roun

The Label:

continue rinsing eye.

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

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

Personal Protective Equipment (PPE)

Applicators and other handlers must wear: long-sleeved shirt and long pants, shoes plus socks. Follow manufacturer's instructions for cleaning/maintaining Personal Protective Equipment (PPE). If there are no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

When handlers use closed systems, enclosed cabs or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240 (d) (4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations

Users should:

- · Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

Admission No. 13

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

Admission No. 14

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

Personal Protection





Multiple Heavy Exposures Nov. 2014: Reports to Monsanto



From: Sent: To:

Subject:

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

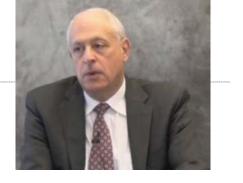
I will call him. The story is not making any sense to me at all.

Dan

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

Spoke with Dewayne Johnson @

and this is his story.



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

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

Thanks in advance for your assistance.

Patricia Biehl Product Support Specialist

Message		
From: Sent:	GOLDSTEIN, DANIEL A [AG/1000] [/O=MONSANTO/OU=NA-3 11/11/2014 8:19:51 PM	1000-01/CN=RECIPIENTS/CN=527246]
To:	BIEHL, PATRICIA M [AG-Contractor/1045] [/O=MONSANTO/	OU=NA-1000-01/cn=Recipients/cn=208718]
Subject:	RE: Ranger Pro Exposure	and the second se
l will call him Dan	. The story is not making any sense to me at all.	
Sent: Tuesda To: GOLDSTI	., PATRICIA M [AG-Contractor/1045] ay, November 11, 2014 2:12 PM EIN, DANIEL A [AG/1000] nger Pro Exposure	
Spoke with D	ewayne Johnson @ and this is his story.	

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

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

Thanks in advance for your assistance.

Patricia Biehl Prod<u>uct Support</u> Specialist

wiessage

Multiple Heavy Exposures Nov. 2014: Reports to Monsanto



From: Sent: To:

Subject:

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

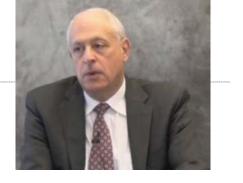
I will call him. The story is not making any sense to me at all.

Dan

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

Spoke with Dewayne Johnson @

and this is his story.



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

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

Thanks in advance for your assistance.

Patricia Biehl Product Support Specialist

Multiple Heavy Exposures Mar. 2015: Reports Problem Again

Message	
From: ient: fo: fo: cC: iubject: Attachments:	Thompson, Joy [4/15/2015 7:04:57 PM GRANETO, MATTHEW J [AG/1000] COLDSTEIN, DANIELA [AG/1000] @monsanto.com]; THURSTON, RUTH M [AG/8070] [] @monsanto.com]; WHITE, EIRI [AG/1000] [] @monsanto.com]; WHITE, EIRI [] ####################################
ilag:	Follow up
or the mont	e the FIFRA 6(a)(2) Reports for the Monsanto Lawn & Garden and Monsanto Agricultural products h of March 2015.
Please call r	ne at 314 f you have any questions.
Thank you, Joy Thomps ndustry liais Missouri Poi	

Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

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

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

Message

From:	Thompson, Joy [.
Sent:	4/15/2015 7:04:57 PM
To:	GRANETO, MATTHEW J [AG/10
CC:	GOLDSTEIN, DANIEL A [AG/100
	@monsant
	ERIN [AG/1000] [@r
	@monsanto.com]; Web
Subject:	March 2015 FIFRA 6(a)(2) Repo
Attachments:	FIFRA March 2015.docx
Flag:	Follow up



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

Good afternoon Matt,

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

Please call me at 314 for the four have any questions.

Thank you,

Joy Thompson RN, CSPI

Industry liaison

Missouri Poison Center

Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

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



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

Date.	03/21/2013
Medical Outcome:	Major Effect H-B
EPA Reg. No.	524-517
Active Ingredients:	Glyphosate 41%
State:	California
History and Notes:	Caller states he has been using Ranger Pro as part of his job for 2 to 3 years. He has recently been diagnosed with cutaneous T cell lymphoma. He has concerns about continuing to use Roundup as part of his job and questions if Roundup could be a source of his cancer. As the call progressed, caller said that doctors are unsure as to how to treat his condition and they are not even sure if it is cancer. Caller states that he works with Ranger Pro using a 50 gallon tank and also using a backpack sprayer. He dilutes 10 ounces of the Roundup per gallon (3.0%) for the 50 gallon tank and 4 ounces of Roundup per gallon (1.25%) when using the backpack sprayer. He recalls having been exposed to Roundup twice in the past 2 to 3 years, both from the backpack leaking/malfunctioning. In one case, he was wearing personal protective equipment (PPE) but it soaked through the PPE and his clothing. Recently, he has had a swollen foot and the MD's cannot figure out what is going on. The caller's level of fear is rising over his continued use of Ranger Pro. He states he continues to get unexplained rashes and nodules over his body. MRPC discussed the product toxicity. The symptoms are not an expected response from the product. Advised MRPC is available, if the treating MD has any questions.

Multiple Heavy Exposures 2015: Reports Problem Again

Message	
From:	Thompson, Jay [
Sent:	4/15/2015 7:04:57 PM
To:	GRANETO, MATTHEW J [AG/1000] [
CC:	GOLDSTEIN, DANIEL A [AG/1000] monsento.com]; NYANGULU, JAMES M [AG/8070]
	Pmonsanto.com); THURSTON, RUTH M [AG/8070] [Pmonsanto.com]; WHITE, ERIN [AG/1000] [Pmonsanto.com]; SEIFERT-HIGGINS, SIMONE [Pmonsanto.com];
	@monsanto.com]; Weber, Julie [@ssmhc.com]
Subject:	March 2015 FIFRA 6(a)(2) Reports
	FIFRA March 2015.docx
Flag:	Follow up
Good after	noon Matt,
Attached are	e the FIFRA 6(a)(2) Reports for the Monsanto Lawn & Garden and Monsanto Agricultural products
for the mont	h of March 2015.
Please call	ne at 314 f you have any questions.
Thank you,	
	ion RN, CSPI
Industry liais	son
Missouri Po	ison Center
	A CONTRACT OF
	A REAL PROPERTY AND A REAL
	State of the second second second second
	a for the second second second second
	Contraction of the local division of the loc
	1999

Human Exposure / Adverse Effect Incidents Involving Monsanto Agricultural Products

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

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

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

His cancer got worse and worse.

Why?

Roundup can promote cancer.







Issues to Consider

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

- 1. What is Roundup?
- 2. Can Roundup cause cancer?

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

- 4. What are Mr. Johnson's damages?
- 5. Should Monsanto be punished for its conduct?

Yes.

es

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

- Economic damages
- Non-economic damages
 - physical pain



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



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



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





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

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

Net Worth: \$6.6 Billion



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



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

How does Roundup work?

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

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

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

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

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

Dr. Kirk Azevedo Sales Representative (former)

"We're about making money, so get it straight."



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

Yes.

