W E I T Z
&
L U X E N B E R G
A PROFESSIONAL CORPORATION
• LAW OFFICES •
700 BROADWAY • NEW YORK, NY 10003
TEL. 212-558-5500 FAX 212-344-5461
WWW.WEITZLUX.COM

August 29, 2017

VIA EMAIL
John Kalas, Esq.
Hollingsworth, LLP
1350 I Street, N.W.
Washington, DC 20005

Re: *In Re: Roundup Products Liability Litigation*, MDL No. 2741,
Document Production for Dr. Portier

Dear Mr. Kalas:

As we discussed yesterday, and subject to Plaintiffs' objections served on August 23, 2017, attached are documents responsive to Schedule A attached to the Notice of Deposition for Dr. Christopher Portier.

Very truly yours,

Robin L. Greenwald

Encl.

Privileged and Confidential
Attorney Client Privilege
Attorney Work Product

In re Glyphosate/Roundup Litigation

March 29, 2015

Hunter W. Lundy
LUNDY, LUNDY SOILEAU & SOUTH, LLP
501 Broad Street
Lake Charles, LA 70601
Email: hlundy@lundylawllp.com
Telephone: 337 439-0707 / Fax: 337 439-1029

Expert Name
Christopher J. Portier, Ph.D.
Email [redacted]

Dear Dr. Portier:

This will confirm that Hunter W. Lundy, acting on behalf of the law firms of Lundy, Lundy, Soileau and South, LLP and Weitz & Luxenberg, PC ("Attorneys" or "Firms"), has retained you for the sole purpose of consulting with these Attorneys in connection with anticipated litigation involving claims arising from injury or damage caused, or potentially caused, by exposure to Roundup and/or other herbicides containing Glyphosate (the "Engagement"). The terms of the Engagement are as follows:

1. You are hereby engaged to provide expert consultation and analysis in connection with the cases to be filed (the "Roundup Cases"), relating to, without limitation, any area of expertise that you have or possess pertaining to the question of whether Roundup and/or Glyphosate-containing herbicides can cause adverse biological/physiological health effects in humans; relevant mechanisms of injury; any research or scientific studies that you have conducted or participated in conducting; and any other related issues.

Privileged and Confidential
Attorney Client Privilege
Attorney Work Product

2. All work conducted in connection with this Engagement as a consulting expert and/or a testifying expert witness pursuant to the direction, authority, and/or funding of the referenced Attorneys, including any reports, drafts, data, notes, work papers, correspondence, or other work documents you may generate or receive in connection with the Roundup Cases shall be considered and treated as confidential work product. All such documents and materials (and any information they contain that is not publicly available data or previously available to you) may be used only for purposes of this Engagement and may not be disclosed to anyone without our written consent in advance. This Engagement does not pertain to nor shall it affect your research and/or scientific studies, and it is expressly understood and acknowledged that we have not, nor will we fund, participate, sponsor or be involved in any of your past, present or future research or scientific studies.

3. In recognition of the confidential nature of this Engagement and subject to the terms of paragraph 2, you agree to not discuss or share any of this work, work product, analysis and/or opinions developed or prepared in connection with this Engagement with anyone else including, but not limited to, media organizations, trade journals, professional publications, members of the public, other purported experts, etc., and to notify us promptly if you receive:

   a. Any request to reveal information related to this Engagement or to examine, inspect or copy any documents you generate or receive; or

   b. Any actual or attempted service of a subpoena, summons or order purporting to require the disclosure of any such information or documents; and

   c. In consequence of such requests, subpoena(s), summons or order to require disclosure, the above-named law firm shall provide whatever legal services that are required to Christopher J. Portier without fee, any resultant out-of-pocket expenses, and payment of hourly rate.

Privileged and Confidential
Attorney Client Privilege
Attorney Work Product

4. You have assured us that you do not have any conflict of interest which might interfere with your performance of services contemplated by this Engagement, and you agree to avoid any such conflict during the term of this Engagement. More specifically, it is understood that until this matter is resolved (including any appeals), you will not accept any Roundup and/or Glyphosate-related engagement with any law firm that is a party to Roundup and/or Glyphosate-related litigation without our written consent in advance. However, if written consent is requested by Christopher J. Portier regarding another matter outside the specifics of this litigation, such consent shall not be unreasonably withheld. The request shall list the reasons why consent is requested. Should requested consent be withheld by Firms, they shall supply specific written reasons referencing the specific reasons listed in the written consent request. If Expert and Firms cannot agree, a single arbiter agreed upon by both parties shall decide.

5. Your fee for specific consultation, analysis and any requested report(s) shall be $450.00 (US Dollars) per hour in addition to reimbursement for any out-of-pocket expenses. You shall receive a retainer of $5,000.00 from which charges shall be drawn. You will send a monthly invoice as necessitated by the requested work which identifies the time spent and services rendered. Upon the depletion of the $5,000.00 retainer, payment will be made within 30 days from receipt of your invoice. Bills should be issued to the attention of Hunter W. Lundy at Lundy, Lundy, Soileau & South, LLP, 501 Broad Street, Lake Charles, LA 70601.

6. You will be working under the exclusive direction of Hunter W. Lundy, Matthew E. Lundy and Kristie M. Hightower with the law firm of Lundy, Lundy, Soileau & South, LLP, and Robin L. Greenwald with the law firm of Weitz and Luxenberg, PC.

7. Any and all work product created by you or on your behalf in whole or in part during the course of this Engagement, authorized by the Committee, shall be considered a work for hire and the property of the Firms.

8. You or we may terminate this agreement in writing at any time, in which event

you must stop work and bill only for the work performed up until receipt of the written termination. However, in the event of such termination, the restrictions described in paragraphs 2, 3 and 4 (related to work product generated) above will remain in effect absent a mutual agreement to the contrary. Such mutual agreement shall not be unreasonably withheld.

9. Any controversy, dispute or claim arising out of or relating to this Engagement or breach of this Agreement, shall be decided by a single arbitrator to be mutually selected in a privately administered arbitration to be held in _____, using the rules of the American Arbitration Association. The Firms and you expressly consent to personal jurisdiction in the courts of _____, and waive any objection thereto.

Please acknowledge that you accept these terms by signing the enclosed copy of this letter and returning it to us.

Sincerely,

LUNDY, LUNDY, SOILEAU & SOUTH, LLP

By:_____
Hunter W. Lundy

Agreed to by:

_____
Christopher J. Portier, Ph.D.

Dated: _____

INVOICE

Christopher Portier

Regarding:

***Bill to*:**
Glyphosate/Roundup Litigation
Attn: Hunter W. Lundy
LUNDY, LUNDY SOILEAU & SOUTH, LLP
501 Broad Street
Lake Charles, LA 70601
Email: hlundy@lundylawllp.com
Telephone: 337 439-0707 / Fax: 337 439-1029

Invoice Date: 10/19/2015
Invoice #: 15002

Quantity	Date	Unit	Description	Rate	Amount Due
0.5	6/17/15	hr	Meet with H. Lundy at BIOEM meeting, general issues regarding Glyphosate	$450.00	$225.00
1	6/19/15	hr	Meet with H. Lundy and Robin Greenwald in Davis, CA, general issues regarding Glyphosate	$450.00	$450.00
2	7/9/15	hr	Background research on glyphosate and AML, cancers in the Ag. Health Study and onset time for NHL	$450.00	$900.00
3.5	10/19/15	hr	Reduce value of retainer (balance $5000.00) by cost this invoice (new balance $3425.00)	-$450.00	-$1575.00
				Total	$0.00

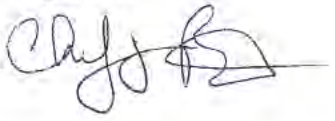
Reimbursement Information:

Name: Christopher Portier

[redacted]

[redacted]

Signature:



INVOICE

Christopher Portier

Regarding:

Bill to:
Glyphosate/Roundup Litigation
Attn: Hunter W. Lundy
LUNDY, LUNDY SOILEAU & SOUTH, LLP
501 Broad Street
Lake Charles, LA 70601
Email: hlundy@lundylawllp.com
Telephone: 337 439-0707 / Fax: 337 439-1029

Invoice Date: 3/29/2016
Invoice #: 15003

Quantity	Date	Unit	Description	Rate	Amount Due
2	12/4/15	hr	Phone call followed by research on glyphosate references	$450.00	$900.00
3	12/16/15	hr	Meet with Robin Greenwald and staff in NYC RE: Glyphosate	$450.00	$1350.00
3	3/11/16	hr	Meet with Hunter Lundy, Kristie Hightower and Rudie Soileau in Lake Charles	$450.00	$1350.00
3	3/11/16	hr	Travel to Lake Charles	$150.00	$450.00
3	3/11/16	hr	Travel from Lake Charles to New Orleans	$150.00	$450.00
			Credit from retainer	$3425.00	-$3425.00
				Total Invoice	$1085.00

Reimbursement Information:

Name: Christopher Portier
[redacted]

Signature:

INVOICE

Christopher Portier

Regarding:

Bill to:
Glyphosate/Roundup Litigation
Attn: Hunter W. Lundy
LUNDY, LUNDY SOILEAU & SOUTH, LLP
501 Broad Street
Lake Charles, LA 70601
Email: hlundy@lundylawllp.com
Telephone: 337 439-0707 / Fax: 337 439-1029

Invoice Date: 6/30/2016
Invoice #: 15004

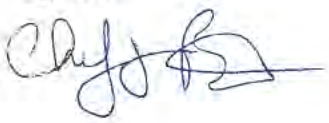
Quantity	Date	Unit	Description	Rate	Amount Due
8	5/12/16	hr	Read and evaluate EPA glyphosate document	$450.00	$3600.00
5	5/13/16	hr	Read and evaluate EPA glyphosate document	$450.00	$2250.00
4	5/14/16	hr	Read and evaluate EPA glyphosate document	$450.00	$1800.00
2	5/15/16	hr	Read and evaluate EPA glyphosate document	$450.00	$900.00
				Total Invoice	$8550.00

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:



INVOICE

Christopher Portier

Regarding:

Bill to:
Glyphosate/Roundup Litigation
Attn: Robin Greenwald, Esq.
Weitz & Luxenberg P.C.
700 Broadway, 5th Floor
New York, NY. 10003
Phone:212-558-5685
Fax: 212-344-5461
Email: RGreenwald@weitzlux.com

Invoice Date: 2/6/2017
Invoice #: 17001

Quantity	Date	Unit	Description	Rate	Amount Due
10	10/1/2016 to 12/31/2016	hr	Multiple phone meetings, reviews and background development	$450.00	$4,500.00
12	1/1/17 to 2/6/17	hr	Multiple phone meetings and slide preparation	$450.00	$5,400.00
1	1/31/17	tckt	Airline ticket for flight to and from San Francisco/NYC (see attached)	$7,777.71	$7,777.71
				Total Invoice	$17,677.71

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:

INVOICE

Christopher Portier

Regarding:

Bill to:
Glyphosate/Roundup Litigation
Attn: Robin Greenwald, Esq.
Weitz & Luxenberg P.C.
700 Broadway, 5th Floor
New York, NY. 10003
Phone:212-558-5685
Fax: 212-344-5461
Email: RGreenwald@weitzlux.com

Invoice Date: 3/7/2017
Invoice #: 17002

Quantity	Date	Unit	Description	Rate	Amount Due
17	2/8/17 to 2/26/17	hr	Slide preparation and discussion for "Science Day"	$450.00	$7,650.00
6	2/25/17	hr	Travel time to San Francisco	$100.00	$600.00
6.5	2/27/17	hr	"Science Day"	$450.00	$2,925.00
4	3/2/17	hr	Preparation of expert report	$450.00	$1,800.00
6	3/3/17	hr	Meet with legal team	$450.00	$2,700.00
5	3/5/17	hr	Travel time to home	$100.00	$500.00
1	2/25/17	cost	Taxi from airport to hotel in San Francisco	$50.00	$50.00
1	2/25/17	cost	Hotel in San Francisco	$560.50	$560.50
1	3/1/17	cost	Taxi to hotel in NYC	$62.84	$62.84
1	3/1/17	cost	Hotel in NYC	$601.40	$601.40
1	3/5/17	cost	Taxi to airport in NYC	$66.34	$66.34
				Total Invoice	$17,516.08

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:

INVOICE

Christopher Portier

Regarding:

***Bill to*:**
Glyphosate/Roundup Litigation
Attn: Robin Greenwald, Esq.
Weitz & Luxenberg P.C.
700 Broadway, 5th Floor
New York, NY. 10003
Phone:212-558-5685
Fax: 212-344-5461
Email: RGreenwald@weitzlux.com

Invoice Date: 4/4/2017
Invoice #: 17003

Quantity	Date	Unit	Description	Rate	Amount Due
163	Various dates	hr	Drafting of Expert Report (individual daily activities on Page 2)	$450.00	$73,350.00
			Total Invoice		$73,350.00

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:

Quantity	Date	Units	Description	Rate	Charge
5.5	3/7/17	hr	Drafting of Expert Report	$450.00	$2,475.00
6.5	3/8/17	hr	Drafting of Expert Report	$450.00	$2,925.00
2	3/9/17	hr	Drafting of Expert Report	$450.00	$900.00
4	3/10/17	hr	Drafting of Expert Report	$450.00	$1,800.00
6	3/13/17	hr	Drafting of Expert Report	$450.00	$2,700.00
8	3/14/17	hr	Drafting of Expert Report	$450.00	$3,600.00
7	3/15/17	hr	Drafting of Expert Report	$450.00	$3,150.00
8	3/16/17	hr	Drafting of Expert Report	$450.00	$3,600.00
6	3/17/17	hr	Drafting of Expert Report	$450.00	$2,700.00
4	3/18/17	hr	Drafting of Expert Report	$450.00	$1,800.00
8	3/19/17	hr	Drafting of Expert Report	$450.00	$3,600.00
9	3/20/17	hr	Drafting of Expert Report	$450.00	$4,050.00
9	3/21/17	hr	Drafting of Expert Report	$450.00	$4,050.00
9	3/22/17	hr	Drafting of Expert Report	$450.00	$4,050.00
8	3/23/17	hr	Drafting of Expert Report	$450.00	$3,600.00
8	3/24/17	hr	Drafting of Expert Report	$450.00	$3,600.00
3	3/25/17	hr	Drafting of Expert Report	$450.00	$1,350.00
8	3/26/17	hr	Drafting of Expert Report	$450.00	$3,600.00
8	3/28/17	hr	Drafting of Expert Report	$450.00	$3,600.00
8	3/29/17	hr	Drafting of Expert Report	$450.00	$3,600.00
8	3/30/17	hr	Drafting of Expert Report	$450.00	$3,600.00
8	3/31/17	hr	Drafting of Expert Report	$450.00	$3,600.00
2	4/1/17	hr	Drafting of Expert Report	$450.00	$900.00
7	4/2/17	hr	Drafting of Expert Report	$450.00	$3,150.00
3	4/3/17	hr	Drafting of Expert Report	$450.00	$1,350.00
Totals					
163	25 days				$73,350.00

INVOICE

Christopher Portier

Regarding:

***Bill to*:**
Glyphosate/Roundup Litigation
Attn: Robin Greenwald, Esq.
Weitz & Luxenberg P.C.
700 Broadway, 5th Floor
New York, NY. 10003
Phone:212-558-5685
Fax: 212-344-5461
Email: RGreenwald@weitzlux.com

Invoice Date: 6/18/2017
Invoice #: 17004

Quantity	Date	Unit	Description	Rate	Amount Due
72	Various dates	hr	Drafting of Expert Report (individual daily activities on Page 2)	$450.00	$32,400.00
			Total Invoice		$32,400.00

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:

Quantity	Date	Units	Description	Rate	Charge
2	4/5/17	hr	Q&A	$450.00	$900.00
3	4/6/17	hr	Q&A, Work on expert report	$450.00	$1,350.00
4	4/7/16	hr	Read parts of various depositions	$450.00	$1,800.00
8	4/13/17	hr	Read FIFRA SAP Report, include in Expert Report	$450.00	$3,600.00
9	4/18/17	hr	Correct typos to Expert Report, explain certain parts, expand explanations of animal data	$450.00	$4,050.00
6	4/23/17	hr	Check all numbers and tables in expert report, clarify text	$450.00	$2,700.00
7	4/24/17	hr	Check all numbers and tables in expert report, clarify text	$450.00	$3,150.00
4	4/30/17	hr	Edit and refine Expert Report	$450.00	$1,800.00
9	5/1/17	hr	Edit and refine Expert Report	$450.00	$4,050.00
3	6/5/17	hr	Edit and refine Expert Report	$450.00	$1,350.00
4	6/6/17	hr	Edit and refine Expert Report	$450.00	$1,800.00
4	6/7/17	hr	Edit and refine Expert Report	$450.00	$1,800.00
5	6/8/17	hr	Edit and refine Expert Report	$450.00	$2,250.00
2	6/9/17	hr	Edit and refine Expert Report	$450.00	$900.00
2	6/13/17	hr	Edit and finalize final Expert Report	$450.00	$900.00
Totals					
72	15 days				$32,400.00

INVOICE

Christopher Portier

Regarding:

***Bill to*:**
Glyphosate/Roundup Litigation
Attn: Robin Greenwald, Esq.
Weitz & Luxenberg P.C.
700 Broadway, 5th Floor
New York, NY. 10003
Phone:212-558-5685
Fax: 212-344-5461
Email: RGreenwald@weitzlux.com

Invoice Date: 7/13/2017
Invoice #: 17005

Quantity	Date	Unit	Description	Rate	Amount Due
1	20-June to 19 July, 2017	ea	Airplane ticket for deposition in NYC in July, 2017 (cancelled)	$4,046.56	$4,046.56
			Total Invoice		$4,046.56

Reimbursement Information:

Name: Christopher Portier

[redacted]

Signature:

From: [redacted]
Subject: REPLY to Letter regarding EFSA Glyphosate Recommendations
Date: December 15, 2015 at 5:09:54 PM GMT+1
To: [redacted]
Cc: [redacted]

Dear Mr Portier,

Please find enclosed letter from Commissioner Andriukaitis.

Best regards,

Egidijus Dapkus
Assistant unknown.gif ¬ **European Commission** Cabinet of Commissioner Vytenis Andriukaitis Health & Food Safety BERL 08/359
+32 229 80729 [redacted]

From: Kurt Straif <[redacted]>
Subject: FW: IARC Monograph on Glyphosate
Date: November 11, 2015 at 11:04:48 PM GMT+1
To: "Chris Portier [redacted]" <[redacted]>

fyi

From: Kurt Straif **Sent:** 11 November 2015 23:04 **To:** [redacted] **Cc:** 'Landrigan, Philip' <[redacted]>
Subject: FW: IARC Monograph on Glyphosate

Dear Ellen,

I am a strong believer in open and transparent (and when needed provocative) discussion among reasonable people, and therefore I would like to respond to your email (appropriately forwarded by Phil, since I'm the first author of that letter and the Head of the IARC Monographs).

- Our response to the letter from our good friend Manolis was very nuanced, including the identification of scenarios where meta-analyses are not the magic cure for causal inference
- Cochrane reviews (even when focusing on RCTs) don't necessarily get it right (mammography screening being one such example)
- With our without meta-analyses, I would argue that the IARC Monographs are systematic reviews, and include a review of all published literature on cancer in humans and in animals pertinent to a given topic. Therefore, I don't understand why we are on weak grounds here.
- The Monograph on glyphosate included reviews of available meta-analyses (the most recent and comprehensive one reporting a statistically significant increased risk of NHL), but concluded that the qualitative review of the individual studies was more informative, and concluded that there is (only) "limited" evidence in humans.

Best,
Kurt

From: Landrigan, Philip [redacted] **Sent:** 11 November 2015 18:46 **To:** Kurt Straif [redacted] **Subject:** FW: IARC Monograph on Glyphosate

FYI

Philip J. Landrigan, MD, MSc, FAAP
Dean for Global Health
Arnhold Institute for Global Health
Professor of Preventive Medicine and Pediatrics
Icahn School of Medicine at Mount Sinai
12 16 Fifth Avenue, Room 556
New York, NY 10029

Tel: 212-824-7952

[redacted]

unknown.png ¬ 1__#$!@%!#__unknown.png ¬ unknown.gif ¬ 2__#$!@%!#__unknown.png ¬ 3__#$!@%!#__unknown.png ¬

WHO Collaborating Centre in Children's Environmental Health

From: Ellen Silbergeld [redacted] **Sent:** Wednesday, November 11, 2015 10:23 AM**To:** Landrigan, Philip**Cc:** [redacted] **Subject:** RE: IARC Monograph on Glyphosate

They are not the same. I think you and Kurt were co authors on a letter published in EHP in 2012 that recommended that IARC examine the use of meta-analyses and SR methods when possible and appropriate. **Use of Meta- analyses by IARC Working Groups**
http://dx.doi.org/10.1289/ehp.1205397

TO QUOTE YOUR LETTER: "With more epidemiological studies becoming

available for each agent, additional cancer sites being investigated, and relatively small effect esti-mates becoming center of the discussion, the need for meta-analyses is likely to increase."

I think this an example of how we are all on weak ground when each group does an assessment with a less than complete review of the literature

Ellen K Silbergeld, PhD
Professor, Environmental Health Sciences
Johns Hopkins Bloomberg School of Public Health
615 North Wolfe Street, Rm E6644
Baltimore MD 21205 USA
tel: 410 955 8678
fax: 443 287 6414

PLEASE NOTE: IF YOU DO NOT RECEIVE A PROMPT RESPONSE FROM ME TO AN EMAIL, PLEASE RESEND IT AS WE ARE HAVING ISSUES WITH OUR EMAIL SYSTEM. IF YOU STILL DO NOT RECEIVE A RESPONSE, YOU MAY HAVE TO CALL ME BY PHONE.

From: Landrigan, Philip [redacted] **Sent:** Wednesday, November 11, 2015 10:03 AM**To:** Ellen Silbergeld**Subject:** Re: IARC Monograph on Glyphosate

In my opinion an IARC review is Cochrane equivalent

Philip J. Landrigan, MD, MSc, FAAP
Dean for Global Health
Arnhold Institute for Global Health
Professor of Preventive Medicine & Pediatrics
Icahn School of Medicine at Mount Sinai
1216 Fifth Avenue, Room 556
New York, NY 10029

Tel: 1 212 824 7952

On Nov 11, 2015, at 9:50 AM, Ellen Silbergeld <[redacted]> wrote:

Phil: I have concerns that no one has done a systematic review on this topic...

Ellen K Silbergeld, PhD
Professor, Environmental Health Sciences
Johns Hopkins Bloomberg School of Public Health
615 North Wolfe Street, Rm E6644
Baltimore MD 21205 USA
tel: 410 955 8678
fax: 443 287 6414

PLEASE NOTE: IF YOU DO NOT RECEIVE A PROMPT RESPONSE FROM ME TO AN EMAIL, PLEASE RESEND IT AS WE ARE HAVING ISSUES WITH OUR EMAIL SYSTEM. IF YOU STILL DO NOT RECEIVE A RESPONSE, YOU MAY HAVE TO CALL ME BY PHONE.

From: Landrigan, Philip[redacted] **Sent:** Wednesday, November 11, 2015 9:26 AM**To:** Chris Portier**Cc:** Dariusz Leszczynski; ronald melnick;[redacted] pcl;[redacted] Bailer, A. John; Julia Gohlke; Dr. Fiorella Belboggi; Morando Morando Soffritti; Woodruff Tracey; Hillary Carpenter III; Harvey Checkoway; Jackson, Richard J.; Devra Davis;[redacted] Elena Craft; Dr Peter Di Marco PhD; Dr. Lutz Edler; Dr. Annette Kopp-Schneider; Silbergeld Ellen; Jon Freedman; Michael Gallo; Kenneth Portier; Ralph Portier; Steven hamburg; Joe Haseman; Tyrone Hayes; Irva Hertz-Picciotto; James Huff; [redacted] Tsuyoshi Nakamura; Ken Ramos; Michael Schwartz; Ray Tice; Sarah Vogel**Subject:** Re: IARC Monograph on Glyphosate

Chris

I stand with you on this. Please add my name

Phil Landrigan Philip J. Landrigan, MD, MSc, FAAP

Dean for Global Health
Arnhold Institute for Global Health
Professor of Preventive Medicine & Pediatrics
Icahn School of Medicine at Mount Sinai
1216 Fifth Avenue, Room 556
New York, NY 10029

Tel: 1 212 824 7952

On Nov 11, 2015, at 9:10 AM, Chris Portier <[redacted]> wrote:

Dear Colleagues,

For IARC Monograph 112, 17 scientists evaluated the carcinogenic hazard for 4 insecticides and the herbicide glyphosate. The Working Group concluded that glyphosate was a probable human carcinogen. This finding stirred great debate globally on the safety of glyphosate and led to a careful evaluation of the IARC monograph results when they became available on July 29, 2015. During this period, the European Food Safety Agency (EFSA) was in the middle of a reassessment of the safety of glyphosate. The German Federal Institute for Risk Assessment (BfR) was the lead country agency in drafting the reassessment report. The draft, prior to the IARC Monograph, concluded there was no carcinogenic potential of glyphosate. In August of this year, following the release of the full Monograph on glyphosate, the BfR drafted an Addendum to their report that specifically addresses the Monograph review. This was presented to EFSA several weeks ago and leaked by the press.

This week, EFSA will release their reassessment of glyphosate. In this review, they will again conclude that glyphosate has no carcinogenic potential. This review is based on the BfR Addendum which has some severe scientific flaws. I am concerned that this evaluation, if it stands,

could weaken the effectiveness of the IARC Monograph Programme. I am also concerned that the serious flaws in the BfR Addendum, if not challenged, could continue to be used by regulatory agencies to dismiss critical science pertinent to a regulatory decision, including broad exclusion of literature data and epidemiological data.

The European Commission ENVI Committee will meet on December 1, 2015 to receive the reassessment report from EFSA. I have drafted a letter of concern that I wish to present to the ENVI Committee as they consider whether to accept or reject the EFSA evaluation. I would like to invite you to join with me in signing this open letter. I have obtained your names from many different lists, mostly from previous IARC monographs but also from other sources. It is possible I have included your name more than once on this list and I apologize for sending you multiple copies.

I am open to changes to improve the letter, but because of the short time-frame, I hope you can agree to sign on with only modest modifications (I am sending this to several hundred colleagues). I have included the letter but have not included the BfR Addendum or the Reassessment Report because of size. These are available at:

Addendum: http://www.mdr.de/fakt/fakt-glyphosat-bfr-bewertung100.html (NOTE: click on Herunterladen to download the report)
RAR: http://dar.efsa.europa.eu/dar-web/provision
The more important report is the Addendum.

If you agree to joining me in signing this letter, please respond by November 25 with the following that I can then add to my letter.

Title (Prof, Dr., …), Name
Position Title (e.g. Director, Named Chair, etc)
Affiliation
City, Country

I look forward to hearing from you.

Sincerely, Christopher Portier

<IARCWG112ResponseV3.docx>

From: FOUCART, Stéphane <[redacted]
Date: November 13, 2015 at 12:59:31 PM GMT+1
To: Chris Portier <[redacted]

Dear Chris Portier,

thank you so much for your time & help.
Please find attached the resulting article, due to be published this afternoon in the print edition (already on line).

again : thanks a lot for you explanations.
best
Stéphane

From: "Adriaanse, Paulien" <[redacted]
Subject: Your request for email address
Date: November 24, 2015 at 3:54:29 PM GMT+1
To: [redacted]

Dear Sir,

Please find below my email address for sending a copy of your letter to EFSA's PPR Panel.

Sincere regards,

Paulien Adriaanse

Paulien Adriaanse

Alterra
Team Environmental Risk Assessment
Senior scientific researcher LUMEN, room B.003 P.O. Box 47 6700 AA Wageningen tel. +31 317 481913
email: paulien.adriaanse@wur.nl
http://www.era.wur.nl

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From: Kathryn Guyton <[redacted]
Subject: FW: glyphosate in the press
Date: April 6, 2016 at 11:23:12 AM GMT+2
To: "Rusyn, Ivan" <[redacted], Chris Portier
[redacted]

Dear Chris, Dear Ivan,

The below may be of interest.

Chris, we gave your contact info to Kate K. of Reuters. I'll forward you the information we provided to her.

Best to you both from sunny Lyon,
Kate

From: Véronique Terrasse <[redacted]
Date: Wednesday 6 April 2016 at 11:09
To: Kurt Straif [redacted], Kate Guyton [redacted], Dana Loomis
[redacted]
Cc: Nicolas Gaudin <[redacted]
Subject: glyphosate in the press

Dear all,

Some lobbying activities on both sides..

Copa and Cogeca send letter to EU Commission & MEPs urging them to keep the herbicide active substance glyphosate on EU market, after EU Foo Safety Authority (EFSA) gave it green light (pdf)

Petition demands EPA revoke license for weed-killer ingredient

The Hill | 05/04/16 21:58

...Environmental Protection Agency (EPA) to revoke the license for ***glyphosate*** the active ingredient i Monsanto s herbicide Roundup. Recent tests.. .

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Véronique Terrasse
Press Officer, IARC Communications Group
Email: [redacted]
Web: www.iarc.fr
Tel: +33 4 72 73 83 66
Cell: +33 6 45 28 49 52

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From: Kathryn Guyton [redacted]
Subject: FYI
Date: April 6, 2016 at 11:26:45 AM GMT+2
To: Chris Portier <[redacted]

Hi Chris,
As mentioned.
Best,
Kate

From: Kathryn Guyton <[redacted]
Subject: Letter to Vol 112 Working Group
Date: April 7, 2016 at 8:55:57 PM GMT+2
To: Chris Portier <[redacted]

Dear Chris,
Please see the attached letter.
Best,
Kate

From: Kathryn Guyton <[redacted]
Subject: FW: Breaking news from EU Food Policy
Date: April 13, 2016 at 3:15:08 PM GMT+2
To: Ivan Rusyn [redacted] Chris Portier [redacted] Lauren Zeise <[redacted]

The latest on the EU vote on glyphosate today...
Best,
Kate

From: EU Food Policy [mailto:news@eufoodpolicy.com] **Sent:** 13 April 2016 14:18
Here's the latest breaking news from EU Food Policy:

MEPs call for 7-year limit on new glyphosate authorisation

MEPs have backed a resolution calling on the European Commission to renew the authorisation of the herbicide, glyphosate, for a maximum of seven years instead of the normal 15-year approval.
read more...
To access previous editions of EU Food Policy, use the Archive tab and select the edition required. When logging in, please remember to enter your email address in lower case, followed by your password. If you have any problems, don't hesitate to contact us.

Yours sincerely, *Patrick Bartlett Director EU Food Policy*
info@eufoodpolicy.com +44 208 567 4569

From: Kathryn Guyton [redacted]
Subject: FW: Reuters attacks IARC over glyphosate cancer link
Date: April 21, 2016 at 11:18:05 AM GMT+2
To: Chris Portier [redacted] Martyn Smith
[redacted]

Dear Chris, Dear Martyn,
Perhaps you did not realise it, but some of the sources in the Reuters article have a pro-industry history. ;-)
Happy reading,
Kate

Hope this is of some use to IARC; I understand they will respond to the recent attacks on them. Sources can be accessed in the online version here:
http://www.gmwatch.org/news/latest-news/16889

Claire Robinson
GMWatch

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From: "ED.Directorate" <[redacted]
Subject: RE: EFSA Glyphosate Recommendations
Date: February 9, 2016 at 3:24:39 PM GMT+1
To: IARC Director <[redacted]
Cc: ANDRIUKAITIS Vytenis <[redacted], HOGAN Phil <[redacted], PRATS MONNE Xavier <[redacted] MIKO Ladislav <[redacted] EFSA PESTICIDES PPR <[redacted] David Allen <[redacted], Kurt Straif <[redacted]

Dear Dr Wild,

In reply to your letter of 5 February 2016, please find attached Dr Url's response for your kind attention.

Yours sincerely,

Anna Azzali
Assistant to the Executive Director

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Via Carlo Magno 1A
43126 Parma (Italy)
Tel. +39 0521 036 201
Fax. +39 0521 036 0201
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twitter.com/EFSA_EU **1__#$!@%!#__unknown.jpg ¬**
youtube.com/EFSAchannel **2__#$!@%!#__unknown.jpg ¬**

From: Margot Geesink [redacted] **On Behalf Of** IARC Director
Sent: 05 February 2016 16:11 **To:** URL Bernhard; ED.Directorate **Cc:** ANDRIUKAITIS Vytenis; CAB ANDRIUKAITIS WEBPAGE; HOGAN Phil; PRATS MONNE Xavier; MIKO Ladislav; [redacted] EFSA PESTICIDES PPR; David Allen; Kurt Straif; IARC Director **Subject:** FW: EFSA Glyphosate Recommendations

Dear Dr Url,

Please find attached a letter from Dr Christopher Wild.

Yours sincerely,

Margot Geesink
Personal Assistant to Dr Christopher P. Wild, Director,
International Agency for Research on Cancer (IARC)
150 cours Albert-Thomas
69008 Lyon, France
Tel. +33-4-72738577; Fax +33-4-72738564
E-mail: [redacted] www.iarc.fr

From: AZZALI Anna [redacted] **On Behalf Of** ED.Directorate **Sent:** 13 January 2016 10:57 **To:** Chris Portier [redacted] **Cc:** ANDRIUKAITIS Vytenis [redacted] HOGAN Phil [redacted] PRATS MONNE Xavier [redacted] IARC Director [redacted] MIKO Ladislav [redacted] **Subject:** RE: EFSA Glyphosate Recommendations

Dear Professor Portier,

In reply to your letter dated 27 November 2015, please find attached Dr. Url's response for your kind attention.

Yours sincerely,

Anna Azzali
Assistant to the Executive Director

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Via Carlo Magno 1A
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Tel. +39 0521 036 201
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twitter.com/EFSA_EU **1__#$!@%!#__unknown.jpg ¬**
youtube.com/EFSAchannel **2__#$!@%!#__unknown.jpg ¬**

From: Chris Portier [redacted] **Sent:** 27 November 2015 09:57
To: CAB ANDRIUKAITIS WEBPAGE; ANDRIUKAITIS Vytenis **Cc:** URL Bernhard; [redacted] EFSA PESTICIDES PPR; HOGAN Phil; MIKO Ladislav; [redacted] **Subject:** EFSA Glyphosate Recommendations

Dear Commissioner Andriukaitis,

Attached to this email is a letter from 96 prominent epidemiologists, toxicologists, statisticians and molecular biologists from 25 countries. We have banded together and write to you at this time to express our deep concern over the recent European Food Safety Agency (EFSA) decision that the widely used herbicide, glyphosate "is

unlikely to pose a carcinogenic hazard to humans." We ask that you read our letter and share it with those who will be advising you on accepting or rejecting EFSA's decision. We would greatly appreciate your sharing this with the members of the Standing Committee on Plants, Animals, Food and Feed before their next meeting on December 10, 2015. I will be in Brussels from November 30 to December 2. If you believe it would be helpful for me to discuss these concerns with you or your staff in person, please send email to this address or call +41 79 605 79 58.

Thank you for your attention to this important issue.

Sincerely,

Prof. Christopher J. Portier

cc: Mr. Phil Hogan, European Commissioner for Agriculture and Human Development
Dr. Ladislav Miko, Deputy Director-General, DG Health & Food Safety
Dr. Bernhard Url, Executive Director, EFSA
Dr. Giovanni La Via, Chair, ENVI Committee
EFSA Panel on Plant Protection Products and their Residues
Mr. Christian Schmidt, Minister of Food and Agriculture
Dr. Helmut Tschiersky, President of the Federal Office of Consumer Protection and Food Safety (BVL)
Professor Dr. Dr. Andreas Hensel, President, BFR
Dr. Christopher Wild, Director, IARC
Mr. Jim Jones, Assistant Administrator, USEPA

From: "ED.Directorate" [redacted]
Subject: RE: EFSA Glyphosate Recommendations
Date: January 13, 2016 at 10:57:15 AM GMT+1
To: [redacted]
Cc: ANDRIUKAITIS Vytenis <[redacted],
HOGAN Phil [redacted]
[redacted] PRATS MONNE Xavier
[redacted]
[redacted] MIKO Ladislav
[redacted]

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youtube.com/EFSAchannel **2__#$!@%!#__unknown.jpg ¬**

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Dr. Helmut Tschiersky, President of the Federal Office of Consumer Protection and Food Safety (BVL)
Professor Dr. Dr. Andreas Hensel, President, BFR
Dr. Christopher Wild, Director, IARC
Mr. Jim Jones, Assistant Administrator, USEPA

From: Kathy Burns [redacted]
Subject: RE: REPLY to Letter regarding EFSA Glyphosate Recommendations
Date: January 18, 2016 at 5:04:29 PM GMT+1
To: 'Chris Portier' [redacted]

This is fantastic. Your efforts on this have made all the difference in moving towards transparency and hopefully a more legitimate EFSA (if that can even be hoped for).

From: Chris Portier [redacted] **Sent:** Monday, January 18, 2016 10:55 AM **To:** Dr. Christopher Portier [redacted] **Subject:** Fwd: REPLY to Letter regarding EFSA Glyphosate Recommendations

FYI. I guess we had some impact.

C.

Begin forwarded message:

From: Kate Trollope <[redacted]
Subject: RE: REPLY to Letter regarding EFSA Glyphosate Recommendations
Date: January 18, 2016 at 4:39:43 PM GMT+1
To: 'Chris Portier' <[redacted]

As discussed, please find article below on EU experts' involvement in the EFSA assessment. Prior to this article, we found that one expert was someone EFSA had already launched a "breach of trust" against a few years ago when he was on their pesticides panel but failed to say that he worked for a consultancy, Melete, which worked for chemical firms. However, this person, Prof Galli was due to attend the teleconference on glyphosate but did not actually tune in so he was invited to participate but did not in the end!

We have also run an article about the fact that the wife of the EFSA head of the pesticides unit ran a chemical consultancy until a few weeks ago.

And we have found that many of the declarations of interest that EFSA publishes for its pesticide experts are blank because the experts refuse to fill them in and EFSA has no power to make them do so!

Best regards, Kate

Secrecy deepens over EU experts involved in glyphosate verdict

The secrecy over the identity of the EU member state experts involved in deciding that glyphosate is safe has deepened after the vast majority refused to allow their name to be made public.

In an effort to be more transparent about the procedure used in the EU for evaluation of pesticides, the European Food Safety Authority (EFSA) asked the 75 experts, who work for member states, if it could publish a list of their names. But only 14 people agreed to be identified, including two who were invited in their personal capacity.

These were Marianne Balmer of the Swiss research institute, Agroscope, and Veronique Poulsen, of the French food safety agency, ANSES.

Following the contrasting verdicts over glyphosate from EFSA and the International Agency for Research on Cancer, a number of organisations applied through the access-to-documents legislation for a list of the 75 experts involved at EFSA.

But none of the five individuals who work at the Federal Institute for Risk Assessment, BfR, which was the rapporteur on glyphosate, would be identified. And most experts working in other member states took a similar stance.

Dirk Detken, head of legal at EFSA, said the Authority was "committed to high standards of transparency and engagement in the risk assessment process, aiming at generating trust and credibility".

But he said this was subject to rules regarding personal data protection and "the

commitment ensured by the subsidiarity principle underpinning the peer review process involving member states".
Therefore, EFSA had asked the experts involved if the fact that they represented their administration at the expert meetings could be made public.
Most said no but EFSA has provided the names of the institutions involved, which brings clarity, as well as the names of people who were prepared to be identified.
Those who refused to be identified work at the following organisations:

- the Austrian food safety agency, AGES, (4)
- the Greek Benaki institute (4)
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- the Central Institute in the Czech Republic (2)
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- the National Institute of Public Health (1)
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- the Scientific Institute of Health in Belgium (1)
- the State Plant Service in Lithuania (1)
- the Germany Environment Agency (4)
- the Slovakian Water Research Institute (1)
- Croatia (1)

Those prepared to be identified included Sten Flodstrom, of the Swedish Chemicals Agency, which argued in a minority Opinion that glyphosate could be carcinogenic.
Others identified include Audra Paltanaviciene, State Plant Service, Ministry of Agriculture, Lithuania; Liga Brence, of the State Plant Protection Service in Latvia; Lucija Perharic, of the National Institute of Public Health in Slovenia; Ana Fandino Carro, of the National Institute for Agricultural and Food Research Technology in Spain; Christian Schlitt and Luca Tosti, of the Italian Centre for Pesticides; Laura Maccalman, of the UK Institute of Occupational Medicine; Wim Hooghe, of the Belgian Federal Public Service Health; Thomasina Barron, of the Department of Agriculture in Ireland; Susy Brescia, of the UK Chemicals

Regulation Directorate; and Eugenia Chaideftou, of the Benaki Institute in Greece.
NGOs have requested the documents and, no doubt, in the coming weeks will be looking into any declarations of interest made.
Corporate Europe Observatory last month launched a €5,000 fundraising campaign to raise funds for an investigation.
EFSA has already published on its website a list of all its member state experts involved in pesticide work. But this does not tell you which particular substances they have been involved in.
Some experts agree to publication of a DoI but many do not. Furthermore, EFSA cannot screen the DoIs because the experts work for member states.
The pesticides risk assessment is done differently to the panel system used for other regulated products such as food additives or GMOs and relies on experts sent by member states, not experts appointed to a panel by the management board.

EFSA pesticides supremo declares wife's chemical interests

The European Food Safety Authority's head of pesticides has revealed that until a few weeks ago his wife ran a private consulting company working for the chemical industry.
Jose Tarazona, head of the EFSA pesticides unit, makes the disclosure in a declaration of interest (DoI) form, which was signed on 2 December.
Dr Tarazona, who presided over EFSA's high profile work on glyphosate, says his wife, Maria Jose Ramos Peralonso, is an expert on hazard and risk communication of chemicals and had her own consulting company, Green Planet Environmental Consulting.
He says she gave advice to public and private bodies on the implementation of REACH, CLP and the communication of hazards and risks.
"She covered industrial and consumer (but not food or feed) products, thus no direct involvement in matters related to EFSA activities. No contracts with private companies since I am EFSA staff," he adds.
A number of organisations requested a copy of Dr Tarazona's declaration of

interest following EFSA's verdict that glyphosate was unlikely to cause cancer, in contrast to the opposite verdict of the International Agency for Cancer Research's.
He was the key staff member at EFSA involved in the assessment and represented EFSA at its press conference and in the European Parliament debate.
The requests for the DoI were made in November and early December and suddenly a new DoI was signed on 2 December. This stated that Dr Tarazona's wife had ended her consultancy in November.
This has created the perception that the consulting firm shut only as people asked more questions about Dr Tarazona's interests.
However, a spokesman for EFSA said that the closure of the consulting firm was a purely personal decision and was taken some time ago.
There was no link between NGOs asking for the DoI and the company closing, he said.
And Dr Tarazona had always declared his wife's interest on his DoI and needed to update his DoI because of the firm's closure.
The EFSA spokesman also stressed that the consulting firm had never been involved in work related to pesticides, or, in particular, to glyphosate.
Dr Tarazona became head of EFSA's pesticides unit in October 2013 after working for the European Chemicals Agency for four years.
Under EFSA independence rules, senior staff have to submit a DoI which includes any interests of "close family members".

EFSA under pressure to publish names of glyphosate experts

The European Food Safety Authority is under pressure to publish the names of exactly who actively contributed to its assessment of glyphosate and their declarations of interest.
This follows the disclosure that some member state experts involved on EFSA's pesticide working groups have refused to provide a declaration of interest.
One of them was the subject of a breach of trust procedure at EFSA in 2011 because he failed to declare interests with chemical firms.
This week, the head of legal affairs at EFSA, Dirk Detken, said that although this scientist, Corrado Galli, was appointed by Italy for the purpose of the assessment, in fact he had failed to attend the discussion.
Following the revelations about Prof Galli, *EU Food Policy* submitted an access-to-documents request to Mr Detken, asking for copies of all the comments made by Prof Grilli, including those made at the teleconference.
Mr Detken replied: "Although Corrado Galli was put forward by Italy as one of its

experts to participate in the teleconference (teleconference 117), together with member state scientists during the peer review, Dr Galli did not attend, meaning that the documents you seek with your request do not exist."
EU Food Policy asked EFSA several times two weeks ago why Prof Galli was allowed to participate and this is the first time that EFSA has said that he did not. Before, we were told that it was up to member states to put forward their experts and that EFSA itself had no control over them, and no power to force them to make a declaration of interest.
EFSA has published the names of all its experts in several working groups on pesticides and the unscreened DoIs of those experts willing to submit one. But so far, it has not issued a list of which experts made written comments and which attended the teleconference.

Back

From: Kate Trollope <[redacted]
Subject: RE: REPLY to Letter regarding EFSA Glyphosate Recommendations
Date: January 18, 2016 at 4:39:43 PM GMT+1
To: 'Chris Portier' <[redacted]

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This week, the head of legal affairs at EFSA, Dirk Detken, said that although this scientist, Corrado Galli, was appointed by Italy for the purpose of the assessment, in fact he had failed to attend the discussion.

Following the revelations about Prof Galli, *EU Food Policy* submitted an access-to-documents request to Mr Detken, asking for copies of all the comments made by Prof Grilli, including those made at the teleconference.

Mr Detken replied: "Although Corrado Galli was put forward by Italy as one of its experts to participate in the teleconference (teleconference 117), together with member state scientists during the peer review, Dr Galli did not attend, meaning that the documents you seek with your request do not exist."

EU Food Policy asked EFSA several times two weeks ago why Prof Galli was allowed to participate and this is the first time that EFSA has said that he did not. Before, we were told that it was up to member states to put forward their experts and that EFSA itself had no control over them, and no power to force them to make a declaration of interest.

EFSA has published the names of all its experts in several working groups on pesticides and the unscreened DoIs of those experts willing to submit one.

But so far, it has not issued a list of which experts made written comments and which attended the teleconference.

From: Chris Portier [redacted] **Sent:** 18 January 2016 13:58

To: kate trollope <[redacted] **Subject:** Re: REPLY to Letter regarding EFSA Glyphosate Recommendations

+41 79 605 7958

On Jan 18, 2016, at 2:48 PM, kate trollope [redacted] wrote:

Yes I would. What number can I reach you on this afternoon. Kate

From: Chris Portier [redacted] **Sent:** 18 January 2016 13:18
To: kate trollope**Subject:** Re: REPLY to Letter regarding EFSA Glyphosate Recommendations**Importance:** High

Kate,

If you wish to chat about the response, I would be happy to talk with you.

C.

On Jan 14, 2016, at 9:56 AM, kate trollope [redacted] wrote:

Dear Prof Portier

I was wondering if you had any response to the letter you received yesterday from EFSA?

I look forward to hearing from you.

Kind regards, Kate
Kate Trollope
Editor
EU Food Policy

www.eufoodpolicy.com

00 44 208 579 0192

From: Chris Portier [redacted] **Sent:** 21 December 2015 14:10
To: kate trollope **Subject:** Re: REPLY to Letter regarding EFSA Glyphosate Recommendations

That was my read on the letter as well. Except the part about ECHA… not sure what happens if they decide to classify as carcinogenic.

On Dec 21, 2015, at 3:07 PM, kate trollope [redacted] wrote:

Thanks very much. I received this from the European Commission last week when they put it on Twitter. I would be grateful if you could let me know when you get the letter from EFSA, addressing the scientific points.

I would also like to know if you have any reaction to the letter from Mr Andriukaitis? He seemed to be saying that the Commission is legally bound to do what EFSA says.

Thanks, Kate

From: Chris Portier [redacted] **Sent:** 21 December 2015 13:59
To: kate trollope **Subject:** Fwd: REPLY to Letter regarding EFSA Glyphosate Recommendations

FYI

Begin forwarded message:

From: [redacted]
Subject: REPLY to Letter regarding EFSA Glyphosate Recommendations
Date: December 15, 2015 at 5:09:54 PM GMT+1
To: [redacted]
Cc: [redacted]

Dear Mr Portier,

Please find enclosed letter from Commissioner Andriukaitis.

Best regards,

Egidijus Dapkus
Assistant

From: "Lowit, Anna" <[redacted]
Subject: FW: Sorry
Date: June 24, 2016 at 8:18:40 PM GMT+2
To: [redacted]

Hi Chris

Jim Jones forwarded me some files from you. thanks for sending them. I have a quick Q for you.

in this PPT file, what is the citation(s) for the metaanalysis of the animal tumor data?

Thanks
Anna

Sent from my Windows Phone

From: Jones, Jim
Sent: 6/24/2016 7:43 AM
To: Housenger, Jack; Lowit, Anna
Subject: FW: Sorry

As per my conversation with Jack. Jim

-----Original Message-----
From: Chris Portier[redacted]
Sent: Thursday, June 23, 2016 2:17 PM
To: Jones, Jim <[redacted]
Subject: Sorry

Jim,

I had an error in one Table that I had to correct. New version attached.

C,

From: "Lowit, Anna" <[redacted]
Subject: RE: Sorry
Date: June 24, 2016 at 9:11:58 PM GMT+2
To: Chris Portier <[redacted]

Ditto on the terse emails, it's too easy on the phone to be quick and even rude! I do it too.

Thanks for the quick response.

Would you mind sharing the code? I'm interested in the analysis, it's a different approach to the data compared to all the others "floating around".

Sent from my Windows Phone

From: Chris Portier
Sent: 6/24/2016 2:22 PM
To: Lowit, Anna
Subject: Re: Sorry

Anna,

Oh, and I wanted to say Hi Anna. Sometimes my emails are a bit short.

If you need any background from me, I'll be happy to help you out. I am also in DC if you want to meet and discuss this.

C.

On Jun 24, 2016, at 2:18 PM, Lowit, Anna <[redacted] wrote:
Hi Chris

Jim Jones forwarded me some files from you. thanks for sending them. I have a quick Q for you.

in this PPT file, what is the citation(s) for the metaanalysis of the animal tumor data?

Thanks
Anna

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Sent: 6/24/2016 7:43 AM
To: Housenger, Jack; Lowit, Anna
Subject: FW: Sorry

As per my conversation with Jack. Jim

-----Original Message-----
From: Chris Portier [redacted]
Sent: Thursday, June 23, 2016 2:17 PM
To: Jones, Jim [redacted]
Subject: Sorry

Jim,

I had an error in one Table that I had to correct. New version attached.

C,

<FiguresandTablesEPA.pptx>

From: "Lowit, Anna" <[redacted]
Subject: RE: Sorry
Date: June 27, 2016 at 2:17:34 AM GMT+2
To: Chris Portier [redacted]

Thanks!

Sent from my Windows Phone

From: Chris Portier
Sent: 6/26/2016 6:42 PM
To: Lowit, Anna
Subject: Re: Sorry

Anna,

Per your request. I believe these are all of the files you will need. Let me know if these do not work for you. I had some minor errors in the tables again because I was not taking direction into account for the trend test (up or down). That is now fixed.

C.

From: "Lowit, Anna" <[redacted]
Subject: RE: Sorry
Date: June 24, 2016 at 9:23:09 PM GMT+2
To: Chris Portier [redacted]

That would be great ☺

Sent from my Windows Phone

From: Chris Portier
Sent: 6/24/2016 3:14 PM
To: Lowit, Anna
Subject: Re: Sorry

No problem. Shall I clean it up a bit first. I can get it to you by monday.

On Jun 24, 2016, at 3:11 PM, Lowit, Anna [redacted] wrote:
Ditto on the terse emails, it's too easy on the phone to be quick and even rude! I do it too.

Thanks for the quick response.

Would you mind sharing the code? I'm interested in the analysis, it's a different approach to the data compared to all the others "floating around".

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To: Lowit, Anna
Subject: Re: Sorry

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If you need any background from me, I'll be happy to help you out. I am also in DC if you want to meet and discuss this.

C.

On Jun 24, 2016, at 2:18 PM, Lowit, Anna [redacted] wrote:
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Jim Jones forwarded me some files from you. thanks for sending them. I have a quick Q for you.

in this PPT file, what is the citation(s) for the metaanalysis of the animal tumor data?

Thanks
Anna

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From: Jones, Jim
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To: Housenger, Jack; Lowit, Anna
Subject: FW: Sorry

As per my conversation with Jack. Jim

-----Original Message-----
From: Chris Portier [redacted]
Sent: Thursday, June 23, 2016 2:17 PM
To: Jones, Jim [redacted]
Subject: Sorry

Jim,

I had an error in one Table that I had to correct. New version attached.

C,

<FiguresandTablesEPA.pptx>

From: Tom Bender [redacted]
Subject: GYPHOSATE ARTICLE
Date: March 14, 2016 at 9:42:21 PM GMT+1
To: [redacted]

Thank you and your colleagues for your recent article in inadequacy of evaluation of toxicity and danger of herbicides. I don't know if you have seen the attached recent articles, but to me, they offer an even deeper perspective. Evaluating the toxicity of a herbicide based on just its "active" ingredient is profoundly deceptive. Many of the "inert" ingredients are also toxic, and their combinations even MORE toxic. The first study shows that 8 out of 9 Roundup products tested were UP TO 1000 TIMES AS TOXIC as the rating for glyphosate. And it is important to acknowledge that all these studies are based on very short test exposures. Long and/or repeated exposures are, of course, even more toxic.

The second article is based on Freedom Of Information documents EPA was forced to provide, which show that Monsanto knew back in the early '80s the toxicity of glyphosate, and that they AND EPA worked together to bury and hide that information.

There also is important recent information on the LARGER effects of VERY LOW exposure levels of herbicides damaging DNA and with effects continuing to future generations.

It would be wonderful for some of this information to be examined/incuded in a study so we get beyond this "possible" toxicity.

Thanks,
Tom

Tom Bender
Sustainable Architecture and Economics
38755 Reed Rd.
Nehalem OR 97131

503-368-6294
[redacted]
www.tombender.org

From: Kathryn Guyton <[redacted]
Subject: Le Monde
Date: March 16, 2016 at 5:50:24 PM GMT+1
To: [redacted]

Hi Chris,
Can we find a few minutes to chat w Stephane F? Perhaps early afternoon today or tomorrow morning? Let me know when works,
Kate

Envoyé de mon iPhone

From: Kathryn Guyton [redacted]
Subject: FW: Don't renew its authorisation, urge MEPs - Glyphosate
Date: March 23, 2016 at 10:43:07 AM GMT+1
To: "Rusyn, Ivan" [redacted] Chris Portier
[redacted]

From: Véronique Terrasse [redacted]
Date: Wednesday 23 March 2016 at 05:19
To: Kurt Straif [redacted], Dana Loomis [redacted], Kate Guyton [redacted]
Cc: IARC Director [redacted], Nicolas Gaudin [redacted]
Subject: Don't renew its authorisation, urge MEPs - Glyphosate

Dear all,

Below is Bloomberg's coverage following the MEPs' call to stop the relicensing of Glyphosate:

"The non-binding resolution calls on the EU executive to table a new draft. MEPs want the European Commission and the European Food Safety Authority to "immediately disclose all the scientific evidence that has been a basis for the positive classification of glyphosate and the proposed re-authorisation, given the overriding public interest in disclosure".

Next steps

The motion for a resolution, co-signed by Katerina Konecn (GUE/NGL, CZ), Bas Eickhout (Greens/EFA, NL) Piernicola Pedicini (EFDD, IT), on behalf of their respective political groups, and MEPs Mark

Demesmaeker (ECR, BE), Sirpa Pietikainen (EPP, FI) and Frederique Ries (ALDE, BE), will be ***put to a vote at the 11-14 April plenary session in Strasbourg****.*

National experts sitting in the Standing Committee on Plants, Animals, Food and Feed (Phytopharmaceuticals Section) **will vote to adopt or reject the Commission proposal by qualified majority in May. If there is no such majority, it will be up to the European Commission to decide.**

http://www.bloomberg.com/research/markets/news/article.asp?docKey=600-201603221059M2 EUPR 766c0000051ccac3 3600-1

Press release from the European Parliament

http://www.europarl.europa.eu/portal/en

Véronique

unknown.png ¬

Véronique Terrasse
Press Officer, IARC Communications Group
Email: [redacted]
Web: www.iarc.fr
Tel: +33 4 72 73 83 66
Cell: [redacted]

unknown.png ¬

From: Kathryn Guyton [redacted]
Subject: FW: Glyphosate: article, NRDC blog
Date: March 29, 2017 at 4:22:20 PM GMT+2
To: Christopher Portier [redacted]

As discussed in http://time.com/4711846/roundup-weed-killer-cancer/, please see attached article.
See also https://www.nrdc.org/experts/jennifer-sass/split-within-epa-glyphosate-carcinogenicity.

From: Kathryn Guyton <[redacted]
Subject: Fwd: Sutherland Investigative Report "Is Glyphosate Legal" and the US NIH RoC
Date: March 17, 2016 at 4:03:08 PM GMT+1
To [redacted]

Envoyé de mon iPhone

Begin forwarded message:

From: Véronique Terrasse [redacted]
Date: 17 March 2016 at 08:34:20 GMT-5
To: Kurt Straif <[redacted], Kathryn Guyton <[redacted]
Dana Loomis <[redacted]
Cc: Nicolas Gaudin <[redacted]
Subject: FW: Sutherland Investigative Report "Is Glyphosate Legal" and the US NIH RoC

Quite impressive overview from a regular citizen..

Véronique Terrasse
Press Officer, IARC Communications Group
Email: [redacted]
Web: www.iarc.fr
Tel: +33 4 72 73 83 66
Cell: [redacted]

From: IARC Communications **Sent:** 17 March 2016 14:02**To:** Véronique Terrasse**Cc:** Nicolas Gaudin**Subject:** FW: Sutherland Investigative Report "Is Glyphosate Legal" and the US NIH RoC

FYI

Bernadette

From: Donald Sutherland [redacted] **Sent:** jeudi 17 mars 2016 12:33**To:** IARC Communications**Subject:** Sutherland Investigative Report "Is Glyphosate Legal" and the US NIH RoC

Good Morning Christopher Wild,
I am a USDA certified organic vegetable farmer in Hopkinton, MA USA and a freelance writer.
I wanted to alert you and the IARC my nomination of glyphosate and its products to the US NIH Report on Carcinogens have been accepted.
Also, I have writen a report "Is Glyphosate Legal" for you and the IARC review.
Please contact me if you have any questions.

Best Wishes,
Donald Sutherland
Hopkinton, MA USA
Long Life Farm
Http://www.longlifefarm.com
Member of the Northeast Organic Farmers Association (NOFA)
Member of the Society of Environmental Journalists (SEJ) Is Glyphosate Legal?
By Donald Sutherland

It is spring time and millions of pounds of the world's most common herbicide are being applied to the agricultural land in the United States.
http://npic.orst.edu/factsheets/archive/glyphotech.html
http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2012&map=GLYPHOSATE&hilo=L

This year the United States Department of Environmental Protection (EPA), who license and regulate glyphosate and its 750 products, must decide if the herbicide is safe for prenatal, infant, child, and adult

consumption in food crops and products- and the agency is stalling.

The EPA's sister European Food Safety Authority (EFSA) is also stalling its' reauthorization of glyphosate under a peer review re-evaluation of EU's list of approved active substances.
http://www.efsa.europa.eu/

Currently, France, Italy, Sweden, and the Netherland's are opposed to the relicensing of glyphosate, and Germany is abstaining.
http://www.theguardian.com/environment/2016/mar/08/eu-vote-on-controversial-weedkiller-licence-postponed-glyphosate

In the United States the EPA is under a federal mandate requiring the agency to re-evaluate all pesticides on a 15-year cycle.
http://www.epa.gov/pesticide-reevaluation
http://www.epa.gov/ingredients-used-pesticide-products/glyphosate

The federal regulatory agencies (EPA, USDA, FDA) who establish food safety regulations claim the world's most commonly used herbicide is as safe as table salt if used under directions.

So, why doesn't the EPA reregister the license for glyphosate use in agriculture?

In 2015 the World Health Organization's International Agency for Research on Cancer (IARC) assessed glyphosate and its products as a probable human carcinogenic health risk, and this year the California state government intends to list the herbicide as a carcinogen.

The California Office of Environmental Health Assessment (OEHHA) intends to list glyphosate as a carcinogen under the mandates of state law Proposition 65 (The Safe Drinking Water and Toxic Enforcement Act of 1986).
http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/090415LCset27.html

"The law requires that certain substances identified by the International Agency for Research on Cancer (IARC) be listed as known to cause cancer under Proposition 65. Labor Code section 6382(b)(1) refers to substances identified as human or animal carcinogens by IARC."
http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/090415LCset27.html

So far, the EPA hasn't agreed with the California OEHHA and World Health Organization's IARC assessment of glyphosate and its products as a human carcinogenic health risk.
http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-09.pdf#page89
https://www.iarc.fr/en/media-centre/iarcnews/pdf/MonographVolume112.pdf
http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/090415LCset27.html

Clinical, peer reviewed studies by science, industry, and government bodies show glyphosate kills plants and bacteria by interfering with an enzyme producing aromatic amino acids which are essential for life in plants, bacteria and humans.
http://www.epa.gov/sites/production/files/2015-06/documents/glyphosate-417300_2015-06-29_txr0057175.pdf
http://www.monsanto.com/glyphosate/pages/how-does-glyphosate-work.aspx
https://en.m.wikipedia.org/wiki/Glyphosate

The EPA and glyphosate manufacturers admit consumers absorb glyphosate in minute amounts from food and drinking water, but assure us decades of clinical studies show it only harms plant life and passes harmlessly through the body in urination.

"All labeled uses of glyphosate are safe for human health and supported

by one of the most extensive worldwide human health databases ever compiled on an agricultural product," states Dr. Philip Miller, Vice President Global Regulatory Affairs, Monsanto.
http://news.monsanto.com/news/monsanto-disagrees-iarc-classification-glyphosate

Not so, says an international contingent of scientists.

These scientists, using peer reviewed clinical data, defend the IARC assessment glyphosate poses a human health risk.
http://www.zeit.de/wissen/umwelt/2015-11/glyphosat-offener-brief.pdf
https://www.researchgate.net/publication/283490944_Glyphosate_pathways_to_modern_diseases_IV_cancer_and_related_pathologies
http://www.mdpi.com/1099-4300/15/4/1416
http://www.nejm.org/doi/full/10.1056/NEJMp1505660?rss=searchAndBrowse
http://www.enveurope.com/content/26/1/14

They argue the US EPA and EFSA have cited biased industry sponsored clinical data to make their case glyphosate is safe, and didn't consider the low dose effects in prenatal, infants, and children.
http://www.efsa.europa.eu/en/efsajournal/pub/4302

"The science consisted solely of toxicologic studies commissioned by the herbicide manufacturers in the 1980s and 1990s and never published, not an uncommon practice in U.S. pesticide regulation," says Philip J. Landrigan, M.D., and Charles Benbrook, Ph.D. in their New England Journal of Medicine report GMOs, Herbicides, and Public Health.
http://www.nejm.org/doi/full/10.1056/NEJMp1505660?rss=mostEmailed

"These studies predated current knowledge of low-dose, endocrine-mediated, and epigenetic effects and were not designed to detect them. The risk assessment gave little consideration to potential

health effects in infants and children, thus contravening federal pesticide law," Landrigan and Benbrook say.
http://www.nejm.org/doi/full/10.1056/NEJMp1505660?rss=searchAndBrowse

The exponential increase in the agricultural use of glyphosate over the past two decades and its' correlation with human health issues involving neurological, intestinal, and cancer disorders, is hotly contested by both sides of the glyphosate safety debate.

"I personally believe that glyphosate is the main reason why we have an epidemic in autism. I think it's also responsible for the rise in Non-Hodgkin's lymphoma, pancreatic cancer, thyroid cancer, inflammatory bowel disease, ADHD, COPD, alzheimer's, diabetes, obesity, and probably several other chronic conditions that we face today," says
Stephanie Seneff, a senior research scientist at the Massachusetts Institute of Technology (MIT).
https://www.researchgate.net/publication/283490944_Glyphosate_pathways_to_modern_diseases_IV_cancer_and_related_pathologies
http://www.mdpi.com/1099-4300/15/4/1416

I don't agree with the WHO's designation as "probably carcinogenic," she says. "I think it is definitely carcinogenic."

The stakes are huge in this political scientific schism.

The future of the global proprietary owned agro-industry glyphosate ready genetically modified organism (GMO) crops lies in the resolution of the split between the World Health Organization's IARC and the US EPA & EFSA.

Food manufacturers using GMO crops also have a huge stake at risk if glyphosate is banned or restricted.

Over 90% of US corn, soy, and sugar beet crops are grown with glyphosate, and these GMO crops and their products constitute over 80% of processed food products. Glyphosate is also used in wheat production.
http://www.ers.usda.gov/media/1282246/err162.pdf
http://www.ers.usda.gov/media/1424185/eib124.pdf

Kellogg's, a Fortune 500 food manufacturer, acknowledges grains purchased on the open market contain agricultural herbicide residues including glyphosate and are consumed by customers in their processed products.
http://www.gmofreeusa.org/food-testing/kelloggs/kelloggs-froot-loops/

"Nearly all crops in the US are treated with herbicides and pesticides, and may leave behind very low residue levels on some foods," says a customer service Kellogg Company spokesman.

"In the US, the acceptable level of pesticide and herbicide use in crops is set by the Environmental Protection Agency (EPA) based on, a standard of reasonable certainty that the use would cause no harm to human health or the environment," says the company spokesman.

US federal agencies in charge of protecting the public's health with a "standard of reasonable certainty", EPA, USDA, and FDA, state they have never tested glyphosate residue in federal aggregate food crop tests (outside of a USDA Soy 2011 test), because manufacturer and EPA cited laboratory tests claim there is no human health risk. They also insist glyphosate herbicides are safe if used under direction.
http://www.epa.gov/pesticides/health/
http://www.epa.gov/pesticides
http://www.monsanto.com/glyphosate/pages/default.aspx
http://www.monsanto.com/iarc-roundup/pages/default.aspx

These same federal agencies also authorized the safety of "Roundup ready" transgenic genetically modified organisms (GMOs) crops as

"substantially equivalent to nature", and give GMO glyphosate ready crops a pass from federal food testing requirements.
http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/labelingnutrition/ucm059098.htm
http://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/introduction-biotechnology-regulation-pesticides#overview

It's a complicated byzantine federal process proving glyphosate isn't a health risk to humans.

But, when it is unraveled a secret is found - the licensing of glyphosate and its products is in violation of the federal laws governing pesticides.

Under the Federal Food Drug and Cosmetic Act (FFDCA) and the Food Quality Protection Act (FQPA) aggregate testing of food crops and products is mandated for all pesticide residue tolerances to account for the accumulated exposures of the herbicide's chemical residue in commonly consumed food.
http://www.epa.gov/laws-regulations/summary-food-quality-protection-act
http://www.epa.gov/laws-regulations/summary-federal-food-drug-and-cosmetic-act

US federal agencies (EPA, USDA, FDA) claim there is no government aggregate food testing of glyphosate residues, so the EPA uses "available information".
http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0132-0009

The EPA also admits to waiving the FQPA Safety Factor additional tenfold risk margin of safety for pesticide maximum residue levels (MRLs) protecting the safety of the most vulnerable population group - prenatal, infants, and children.
http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0

132-0009
http://www.epa.gov/sites/production/files/2015-07/documents/determ.pdf
http://www.epa.gov/laws-regulations/summary-federal-food-drug-and-cosmetic-act
http://www2.epa.gov/pesticide-tolerances/about-pesticide-tolerances
http://www.ecfr.gov/cgi-bin/text-idx?SID=14480e45fa5ca0522865d765eec6bb72&mc=true&node=se40.24.180_1364&rgn=div8

Clinical laboratory glyphosate health risk testing data cited by the EPA Hazard Identification Assessment Review Committee (HIARC) is used in the federal agency's Office of Pesticide Programs (OPP) and Health Effects Division (HED) ruling the safety of infants and children is adequately protected if the FQPA Safety Factor were reduced to 1X instead of 10X.
http://www.monsanto.com/glyphosate/pages/default.aspx
http://www.monsanto.com/iarc-roundup/pages/default.aspx
http://www.epa.gov/pesticide-contacts/contacts-office-pesticide-programs-health-effects-division#teb
http://www.epa.gov/pesticides

For now, the EPA insists glyphosate and its MRLs, established before the herbicide was declared a probable carcinogenic health risk by the World Health Organization, is safe for humans.
http://www.epa.gov/oppsrrd1/reregistration/REDs/factsheets/0178fact.pdf
http://www.ecfr.gov/cgi-bin/text-idx?SID=14480e45fa5ca0522865d765eec6bb72&mc=true&node=se40.24.180_1364&rgn=div8

"If you are asking if glyphosate is safe, then yes, we have said that that glyphosate does not cause unreasonable adverse effects to human health and the environment so long as it is used according to the pesticide labels," says Khue Nguyen, ChemicalReview Manager, Risk Management and Implementation Branch 1
PesticideRe-evaluation Division, Office of Pesticide Programs, EPA

"EPA regulates pesticides, which means we deal primarily with pesticide policy and we determine what appears on the pesticide labels. We do not do food safety inspections or testing on food/feed commodities. To be clear, we set tolerances for all pesticides that are used on food/feed commodities. A pesticide having a tolerance or multiple tolerances does not mean that it is unsafe," says Nguyen.

Section408(b)(2)(A)(i) of the Federal Food Drug and Cosmetics Act states that EPA can establish a tolerance for a pesticide chemical residue in or on food only if EPA determines that the tolerance is safe. "Safe" is then defined as a "reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures.
http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterIVFood/
http://www.epa.gov/laws-regulations/summary-federal-food-drug-and-cosmetic-act

Consumer advocates claim without the government providing a transparent aggregate testing of glyphosate chemical residue in food there is no total accounting for the public's cumulative exposure to the herbicide in a daily diet, and no safety MRL can be established.

"The legal process for tolerance setting must be based on human health effects from dietary exposures. However, without data on actual residues on these crops, this cannot be verified. We have challenged EPA's tolerance setting before and will continue to do so," says Nichelle Harriott, Science and Regulatory Director, Beyond Pesticides.
http://www.beyondpesticides.org

In a little publicized federal government sponsored program called the IR-4 Project the USDA, EPA, and glyphosate manufacturers do test glyphosate tolerance residue on crops, but without transparency to the public.

The United States Department of Agriculture funded IR-4 Project partnering with the EPA, state government agencies, glyphosate manufacturers, and universities have been testing glyphosate residues in food crops and feed to facilitate the herbicide's use in agriculture.
http://ir4.rutgers.edu

IR-4 sounds like a federal secret, but when it petitioned the Environmental Protection Agency(EPA) in the federal register to increase food crop MRL residue tolerance levels of the world's most popular herbicide it gave away its cover.
http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0132-0009

The IR-4 petition went unnoticed in the shadow of Monsanto's (an IR-4 member) EPA petition, and was approved by the EPA (also an IR-4 member).
http://www.regulations.gov/#%21docketDetail;D=EPA-HQ-OPP-2012-0132
https://www.gpo.gov/fdsys/pkg/FR-2013-05-01/pdf/2013-10316.pdf
http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0132-0009

Headquartered in Princeton, N.J., the IR-4 operates as a "unique" partnership between the USDA, EPA, the National Institute of Food and Agriculture (NIFA), the Agricultural Research Service (ARS), the State Agricultural Experiment Stations (SAES), agrochemical industry, universities, commodity groups, and growers.
http://nifa.usda.gov/topics
http://ir4.rutgers.edu/directory.cfm?nd=nd&letter=B

Monsanto, Syngenta, DuPont, Dow, Bayer, and BASF are listed in the IR-4 directory.
http://ir4.rutgers.edu/directory.cfm?nd=nd&letter=B

With a staff of over 125 full time members the mission statement for the IR-4 Project is to "facilitate registration of sustainable pest management technology for specialty crops and minor uses."

Specialty crops tested by IR-4 include commonly consumed food crops (ie. fruits, vegetables, nuts, herbs, spices,) and non-food plants and flowers used in landscape.

"As some background, for more than 50 years, the USDA funded IR-4 Project is the only resource for facilitating registrations of conventional chemical pesticides, biopesticides, and organic products for growers of specialty crops and other minor uses (specialty uses) in the United States. These are uses not supported by registrants. IR-4 is a partnership with government, industry and growers," says Jerry J. Baron, Ph.D, Executive Director, IR-4 Project.

"We typically develop residue exposure data to assist EPA with their risk assessment. Basically we apply the test product the way the farmer would potentially use the pesticide or biopesticide. When the crop is mature, we harvest the raw agriculture commodity and analyze for the presences of the chemical, biochemical and/or metabolites, " says Baron.

What was the IR-4's urgent need to exponentially increase the herbicide residue levels on such foods as carrots, sweet potatoes, fruits, grains, and berries?

"The IR-4 Project received multiple request for assistance to facilitate modifications to the registration of glyphosate from public sector scientists with USDA and the State Agricultural Experiment Stations. These requests were reviewed during IR-4 Project Food Use Workshops and classified as high priority," says Baron.

The IR-4 insists there is no conflict of interest with government regulatory bodies and glyphosate industry manufacturers collectively

using their testing data to petition the EPA in the federal register to increase glyphosate MRL levels for crops.
http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0132-0009

"Though IR-4's data development is independent of the companies, IR-4 submissions are coordinated with the companies. Due to provisions of the Pesticide Registration Improvement Act, IR-4 submissions are often classified as part of a company submission," says the IR-4 Executive Director.

The IR-4 also insists their hidden glyphosate residue data developed under USDA and EPA testing standards is "different" from the USDA MRL monitoring data used in national USDA food survey's to protect the health of the public.

"The data IR-4 develops is much different than glyphosate monitoring data by EPA and USDA ; we are fully removed from that activity. USDA just released a report within the last couple of weeks from their Pesticide Data Program out of the Agriculture Marketing Service. You may find some glyphosate monitoring data in that sample set," says Baron.

The USDA Pesticide Data Program (PDP)Annual Summary report is conducted by the USDA Agricultural Marketing Service (AMS) to collect data on pesticide/herbicide residues in over 10,000 samples of fruit, vegetables, fresh and processed products, and infant formulas throughout the US using the MRL tolerances set by the EPA. This PDP data is presented to the public to assure consumers the food they feed their families is safe.
https://www.ams.usda.gov/sites/default/files/media/2014%20PDP%20Annual%20Summary.pdf

"Ultimately, if the EPA determines a pesticide is not safe for our families it is removed from the market," states the USDA in their 2014

PDP report.
http://www.ams.usda.gov/sites/default/files/media/PDP%20factsheet.pdf

The USDA admit they don't test in the PDP for the mostly commonly used herbicide in the US (glyphosate) in food crops and food products - except for a USDA soy test in 2011.
https://www.ams.usda.gov/sites/default/files/media/2014%20PDP%20Annual%20Summary.pdf

"The PDP tests a wide variety of domestic and imported foods using a sound statistical program and the most current laboratory methods. Glyphosate is not detectable using the multi-residue methods (MRM) the PDP testing laboratories use and would require a specialized method. Glyphosate requires the single analyte method to test for residues," says Peter Wood, spokesman for the Public Affairs Office of the USDA AMS.

When asked why didn't the USDA PDP use USDA funded IR-4 glyphosate residue MRL data for those foods listed in the annual survey the USDA spokesman said, "the report does not include data from other sources."

Why then doesn't the USDA use the single analyte method used in the 2011, PDP testing of 300 soybean samples for glyphosate and its metabolite AMPA (aminomethylphosphonic acid)?
http://www.ams.usda.gov/sites/default/files/media/2011%20PDP%20Annual%20Summary.pdf

"USDA and EPA specialists discuss the selection of commodities and pesticides for testing. With USDA's scientific input and EPA's data needs, EPA makes the determination which commodities and pesticides are tested," says Wood.

"Currently, the U.S. Food and Drug Administration (FDA) is testing corn and soybean grains for glyphosate residues. EPA is waiting on the

results from FDA testing before making the determination if additional data is needed for its ongoing evaluation of glyphosate tolerances to ensure that the levels set by EPA meet the safety standards prescribed by the law," he says.
http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/ucm184293.htm

The FDA is responsible for enforcing EPA pesticide tolerances, but admits it is the first time they have ever tested for glyphosate MRLs in any food commodity.

"FDA has not routinely looked for glyphosate in its pesticide monitoring regulatory program for several reasons, including that available methods for detecting glyphosate were selective residue methods that would have been very expensive and labor intensive to implement in FDA field labs," says Charlotte Lian, Ph.D., Plant Products Branch, Division of Plant Products and Beverages, Office of Food Safety Center for Food Safety and Applied Nutrition, Food and DrugAdministration
http://www.fda.gov/downloads/Food/ComplianceEnforcement/ucm073186.pdf

"FDA is aware of the 2015 IARC World Health Organization's assessment of glyphosate. In the U.S., risk assessments of pesticides are conducted by EPA," says Lian.

How was glyphosate and 750 products licensed without abiding by the aggregate tolerance residue testing data mandates for risk assessments under the Food Quality Protection Act?

The EPA dodges the question.

Anne Overstreet, Chief Communication Services Branch, Field and External Affairs Division Office of Pesticide Programs, Environmental

Protection Agency says, "the Federal Food, Drug, and Cosmetic Act states: To make the safety finding, EPA *considers*, among other things: the toxicity of the pesticide and its break-down products, aggregate exposure to the pesticide in foods and from other sources of exposure, and any special risks posed to infants and children."

"While testing for aggregate exposure is nearly impossible – people eat different foods, combinations of foods, and amounts of foods – EPA uses *models* to assess likely aggregate exposure and adds an additional safety factor to further protect consumers, especially children, as required by the Food Quality Protection Act," she continues. http://www.epa.gov/laws-regulations/summary-food-quality-protection-act

"In setting tolerances, EPA must make a finding that the tolerance is "safe," with safe being defined as meaning that there is a "reasonable certainty that no harm will result from aggregate exposure to the pesticide residue," she says.

Anne Overstreet then refers to the USDA PDP aggregate exposure testing as proof consumers shouldn't worry about pesticides residues on their food - even though the 2014 PDP didn't test for glyphosate.

"The PDP data demonstrate that overall pesticide residues found on foods tested are at levels below the tolerances established by EPA and pose no safety concern. Based on the PDP data, consumers can feel confident about eating a diet that is rich in fresh fruits and vegetables," says Overstreet.

"Glyphosate residue data are not part of 2014 PDP sampled pesticides. To find out whether FDA has plans to test for glyphosate residues, please contact FDA directly," she says.

This type of circular non-answer on glyphosate's safety is how the EPA has been stalling their decision to reregister the herbicide and its products - while permitting its' continued use.

And after exposing a generation to glyphosate, the EPA also refuses to answer if the herbicide's current MRL tolerance residue levels are in violation of the FQPA Safety Factor protecting prenatal, infants, and children.

"The real question is whether the EPA was in violation of the law when glyphosate was approved then and now," says Jonathan Evans, Environmental Health Legal Director and Senior Attorney for the Center for Biological Diversity.

Donald Sutherland is a freelance writer, USDA certified organic vegetable farmer, member of the Northeast Organic Farmers Association (NOFA), and the Society of Environmental Journalists (SEJ).
https://www.linkedin.com/in/donaldsutherland
He farms with his wife Laura, and their two daughters Mei and Li, in Hopkinton, Ma
Long Life Farm
http://www.longlifefarm.com
His last story on food was published in Food Safety News.
http://www.foodsafetynews.com/author/dsutherland/#.Vq-RRvA8KrU

Begin forwarded message:

From: "Lunn, Ruth (NIH/NIEHS) [E]" [redacted] **Date:** January 14, 2016 at 4:23:33 PM EST **To:** Donald Sutherland

[redacted] **Subject: FW: [NTP Web] Received nomination to the National Toxicology Program**

Dear Mr. Sutherland, This email acknowledges your nomination of glyphosate and its products for review for possible listing in the Report on Carcinogens and the list of websites/documents supporting your nomination. The process for preparing the Report of Carcinogen is available at http://ntp.niehs.nih.gov/go/rocprocess; please see Part 1 of the process for steps regarding nominations and selection of candidate substances. We appreciate your interest in the Report on Carcinogens and National Toxicology Program and your previous correspondence regarding this topic. Sincerely, Ruth M. Lunn, DrPH Director, Office of the Report on Carcinogens Division of the National Toxicology Program, NIEHS Phone: 919-316-4637 Mailing address PO Box 12233, MD K2-14 Research Triangle Park, NC 27709 Courier 530 Davis Dr., Room 2138 Morrisville, NC 27560 On 1/7/16, 10:05 AM, "NTP Website" <ntpweb-noreply@ntp.niehs.nih.gov> wrote:

The following has been submitted as a nomination.

Name: Donald Sutherland
Telephone: 508-497-3676
Email: [redacted]
Affiliation Type: Individual
Additional Contact Information: The best way to contact me is by email: [redacted]

From: Kathryn Guyton [redacted]
Subject: Fwd: Correction in NR article
Date: May 5, 2016 at 11:47:08 AM GMT+2
To: [redacted]

Et voila. Thanks to Ivan for alerting me to this article!

Envoyé de mon iPhone

Begin forwarded message:

From: Kathryn Guyton [redacted]
Date: 5 May 2016 at 11:40:34 GMT+2
To: [redacted]
Cc: [redacted] Kurt Straif [redacted] Nicolas Gaudin [redacted], Véronique Terrasse [redacted]
Subject: Correction in NR article

Dear Sir, Dear Madam,

I hereby request correction of false and defamatory statements in the recent NR article below.

The presentation in question noted that many studies had examined a link to breast cancer with some pesticides (not herbicides in particular), a factual statement. Further, a publication that I coauthored in The Lancet Oncology reached the opposite conclusion from "clear indications of a link to breast cancer" that you attribute to me in your article. Contrary to your assertion of a "total lack of objectivity", our publications states specifically: "Although more than 40 studies conducted since 1993 were reviewed, no clear association was found between breast cancer and DDT or DDE"

http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(15)00081-9/fulltext

I will look forward to your reply.

Sincerely yours,

Kate Z. Guyton PhD DABT
Monographs Section
International Agency for Research on Cancer
150, cours Albert Thomas
69372 Lyon Cedex 08
France
Tel: [+33] (0)4 72 73 86 54
[redacted]

The lead author of the glyphosate report, Kathryn Guyton, gave a speech in 2014 to an NGO group — before the review process had begun — in which she stated that the herbicide studies planned for 2015 had shown clear indications of a link to breast cancer, demonstrating her total lack of objectivity.

Read more at:
http://www.nationalreview.com/article/434845/WHO-cancer-agency-bad-science-labels-glyphosate-probably-carcinogenic

From: Kathryn Guyton <[redacted]
Subject: Fwd: Clarification- NR article
Date: May 5, 2016 at 12:19:15 AM GMT+2
To: "[redacted]

Envoyé de mon iPhone

Begin forwarded message:

From: Kathryn Guyton <[redacted]
Date: 4 May 2016 at 22:59:11 GMT+2
To: Kurt Straif <[redacted] Dana Loomis <[redacted]
"Nicolas Gaudin" <[redacted]
Subject: Clarification- NR article

Dear Kurt, Dear Dana,

I have spoken to Chris Portier, and EDF is taking steps to correct false statements about him/EDF in the NR article. I have taken the step of contacting NR by phone and noting that false and potentially defamatory statements about me have appeared in their article, and asking what steps had been taken to verify any of the facts presented. I was told to contact the below NR folks in writing, and have drafted this email for your review and further comment.

Bonne soiree,
Kate

Dear Sir, Dear Madam,

I was wondering what steps could be taken to correct the record concerning false and potentially defamatory statements in this article: http://www.nationalreview.com/article/434845/WHO-cancer-a

gency-bad-science-labels-glyphosate-probably-carcinogenic, particularly:

The lead author of the glyphosate report, Kathryn Guyton, gave a speech in 2014 to an NGO group — before the review process had begun — in which she stated that the herbicide studies planned for 2015 had shown clear indications of a link to breast cancer, demonstrating her total lack of objectivity.

The presentation in question noted that many studies had examined a link to breast cancer with some pesticides (not herbicides in particular), a factual statement. Further, a publication that I coauthored in The Lancet Oncology reached the opposite conclusion from "clear indications of a link to breast cancer", specifically: "Although more than 40 studies conducted since 1993 were reviewed, no clear association was found between breast cancer and DDT or DDE measured in samples of blood or adipose taken in adulthood" http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(15)00081-9/fulltext

I will look forward to your reply.

With kind regards,

nbrown@nationalreview.com
kconnell@nationalreview.com

From: Kurt Straif [redacted]
Subject: FW: Conflict of Interest Concerns Cloud Meeting as International Experts Review Herbicide Risks | U.S. Right to Know
Date: May 12, 2016 at 10:26:48 PM GMT+2
To: "Christopher Portier [redacted]
"Emmerig Hedwig (Ref. Biotechnologie und Bioethik)"
[redacted]

FYI, Boobis is Chair of the current JMPR meeting and Moretto vice-Chair.
http://usrtk.org/pesticides/conflict-of-interest-concerns-cloud-meeting-as-international-experts-review-herbicide-risks/

From: Kathryn Guyton [redacted]
Subject: Fwd: Breaking news from EU Food Policy
Date: May 17, 2016 at 4:26:08 PM GMT+2
To: [redacted]

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From: Kathryn Guyton <[redacted]
Subject: FW: Latest issue from EU Food Policy
Date: May 20, 2016 at 3:11:40 PM GMT+2
To: Ivan Rusyn [redacted] Christopher Portier
[redacted]

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From: Kurt Straif <[redacted]
Date: Friday 20 May 2016 11:30
To: Nicolas Gaudin <[redacted]
Subject: FW: Latest issue from EU Food Policy

As usual,
Merci, Kurt

From: EU Food Policy [mailto:news@eufoodpolicy.com] **Sent:** 20 May 2016 11:00 **To** [redacted] **Subject:** Latest issue from EU Food Policy

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Hi Mr Straif,

The latest edition is ready for you to view at www.eufoodpolicy.com. You can download this week's full newsletter or read all the top stories and analysis online. If you have any problems please email info@eufoodpolicy.com. These are some of this week's headlines:

EU will act over EFSA palm oil Opinion - Commission Read more... **Swedish agency launches probe into glycidyl levels in food**Read more... **Glyphosate - member states fail to support nine year renewal**Read more... **Ombudsman to probe "EU pilot" system for infringement cases**Read more... **EFSA pesticide expert advises CEFIC chemical lobby**Read more... **Choices label is not "licence" to eat more, finds study**Read more... **Action Plan on mutual recognition changes published**Read more... **Glyphosate unlikely to cause cancer, says WHO/FAO panel**Read more... **WHO/FAO conclusions on glyphosate irrelevant to renewal, say critics**Read more... **WHO defends glyphosate experts**Read more...

Also in the latest issue

US tells Commission to act over French BPA ban Commission rules out EU ecolabel for fish Launch of new standard for measuring food waste Andriukaitis promises raft of food waste measures Eating bigger breakfast doesn't dramatically cut lunch calories A colour on a food packet is worth a thousand words Coke under attack over marketing pledges BfR endocrine consensus breaks as participants give different message Dutch raids over country of origin fraud FSA board supports major changes to delivery of scientific advice Commission censure motion collapses Commission takes case-by-case view of East-West food quality divide FSA to look after mandatory CCTV in slaughter houses EU could ban DNP supplements TTIP - more conspiracy theories than Middle Ages, says Andriukaitis

Swedish government looks at new plan on reformulation Health NGOs say advertising reforms don't go far enough EFSA seeks experts to serve for just one year MEPs hold another non-binding vote on GMOs Hogan calls for more substantial proposals from US in TTIP EFSA gives green light to liquid absorber EFSA issues positive verdict on GM food contact ingredient Dieticians call on Parliament to act on obesity EFSA issues verdict on material to extend shelf life of wine Italy notifies changes in national olive oil labelling law In brief

To access previous editions of EU Food Policy, use the Archive tab and select the edition required. When logging in, please remember to enter your email address in lower case, followed by your password. If you have any problems, don't hesitate to contact us.

Yours sincerely, *Patrick Bartlett Director EU Food Policy*
info@eufoodpolicy.com +44 208 567 4569

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From: Kathryn Guyton [redacted]
Subject: Fwd: Emailing: EUFoodPolicy_ECHA.pdf, EUFoodPolicy_MEPs-vote.pdf, EUFoodPolicy_mediation.pdf
Date: March 22, 2016 at 1:06:47 PM GMT+1
To: [redacted]

Envoyé de mon iPhone

Begin forwarded message:

From: Kurt Straif [redacted]
Date: 22 March 2016 at 08:04:06 GMT-4
To: Dana Loomis <[redacted] Kathryn Guyton [redacted]
Nicolas Gaudin <[redacted] Véronique Terrasse
[redacted]
Subject: Emailing: EUFoodPolicy_ECHA.pdf, EUFoodPolicy_MEPs-vote.pdf, EUFoodPolicy_mediation.pdf

Dear all,

I have managed to get trial access to EUFoodPolicy and have now downloaded and attached fyi the recent 3 possibly important, short articles.

Kurt

Your message is ready to be sent with the following file or link attachments:

EUFoodPolicy_ECHA.pdf
EUFoodPolicy_MEPs-vote.pdf
EUFoodPolicy_mediation.pdf

From: Kathryn Guyton [redacted]
Subject: FW: RAC-40_Invitation to IARC_glyphosate
Date: February 7, 2017 at 10:12:52 AM GMT+1
To: Christopher Portier [redacted]

Hi Chris,
Did you also receive this invitation? I'll be in the US 4-17 March, and know you will also be at SOT (as will Jose T). I can check if someone else can attend from IARC.
Kate

From: ECHA Committee Risk Assessment <rac@echa.europa.eu>
Date: Tuesday, 7 February 2017 at 09:00
To: Kate Guyton [redacted]
Cc: BOWMER Tim [redacted] VAN HAELST Anniek [redacted], Kurt Straif [redacted], ECHA Committee Risk Assessment [redacted]
Subject: RAC-40_Invitation to IARC_glyphosate

RE: 40th meeting of the Committee for Risk Assessment (6-10 March and 14-15 March 2017)

For the attention of IARC - glyphosate

Dear Dr Kate Z. Guyton,

Please find attached your invitation to the 40th Meeting of the Committee for Risk Assessment (RAC-40). Glyphosate is scheduled to be discussed on Wednesday 8 March at 11.30 – 18.30 and on Wednesday 15 March at 09.15-11.15 Helsinki time. The working language of the meeting will be English.

Preparation for the meeting
The provisional Draft Agenda and the provisional timelines are attached to this invitation.

Practicalities
You are kindly asked to make your own travel and any hotel

arrangements. A list of local hotels is available on request.

Please confirm your attendance, and for any further information or assistance you may need, please contact RAC Secretariat (rac@echa.europa.eu).

Data protection notice
This meeting will be video recorded for minute taking purposes. The recordings will only be accessible to the Secretariat and will be permanently deleted once no longer needed. Please note that the minutes, which are published on the ECHA website, include a list of participants. The European Chemicals Agency will ensure on its part that your personal data is processed as required by Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. You have the right to access and rectify that data. To exercise these rights, please contact the data controller at rac@echa.europa.eu
For any further information or assistance you may need, please contact the RAC Secretariat (rac@echa.europa.eu).

Best regards,

Leila Kokkola Committee for Risk Assessment (RAC) Unit B.1 - Committees Secretariat European Chemicals Agency Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland Tel. +358 9 6861 8288
[redacted]
http://echa.europa.eu/
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From: "Peltonen Kimmo (Tukes)" <[redacted]
Subject: glycophosphate
Date: March 6, 2017 at 5:08:52 PM GMT+1
To: Tuomisto Jouko <[redacted], "Chris Portier
[redacted] "Putkonen Tiina (Tukes)"
[redacted]

Dear Jouko, Chris and Tiina,

I have contacted EFSA and ECHA and the message is clear. They will not participate any meeting or share any data dealing with glycophosphate before ECHA's opinion is adopted and released. When that will happen – your guess is as good as mine.

I talked today with Jose Tarazona from EFSA and he made a proposal to have a meeting which has a more general topic focusing methodological differences between WHO/EU in chemical risk assessment. Furthermore he suggested that one should have 5 different pesticides and some industrial chemicals as examples.

Please, let me know your thoughts about the more general workshop, which could preferentially be a joint one with all parties.

Sorry to disappoint you, but I don't see any point of trying to arrange a meeting on this subject anymore.

All the best,

Kimmo

Kimmo Peltonen Pääjohtaja | Director General

Turvallisuus- ja kemikaalivirasto (Tukes) | Finnish Safety and Chemicals Agency
PL 66 (Opastinsilta 12 B), 00521 Helsinki, FINLAND
Puh. 040 5002 614 | Tel. +358 40 5002 614
[redacted]

Tukes: Suojan tuoja – turvallisen toiminnan edistäjä ja mahdollistaja.

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From: [redacted]
Subject: Automatic reply: EFSA Glyphosate Recommendations
Date: November 27, 2015 at 9:57:24 AM GMT+1
To: [redacted]

We acknowledge receipt of your email. If your message concerns a request for a meeting or a petition please see the information below.

Important notice on Transparency: Meetings with organisations or self-employed individuals

I would like to draw your attention to the Commission's new policy on transparency which entered into force on 1 December 2014. More details can be found here.

Before we can proceed with your request for a meeting, could you please confirm whether you, or your organisation, are registered in the Transparency Register and provide your Register ID number? If you are not registered, you are kindly invited to register on this website. The meeting can only take place once we have received the confirmation of your registration.

Please be aware that the European Commission is committed to enhanced transparency. Therefore, Commissioners and their Cabinets only meet organisations or self-employed individuals that are registered in the EU's Transparency Register.

Petitions

Replies to petitions are published on the Transparency Portal of the European Commission.

From: Sönke Guttenberg - Harald Ebner MdB [redacted]
Subject: AW: EFSA Glyphosate Recommendations
Date: November 27, 2015 at 9:58:57 AM GMT+1
To: Chris Portier [redacted]

Thank you! Then I will start sending now.

Von: Chris Portier [redacted] **Gesendet:** Freitag, 27. November 2015 09:58 **An:** Sönke Guttenberg - Harald Ebner MdB **Betreff:** Fwd: EFSA Glyphosate Recommendations

It has been sent.

Begin forwarded message:

From: Chris Portier [redacted]
Date: November 27, 2015 at 9:56:57 AM GMT+1
To: [redacted]
Cc: [redacted]

Subject: EFSA Glyphosate Recommendations

Dear Commissioner Andriukaitis,

Attached to this email is a letter from 96 prominent epidemiologists, toxicologists, statisticians and molecular biologists from 25 countries. We have banded together and write to you at this time to

express our deep concern over the recent European Food Safety Agency (EFSA) decision that the widely used herbicide, glyphosate "is unlikely to pose a carcinogenic hazard to humans." We ask that you read our letter and share it with those who will be advising you on accepting or rejecting EFSA's decision. We would greatly appreciate your sharing this with the members of the Standing Committee on Plants, Animals, Food and Feed before their next meeting on December 10, 2015. I will be in Brussels from November 30 to December 2. If you believe it would be helpful for me to discuss these concerns with you or your staff in person, please send email to this address or call +41 79 605 79 58.

Thank you for your attention to this important issue.

Sincerely,

Prof. Christopher J. Portier

cc: Mr. Phil Hogan, European Commissioner for Agriculture and Human Development
Dr. Ladislav Miko, Deputy Director-General, DG Health & Food Safety
Dr. Bernhard Url, Executive Director, EFSA
Dr. Giovanni La Via, Chair, ENVI Committee
EFSA Panel on Plant Protection Products and their Residues
Mr. Christian Schmidt, Minister of Food and Agriculture
Dr. Helmut Tschiersky, President of the Federal Office of Consumer Protection and Food Safety (BVL)
Professor Dr. Dr. Andreas Hensel, President, BFR
Dr. Christopher Wild, Director, IARC
Mr. Jim Jones, Assistant Administrator, USEPA

From: FOUCART, Stéphane <[redacted]
Subject: bombshell
Date: March 16, 2017 at 10:07:17 PM GMT+1
To: Chris Portier <[redacted] Chris Portier <[redacted]

Hi Chris

you NEED to check out this file (New documents unsealed). It is so huge I am not sure I properly understand : did Monsanto itself had serious evidence that glyphosate is a potential clastogenic compound, back in 1999 ??? look at exhibit 5 !! I would very much appreciate your interpretation of the content of the file (released the very day ECHA said glyphosate is not a CMR !!)

best regards
Stef

--
Stéphane Foucart
Le Monde
service Planète/Science - *Environment/Science desk*
80 boulevard Auguste Blanqui
75 707 Paris cedex 13
tel. +33 1 57 28 27 02
[redacted]

From: Volker Barth <[redacted]
Subject: engl version - documentary on risk assessment / glyphosate
Date: January 17, 2016 at 11:45:53 AM GMT+1
To: Chris Portier <[redacted]

Dear Chris

EFSA spread the news about your letter, and meeting with the Commission coming up.

Nice to see your irritation is still unsatisfied about EFSA and BfR at present. My guess is that they were bought by the bio-organic farm industry, as it is a clear case, the more openly their work is flawed, the more customers will switch of to the organic food counter. But that is just a guess.

Just in case, the engl version has just been translated, is officially not yet published, but is already asked for by various European Broadcasters, and can be used for review and internal communication.

https://vimeo.com/141141148
PW agriculture

what I sometimes wonder, if the procedures of EFSA and the EC Commission
are in perfect harmony - what they seem to be

or if the commission is totally uninterested or simply unaware that e.g. the BfR risk asssessment was entirely prewritten/preformulated by the industry Glyphosate Task Force GTF, and not by BfR.
(As declared in plain sight on the original BfR report on page one, which is referred in the movie at TC 31:18)

(interestingly the job was granted by GTF to the same intertek team, which later re-evaluated the IARC work - with central author Williams GM)

Well, if you find time on such a beautiful day to watch the movie - now it is in English, and please let me know if you detect any wrong interpretation of your words or science immediately

over here the snow seems to stay, means likely we can xcountry ski to Gruene Woche the upcoming week

hope all is well on your side

with greetings

Volker

--
soweit, mit herzlichen Grüssen

Ihr

Volker Barth

Anthro Media

Documentary and iTV Production
Nature, Science, and Living History

Nansenstr. 19
D- 12047 Berlin

tel :: +49 (0) 30 62 7278 62
fax :: +49 (0) 30 62 7278 32
[redacted]

LONGER ARE
PASSIVELY DATA MINED, BUT ACTIVELY MONITORED

From: FOUCART, Stéphane <[redacted]
Subject: EPA ORD OPP glyphosate
Date: March 14, 2017 at 11:32:24 AM GMT+1
To: Chris Portier <[redacted] Chris Portier [redacted]

FYI

http://www.lemonde.fr/planete/article/2017/03/14/glyphosate-discorde-a-l-agence-de-protection-de-l-environnement-americaine_5094158_3244.html

best
Stef

--
Stéphane Foucart
Le Monde
service Planète/Science - *Environment/Science desk*
80 boulevard Auguste Blanqui
75 707 Paris cedex 13
tel. +33 1 57 28 27 02
[redacted]

From: FOUCART, Stéphane [redacted]
Subject: glyphosate letter
Date: December 7, 2015 at 2:22:16 PM GMT+1
To: Chris Portier [redacted]

Dear Chris Portier,

I hope this message finds you well. I mentioned the letter to european authorities on glyphosate at the last paragraph of my weekly column (here http://abonnes.lemonde.fr/idees/article/2015/12/07/petits-arrangements-avec-la-verite_4826110_3232.html for subscribers, and in the print edition, PDF attached).

Please do not hesitate to send updates if necessary (these last days, the timing was bad in France, virtually all environmental journalists are working on the COP21).

best regards,
Stéphane

From: FOUCART, Stéphane <[redacted]
Subject: Fwd: Gly
Date: March 8, 2016 at 5:04:26 PM GMT+1
To: Chris Portier <[redacted]

FYI

From: Christopher Watts <[redacted]
Subject: Fwd: Ramazzini Institute
Date: September 7, 2016 at 1:30:31 PM GMT+2
To: [redacted]

Christopher,

I am following up on our recent introduction to try to schedule a short call to hear your insights into the Ramazzini Institute.

I'm conducting some background research to try to better understand the aims and the activities of the Institute.

It's not for any specific article or publication, at this stage, so our conversation will be off the record, for background only.

Would you like to suggest a time that is convenient for you?

Thank you very much for letting me know.

Kind regards,

Christopher.

---------- Forwarded message ----------
From: **Devra Davis** [redacted]
Date: 10 August 2016 at 17:26
Subject: Re: Ramazzini Institute
To: Christopher Watts <[redacted]
Cc: Chris Portier <[redacted]

yes....also recommend Christopher Portier, copied here

Devra Davis, PhD MPH
Fellow American College of Epidemiology

Visiting Prof. Hebrew Univ. Hadassah Medical Center & Ondokuz Mayis Univ. Medical School
Associate Editor, Frontiers in Radiation and Health
President Environmental Health Trust
P.O. Box 58
Teton Village, WY 83025

Web: EHTRUST.ORG
Please Sign up for the EHT Newsletter
Follow me on Twitter @DevraLeeDavis
www.facebook.com/devra.davis
www.facebook.com/EHTrust

See our new music video: "A Little Chat"
http://ehtrust.org/music-video-on-cell-phone-safety/

Disconnect:the truth about cell phone radiation
http://amzn.to/1OGZJwT

The Secret History of the War on Cancer
http://amzn.to/1FIMzfJ

On Wed, Aug 10, 2016 at 12:43 AM, Christopher Watts [redacted] wrote:

Dear Dr Davis,

I am conducting some background research on the Ramazzini Institute to try to get greater insight into its goals and its activities.

Would you be available for a short off-the-record briefing by phone in the coming 1-2 weeks to share your insights and experiences of the institute, please?

Alternatively, are you able to recommend me any names of other well-placed individuals who are familiar with the institute?

I would be grateful for any support you are able to offer. Thank you very much for letting me know.

Yours sincerely, Christopher Watts.

--
Christopher Watts
Contributing Editor
The Economist Group
[redacted]

--
Christopher Watts
Contributing Editor
The Economist Group
[redacted]

From: Kathryn Guyton <[redacted]>
Subject: Glyphosate-Information requests
Date: April 1, 2016 at 3:25:41 PM GMT+2
To: [redacted] "Blair, Aaron (NIH/NCI) [V]" <[redacted]> Bill Jameson <[redacted]> "Kromhout, J. (Hans)" <[redacted]> frank lecurieux <[redacted]> Teresa Rodriguez <[redacted]> Consolato Sergi <[redacted]> Chris Portier <[redacted]>
Cc: Kurt Straif <[redacted]> Dana Loomis <[redacted]>

Dear Vol 112 Working Group members,

Although you are not employed by a US state or federal institution, you may find of interest that two state universities in the US have received information requests, issued under US state open records laws, concerning the IARC evaluation of glyphosate. IARC is not in a position to offer legal advice concerning such information requests. However, it is the position of IARC that Working Group members prepare all materials on behalf of IARC, and not as part of their official employment duties; and that IARC is the sole owner of all such materials. IARC does not encourage participants to retain working drafts of documents after the related Monograph has been published.

Don't hesitate to inform us if you have similarly received such information requests, or if we can facilitate or help with any responses.

With kind regards,
Kate

Kate Z. Guyton PhD DABT
Responsible Officer, Volume 112

Monographs Section
International Agency for Research on Cancer 150, cours Albert Thomas
69372 Lyon Cedex 08
France Tel: [+33] (0)4 72 73 86 54
[redacted]

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Here is the article
Date: September 29, 2016 at 5:55:39 PM GMT+2
To: Christopher Portier <[redacted]

http://www.huffingtonpost.com/carey-gillam/upcoming-epa-meetings-on_b_12245584.html

--

Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

From: Geets Siobhan [redacted]
Subject: AW: press inquiry glyphosate
Date: December 1, 2015 at 11:17:22 AM GMT+1
To: Chris Portier <[redacted]

Great, when can I call in the afternoon? I think it is a six hour time difference?

Mit freundlichen Grüßen Mag. Siobhan Geets Redaktion
unknown.gif ¬ **Wiener Zeitung GmbH** Media Quarter Marx 3.3 (
Anfahrtsplan) 1030 Wien I Maria-Jacobi-Gasse 1 T: +43 1 206 99-315
[redacted] I http://www.wienerzeitung.at

1__#$!@%!#__unknown.gif ¬

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Von: Chris Portier [redacted] **Gesendet:** Montag, 30. November 2015 18:40 **An:** Geets Siobhan **Betreff:** Re: press inquiry glyphosate

I am available tomorrow afternoon or now.

==========

Text entered on a small quadrilateral of aluminosilicate glass using thick fingers with a confused spelling checker running on a processor more powerful than the combined computing power of the planet when I started college and sent over digitally-controlled electromagnetic fields that are probably scrambling my brain. Mistakes are inevitable.

On Nov 30, 2015, at 18:06, Geets Siobhan [redacted] wrote:

Dear Prof. Portier,

I am writing to you on behalf of the Austrian daily newspaper „Wiener

Zeitung", we would like to print an interview with you on the dangers of glyphosate.
Are you available on phone or Skype in the next days?
I hope we'll be able to talk about this very important subject soon!

Sincerely,
best wishes from Vienna,

Siobhán Geets

Mag. Siobhan Geets Redaktion <image001.gif> **Wiener Zeitung GmbH** Media Quarter Marx 3.3 (Anfahrtsplan)
1030 Wien | Maria-Jacobi-Gasse 1 T: +43 1 206 99-315
[redacted] | http://www.wienerzeitung.at

<image002.gif>

From: Carey Gillam <careygillamnewsnow@yahoo.com>
Subject: Re: can you review this please??
Date: September 27, 2016 at 9:03:17 PM GMT+2
To: Chris Portier [redacted]
Reply-To: Carey Gillam <careygillamnewsnow@yahoo.com>

Thank you for the quick reply. I have another question for you, if and when you have time to address it. I'm interested in the EPA scientist listing as sitting on the IARC working group... A Matthew T. Martin. He appears to have no involvement with the EPA's own cancer assessments of glyphosate. Did he agree wholeheartedly with the rest of the working group, as far as you recall? Do you know much about his position? He seems fairly young. He is listed as a research Biologist at the EPA's National Center for Computational Toxicology in North Carolina. I wonder if he was in that role last year when he was on the IARC working group, or if he has been since reassigned. Do you know anything about him??

Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@yahoo.com
carey@usrtk.org
https://twitter.com/careygillam
http://www.careygillam.com/

From: Chris Portier <[redacted]
To: Carey Gillam <careygillamnewsnow@yahoo.com>
Sent: Tuesday, September 27, 2016 1:52 PM
Subject: Re: can you review this please??

I have no concerns with your quotes. A very balanced article I think.

On Sep 27, 2016, at 8:17 PM, Carey Gillam <careygillamnewsnow@yahoo.com> wrote:

I have an article I plan to publish perhaps tomorrow. Can you please look over these few paragraph excerpts and tell me if you see anything inaccurate??

The company clearly does not welcome the public scrutiny the meetings bring, but it should be satisfied that the EPA has no intention of contradicting Monsanto's claims of glyphosate's safety. After all, earlier this month the EPA publicized a 227-page "evaluation" of glyphosate's cancer-causing potential that ended with a "proposed" conclusion that glyphosate was "'not likely to be carcinogenic to human' at doses relevant to human health risk assessment."

To its credit, the EPA did issue several caveats in that report, acknowledging that numerous research studies do link glyphosate to cancer, but offering various explanations as to why the agency doesn't believe those study results are significant. The agency also added a host of qualifiers, including stating that the data it was relying on was largely limited and outdated. And the EPA specifically noted that "with the increased use of glyphosate following the introduction of glyphosate-tolerant crops in 1996, there is a need for more recent studies…" The EPA also offered a specific caveat with respect to research tying glyphosate to non-Hodgkin lymphoma (NHL), saying: "There are conflicting views on how to interpret the overall results for NHL. Some believe that the data are indicative of a potential association between glyphosate exposure and risk of NHL."

The EPA's appearance of aligning with Monsanto over independent international scientists with decades of specific

experience in cancer research, angers many in the scientific community who say the EPA is straying from established scientific principles and ignoring key evidence so it can keep the corporate interests who profit from glyphosate herbicides happy

"This chemical is a probable human carcinogen by any reasonable definition. It is nonsense to say otherwise," said Christopher Portier, former director of the National Center for Environmental Health and Agency for Toxic Substances and Disease Registry at the U.S. Centers for Disease Control and Prevention (CDC). Prior to that role, Portier spent 32 years with the National Institute of Environmental Health Sciences (NIEHS), where he served as the NIEHS associate director, director of the Environmental Toxicology Program, and associate director of the National Toxicology Program. In retirement, Portier, who was an "invited specialist" to the IARC review on glyphosate, has done some part-time work for the Environmental Defense Fund.

Portier and more than 90 other international scientists have issued a detailed report laying out the specific research that ties glyphosate to cancer both in animal studies and in human observations. The scientists said the only way for the EPA or other regulatory bodies to discount the evidence is to bend well-established rules for scientific evaluations. They say available human evidence shows an association between glyphosate and a blood cancer called non-Hodgkin lymphoma; while significant carcinogenic effects are seen in laboratory animals for rare kidney and other types of tumors. There is also "strong evidence of genotoxicity and oxidative stress," including findings of DNA damage in the peripheral blood of people exposed to glyphosate, the scientists said.
"The most appropriate and scientifically based evaluation of the cancers reported in humans and laboratory animals as well as supportive mechanistic data is that glyphosate is a probable human carcinogen*,"* the report states. *"On the basis of this*

conclusion and in the absence of evidence to the contrary, it is reasonable to conclude that glyphosate formulations should also be considered likely human carcinogens."

"The EPA is in a bad spot with this. The pushback really has come out of the industry based on things that are not scientifically sound," said Maarten Bosland, one of the authors of the report on glyphosate research. Bosland is director of the Center for Global Health Outreach Department of Pathology at the University of Chicago /Illinois and holds a Ph.D. in experimental pathology. "The amount of money that is involved in this compound is gigantic. It's a worldwide conglomerate of financial interests that are affected by this."

It seems more than coincidental that the EPA's rationale for dismissing scientific studies that IARC said showed cancer links closely dovetails with the findings of a 16-member Monsanto-funded panel. That group of 16 scientists, all but four of whom had previously worked either as employees or consultants for Monsanto, issued a report in 2015 that supported Monsanto's contention that there is no real evidence that glyphosate can cause cancer. Leading the work was Gary M. Williams, director of environmental pathology and toxicology at New York Medical College, who has a long history of publishing positive findings about glyphosate while working as a consultant for Monsanto. Williams was an author of one of Monsanto's most-touted studies, a 2000 research report that concluded glyphosate is not only not a carcinogen, but "is considered to be practically nontoxic."

Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@yahoo.com
carey@usrtk.org
https://twitter.com/careygillam
http://www.careygillam.com/

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Re: CD-1 mouse study
Date: June 7, 2017 at 6:11:14 PM GMT+2
To: Chris Portier <[redacted]

One quick quote perhaps? I'm writing about Monsanto's manipulation of the kidney study results, or their efforts to convince regulators of their industry-friendly "interpretation." I see dog studies, rats, mice, rabbits, etc..that show tumors, reduced pregnancy rates, other negative impacts, and yet the data all eventually are discounted by regulators as not statistically significant. Can you offer a reader-friendly quote addressing this?
Carey

On Mon, Jun 5, 2017 at 9:32 PM, Chris Portier [redacted] wrote:
The kidney tumors in the 1983 study are definitely important. When the two 24 month mouse studies are combined, the kidney tumors are statistically significant. Individually, when historical controls are used against the rates seen in the 1983 study, the finiding is highly statistically significant. The argument used by the regulatory agencies that these tumors fall within the range of historical controls is an incorrect statistical comparison and a mor rigorous approach needs to be used - this leads to significance as noted by IARC. In general, all four mouse studies in CD-1 mice showed some positive trend in kidney tumors that, when combined, is highly significant. The same is true for hemangiosarcomas in male mice and malignant lymphoma in male mice in the 18-month studies. They are all important.

C.

On Jun 6, 2017, at 4:37 AM, Carey Gillam <careygillamnewsnow@gmail.com> wrote:

Hello again - I'm writing up a piece about the twisted path of the 1983 CD-1 mouse study that has appeared fairly pivotal when it comes to glyphosate carcinogenicity classifications. You know the saga of the non-existent tumor in the control group that then appeared after Monsanto enlisted an outside pathologist to review tissue slides.
I'm wondering how you view this study and how much weight it carries, or

does not carry, in your evaluations of the research surrounding glyphosate and cancer.
You are aware, I believe, that the plaintiffs' attorneys in the Roundup cancer litigation in San Francisco received court approval to review the tissue slides. I'd be most interested in your view on that study. This is the one prepared by BioDynamics for Monsanto's submission to EPA.

--
Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

--
Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

From: Kathryn Guyton <[redacted]
Subject: Re: EFSA "criteria"
Date: November 17, 2015 at 5:12:54 PM GMT+1
To: Chris Portier
Cc: "Rusyn, Ivan"[redacted]

Apologies, they are both wrong- should be:
·Carcinoma [P=0.037]
Adenoma or carcinoma (combined)[P=0.034]

From: Chris Portier <[redacted]
Date: Tuesday 17 November 2015 at 17:09
To: Kate Guyton <[redacted]
Subject: Re: EFSA "criteria"

One of these p-values is wrong.

On Nov 17, 2015, at 4:30 PM, Kathryn Guyton <[redacted] wrote:
Dear Chris, Dear Ivan,

We have noted that EFSA has invoked a number of "additional criteria" in a weight of evidence approach in concluding "no evidence of carcinogenicity" of glyphosate in experimental animals.

I append for your review and comment a preliminary review of the criteria referenced by EFSA (see below), identifying relevant IARC and OECD guidance, and (consistent with the IARC systematic review approach) indicating the applicability of each to the two studies that provided "sufficient evidence" of carcinogenicity in the Monograph.

Many thanks,
Best from Lyon,
Kate

http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/4302.pdf

No evidence of carcinogenicity was confirmed by the large majority of the experts (with the exception of one minority view) in either rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies and slightly increased incidences only at dose levels at or above the limit dose/MTD, lack of pre- neoplastic lesions and/or being within historical control range. The statistical significance found in trend analysis (but not in pair-wise comparison) per se was balanced against the former considerations.
<Additional criteria- EFSA.docx>

From: Kathryn Guyton [redacted]
Subject: Re: EFSA Glyphosate Recommendations
Date: November 27, 2015 at 10:59:16 AM GMT+1
To: Chris Portier [redacted]

AWESOME! FYI, it will be me and Chris Wild at the ENVI meeting.
Kate

From: Chris Portier [redacted]
Date: Friday 27 November 2015 at 10:26
To: Kate Guyton [redacted] Kurt Straif [redacted]
Subject: Fwd: EFSA Glyphosate Recommendations

Embargoed until monday.

Begin forwarded message:
From: Chris Portier [redacted]
Date: November 27, 2015 at 9:56:57 AM GMT+1
[redacted]
Subject: EFSA Glyphosate Recommendations

Dear Commissioner Andriukaitis,

Attached to this email is a letter from 96 prominent epidemiologists, toxicologists, statisticians and molecular biologists from 25 countries. We have banded together and write to you at this time to express our deep concern over the recent European Food Safety

Agency (EFSA) decision that the widely used herbicide, glyphosate "is unlikely to pose a carcinogenic hazard to humans." We ask that you read our letter and share it with those who will be advising you on accepting or rejecting EFSA's decision. We would greatly appreciate your sharing this with the members of the Standing Committee on Plants, Animals, Food and Feed before their next meeting on December 10, 2015. I will be in Brussels from November 30 to December 2. If you believe it would be helpful for me to discuss these concerns with you or your staff in person, please send email to this address or call [redacted]

Thank you for your attention to this important issue.

Sincerely,

Prof. Christopher J. Portier

cc: Mr. Phil Hogan, European Commissioner for Agriculture and Human Development

Dr. Ladislav Miko, Deputy Director-General, DG Health & Food Safety

Dr. Bernhard Url, Executive Director, EFSA

Dr. Giovanni La Via, Chair, ENVI Committee

EFSA Panel on Plant Protection Products and their Residues

Mr. Christian Schmidt, Minister of Food and Agriculture

Dr. Helmut Tschiersky, President of the Federal Office of Consumer Protection

and Food Safety (BVL)

Professor Dr. Dr. Andreas Hensel, President, BFR

Dr. Christopher Wild, Director, IARC

Mr. Jim Jones, Assistant Administrator, USEPA

From: [redacted]
Subject: RE: EFSA Glyphosate Recommendations
Date: December 4, 2015 at 4:49:01 PM GMT+1
To: [redacted]
Cc: [redacted]

Dear Mr Portier,

Thank you for your prompt reply. Unfortunately, the Commissioner will not be in Brussels after 17 December so in this case, we would like to instead offer a meeting on 8 January at 13:00-14:00, would this be suitable?

Best regards,

Tuuli Kytölä

From: Chris Portier [redacted] **Sent:** Friday, December 04, 2015 3:54 PM**To:** KYTOLA Tuuli (CAB-ANDRIUKAITIS)**Cc:** CHAZE Nathalie (CAB-ANDRIUKAITIS); DAPKUS Egidijus (CAB-ANDRIUKAITIS); LIUTVINSKAITE Dovile (CAB-ANDRIUKAITIS)**Subject:** Re: EFSA Glyphosate Recommendations

Dear Tuuli Kytölä,

I am honored that the Commissioner would take the time out of his busy schedule to meet with me. The issue of glyphosate carcinogenicity is one that is important to everyone in Europe on both economic and safety levels and it is important that we all have a clear understanding of what the data are implying. Regretfully, I will be flying to the United States on December 11 and will be unavailable at that time. I will return from the United States on December 17 but have a commitment on December 18. I am free the following week if that could be arranged.

Sincerely,

Prof. Christopher Portier

On Dec 4, 2015, at 1:04 PM, [redacted] wrote:

Dear Mr Portier,

On behalf of Commissioner Vytenis Andriukaitis, I would like to thank you for your e-mail of 27 November 2015, sharing concerns about the EFSA Glyphosate Recommendations.

The Commissioner would be available for a meeting with you on 11 December at 13:30-14:30, would this be suitable for you?

Yours sincerely,

Tuuli Kytölä Assistant <image001.gif> **European Commission**
Cabinet of Commissioner Vytenis Andriukaitis Health and Food Safety
BERL 08/376 +32 229 58938 [redacted]

From: Chris Portier [redacted] **Sent:** Friday, November 27, 2015 9:57 AM**To:** CAB ANDRIUKAITIS WEBPAGE; ANDRIUKAITIS Vytenis (CAB-ANDRIUKAITIS)**Cc:** URL Bernhard (EFSA); LA VIA Giovanni (EP); [redacted] HOGAN Phil (CAB-HOGAN); MIKO Ladislav (SANTE); [redacted] **Subject:** EFSA Glyphosate Recommendations

Dear Commissioner Andriukaitis,

Attached to this email is a letter from 96 prominent epidemiologists, toxicologists, statisticians and molecular biologists from 25 countries. We have banded together and write to you at this time to express our deep concern over the recent European Food Safety

Agency (EFSA) decision that the widely used herbicide, glyphosate "is unlikely to pose a carcinogenic hazard to humans." We ask that you read our letter and share it with those who will be advising you on accepting or rejecting EFSA's decision. We would greatly appreciate your sharing this with the members of the Standing Committee on Plants, Animals, Food and Feed before their next meeting on December 10, 2015. I will be in Brussels from November 30 to December 2. If you believe it would be helpful for me to discuss these concerns with you or your staff in person, please send email to this address or call [redacted]

Thank you for your attention to this important issue.

Sincerely,

Prof. Christopher J. Portier

cc: Mr. Phil Hogan, European Commissioner for Agriculture and Human Development

Dr. Ladislav Miko, Deputy Director-General, DG Health & Food Safety

Dr. Bernhard Url, Executive Director, EFSA

Dr. Giovanni La Via, Chair, ENVI Committee

EFSA Panel on Plant Protection Products and their Residues

Mr. Christian Schmidt, Minister of Food and Agriculture

Dr. Helmut Tschiersky, President of the Federal Office of Consumer Protection

and Food Safety (BVL)

Professor Dr. Dr. Andreas Hensel, President, BFR

Dr. Christopher Wild, Director, IARC

Mr. Jim Jones, Assistant Administrator, USEPA

<EFSA-Glyphosate-Letter.pdf>

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Re: FYI - maybe we can talk again
Date: October 25, 2016 at 11:44:43 PM GMT+2
To: Chris Portier <[redacted]

There is also this out today. They are really turning up the heat now on EPA, moving from attacking IARC credibility to threatening careers of EPA officials, including pointing fingers at Jim Jones, the top pesticide program guy at EPA. The fact that they are so focused on obtaining emails from anyone EXCEPT Monsanto Co, (which we know there are Monsanto emails to and from EPA on this topic) shows how the wind is blowing. I think they are pushing so hard to get EPA to officially and finally repudiate the cancer connection both to hopefully influence EU decision and to use as lever to try to halt or limit the MDL. Anyway, this is latest from DC:
https://science.house.gov/sites/republicans.science.house.gov/files/documents/10.25.16%20SST%20Letter%20to%20Administrator%20McCarthy%20re%20Glyphosate.pdf

On Tue, Oct 25, 2016 at 1:55 PM, Chris Portier [redacted] wrote:

NIH needs public examination after giving millions to rogue UN agency

By: Bruce Chassy
Published: October 24, 2016
Source: The Hill
http://thehill.com/blogs/pundits-blog/healthcare/302484-nih-needs-public-examination-after-giving-millions-to-rouge-un

The National Institutes of Health (NIH) is being **called** on the carpet to explain why it gave tens of millions of dollars to the International Agency for Research on Cancer (IARC), a United Nations agency that has been accused of "**quackery**" and "**cherry picking**" its facts.

The NIH agreed to appear before Rep. **Jason Chaffetz**'s House Oversight Committee — but only on the condition that the hearing is closed-press and off-limits to the public. We don't even know the exact date the hearing will be held.

Meanwhile, the NIH is **stonewalling** FOIA requests for its emails with IARC staff, claiming — absurdly — that U.S. freedom of information laws somehow don't apply to U.S. government employees communicating with the IARC.

Why all the secrecy? The growing scandal over the IARC's finding that the widely used herbicide glyphosate is "probably carcinogenic" to humans has nothing do with national security, terrorism or classified information.

Congress simply wants the NIH to explain its support and staff involvement with an agency that has been widely criticized for its shoddy science and plagued by questions of bias. Science claims upon which public health policies are set demand transparency, expert review and demonstrated replicability.

Because of the IARC's flawed assessment and its unprecedented political lobbying, glyphosate's re-approval is now threatened in Europe, and the U.S. Environmental Protection Agency has delayed what should have been an easy re-approval. Losing glyphosate would be a **massive blow** to American farmers, consumers and the agricultural economy.

If we want the American people to continue to trust the integrity of our regulatory system, the NIH needs to answer the questions raised by the IARC's actions.

In March of this year, David Zaruk **published a series** detailing the conflicts of interest of the IARC's "independent expert," Chris Portier.

An ex-staffer at the NIH's sub-agency, the National Institute for Environmental Health Sciences (NIEHS), Portier drove the current IARC monograph process, determining which chemicals would be reviewed and influencing who would be selected to participate on the review panels — all the while taking a pay check

from the anti-pesticide Environmental Defense Fund.

Despite the IARC's purported strict conflict of interest rules, which it routinely uses to exclude scientists with any connection to industry, the agency covered up Portier's activist connections for years, identifying him only as "retired" from the NIEHS.

Portier isn't the only one in the IARC's revolving door of activist groups and those who profit by disparaging chemicals. Other monograph panelists with undisclosed conflicts include:

- Martyn Smith, reported to be a founding incorporator of the Council for Education and Research on Toxics (CERT) — an activist litigator group that sues companies over cancer claims **linked** to California Prop 65 issues — and an expert **witness** in lawsuits against chemical and pharmaceutical companies;

- Mary Wolff, an advisory board member of the anti-pesticide NGOs **Breast Cancer Action** and the **Silent Spring Institute**; and

- R. Thomas Zoeller, advisory board member of the anti-pesticide **Organic Center**.

Others, like **Aaron Blair**, **Isabelle Baldi**, **Matthew Ross** and **Ivan Rusyn**, frequently collaborate in activist conferences, co-publish papers with activists, or publicly lobby to ban pesticides. Many also serve as expert witnesses for lawsuits claiming chemicals cause cancer and are positioned to directly profit from the IARC's skewed and misleading hazard-based cancer rankings.

Congress needs to know what role the NIEHS has played in all of this, to wit:

- What role did the NIEHS and other U.S. government employees have in the IARC monograph process?

- Was the NIEHS aware of Chris Portier's and others' conflicts of interest when it provided millions in taxpayer funds to the IARC?

- Will the NIH comply with U.S. law and release their FOIA communications with the IARC to the public?

•

Finally, serious concerns have been raised about NIH and EPA procedures involving Chris Portier's brother, Kenneth Portier. The two sat on multiple **NIEHS** and **EPA** panels and other meetings without disclosing their relationship — even when Ken sat in review of Chris's work.

Despite declaring his belief that glyphosate should be taken off the market and the fact that his brother's reputation as an expert claiming glyphosate causes cancer is directly tied to the review findings, Kenneth Portier has been named to sit on EPA's glyphosate review panel.

Given this troubling conflict of interest, will the NIH and EPA disclose who recommended Kenneth Portier to this panel, release any official correspondence with Kenneth Portier and his brother Chris, and ask Kenneth Portier to make public any correspondence he has had with Chris regarding glyphosate?

The NIH needs to divulge what it knew and when it knew it. It must comply with U.S. transparency laws and rectify any internal conflicts that led to U.S. taxpayer dollars funding a rogue U.N. agency.

That's how things are supposed to be done in the United States. Not in secret, behind closed doors.

Chassy served as a researcher at the NIH for 21 years before moving to the University of Illinois at Urbana-Champaign as a department head and assistant dean, and is now professor emeritus of Food Science and Human Nutrition.

--

Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com

https://twitter.com/careygillam

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Re: Glyphosate Letter
Date: May 30, 2017 at 10:34:43 PM GMT+2
To: Chris Portier [redacted]

Thank you! Hey, I shared this on social media outlets but would like to write more if possible. It seems it has gotten quite a bit of attention in European press. Have you gotten much interest from U.S. journalists?
And can you illuminate for me the key distinctions or additions in this letter from the excellent piece you and the other scientists put out last year that made similar points: in essence, European regulators are ignoring and/or missing increases in tumor responses.
What are the newest, salient points, if you can direct me?
And have you heard anything back from Juncker's office, EFSA or EChA?
Best regards,
Carey

On Sat, May 27, 2017 at 7:55 AM Chris Portier <[redacted] wrote:
Carey,

FYI. Please treat this as embargoed until Monday, May 29 at 1:00 pm CET.

C.

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Re: glyphosate questions from a reporter
Date: September 21, 2016 at 1:45:36 PM GMT+2
To: Chris Portier <[redacted]

Thank you - I have to get my little chickens (children) off to school and then will be free by 9 a.m central/10 ET. I'd be grateful if you would call. My cell is[redacted]
Best regards,
Carey

On Wed, Sep 21, 2016 at 6:17 AM, Chris Portier <[redacted] wrote:
I am able to speak today before noon Eastern Standard time. Phone is [redacted] If you prefer, I can call you since I have unlimited international calling.

C.

On Sep 20, 2016, at 6:57 PM, Carey Gillam <careygillamnewsnow@gmail.com> wrote:

Greetings Dr. Portier- Prof. Bosland was kind enough to share your email address and your phone number. I'm hoping to arrange a time to talk to you via phone, or perhaps to ask you a few questions via email, if you prefer. I'm a reporter/researcher looking into a range of concerns surrounding glyphosate for a book I'm writing on the topic. I'm using expert voices like yours to help guide readers through this complicated, but important, issue. So with all that in mind, I'm asking if you might have time to speak on the phone Wednesday, or if you might entertain some questions via email?
If you need to know more about me, you can look at my work here http://www.huffingtonpost.com/author/careygillamnewsnow-194 and here http://www.reuters.com/journalists/carey-gillam/
My latest story from last week http://www.huffingtonpost.com/carey-gillam/fda-finds-monsantos-weed_b_12008680.html got 133,000 Facebook 'likes' on the HuffPo website, so people are reading about glyphosate!
Please let me know if we can speak.

--
Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

--
Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

From: "Sass, Jennifer" <[redacted]
Subject: RE: Glyphosate SAP Hearing
Date: December 12, 2016 at 6:13:06 PM GMT+1
To: Chris Portier <[redacted]

Great - thanks!

-----Original Message-----
From: Chris Portier [redacted]
Sent: Monday, December 12, 2016 12:10 PM
To: Sass, Jennifer
Subject: Re: Glyphosate SAP Hearing

I I'll send you a revised version in word. Thanks for sharing this.

Sent from my iPad

On Dec 12, 2016, at 17:51, Sass, Jennifer [redacted] wrote:

Thanks for pulling this together Chris - you are truly a superhero.

My problem is that I won't be able to attend the SAP either, since it is now overlapping with the NIEHS BSC, and I have to be at NIEHS for that. I'll be able to webinar into the SAP on Friday, but will have to miss Tue-Thurs. Aargh.

Kristi Pullen is unable to attend the SAP for me, since she got pulled into another all-day meeting. I'm going to have to get an intern or someone without technical ability to attend and just give a word of introduction and then circulate my comments. I can also include yours at that time. Getting them circulated in writing is probably best anyway, so the panelists can refer to them at the appropriate times.

My scheduled comment time is Thurs AM. Let me know if you'd like me to include your comments. I can put them together as a one-page from you, and have them circulated on Thurs AM along with mine.

-----Original Message-----
From: Chris Portier [redacted]
Sent: Monday, December 12, 2016 7:23 AM
To: Sass, Jennifer
Subject: Glyphosate SAP Hearing

Jenn,

Dr. Joe Haseman has submitted comments to the SAP that are critical of my analysis. I only noticed these yesterday so I will not have an opportunity to respond in writing to the SAP. I was wondering if you could find someone who is speaking who could present my comments to the committee. I have drafted below something simple and easily read. I don't know the rules, but if they could hand over additional written comments, this would be helpful. But if they could just make a few observations in their prepared talk, this would help as well. I am concerned that Dr. Haseman's comments will carry great weight, especially if he is present. Here are the points I would make:

Major Points:

1. Dr. Haseman's analysis of p-values across the fifteen studies is flawed because (1) some of these studies are not valid tests of the compound as noted by the EFSA, EPA and others; (2) The approach is inappropriate for rare tumors and (3) the approach does not address the issue of the same tumor site appearing in multiple studies in the male mouse (he groups his analysis with rats and mice to say the three findings occur by chance in the male mice).

2. Dr. Haseman's dismissal of the tumor findings in mice fails to clarify the picture. For tumors with low historical control rates, the exact test has very limited power and it is where historical controls should be used to characterize the response (e.g. the p-value of 0.062 calculated by Dr. Haseman and estimated by me for the 2 tumors in the high dose of the 1997 study is the smallest p-value possible under the exact test as this is the most extreme case for a marginal of two tumors). The historical control data set I used was that cited by EPA. The IARC used a different study but for simplicity in my presentation, I used the study cited by EPA. For this rare tumor, the p-value calculated by the historical controls is very

significant in 3 studies. This is even more obvious for hemangiosarcomas where the historical control base cited by the EPA shows no tumors in 26 control groups for 18 months; the 1997 study saw 2 tumors in the high dose group. If nothing else, the SAP should request that EPA use a formal test of significance of historical controls in these evaluations.

3. EPA, in their document, compares the results from the 18 month mouse studies with those of the 24 month studies and concludes they are inconsistent. The analysis presented with the poly-3 adjusted pooled data is an attempt to address this question rigorouusly; if the studies were indeed inconsistent, then any trend in the data should be removed by the pooled analysis. Dr. Haseman's comments fail to address this part of the arguments by the EPA.

Minor Points:

1. The Poly-3 adjustments are used appropriately. EPA based their analysis on tumor counts and did not provide the actual survival for the animals. The analysis was simply an attempt to make the 18-month studies match the 24-month studies. There was no attempt to hide the fact that the 24-month study denominators would not change. I could only use the data available to me.

2. The randomization test (20,00 random samples) I used to estimate the exact p-value for the trend test is sufficient to give reasonable p-values. While it is simple to calculate p-values for responses at the extreme, this is much more difficult for the pooled data and I did not have access to a program to calculate truly exact p-values. The one randomization test was applied to all of my exact analyses.

3. Dr. Haseman is not actually reviewing the EPA evaluation but pretty much only my comments to the analyses. Both he and Dr. Tarone correctly point out the flaws in using the approximate trend test p-value. What he fails to see is the limitations of any of these tests for rare tumors which are the last 2 columns in my response to Dr. Tarone.

4. I did not play a significant role in the IARC review; I was an invited specialist. In that capacity I did not write any of the report or participate in the discussion to finally list glyphosate as a "Probable Human Carcinogen".

The positive findings for renal tubule adenomas (0/49, 0/49, 1/50, 3/50) in the 1983 study by the IARC Working Group was based upon both p-value and historical control data but is also significant under the exact test. The finding of a significant effect on hemangiosarcomas in the 1993 study is significant by the exact test and the test against historical controls. The IARC could only evaluate 2 of the mouse studies.

C.

From: Carey Gillam <careygillamnewsnow@gmail.com>
Subject: Re: Industry complaint about Infante here if you are interested
Date: October 19, 2016 at 10:22:07 PM GMT+2
To: Chris Portier [redacted]

http://www.huffingtonpost.com/carey-gillam/epa-bows-to-chemical-indu_b_12563438.html

On Tue, Oct 18, 2016 at 2:15 PM, Carey Gillam <careygillamnewsnow@gmail.com> wrote:
http://191hmt1pr08amfq62276etw2.wpengine.netdna-cdn.com/wp-content/uploads/2016/01/CLA-Comments-on-SAP-Disqualification-10-12-16.pdf

--
Best regards,
Carey Gillam
913-526-6190
careygillamNewsNow@gmail.com
www.careygillam.com
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Best regards,
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careygillamNewsNow@gmail.com
www.careygillam.com
https://twitter.com/careygillam

From: Erika Sanders <[redacted]
Subject: RE: Invitation to speak on CHE call on glyphosate, Thur April 28
Date: April 8, 2016 at 5:57:49 PM GMT+2
To: 'Chris Portier' [redacted]
Cc: 'Lorelei CHE Walker' <[redacted]

Wonderful, Dr. Portier. We're so pleased.

Yes, the "technology" for these calls is really simple. You simply need to dial in to a phone number I'll send you (with an access code).

The only other thing you would need is access to your computer or other device to view your own slides, if you choose to use them. We post them as PDFs on the call's webpage on our website and participants download them to their own devices and follow along on their own. Everyone advances their own slides. So, as you move through your presentation you simply need to say "next slide" or let the audience know what number slide you're on. This isn't a webinar, so no connecting via computer or need for other equipment of any kind.

I will be posting the call announcement on our webpage today. **If you had a moment to send me a brief bio to use and a preferred photo** (I can also look online), then I'll get you added as a speaker. Once that webpage is up, I'll send additional logistical details to the whole group next week.

You would have about 12 minutes or so for your presentation. We do leave time for some Q&A following all the presentations with participants. The call will last a total of 1 hour.

We very much appreciate your willingness to participate. It feels important to have IARC's evaluation of glyphosate represented.

If you have any further questions at this time, please be in touch. Otherwise, you'll be hearing more from us next week.

Best,

Erika

Erika Sanders
CHE Programs Administrative Coordinator
[redacted]
360-331-7904
www.HealthandEnvironment.org

From: Chris Portier [redacted] **Sent:** Friday, April 8, 2016 6:45 AM **To:** Erika Sanders [redacted] **Cc:** Kate Guyton [redacted] Lorelei CHE Walker [redacted] **Subject:** Re: Invitation to speak on CHE call on glyphosate, Thur April 28

Erika,

I assume I would do this from my office via electronic means. If that is true, I am happy to help you out.

C.

On Apr 7, 2016, at 6:30 PM, Erika Sanders [redacted] wrote:

Thank you, Dr. Guyton, for you quick response.

Dr. Portier, we would of course be delighted if you would consider joining the call on April 28th as a speaker to discuss IARC's evaluation of glyphosate. The details are below, but if I can answer any questions, please don't hesitate to be in touch.

Best,
Erika

Erika Sanders
CHE Programs Administrative Coordinator
[redacted]
360-331-7904
www.HealthandEnvironment.org

From: Kathryn Guyton [redacted] **Sent:** Thursday, April 7, 2016 7:37 AM **To:** Erika Sanders <[redacted] **Cc:** 'Lorelei CHE Walker' <[redacted]>; Chris Portier [redacted] **Subject:** Re: Invitation to speak on CHE call on glyphosate, Thur April 28

Dear Erika,

Thank you for your email, and for the kind invitation. Unfortunately, I wouldn't be able to provide the presentation you request. May I kindly suggest you contact Professor Chris Portier, cc'd here, as he may be willing to help.

With best regards,
Kate

Kate Z. Guyton PhD DABT
Monographs Section
International Agency for Research on Cancer 150, cours Albert Thomas
69372 Lyon Cedex 08
France Tel: [+33] (0)4 72 73 86 54
[redacted]

From: Erika Sanders <[redacted] **Date:** Wednesday 6 April 2016 at 19:17 **To:** [redacted] Kate Guyton [redacted] **Cc:** 'Lorelei CHE Walker' <[redacted] **Subject:** Invitation to speak on CHE call on glyphosate, Thur April 28

Dear Dr. Guyton,

I am the Programs Administrative Coordinator with the Collaborative on the Health and the Environment (CHE, see: http://www.healthandenvironment.org). Lisette van Vliet, director of the Health and Environment Alliance (HEAL) in Brussels recommended I reach out to you with an invitation to speak on an upcoming teleconference CHE is hosting on glyphosate and health on **Thursday April 28, 2016 at noon US Eastern**.

Dr. Belpoggi of the Ramazzini Institute in Italy, an author of the recently released consensus statement Concerns over us of glyphosate-based herbicides associated with exposures: a consensus statement(February 17, 2016, Environmental Health),has agreed to speak both to the consensus statement's recommendations as well as to her own research on glyphosate and health. Lisette will speak as well to the policy considerations of glyphosate research and recent policy movement in the EU.

We would like to invite you to speak to IARC's evaluation of glyphosate.

Our overall aim for this call is to give participants an understanding of the latest science on glyphosate, where leading institutions such as IARC stand on its potential human health impacts and what policy recommendations are being made, particularly in the EU.

The teleconference would last one hour. If you agree to speak that will give us 3 speakers, so you would each have approximately 12 minutes or so to present. You're welcome to use slides to accompany your remarks.

Our teleconferences are attended by environmental health researchers, medical professionals, government representatives (EPA, NIEHS, etc.), NGO representatives and some members of the general public. We typically have 75-100 participants. They last for one hour, and include a brief Q&A period following the speaker presentations.

Again, the call is scheduled for Thursday April 28th. If you can join us, you'd only need to send me a brief bio and a photo you'd like me to use for our

advertising. I will then send you additional logistical information for the call.

Thank you for your consideration.

Best,

Erika

Erika Sanders
CHE Programs Administrative Coordinator
[redacted]
360-331-7904
www.HealthandEnvironment.org

From: Kathryn Guyton <[redacted]
Subject: Re: Joint FAO/WHO Meeting on Pesticide Residues - JMPR summary report
Date: May 16, 2016 at 3:51:52 PM GMT+2
To: Chris Portier <[redacted]

Yes. I'm still in Geneva, through tomorrow…

From: Chris Portier <[redacted]
Date: Monday 16 May 2016 at 15:15
To: Kate Guyton <[redacted]
Subject: Re: Joint FAO/WHO Meeting on Pesticide Residues - JMPR summary report

And, do we need to chat?

On May 16, 2016, at 1:14 PM, Kathryn Guyton <[redacted] wrote:

Envoyé de mon iPhone

Begin forwarded message:

A Joint Meeting of the Food and Agriculture Organization of the United Nations (FAO) Panel of Experts on Pesticide Residues in Food and the Environment and the World Health Organization (WHO) Core Assessment Group on Pesticide Residues (JMPR) was held at WHO Headquarters, Geneva (Switzerland), from 9 to 13 May 2016. **Diazinon**, **glyphosate** and **malathion** were placed on the agenda by the JMPR Secretariat, based on the recommendation of the last session of JMPR to re-evaluate these compounds given the number of new studies that had become available since their last full assessments. The

extracts of the results of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) have now been published under the following link: http://www.who.int/foodsafety/jmprsummary2016.pdf?ua=1 You will also find a set of Q&As following this link: http://www.who.int/foodsafety/faq/en/ **For media queries, please contact** Paul Garwood Telephone: +41 22 791 1578 Mobile: [redacted] Email: [redacted] Christian Lindmeier Telephone: +41 22 791 1948 Mobile: [redacted] E-mail: [redacted]

----------This message and its attachments are strictly confidential. If you are not the intended recipient of this message, please immediately notify the sender and delete it. Since its integrity cannot be guaranteed, its content cannot involve the sender's responsibility. Any misuse, any disclosure or publication of its content, either whole or partial, is prohibited, exception made of formally approved use.

From: ECHA Committee Risk Assessment <rac@echa.europa.eu>
Subject: RE: Portier slides for ECHA Committee Risk Assessment
Date: November 21, 2016 at 4:21:40 PM GMT+1
To: Chris Portier [redacted]
Cc: Lisette van Vliet [redacted], Dolores Romano [redacted] Tatiana Santos [redacted], pcl [redacted] DVORAKOVA Dana [redacted] ECHA Committee Risk Assessment [redacted]

Dear Chris,
Thank you for your quick response and for the slides!
Best regards,
Dana

-----Original Message-----
From: Chris Portier [redacted]
Sent: 21 November 2016 17:18
To: ECHA Committee Risk Assessment <rac@echa.europa.eu>
Cc: Lisette van Vliet [redacted] Dolores Romano [redacted] Tatiana Santos [redacted] pcl [redacted]
Subject: Portier slides for ECHA Committee Risk Assessment

Dear Dana,

Per your request through Tatiana Santos and Peter Clausing, I have attached my slides.

C. Portier

From: Chris Portier <[redacted]
Subject: Re: query to you.
Date: August 4, 2017 at 3:33:52 PM GMT+2
To: Carey Gillam <carey@careygillam.com>

The European Parliament is not like the US House or Senate. They take these discussions seriously and ask reasonable questions (in my experience). There will be some members who clearly are on one side of the issue or the other, but many fall in between. You can certainly expect to be attacked by Monsanto and I expect to be attacked by both BfR and EFSA. But that is the nature of the beast.

C.

On Aug 4, 2017, at 1:44 PM, Carey Gillam <carey@careygillam.com> wrote:
I see you are slated to speak to Euro Parl hearing Oct. 11 as am I.
I hope you are planning to attend.
I also see BfR and EFSA and Monsanto on agenda.
Is there any reason I should be skeptical about participation?
And thank you for your reply. I know you are quite busy.
Bests,
Carey

On Fri, Aug 4, 2017 at 4:20 AM, Chris Portier <[redacted]> wrote:
On point 1, I agree that this appears to be a deceit by the Agency asking about formulations only after the fact,

On point 2, by statute, EPA is required to base their decision on the active ingredient (glyphosate) and not the formulated product. So, in doing there evaluations, they tend to ignore studies regarding the formulated product and they don't necessarily feel they even need to know about the adjuvants.

Sorry I took so long to reply, I have been busy. I found more positive tumors in the publicly available glyphosate data and I am trying to decide what is worth doing at this point to expose how poorly these data have been evaluated.

C.

On Aug 2, 2017, at 9:56 PM, Carey Gillam <carey@careygillam.com> wrote:

I have some EPA emails and notes that show the agency trying in April 2016 to get information from Monsanto about formulated Roundup products

An EPA scientist wrote this: "EPA was interested in any data or information Monsanto may have on how the formulations may differ from data on the active ingredient and surfactants independently of one another." The notes go on to ask for information about changes in Monsanto's Roundup formulation "over the years." "Monsanto indicated that up until 2000, nearly all glyphosate products on the market were its Roundup formulation which used some form of tallow amine as a surfactant. Afterwards, the properties of surfactants used and the ratio of surfactant to active ingredient were changed in most formulations… EPA suggested that Monsanto provide in writing any information that documents the changes of glyphosate formulations over time and across the globe."

This comes three months after the same EPA official Khue Nguyen reassured a concerned member of the public who had been asking questions. Nguyen told that man this: "Often, glyphosate products contain water, dyes, and/or surfactants that help facilitate movement of glyphosate into the plant…" . "While manufacturers of pesticide products do not always disclose all "other ingredients" on their labels…. they are required to disclose those ingredients to EPA. Inert ingredients in a product such as Roundup are not of concern for the consumer when pesticide products are used according to the label."

To me this is troubling because
1. it appears that the EPA is acting as though it has all the information it needs on formulated Roundup products to assure they are safe while at the same time asking Monsanto to provide it with information on what its using and in what ratio in these formulated Roundup products.
2. Why is EPA asking Monsanto for information on formulations in 2016, after

some 40 years of this stuff being on the market? Shouldn't EPA already know in detail what is out there and have the database to show its safe if its telling consumers its safe?

Obviously, I'm aware of Monsanto's own internal discussions of formulations v. glyphosate-only research and I'm aware of the studies that have shown formulations to be more toxic.
I'm simply asking you if the language I've shared above, which is pulled verbatim from these EPA records, indicates to you a hypocrisy or perhaps even a deceit by the agency. Or just a lack of knowledge? I may be reading it all wrong or not considering factors I'm not aware of and thought you had the experience and background to address this.
I'd welcome your comments.
Bests,
Carey

Friday, August 18, 2017 at 12:57:17 PM Central European Summer Time

Subject: RE: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation
Date: Friday, August 18, 2017 at 12:20:14 PM Central European Summer Time
From: NEUMANN Nina
To: [redacted]
CC: Portier Chris (TGX), MITTERMAYER Felix
Attachments: image001.png

Dear Prof Dr Portier,

Thank you for your email.

We are delighted that you will participate in the public hearing in the European Parliament, and we will send you further information in early September.

Best wishes

Nina Neumann

From: Portier Chris (TGX) [redacted]
Sent: 18 August 2017 10:57
To: NEUMANN Nina
Subject: Re: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation

Dear Ms. Neumann,

Did I answer this email? It went to my Maastricht account that I seldom check. I would be happy to participate. Please address any further emails to [redacted]

C.

From: NEUMANN Nina [redacted]
Date: Friday, August 4, 2017 at 10:57 AM
To: "Portier Chris (TGX)" [redacted]
Cc: MITTERMAYER Felix [redacted]
Subject: RE: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation

Dear Prof. Dr. Portier,

Considering the importance that many of our Members attach to your presence at the public hearing in the European Parliament on the Monsanto papers and glyphosate, I allow myself to re-send our invitation (just in case my previous email got lost).

Thank you very much in advance.

Best wishes,

Nina Neumann

From: NEUMANN Nina
Sent: 28 July 2017 16:57
To: [redacted]
Cc: MITTERMAYER Felix [redacted]
Subject: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation

Dear Prof. Dr. Portier,

The Committee on the Environment, Public Health and Food Safety (ENVI) and the Committee on Agriculture and Rural Development (AGRI) of the European Parliament will hold a joint Public Hearing entitled "The Monsanto papers and glyphosate" on Wednesday, 11 October, from 9h00 to 12h30, in the premises of the European Parliament in Brussels.

The aim is to discuss the credibility of scientific studies behind both the decision of US regulatory agencies to authorise the plant protection product Roundup™, as well as the conclusions of the EU risk assessment agencies ECHA and EFSA regarding its active substance glyphosate, with a specific focus on the questions raised by the so-called Monsanto papers. The hearing is expected to give a good insight into the matters at stake and to provide Parliament with the necessary information to decide on possible follow-up action.

Given your profile as one of the leading scientists familiar with the risk assessment of glyphosate, the Members of both committees would highly appreciate it if you could speak at this event and present your views.

Considering the fact that the hearing is already in a few weeks' time, we would be grateful if you could let us know as soon as possible whether you will be able to speak at this public hearing.

Many thanks in advance!

Best wishes,

Nina Neumann

Nina NEUMANN
Administrator for a parliamentary body

European Parliament
IPOL
Directorate for Economic and Scientific Policies
Secretariat of the Committee on the Environment, Public Health and Food Safety
BRU - SQM 10Y020 - Tel. +32 228 46022
[redacted]
www.europarl.europa.eu

Friday, August 18, 2017 at 12:57:17 PM Central European Summer Time

Subject: Automatic reply: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation
Date: Friday, August 18, 2017 at 10:57:03 AM Central European Summer Time
From: NEUMANN Nina
To: Portier Chris (TGX)

Thank you for your email. Please note that I am on leave until 30 August. I will be back in the office on 31 August.

Friday, August 18, 2017 at 12:57:17 PM Central European Summer Time

Subject: RE: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation
Date: Friday, August 4, 2017 at 10:52:02 AM Central European Summer Time
From: NEUMANN Nina
To: Portier Chris (TGX)
CC: MITTERMAYER Felix
Attachments: image001.png

Dear Prof. Dr. Portier,

Considering the importance that many of our Members attach to your presence at the public hearing in the European Parliament on the Monsanto papers and glyphosate, I allow myself to re-send our invitation (just in case my previous email got lost).

Thank you very much in advance.

Best wishes,

Nina Neumann

> **From:** NEUMANN Nina
> **Sent:** 28 July 2017 16:57
> **To:** [redacted]
> **Cc:** MITTERMAYER Felix [redacted]
> **Subject:** Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation
>
> Dear Prof. Dr. Portier,
>
> The Committee on the Environment, Public Health and Food Safety (ENVI) and the Committee on Agriculture and Rural Development (AGRI) of the European Parliament will hold a joint Public Hearing entitled "The Monsanto papers and glyphosate" on Wednesday, 11 October, from 9h00 to 12h30, in the premises of the European Parliament in Brussels.
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>
> Considering the fact that the hearing is already in a few weeks' time, we would be grateful if you could let us know as soon as possible whether you will be able to speak at this public hearing.
>
> Many thanks in advance!

Best wishes,

Nina Neumann

Nina NEUMANN
Administrator for a parliamentary body

European Parliament
IPOL
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Secretariat of the Committee on the Environment, Public Health and Food Safety
BRU - SQM 10Y020 - Tel. +32 228 46022
[redacted]
www.europarl.europa.eu

Friday, August 18, 2017 at 12:57:17 PM Central European Summer Time

Subject: Public Hearing on "The Monsanto papers and glyphosate" in the European Parliament on 11 October 2017 - invitation
Date: Friday, July 28, 2017 at 4:57:10 PM Central European Summer Time
From: NEUMANN Nina
To: Portier Chris (TGX)
CC: MITTERMAYER Felix
Attachments: image001.png

Dear Prof. Dr. Portier,

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Given your profile as one of the leading scientists familiar with the risk assessment of glyphosate, the Members of both committees would highly appreciate it if you could speak at this event and present your views.

Considering the fact that the hearing is already in a few weeks' time, we would be grateful if you could let us know as soon as possible whether you will be able to speak at this public hearing.

Many thanks in advance!

Best wishes,

Nina Neumann

Nina NEUMANN
Administrator for a parliamentary body

European Parliament
IPOL
Directorate for Economic and Scientific Policies
Secretariat of the Committee on the Environment, Public Health and Food Safety
BRU - SQM 10Y020 - Tel. +32 228 46022
[redacted]
www.europarl.europa.eu

From: no-reply@echa.europa.eu
Subject: Your ECHA submission data: glyphosate (ISO); N-(phosphonomethyl)glycine, 1071-83-6, 213-997-4
Date: July 8, 2016 at 9:21:09 PM GMT+2
To: [redacted]

Your submission is successfully received. Your reference number is 702fd2a8-3afd-41ea-ac94-fc89eb76cbd5. This message has been generated automatically by comments.echa.europa.eu
Substance Name: glyphosate (ISO); N-(phosphonomethyl)glycine
CAS Number: 1071-83-6
EC Number213-997-4

IARC Monograph Review Process and Glyphosate

Christopher J. Portier, Ph.D.

Cancer by Glyphosate – how dangerous is the herbicide?

Deutscher Bundestag, Berlin

June 6, 2015

The IARC Monographs Program

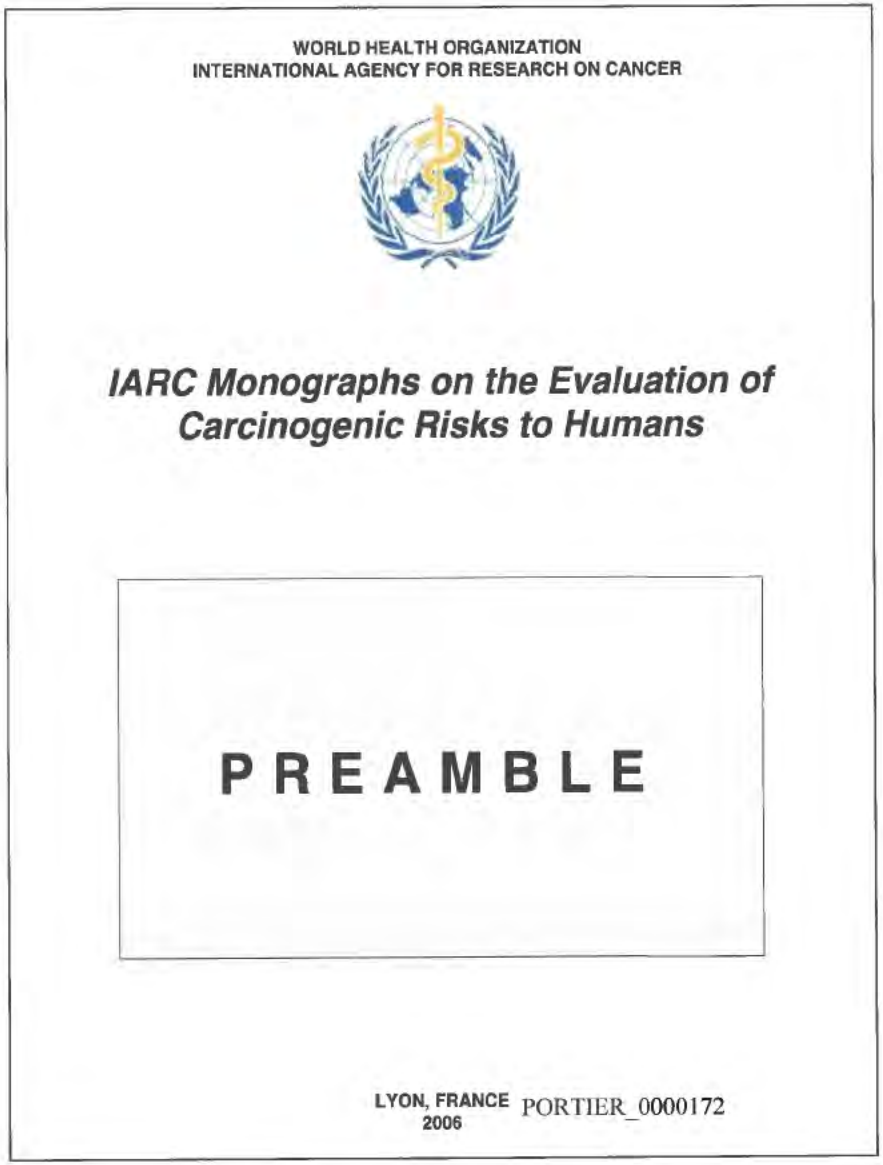
- IARC Monographs Evaluate
  - Chemicals
  - Complex substances and mixtures
  - Occupational exposures
  - Physical and biological agents
  - Personal habits

The IARC Monographs Program

- 980 Agents have been reviewed
  - 116 **known** human carcinogens
    - Group 1
  - 73 **probable** human carcinogens
    - Group 2A
  - 287 **possible** human carcinogens
    - Group 2B
  - 503 **not classifiable**
    - Group 3
  - 1 **probably not** carcinogenic

IARC Monographs Process

- Written Guidelines
  - Public Document
  - Who? What? How?
  - Roles
  - Responsibilities
  - Instructions
    - Review
    - Summary of Evidence



IARC Monograph 112 Process

- Working Group Members
  - No real or apparent conflicts of interest
    - Formal process, written declarations of interest
  - Membership
    - Working Group members – review, evaluate
    - Invited Specialist – review only
    - Representatives – government, observe only
    - Observers – interested party, observe only
    - Secretariat – support the Working Group

IARC Monograph Timeline

- 1 year before Monograph Meeting
  - Meeting announced
  - Call for experts
  - Call for data
- 8 months before Monograph Meeting
  - Working Group membership selected
  - Request for observer status opened
  - Draft sections of Monograph developed by Working Group Members

IARC Monograph Timeline

- 1 month before Monograph Meeting
  - Call for data closed
  - Draft sections distributed to Working Group members for review and comment
- At Monograph Meeting
  - Finalize review of all literature
  - Evaluate the evidence in each category
  - Complete the overall evaluation

IARC Monograph Timeline

- 1-2 weeks after Monograph Meeting
  - Publish summary in Lancet Oncology
- 4-12 months after Monograph Meeting
  - Finalize Monograph and publish

The IARC Monograph

Preamble

General Remarks

Several *Monographs* in one volume:

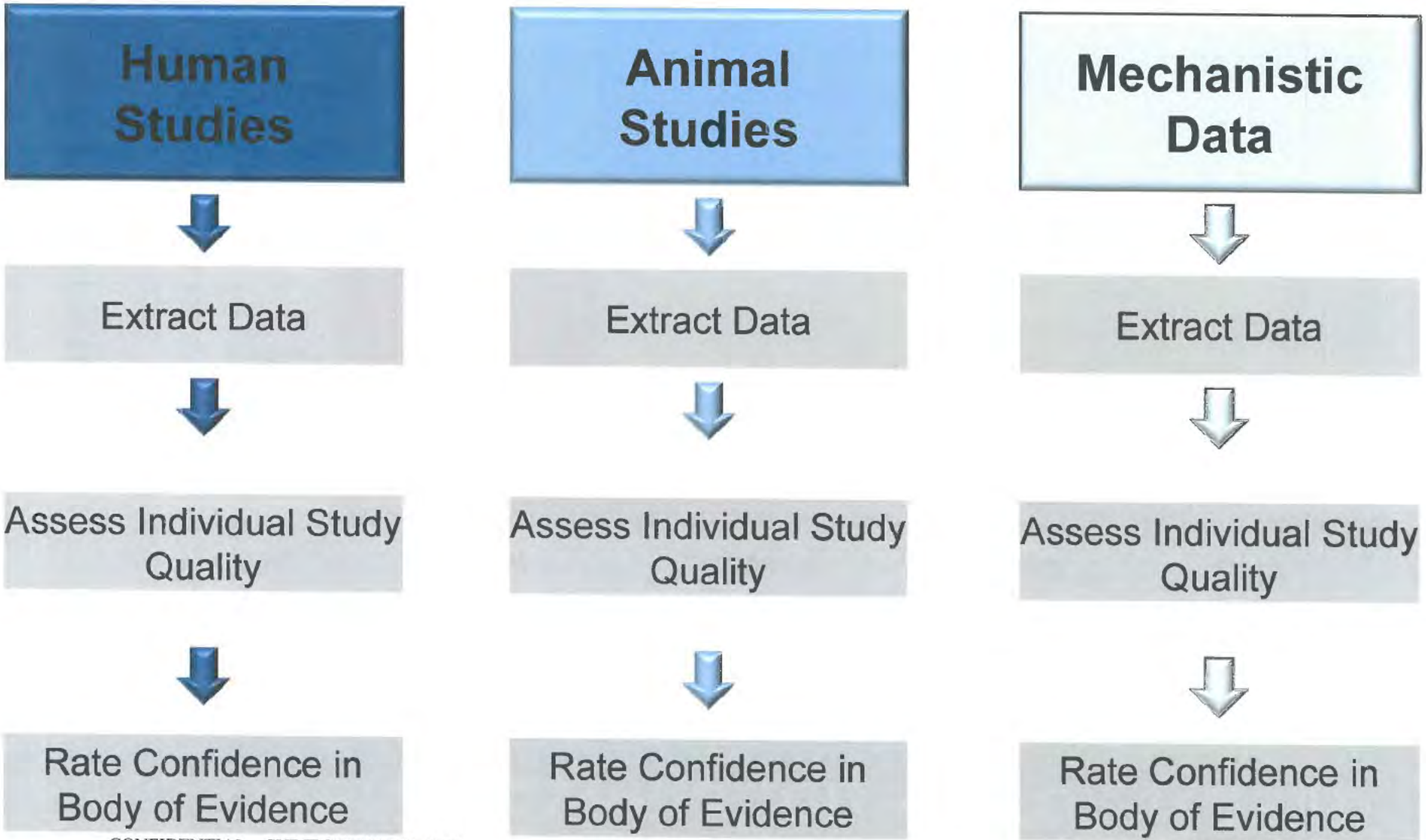
1. Exposure data
2. Cancer in humans
3. Cancer in animals
4. Mechanistic and other relevant data
5. Summary
6. Evaluation and rationale

References

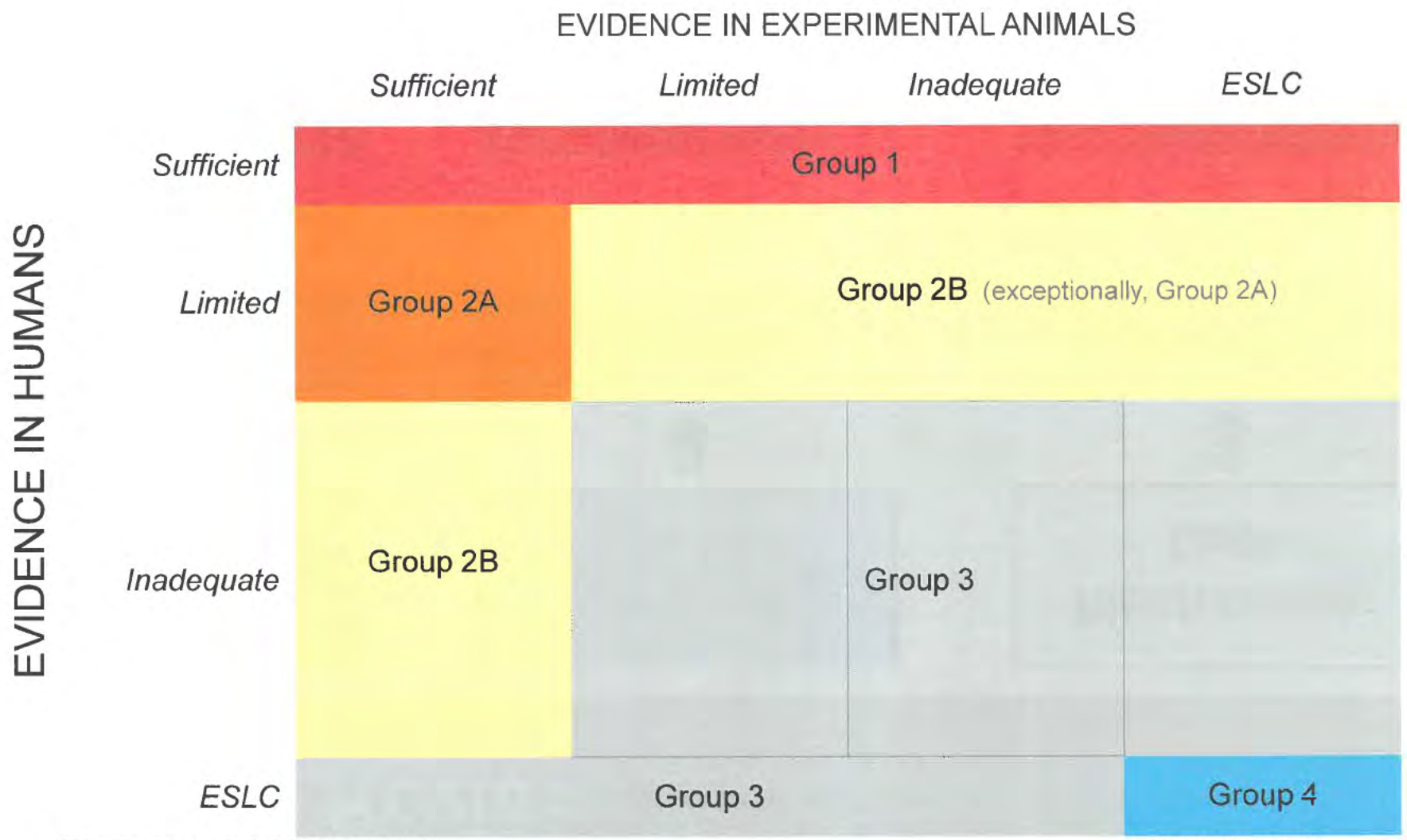
What is reviewed?

- Systematic review of human, experimental and mechanistic data
- All pertinent epidemiological studies and cancer bioassays
- Representative mechanistic data
- Studies must be publicly available
  - Sufficient detail to review
  - Reviewers cannot have been associated with the study

Evidence Review



IARC Overall Evaluation – Prof. Rusyn



Modified from Vincent Cogliano, IARC

Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship is **established**
  - Chance, bias and confounding ruled out with reasonable confidence
- Limited Evidence
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence

Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Inadequate Evidence
  - Studies permit no conclusion regarding causality
- Evidence suggesting lack of carcinogenicity
  - Several strong studies showing consistent lack of positive association
  - Conclusion limited to cancer sites and conditions studied

Glyphosate - Background

- Broad-spectrum, non-selective herbicide
- First synthesized by Cilag (1950) as a possible drug
- Re-synthesized by Monsanto (1970)
- Patent expired [1991, 2000 (US)]
- Hundreds of trade names
- Approximately 91 producers in 20 countries

Glyphosate - Background

- Believed to be the most heavily used herbicide in the world
  - 2012 production volume > 700 million kg
- Production has increased sharply in recent years
  - Genetically modified glyphosate-resistant crop varieties
- Exposure pathways
  - Air (during spraying)
  - Water
  - Food

Glyphosate – Human Evidence

- Literature
  - US Agricultural Health Study (AHS)
  - Multiple independent case-control studies

Glyphosate – Human Evidence

- Epidemiological studies of cancer in humans
  - More than 2 studies
    - Non-Hodgkin Lymphoma (NHL)
    - Multiple Myeloma (MM)
  - Two studies
    - Leukemia, breast cancer, prostate cancer
  - One Study
    - Adult brain, oesophageal, stomach, prostate, soft-tissue sarcoma, lung, oral cavity, colorectal, pancreas, kidney, bladder, melanoma

Glyphosate – Key Epidemiology Studies for Non-Hodgkin Leukemia

Study	Type	Size
Agricultural Health Study *(Alavanja et al., 2003)*	Cohort – pesticide applicators and spouses	52 395 (+32 347 spouses)
US Midwest *(De Roos et al., 2003)*	Pooled analysis of 3 case-control studies	NHL: 650 cases, 1933 controls
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control	517 cases, 1506 controls
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)

Glyphosate Evaluation – Human Evidence

- Limited Evidence for NHL
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence
- Basis
  - De Roos et al., 2003 (US), McDuffie et al., 2001 (Canada), Eriksson et al., 2008 (Sweden)
    - Positive association
    - Adjustment for other pesticides
  - Agricultural Health Study
    - No additional support for association, does not contradict

Monograph should be available in July!

Questions?

Carcinogenicity of Glyphosate
A Systematic Review of the Available Evidence

Christopher J. Portier, Ph.D.

Swiss Society of Toxicology

18 November, 2016, Basel

Glyphosate - Background

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- Exposure pathways
  - Air (during spraying)
  - Water
  - Food

Recent Cancer Assessments of Glyphosate

- IARC – March, 2015
  - Probable human carcinogen
- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- Portier et al. – January, 2016
  - Probable human carcinogen
- WHO/JMPR – March, 2016
  - Unlikely to pose a carcinogenic risk to humans from exposure through the diet
- ECHA – May, 2016 (draft)
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment

Comparison Across Evaluations

Study	Authors Known	COI Made Public	Proprietary Studies	Open Literature	Guidelines	Evaluated Dose-Response
IARC	Yes	Yes	No	Yes	Yes	No
EFSA	No	No	Yes	Yes	Yes	No
Portier	Yes	Yes	Yes	Yes	Yes	No
JMPR	Yes	?	Yes	Yes	Yes	Yes
ECHA	No	No	Yes	Yes	Yes	No
EPA	?	Some	Yes	Yes	Yes	No

Why are they different?

- Human Data
  - Limited evidence versus Insufficient Evidence
- Animal Cancer Studies
  - Sufficient Evidence versus Insufficient Evidence
- Mechanisms
  - Genotoxic or not genotoxic
  - Induces oxidative stress is or is not important

IARC: Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship is **established**
  - Chance, bias and confounding ruled out with reasonable confidence
- Limited Evidence
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence

IARC: Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Inadequate Evidence
  - Studies permit no conclusion regarding causality
- Evidence suggesting lack of carcinogenicity
  - Several strong studies showing consistent lack of positive association
  - Conclusion limited to cancer sites and conditions studied

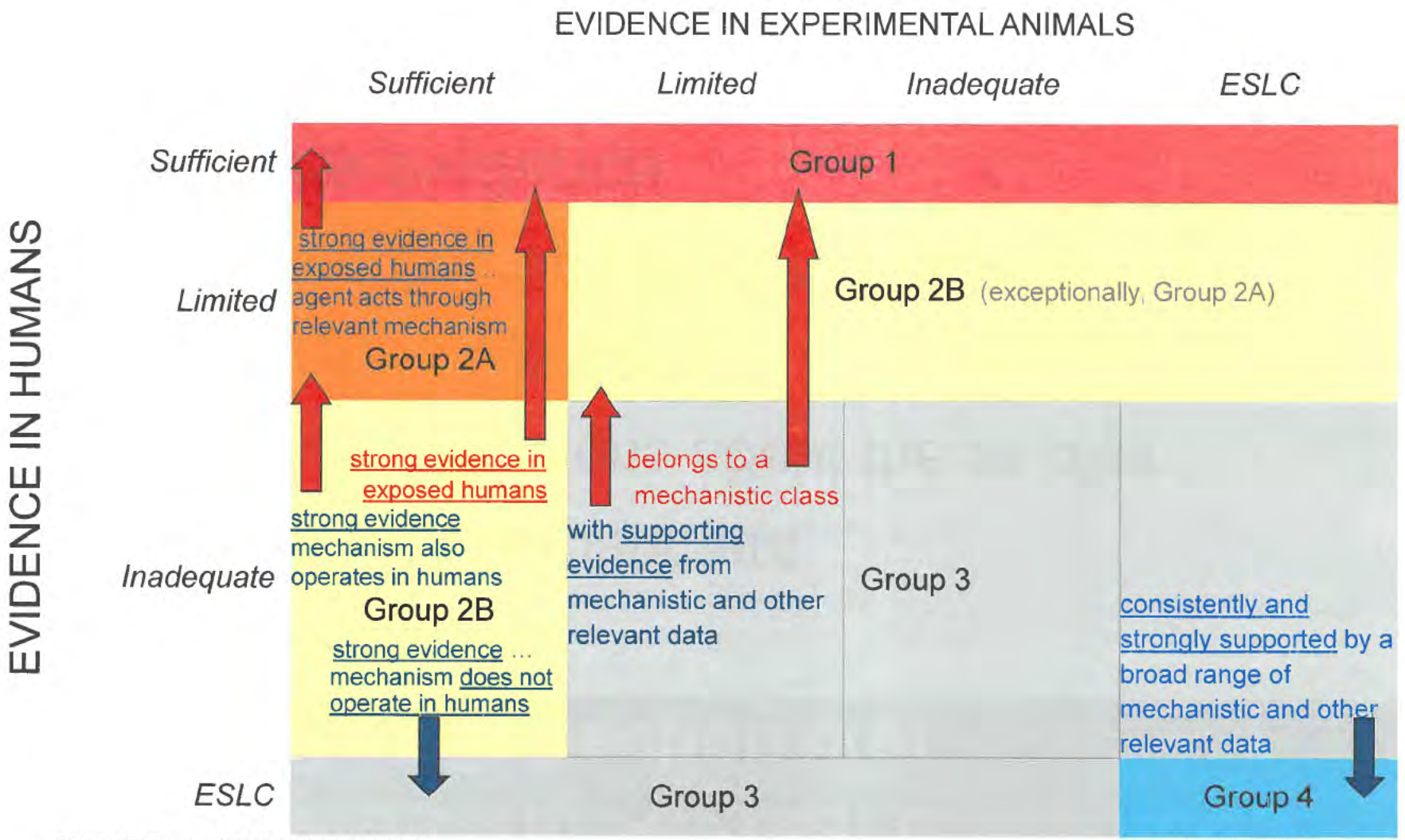
IARC: Evaluating Animal Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship established
  - Two or more species of animals or two or more studies
  - One study where malignant neoplasms occur to an unusual degree
    - Incidence (rare tumors)
    - Site (unusual tumors)
    - Age at onset
    - Strong findings at multiple sites

IARC: Evaluating Animal Evidence
Preamble Part B, Section 6(a)

- Limited Evidence
  - Single positive experiment
  - Unresolved questions about the studies
  - Only benign neoplasms
  - Only promoting activity demonstrated
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity
  - All studies negative or inadequate
  - At least two well-conducted negative studies

IARC Overall Evaluation



Modified from Vincent Cogliano, IARC

CLP Guidance on Carcinogenicity
(continued)

- The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:
  - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or
  - animal experiments for which there is sufficient (1) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).
- In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing **limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals**

Guidance on the Application of the CLP Criteria, ECHA (2015)

Table 1: Human Epidemiology Studies

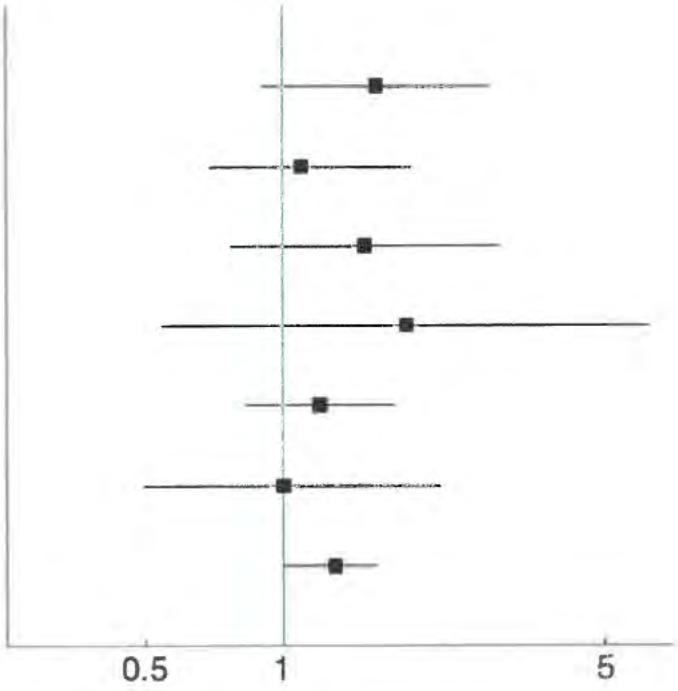
Study	Type	Size	Findings	Exposed Cases
Agricultural Health Study *(De Rooset al., 2005)*	Cohort – licensed pesticide applicators	52 395 (+32 347 spouses), 92 cases, 4-8 years follow-up	1.1 (0.7-1.9) C 0.7 (0.4-1.4) 21-56% tertile compared to <20% tertile 0.9 (0.5-1.6) 21-56% tertile compared to >57% tertile (31 cases no quantification of exposure)	73
US Midwest *(De Roos et al., 2003)*	Pooled analysis 3 case-control studies	NHL: 650 cases, 1933 controls	2.1 (1.1-4) U 1.6 (0.9-2.8) C	36 36
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control study	517 cases, 1506 controls	1.2 (0.83-1.74) U 1.0 (0.63-1.57) ≤2 d/Y 2.12 (1.2-3.73) >2 d/Y	51 28 23
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control	2.02 (1.1-3.71) U 1.51 (0.77-2.94) C 1.69 (0.7-4.07) ≤10 d/Y 2.36 (1.04-5.37) >10 d/Y 1.11 (0.24-5.08) ≤10 Y 2.26 (1.16-4.4) >10 Y	29 29 12 17 NR NR
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)	2.3 (0.4-1.3) U 5.8 (0.6-5.4) C (not specified)	4 NR
France Case-Control *(Orsi et al, 2009)*	Hospital-based case-control study	244 cases, 456 controls	1.0 (0.5-2.2) U	12
Swedish Case-Control Study *(Hardell et al., 2002)*	Population-based case-control study	515 cases, 1141 controls	3.04 (1.08-8.5) U 1.85 (0.55-6.2) C (not specified)	8 8
US Case-Control Study *(Lee et al., 2004)*	Population-based case-control study	872 cases, 2381controls	1.4 (0.98-2.1) U – no asthma 1.2 (0.4-3.3) U - asthma	53 6

Meta Analyses

Study	Included Studies	Findings
Schinasi and Leon, 2014	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.5 (1.1-2.0)
IARC Monograph Working Group	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.103-1.65) – used adjusted risk estimates from Hardell et al., 2003 and Eriksson et al., 2008
Chang and Delzell, 2016	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.0-1.6)

Tree Plot of Epidemiology Studies
(using analyses corrected for potential confounders)

Study	RR	Lower	Upper	Weight
De Roos et al. (2003)	1.600	0.900	2.800	16.2
De Roos et al. (2005)	1.100	0.700	1.900	21.0
Eriksson et al., (2008)	1.510	0.770	2.940	11.6
Hardell et al. (2002)	1.850	0.550	6.200	3.6
McDuffie et al. (2001)	1.200	0.830	1.740	38.1
Oris et al. (2009)	1.000	0.500	2.200	9.5
Meta-Analysis	1.300	1.000	1.600	100.0



Chang and Delzell (2016)

Summary of Human Evidence

- Limited Evidence in Humans
  - IARC, Portier et al.
- Insufficient evidence in humans
  - EFSA, ECHA, EPA
- Did not evaluate
  - WHO/JMPR

Carcinogenicity Studies in Male Mice

Year	Strain	Length[1]	Top Dose[2]	Renal Tumors	Hemangio-sarcomas	Malignant Lymphoma
1983[5]	Crl:CD-1	24	4,841	+[3]		
1993[5]	?:CD-1	24	1,000		+	+/-[4]
1997	CrJ:CD-1	18	4,843	+	+	+
2001	SW	18	1,460	+		+/-[6]
2009	Crl:CD-1	18	810			+

1 – months; 2 – mg/kg bw/day; 3 - + indicates a p-value of <0.05 as calculated by BfR using the Armitage linear trend test in proportions; 4 – p=0.08; 5 – studies evaluated in IARC review; 6 – p=0.053

+ indicates studies evaluated by IARC

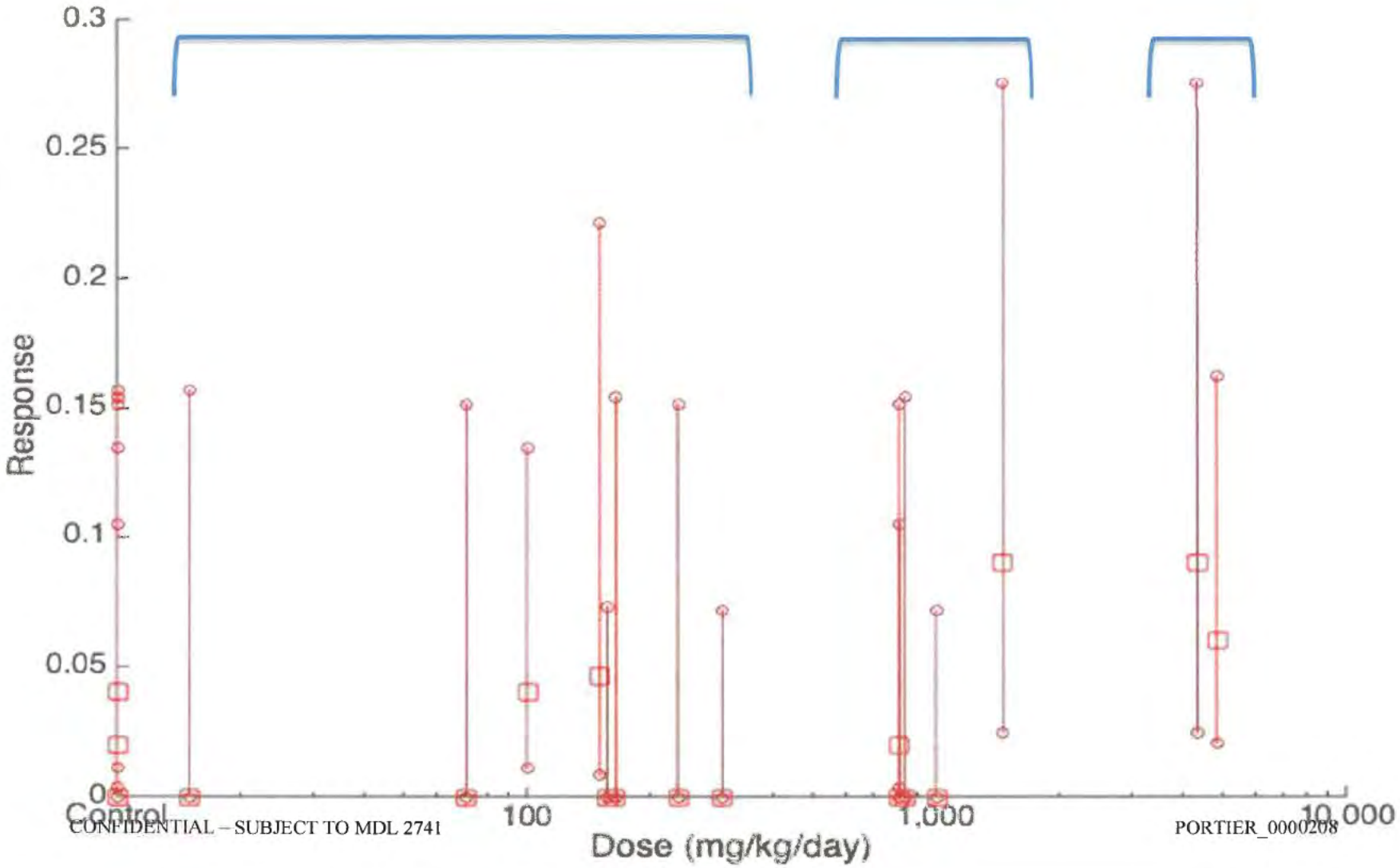
Tale based on Table 5.3-1 in the EFSA Renewal Assessment Report, Addendum I (8/31/2015)

Analysis of Male Mouse Renal Tumors From the Individual Studies

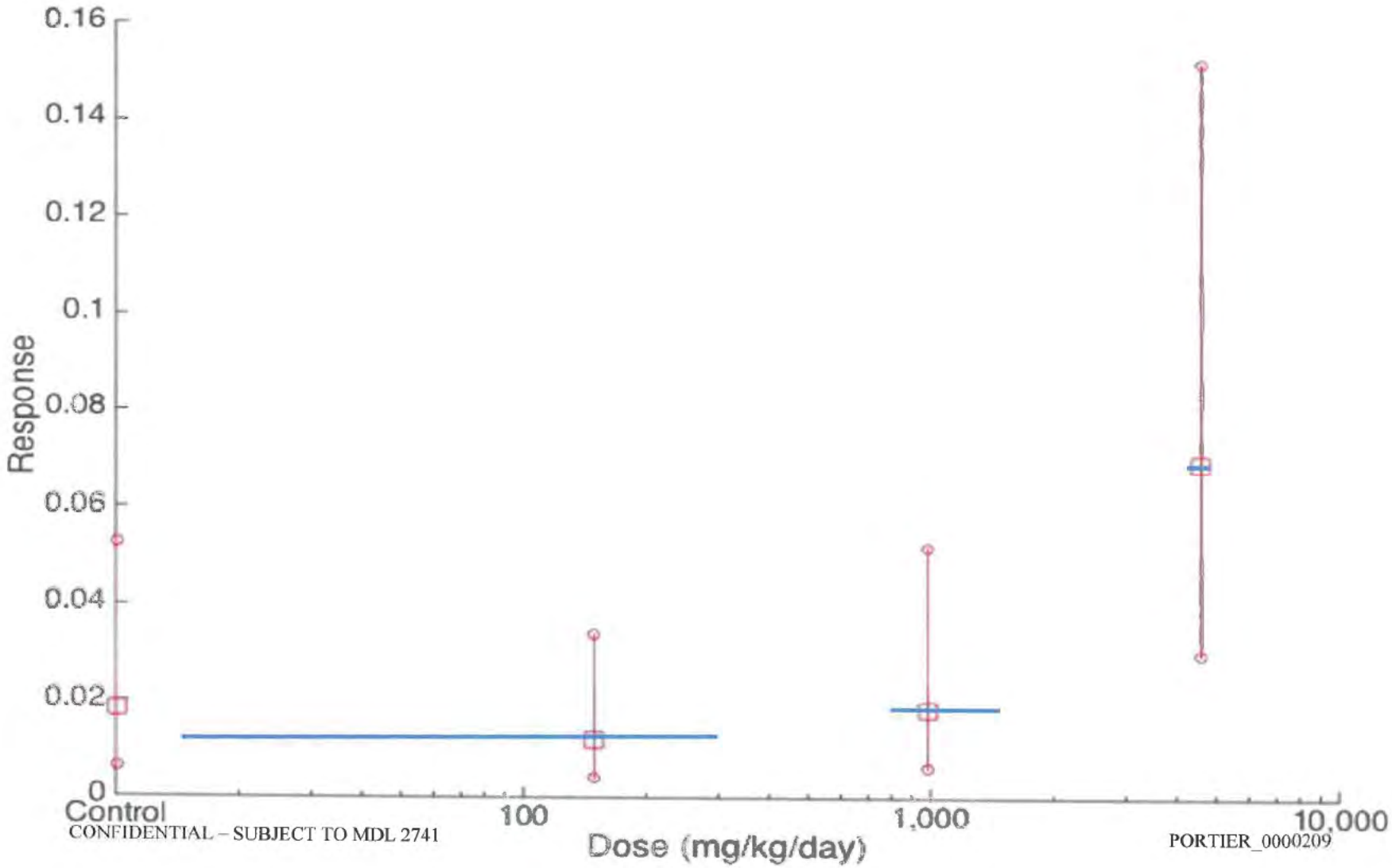
Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[1]
1983	Crl:CD-1	24	157, 814, 4841	1/50, 0/49, 1/50, 3/50	**0.03 (0.03)**
1993	?:CD-1	24	100, 300, 1000	2/50, 2/50, 0/50, 0/50	0.94 (0.94)
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	0/49, 0/49, 1/50, 2/50	**0.04 (0.04)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51	-

1 – Poly-3 adjustment used to predict response at 24 months from response at 18 months; see Bailer and Portier (1988)

Renal tumors in male mice poly-3 adjusted showing individual dose groups



Renal tumors in male mice poly-3 adjusted and clustered by similar doses



Renal Tumors in Male Mice

Study	Approx. Trend	Exact Trend	Historical Trend
Knezevich and Hogan, 1983	0.033	0.063	0.009
Atkinson, 1993b	0.94	0.982	1
Sugimoto, 1997	0.008	0.061	0.009
Kumar, 2001	0.04	0.059	0.011
Wood et al., 2009b	0.5	1	0.629
All experiments combined	<0.001	0.003	0.004
All CD-1 Studies Combined	<0.001	0.005	0.008
All experiments combined, doses<1500	0.212	0.209	0.206
All CD-1 experiments combined, doses<1000	0.851	0.856	0.867

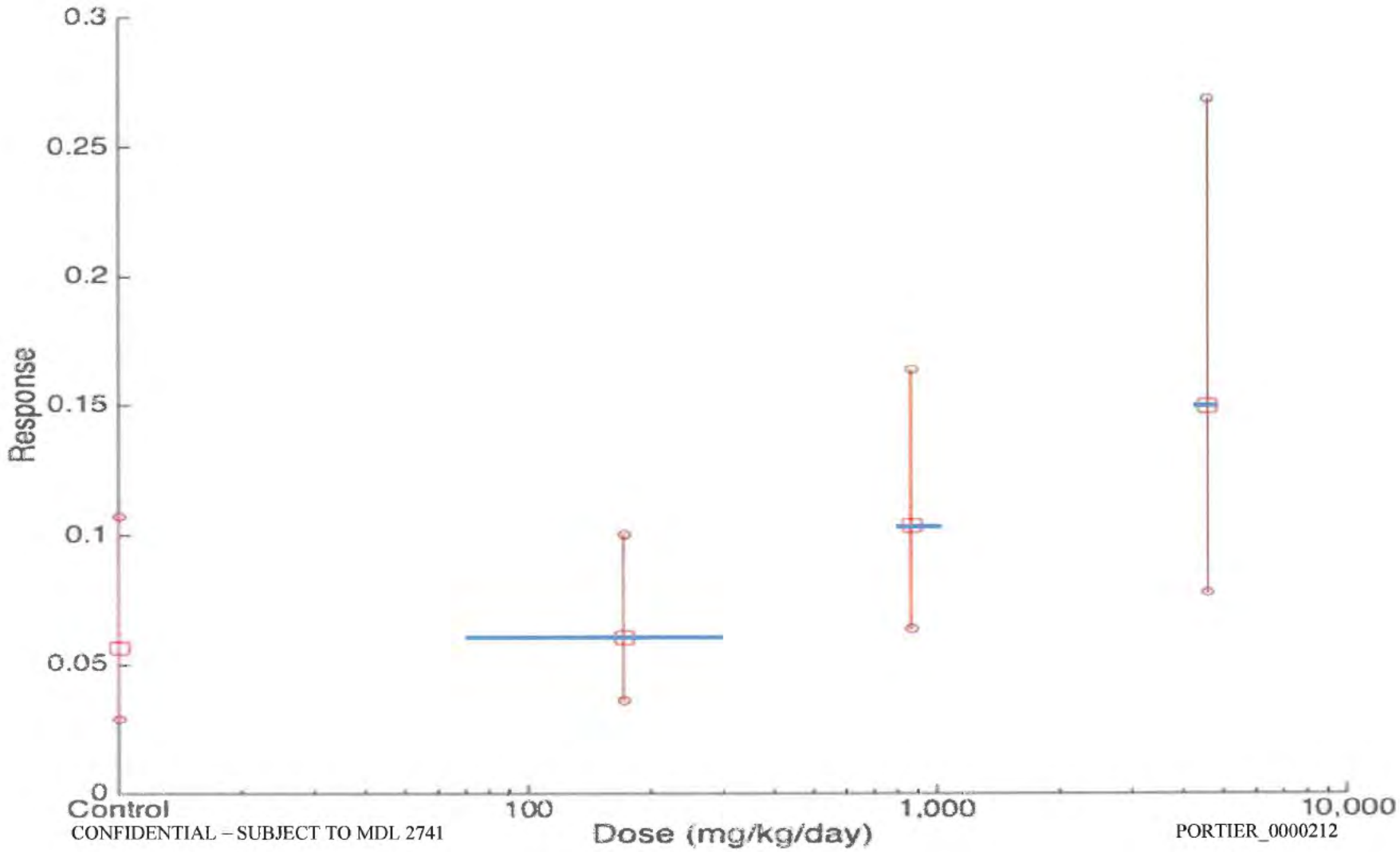
Historical trend test is based upon historical control data from Giknis and Clifford (2005)

Analysis of Male Mouse Malignant Lymphoma From the Individual Studies

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[1]
1983	Crl:CD-1	24	157, 814, 4841	2/50, 5/49, 4/50, 2/50	0.51 (0.51)
1993	?:CD-1	24	100, 300, 1000	4/50, 2/50, 1/50, 6/50	0.08 (0.08)
1997	CrJ:CD-1	18	165, 838, 4348	2/50, 2/50, 0/50, 6/50	**0.008 (0.012)**
2001	SW	18	15, 151, 1460	10/49, 15/49, 16/49, 19/49	**0.05 (0.09)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 1/51, 2/51, 5/51	**0.004 (0.005)**

1 – Poly-3 adjustment used to predict response at 24 months from response at 18 months; see Bailer and Portier (1988)

Malignant lymphomas in male CD-1mice poly-3 adjusted and clustered by similar doses



Malignant Lymphomas in Male Mice

Study	Approx. Trend	Exact Trend	Historical Trend
Knezevich and Hogan, 1983	0.515	0.736	0.484
Atkinson, 1993b	0.076	0.095	0.087
Sugimoto, 1997	0.008	0.02	0.013
Kumar, 2001	0.053	0.105	0.072
Wood et al., 2009b	0.004	0.008	0.007
All experiments combined	0.173	0.426	0.172
All CD-1 Studies Combined	0.015	0.084	0.021
All experiments combined, doses<1500	<0.001	0.002	0.001
All CD-1 experiments combined, doses<1000	0.031	0.036	0.039

Historical trend test is based upon historical control data from Giknis and Clifford (2005)

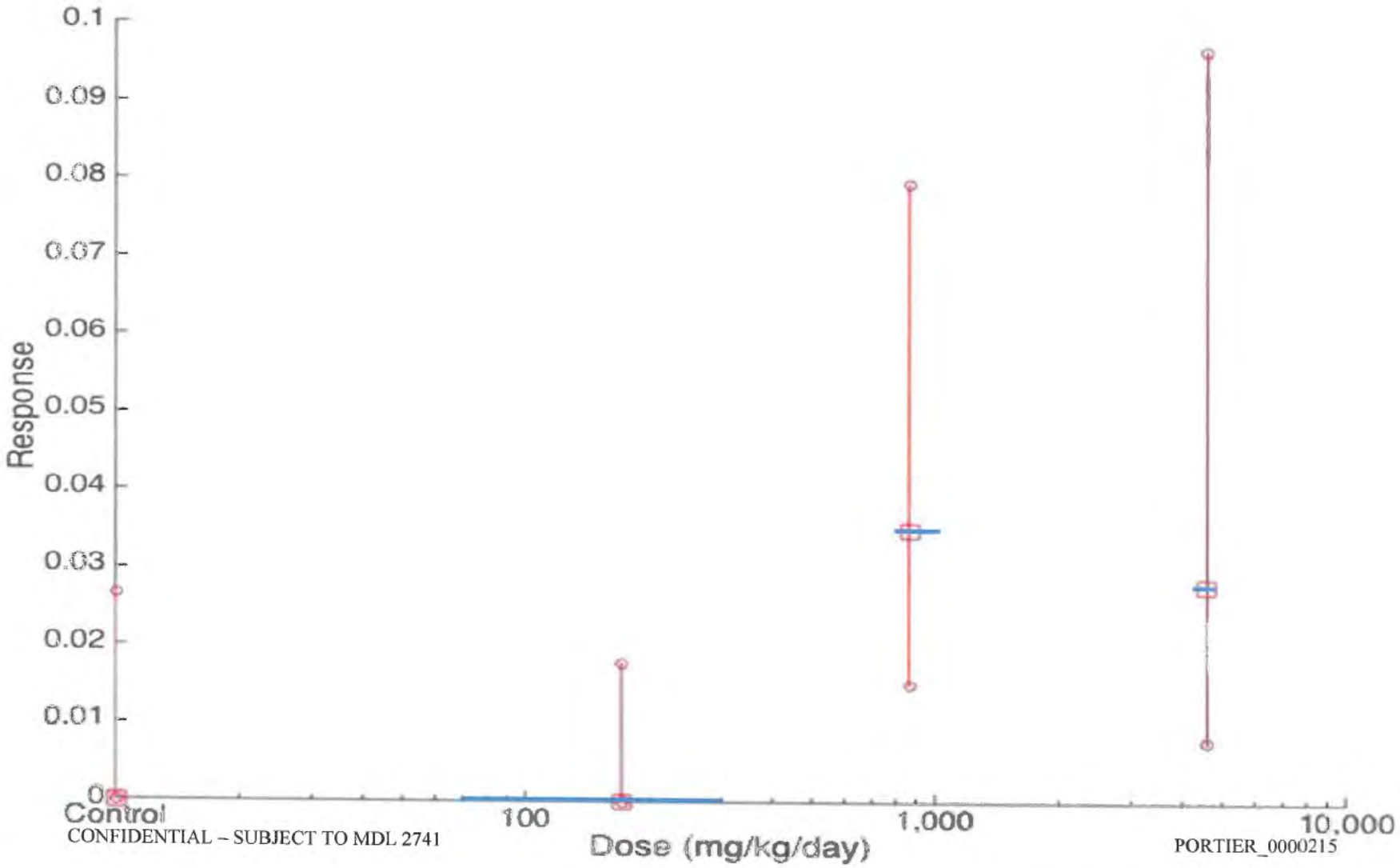
Analysis of Male Mouse Hemangiosarcomas From the Individual Studies

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[1]
1983	Crl:CD-1	24	157, 814, 4841	0/50, 0/49, 1/50, 0/50	0.63 (0.63)
1993	?:CD-1	24	100, 300, 1000	0/50, 0/50, 0/50, 4/50	**0.0004 (0.0004)**
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	0/50, 0/50, 2/50, 0/50	0.724 (0.724)
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51[2]	0.5 (0.50

1 – Poly-3 adjustment used to predict response at 24 months from response At 18 months; see Bailer and Portier (1988)

2 – EChA Table 42 lists tumor counts for this study of 2/51, 1/51, 2/51 and 1/51. However, these rates include hemangiomas from liver and kidney, making them different from the other studies and not applicable for the comparisons that follow

Hemangiosarcomas in male CD-1 mice poly-3 adjusted and clustered by similar



Hemangiosarcomas in Male Mice

Study	Approx. Trend	Exact Trend	Historical Trend
Knezevich and Hogan, 1983	0.628	0.5	0.592
Atkinson, 1993b	<0.001	0.004	<0.001
Sugimoto, 1997	0.008	0.061	0.021
Kumar, 2001	0.5	0.494	0.621
Wood et al., 2009b	0.5	1	0.49
All experiments combined	0.041	0.056	0.060
All CD-1 Studies Combined	0.024	0.044	0.041
All experiments combined, doses<1500	0.007	0.016	0.014
All CD-1 experiments combined, doses<1000	<0.001	<0.001	<0.001

Historical trend test is based upon historical control data from Giknis and Clifford (2005)

Carcinogenicity Studies in Rats

Year	Strain	Length[1]	Top Dose[2]	Finding
+Atkinson et al., 1993	SD	24	1000	none
+Lankas, 1981	SD	26	~32	inadequate dose, testicular tumors (M), pancreas islet cell aden. (M, weak)
+Stout & Ruecker, 1990	SD	24	1183	liver aden. (M), pancreas islet cell aden. (M), thyroid aden. (F)
Enemoto, 1997	SD	24	1127	none
Pavkov & Wyand, 1987	SD	24	41.8	inadequate dose and purity

1 – months; 2 – mg/kg bw/day;
+ indicates studies evaluated by IARC

Carcinogenicity Studies in Rats

Year	Strain	Length[1]	Top Dose[2]	Finding
+Seralini et al., 1993	SD	24	2250 mg/L in water	inadequate, mammary tumors
+Suresh, 1996	Wistar	24	886	none
Wood et al., 2004	Wistar	24	1229.7	mammary gland tumors (F)
Brammer, 2001	Wistar	24	1,498	Liver aden. (M)
+Chru-scielska et al., 2000	Wistar	24	2250 mg/L in water	inadequate documentation
+Syngenta , 1996	Wistar	12	1409	Inadequate length of study

1 – months; 2 – mg/kg bw/day;

+ indicates studies evaluated by IARC

Summary of Animal Cancer Data

- Sufficient Evidence
  - IARC, Portier et al.
- Insufficient Evidence
  - EFSA, ECHA, USEPA, WHO/JMPR
    - Excluded high dose effects
    - Used historical controls inappropriately
    - Generally excluded trend tests
    - Down-played or ignored consistency across mouse studies

Glyphosate Monograph – Mechanistic and Other Considerations:

Key Characteristic of Carcinogens #2 (Genotoxic)

Agent	Strength of the evidence	Evidence base includes	Endpoints considered in the evaluation
Glyphosate	Strong	1. ***Largely positive*** studies: • in human cells *in vitro*, • in mammalian model systems *in vivo* and *in vitro*, • studies in other non-mammalian organisms 2. ***Generally positive*** studies in liver *in vivo* in mammals 3. ***Mixed*** results for kidney and bone marrow *in vivo* in mammals 4. ***Consistently negative*** results from tests in bacterial assays	• Biomarkers of DNA adducts • Biomarkers of various types of chromosomal damage
Glyphosate formulations	Strong	1. ***Evidence in exposed humans***: • three studies of genotoxicicity endpoints in community residents exposed to glyphosate formulations, two of which reported positive associations • one of these studies examined subjects before and after aerial spraying and found a significant increase in micronuclei after exposure in 3 of 4 different geographical areas 2. ***Largely positive*** studies: • in human cells *in vitro*, • in mammalian model systems *in vivo* and *in vitro*, • studies in other non-mammalian organisms 3. ***Generally negative*** results from tests in bacterial assays 4. The ***pattern*** of tissue specificity of genotoxicity endpoints observed with glyphosate formulations is similar to that observed with glyphosate alone	• Chromosomal damage (micronuclei) in circulating blood cells from humans • Biomarkers of DNA adducts • Biomarkers of various types of chromosomal damage
AMPA	Moderate	1. Two human *in vitro* studies 2. One mammalian *in vivo* study 3. One mammalian *in vitro* study 4. One study in eel	While the number of studies is not large, all of the studies were ***positive***

Glyphosate Monograph – Mechanistic and Other Considerations:

Key Characteristic of Carcinogens #5 (Oxidative Stressor)

Agent	Strength of the evidence	Evidence base includes	Endpoints considered in the evaluation
Glyphosate	Strong	1. Rodent studies *in vivo* (including similar effects observed in many tissues) 2. Rodent cells *in vitro* 3. Human cells *in vitro*	• Lipid peroxidation markers • Oxidative DNA adducts • Dysregulation of antioxidant enzymes • Some studies challenged this mechanism experimentally (*e.g.*, by co-administering antioxidants)
Glyphosate formulations	Strong		
AMPA	Strong		

What have I learned from disagreements with EPA, EFSA and EChA?

- Almost impossible to reproduce a regulatory decision
  - Lack of access to data
  - Subjective decisions made with unclear justification
    - Weight-of-evidence
  - Lack of strict adherence to guidelines
- Independent evaluations (like that done by IARC) are critical in order to keep all of the groups involved in regulatory decisions honest
- EC needs an outside set of experts, with no conflicts of interest, to review these types of risk assessments in an open forum

What needs to be done?

- Transparency of regulatory decisions needs to be re-evaluated
  - Authors and any conflicts need to be made public
  - Reviewers and any conflicts need to be made public
  - Literature used to make these decisions need to be made public
- Relationship between industry and regulatory communities needs to be carefully reviewed and guidelines put into place
- Scientific review and oversight of regulatory decisions needs to be done in an open and transparent fashion

Glyphosate Cancer Classification

Christopher J. Portier, Ph.D.

17 May, 2017

EAPCCT Meeting

Basel, Switzerland

IARC Working Group Classifies Glyphosate as "Probably Carcinogenic to Humans"

NATURE | NEWS: EXPLAINER

Widely used herbicide linked to cancer

As the World Health Organization's research arm declares glyphosate a probable carcinogen, *Nature* looks at the evidence.

Roundup weedkiller 'probably' causes cancer, says WHO study

The Monsanto product – the world's most widely used herbicide – contains glyphosate, which may also be carcinogenic for non-Hodgkin's lymphoma

A Top Weedkiller Could Cause Cancer. Should We Be Scared?

ROUNDUP AND RISK ASSESSMENT

By Michael Specter April 10, 2015

A farmer sprays glyphosate across his cornfield.

Participants

Consolato Maria Sergi

Department of Laboratory Medicine and Pathology
University of Alberta
Edmonton, Alberta
Canada

Andrea 't Mannetje

Centre for Public Health Research
Massey University, Wellington Campus
Wellington
New Zealand

Lauren Zeise

Reproductive and Cancer Hazard Assessment
California Environmental Protection Agency
Oakland, CA
USA

Invited Specialist

Christopher J. Portier [retired] [3]

National Center for Environmental Health and Agency for Toxic Substances and Disease Registry
Centers for Disease Control and Prevention
Atlanta, GA
USA

Representatives

Amira Ben Amara [unable to attend] [4]

Agence Nationale de Contrôle Sanitaire et Environnementale des Produits (ANCSEP)
Montplaisir, Tunis
Tunisia

Catherine Eiden [unable to attend] [5]

Office of Pesticide Programs
United States Environmental Protection Agency
Washington, DC
USA

Marie-Estelle Gouze [6]

French Agency for Food, Environment and Occupational Health Safety (ANSES)
Maisons-Alfort
France

Jesudoss Rowland [7]

Office of Pesticide Programs
United States Environmental Protection Agency
Washington, DC
USA

[3] Christopher J. Portier receives a part-time salary from the Environmental Defense Fund, a United States–based non-profit environmental advocacy group.
[4] Amira Ben Amara attended as a representative of the National Agency of Sanitary and Environmental Control of Products, Tunisia.
[5] Catherine Eiden attended as a representative of the United States Environmental Protection Agency.
[6] Marie-Estelle Gouze attended as a representative of ANSES, France.
[7] Jesudoss Rowland attended as a representative of the United States Environmental Protection Agency.

IARC Working Group Findings

- Consistent positive association for NHL but bias and confounding possible
- Renal tumors (1 study) and hemangiosarcomas (1 study) in mice (2 studies evaluated)
- Pancreas islet-cell tumors (2 studies), liver adenomas (1 study), Thyroid C-cell adenomas (1 study) in rats (5 studies evaluated)
- Genotoxicity and oxidative stress

Regulatory Authorities

- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- WHO/JMPR – March, 2016
  - Unlikely to pose a carcinogenic risk to humans from exposure through the diet
- ECHA – March, 2017
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment
- Australia Pesticides and Veterinary Medicines Authority – 2015
  - the use of glyphosate in Australia does not pose a cancer risk to humans

CLP Guidance on Carcinogenicity

- Category 1: Known or presumed human carcinogens
  - Category 1A, known to have carcinogenic potential for humans, classification is largely based on human evidence
  - Category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence

Guidance on the Application of the CLP Criteria, ECHA (2015)

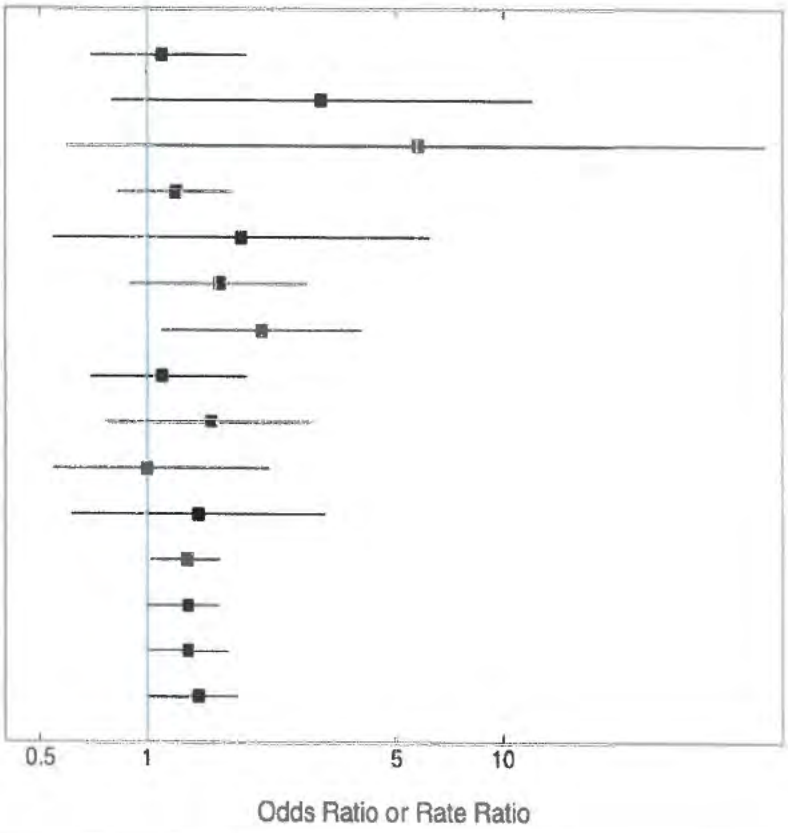
CLP Guidance on Carcinogenicity
(continued)

- The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:
  - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or
  - animal experiments for which there is sufficient (1) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).
- In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing **limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals**

Guidance on the Application of the CLP Criteria, ECHA (2015)

Epidemiology Data – Non-Hodgkin Lymphoma

Study	RR	Lower	Upper	Weight (Model 1)
Cantor et al. (1992)	1.10	0.70	1.90	0.0
Nordstrom et al. (1998)	3.10	0.80	12.00	0.0
Hardell and Eriksson (1999)	5.80	0.60	54.00	0.0
McDuffie et al. (2001)	1.20	0.83	1.74	38.1
Hardell et al. (2002)	1.85	0.55	6.20	3.6
De Roos et al. (2003)	1.60	0.90	2.80	16.2
logistic regression	2.10	1.10	4.00	0.0
De Roos et al. (2005)	1.10	0.70	1.90	21.0
Eriksson et al., (2008)	1.51	0.77	2.94	11.6
Orsi et al. (2009)	1.00	0.55	2.20	3.6
Hohenadel et al. (2011)	1.40	0.62	3.15	0.0
Meta-Analysis: Model 1	1.30	1.03	1.60	
Meta-Analysis: Model 2	1.30	1.00	1.60	
Meta-Analysis: Model 3	1.30	1.00	1.70	
Meta-Analysis: Model 4	1.40	1.00	1.80	



Limited Evidence of Carcinogenicity

- EChA: a positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
- IARC: 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.

Human Data Conclusions

EFSA – very limited?

From the wealth of epidemiological studies, the majority of experts concluded that there is very limited evidence for an association between glyphosate-based formulations and non-Hodgkin lymphoma, overall inconclusive for a causal or clear associative relationship between glyphosate and cancer in human studies. Minority views nevertheless were expressed that there was either inadequate or limited evidence of an association. [redacted]

IARC Working Group – limited evidence

There is *limited evidence* in humans for the carcinogenicity of glyphosate. A positive association has been observed for non-Hodgkin lymphoma.

Reasons used by EFSA to dismiss positive findings in an animal study?

- The trend test was significant but the pair-wise tests were not and/or
- Studies were not consistent and/or
- No positive results at doses below 1000 mg/kg/day and/or
- No dose-response for pre-malignant lesions and/or
- The response was within the historical control range.

Are these reasonable?

Probability of a False Positive Error[1] When Excluding Positive Trend Tests with Responses Inside the Historical Control Range

# Historical Controls Groups	Expected Control Response		
	0.05	0.10	0.20
None	0.056	0.052	0.055
5	0.046	0.046	0.051
10	0.032	0.036	0.036
20	0.020	0.024	0.028
50	0.007	0.013	0.013

1 – doses used are 0, 1, 2, and 4 with 50 animals per group and with the expected response in all dose groups equal to the expected control response, 10,000 simulations

Probability of Detecting a True Positive [1] When Excluding Positive Trend Tests with Responses Inside the Historical Control Range

# Historical Controls Groups	Expected Control Response		
	0.05	0.10	0.20
None	0.404	0.613	0.900
5	0.365	0.591	0.896
10	0.307	0.551	0.886
20	0.252	0.496	0.861
50	0.165	0.398	0.798

1 – doses used are 0, 1, 2, and 4 with 50 animals per group and with the expected response in the high dose group equal to twice (2x) the expected control response and other doses with proportionate response, 10,000 simulations

Use of Historical Controls

- IARC Recommendations
  - Use a formal statistical method
  - *"Generally not appropriate to discount a tumor response that is statistically significantly increased in comparison to concurrent controls by arguing it falls within the range of concurrent controls"*
  - Can be used for rare tumors

Major Tumors in CD-1 Mice

Summary of significance tests for 5 tumors from 4 studies in CD-1 Mice

Study	Months on Study	Neoplasm				
		Hemangio-sarcoma (male)	Hemangi-sarcoma (female)	Malignant Lymphoma (male)	Kidney Tumor (male)	Lung Adeno-carcinoma (male)
Sugimoto 1997	18	+/+++[1]	+++/+++	++/++	+/+++	-/-
Wood 2009	18	-/-	-/-	+++/+++	-/-	++/++
Sugimoto & Wood Pooled		++/+++	+++/+++	+++/+++	++/+++	-/-
Atkinson 1993	24	+++/+++	-/-	+/+	-/-	-/-
Knezevich 1983	24	-/-	NA	-/-	+/++	-/-
Atkinson & Knezevich Pooled		-/-	NA	-/-	++/+	-/-
All CD-1 Studies Pooled		++/++	+++/+++	+/+	+++/+++	-/-

[1]entries are p_{Trend}/p_{Hist} with values: – p>0.1, + 0.1≥p>0.05, ++ 0.05≥p>0.01, +++ p≤0.01

Major Tumors in Rats

Table 8: Summary of significance tests for 5 tumors from 7 studies in Rats

Study	Strain	Neoplasm						
		Liver Adenomas (males)	Mammary Gland Tumors (females)	Thyroid C-Cell Tumors (females)	Thyroid C-Cell Tumors (males)	Thyroid Follicular Cell Tumors (males)	Testis Interstitial Cell Tumors (male)	Kidney Adenomas (males)
Brammer (2001)	Wistar	+++[1]	-					
Wood (2009)		-	+++					
Suresh (1996)		-	-					
Pooled Wistar Rats		++	++					
Lankas (1981)	Sprague Dawley	-		+	-	-	++	-
Enemoto (1997)		-		-	-	-	-	+++
Atkinson et al. (1993)		-		+	-	++	-	-
Stout and Ruecker (1990)		++		-	+	-	-	-
Pooled Sprague-Dawley Rats		++		-	++	-	-	++

[1]entries are p_{Trend}/p_{Hist} with values: – p>0.1, + 0.1≥p>0.05, ++ 0.05≥p>0.01, +++ p≤0.01

Observed versus expected tumor sites with significant trends

Species	Strain	Sex	Total Sites[1]	Exp. <0.05	Obs. <0.05	Tumors[2] p<0.05	Exp. <0.01	Obs. <0.01	Tumors p<0.01
Rat (7 studies)	Sprague-Dawley (4 studies)	M	86	4.3	4	TICT, TFAC, KA, HA	0.9	2	TICT, KA
		F	102	5.1	1	TCCC	1.0	1	TCCC
	Wistar (3 studies)	M	64.5	3.2	2	HA, SK	0.6	1	HA
		F	76.5	3.8	2	MC, MAC	0.8	1	MAC
Mouse (5 studies)	CD-1 (4 studies)	M	42	2.1	8	KA, KC, KAC, H(2)[3], ML(2), LAC	0.4	5	KA,KC, H(2), ML
		F	60	3	1	H	0.6	1	H
	Albino (1 study)	M	10.5	0.5	0		0.1	0	
		F	15	0.8	0		0.2	0	
Rats (7 studies)	All (7 studies)	M	150.5	7.5	6	TICT, KA, HA(2), TFAC, SK	1.5	3	TICT, KA, HA
		F	178.5	8.9	3	TCCC, MC, MAC	1.8	2	TCCC, MAC
		Both	329	16.5	9	TICT, KA, HA(2), TFAC, SK, TCCC, MC, MAC	3.3	5	TICT, KA, HA, TCCC, MAC
Mice (5 studies)	All (5 studies)	M	52.5	2.6	8	KA, KC, KAC, H(2), ML(2), LAC	0.5	5	KA,KC, H(2), ML
		F	75	3.8	1	H	0.7	1	H
		Both	127.5	6.4	9	KA, KC, KAC, H(3)[3], ML(2), LAC	1.3	6	KA,KC, H(3), ML
All (12 studies)	All (12 studies)	M	203	10.1	14	TICT, KA(2), HA(2), TFAC, SK, KC, KAC, H(2), ML(2), LAC	2.0	8	TICT, HA, KA(2),KC, H(2), ML
		F	253.5	12.7	4	TCCC, MC, MAC, H	2.5	3	TCCC, MAC, H
		Both	456.5	22.8	18	TICT, KA(2), HA(2), TFAC, SK, KC, KAC, H(3), ML(2), LAC, TCCC, MC, MAC	4.6	11	TICT, HA, KA(2), KC, H(3), ML, TCCC, MAC

[1]Number of sites examined is based upon suggestions by Dr. J. Haseman in his written testimony to the EPA; male mice – 10.5 sites; female mice – 15 sites; male rats – 21.5 sites; female rats – 25.5 sites

[2]Tumor abbreviations are: KA – kidney adenoma; KC – kidney carcinoma; KAC – kidney adenoma or carcinoma; H – hemangiosarcoma; HA – hepatocellular adenoma; LAC – lung adenoma or adenocarcinoma; ML – malignant lymphoma; MC – mammary gland carcinoma; MAC

Sufficient Evidence in Animals

- ECHA
  - 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. A single study in one species and sex might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites
- IARC – exactly the same

Limited Evidence in Animals

- ECHA
  - the data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.
- IARC – exactly the same

Conclusions

EFSA

[redacted] No evidence of carcinogenicity was confirmed by the large majority of the experts (with the exception of one minority view) in either rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies and slightly increased incidences only at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions and/or being within historical control range. The statistical significance found in trend analysis (but not in pair-wise comparison) *per se* was balanced against the former considerations. [redacted]

IARC Working Group

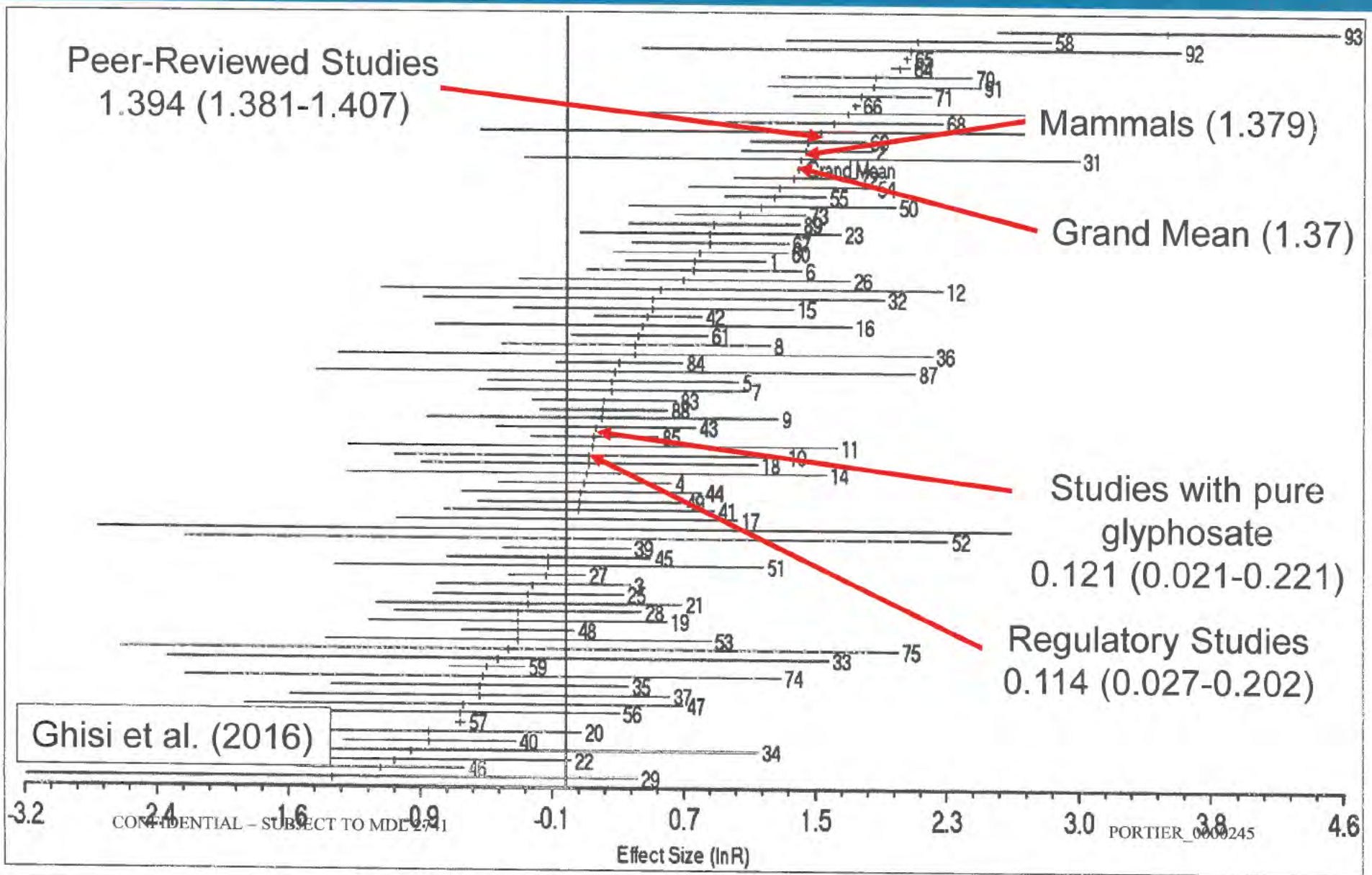
There is *sufficient evidence* in experimental animals for the carcinogenicity of glyphosate.

Summary of in vivo and in vitro genetox studies of glyphosate and glyphosate formulations in mammals[1]

In vivo or in vitro	Species	Cell type or tissue	Glyphosate[2]		Glyphosate Formulations	
			Number Positive	Number Negative	Number Positive	Number Negative
In vivo	Humans	Peripheral blood			2	1
in vitro	Humans	lymphocytes	5	2(1)	2	
		Hep 2	1			
		GM 38 HT1080	1			
		GM 5757	1			
		TR146	1		1	
In vivo	Swiss CD-1 Mouse	Liver/Kidney	1	1	2	
In vivo (micro-nucleus assay)	NMRI mouse	Erythrocytes		4(3)		2(1)
	Swiss CD-1 mouse		1		2	
	Balb C mouse		1			
	$B6C3F_1$ mouse			1		
	Swiss mouse		1(1)			3(2)
	CD-1 mouse		2(2)	1(1)	2 (2)	6 (6)
	Swiss albino mouse		1(1)	3(3)	1	
	C57BL mouse					1
	Mouse (not specified)				1	
	Rats (all)			2(1)		1(1)
In vitro	Mouse	L5178 lymphoma		2(2)		
	Chinese hamster	Lung		3(3)		
	Chinese hamster	ovary	1	1		
	Fischer rat	liver		1		
	Rat	Lymphocytes		1(1)		
	Bovine	Lymphocytes	1		2	

[1]each entry in the table corresponds to a single study where a study is positive if at least one valid positive finding emerged from the study p<0.05; entries in the table are only for studies where data was available to review including data from EFSA[88] and Kier and

Forest Plot of Micronucleus Frequency



Conclusions

EFSA

[redacted]During the teleconference 117, the experts also agreed to the conclusion of the RMS, that for the active substance glyphosate no classification for mutagenicity is warranted. However, there were two minority views, that a Comet assay should be requested for confirmation.

IARC Working Group

There is strong evidence that exposure to glyphosate or glyphosate-based formulations is genotoxic based on studies in humans in vitro and studies in experimental animals.

Is seeing the studies important?

Tumors with significant ($p<0.05$) trends in the carcinogenicity studies not cited in the EFSA and EChA Risk Assessments

Study (Species)	Tumor type Sex; Incidences	p-value (one-sided)
Sugimoto, 1997 (Mouse)	Total number of animals with malignant neoplasms Males; 5/50, 5/50, 11/50, 16/50	0.004
Wood et al., 2009 (Mouse)	Lung adenocarcinomas Males; 5/51, 5/51, 7/51, 11/51	0.038
Atkinson et al., 1993 (Rat)	Thyroid follicular cell adenomas and carcinomas Males; 0/50, 0/21, 0/17, 2/21, 2/49	0.036
Suresh, 1996 (Rat)	Thyroid c-cell Carcinomas Females; 1/47, 0/49, 2/50, 6/47	0.003
Enomoto, 1997 (Rat)	Kidney adenoma Males; 0/50, 0/50, 0/50, 4/50	0.004
Brammer, 2001 (Rat)	Hepatocellular Adenoma Males; 0/52, 2/52, 0/52, 5/52	0.009
Wood et al., 2009 (Rat)	Skin Keratocanthoma Males; 2/51, 3/51, 0/51, 6/51	0.034
Wood et al., 2009 (Rat	Mammary gland adenocarcinomas Males; 2/51, 3/51, 1/51, 6/51	0.046

Take Home Messages

- Transparency is necessary
- Guidelines should be peer-reviewed and applied uniformly
- Proper statistical methods need to be applied and understood

Glyphosate Carcinogenicity

Christopher J. Portier, Ph.D.

Fachanlass: Pesticid-Zukunft Schweiz

28 September, 2016, Bern

Recent Cancer Assessments of Glyphosate

- IARC – March, 2015
  - Probable human carcinogen
- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- Portier et al. – January, 2016
  - Probable human carcinogen
- WHO/JMPR – March, 2016
  - Unlikely to pose a carcinogenic risk to humans from exposure through the diet
- ECHA – May, 2016 (draft)
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment

Comparison Across Evaluations

Study	Authors Known	COI Made Public	Proprietary Studies	Open Literature	Guidelines	Followed Guidelines	Evaluated Dose-Response
IARC	Yes	Yes	No	Yes	Yes	Yes	No
EFSA	No	No	Yes	Yes	Yes	No	No
Portier	Yes	Yes	Yes	Yes	Yes	Yes	No
JMPR	Yes	?	Yes	Yes	Yes	Yes	Yes
ECHA	No	No	Yes	Yes	Yes	No	No
EPA	?	Some	Yes	Yes	Yes	No	No

Why are they different?

- Human Data
  - Limited evidence versus Insufficient Evidence
- Animal Cancer Studies
  - Sufficient Evidence versus Insufficient Evidence
- Mechanisms
  - Genotoxic or not genotoxic
  - Induces oxidative stress is or is not important

Table 1: Human Epidemiology Studies

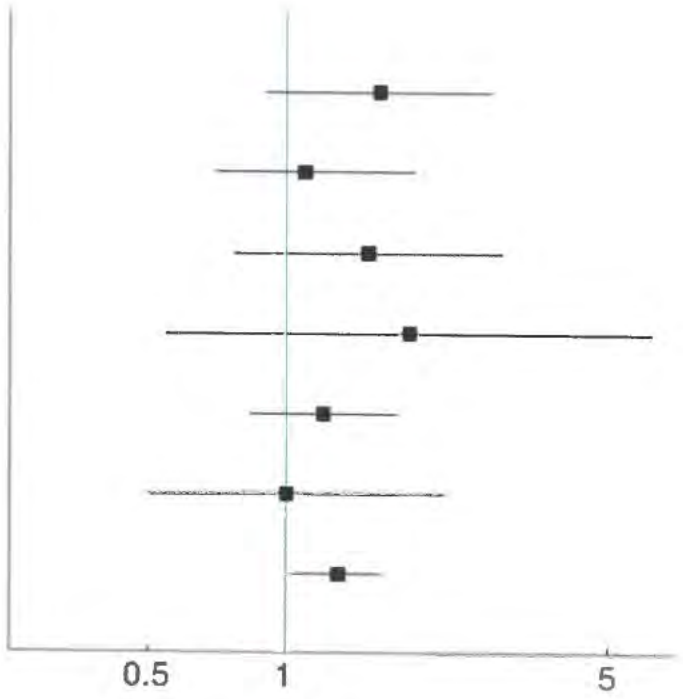
Study	Type	Size	Findings	Exposed Cases
Agricultural Health Study *(De Rooset al., 2005)*	Cohort -- licensed pesticide applicators	52 395 (+32 347 spouses), 92 cases, 4-8 years follow-up	1.1 (0.7-1.9) C 0.7 (0.4-1.4) 21-56% tertile compared to <20% tertile 0.9 (0.5-1.6) 21-56% tertile compared to >57% tertile (31 cases no quantification of exposure)	73
US Midwest *(De Roos et al., 2003)*	Pooled analysis 3 case-control studies	NHL: 650 cases, 1933 controls	2.1 (1.1-4) U 1.6 (0.9-2.8) C	36 36
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control study	517 cases, 1506 controls	1.2 (0.83-1.74) U 1.0 (0.63-1.57) ≤2 d/Y 2.12 (1.2-3.73) >2 d/Y	51 28 23
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control	2.02 (1.1-3.71) U 1.51 (0.77-2.94) C 1.69 (0.7-4.07) ≤10 d/Y 2.36 (1.04-5.37) >10 d/Y 1.11 (0.24-5.08) ≤10 Y 2.26 (1.16-4.4) >10 Y	29 29 12 17 NR NR
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)	2.3 (0.4-1.3) U 5.8 (0.6-5.4) C (not specified)	4 NR
France Case-Control *(Orsi et al, 2009)*	Hospital-based case-control study	244 cases, 456 controls	1.0 (0.5-2.2) U	12
Swedish Case-Control Study *(Hardell et al., 2002)*	Population-based case-control study	515 cases, 1141 controls	3.04 (1.08-8.5) U 1.85 (0.55-6.2) C (notspecified)	8 8
US Case-Control Study *(Lee et al., 2004)*	Population-based case-control study	872 cases, 2381controls	1.4 (0.98-2.1) U – no asthma 1.2 (0.4-3.3) U - asthma	53 6

Table 2: Meta Analyses

Study	Included Studies	Findings
Schinasi and Leon, 2014	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.5 (1.1-2.0)
IARC Monograph Working Group	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.103-1.65) – used adjusted risk estimates from Hardell et al., 2003 and Eriksson et al., 2008
Chang and Delzell, 2016	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.0-1.6)

Figure 1: Tree Plot of Epidemiology Studies
(using analyses corrected for potential confounders)

Study	RR	Lower	Upper	Weight
De Roos et al. (2003)	1.600	0.900	2.800	16.2
De Roos et al. (2003)	1.100	0.700	1.900	21.0
Eriksson et al., (2008)	1.510	0.770	2.940	11.6
Hardell et al. (2002)	1.850	0.550	6.200	3.6
McDuffie et al. (2001)	1.200	0.830	1.740	38.1
Oris et al. (2009)	1.000	0.500	2.200	9.5
Meta-Analysis	1.300	1.000	1.600	100.0



Chang and Delzell (2016)

Summary of Human Evidence

- Limited Evidence in Humans
  - IARC, Portier et al.
- Insufficient evidence in humans
  - EFSA, ECHA, EPA
- Did not evaluate
  - WHO/JMPR

Table 3: Carcinogenicity Studies in Male Mice

Year	Strain	Length[1]	Top Dose[2]	Renal Tumors	Hemangio-sarcomas	Malignant Lymphoma
1983[5]	Crl:CD-1	24	4,841	+[3]		
1993[5]	?:CD-1	24	1,000		+	+/-[4]
1997	CrJ:CD-1	18	4,843	+	+	+
2001	SW	18	1,460	+	**Data Not Available**	+/-[6]
2009	Crl:CD-1	18	810			+

1 – months; 2 – mg/kg bw/day; 3 - + indicates a p-value of <0.05 as calculated by BfR using the Armitage linear trend test in proportions; 4 – p=0.08; 5 – studies evaluated in IARC review; 6 – p=0.054

Table 4: Analysis of Male Mouse Renal Tumors From the Individual Studies

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)
1983	Crl:CD-1	24	157, 814, 4841	1/50, 0/49, 1/50, 3/50	**0.03 (0.03)**
1993	?:CD-1	24	100, 300, 1000	2/50, 2/50, 0/50, 0/50	0.94 (0.94)
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	0/49, 0/49, 1/50, 2/50	**0.04 (0.04)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51	-

Table 5: Pooled Analysis of Male CD-1 Mouse Renal Tumors

Year	Strain	p-Trend (p-poly3)
CD-1 Combined	CD-1	**0.001 (0.001)**
CD-1 Combined and Doses Pooled[1]	CD-1	**0.001(0.001)**
CD-1 Combined, doses>1000 dropped	CD-1	0.85 (0.86)
CD-1 Combined, doses>1000 dropped and Doses Pooled[2]	CD-1	0.80 (0.80)

[1] – Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, doses between 310 and 1500 mg/kg/day, and doses greater than 1500 mg/kg/day. Average doses in each pooled group were used in the analysis. [2]- Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, and doses between 310 and 1500 mg/kg/day. Average doses in each pooled group were used in the analysis.

Figure 2: Renal tumors in male mice poly-3 adjusted showing individual dose groups

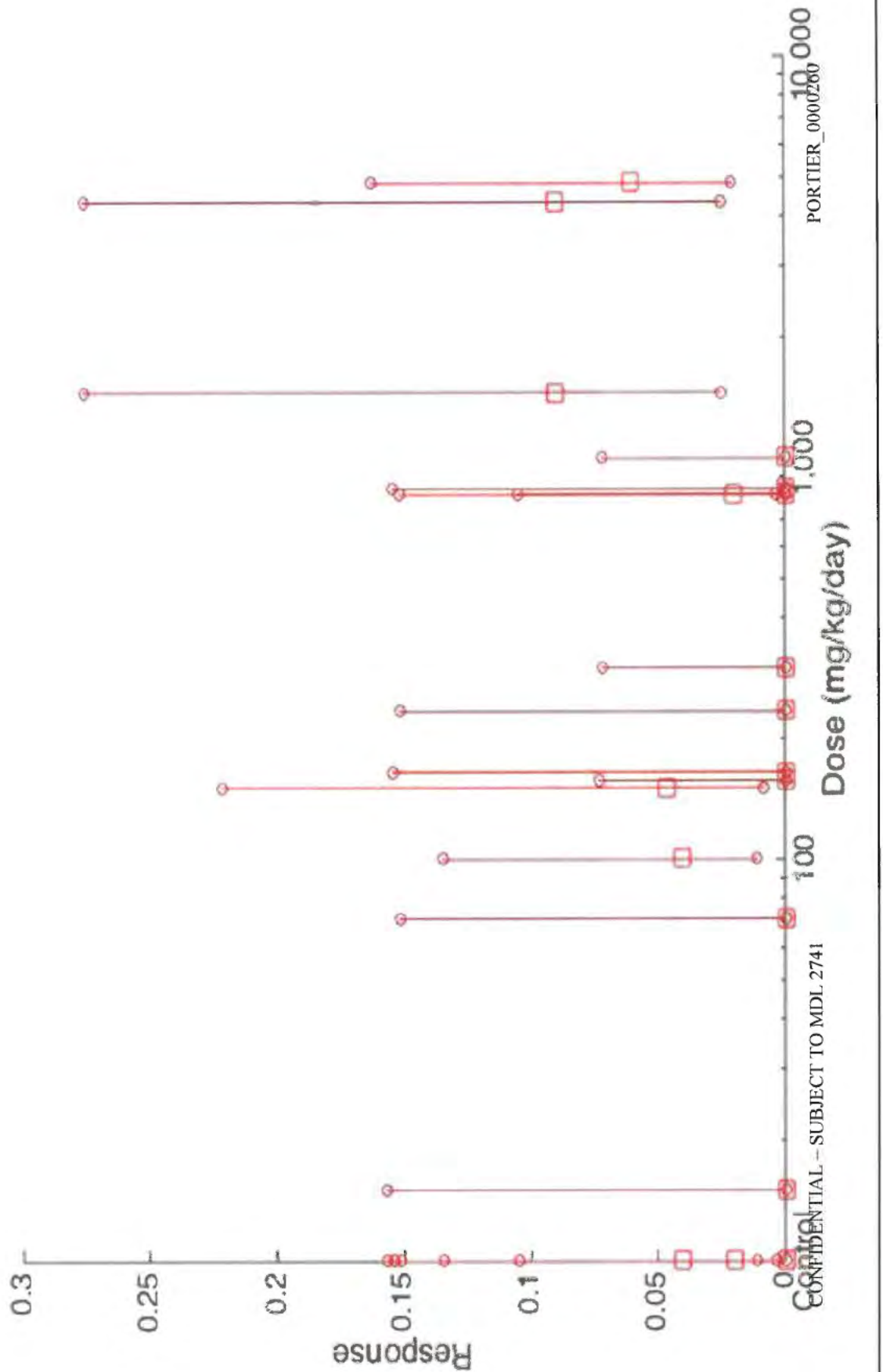


Figure 3: Renal tumors in male mice poly-3 adjusted and clustered by similar doses

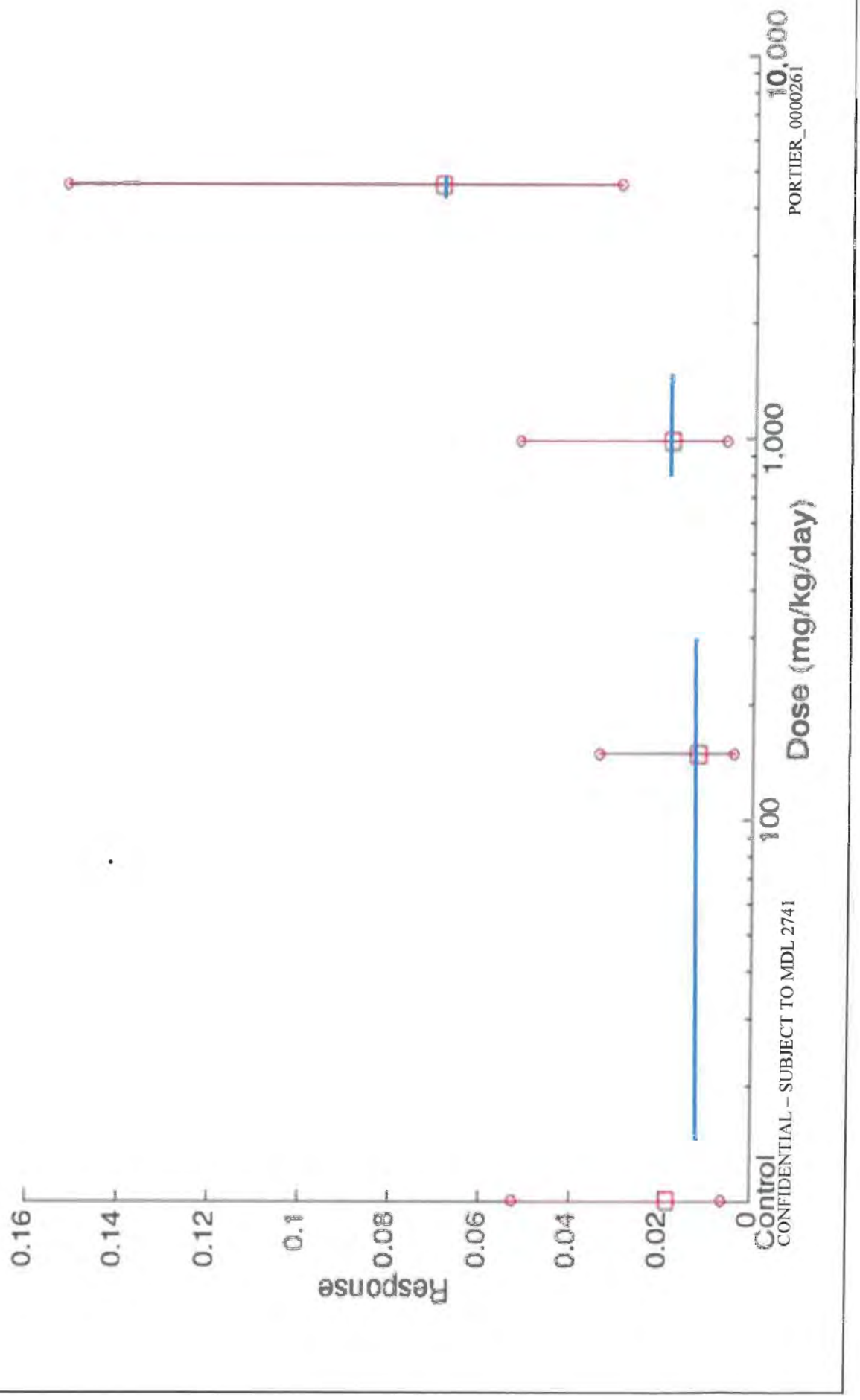


Table 6: Analysis of Male Mouse Malignant Lymphoma From the Individual

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)
1983	Crl:CD-1	24	157, 814, 4841	2/50, 5/49, 4/50, 2/50	0.51 (0.51)
1993	?:CD-1	24	100, 300, 1000	4/50, 2/50, 1/50, 6/50	0.08 (0.08)
1997	CrJ:CD-1	18	165, 838, 4348	2/50, 2/50, 0/50, 6/50	**0.008 (0.012)**
2001	SW	18	15, 151, 1460	10/49, 15/49, 16/49, 19/49	**0.05 (0.09)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 1/51, 2/51, 5/51	**0.004 (0.005)**

Table 7: Pooled Analysis of Male Mouse Malignant Lymphoma

Year	Strain	p-Trend (p-poly3)
CD-1 Combined	CD-1	0.02 (0.01)
CD-1 Combined and Doses Pooled[1]	CD-1	0.01(0.009)
CD-1 Combined, doses>1000 dropped	CD-1	0.03 (0.05)
CD-1 Combined, doses>1000 dropped and Doses Pooled[2]	CD-1	0.04 (0.04)

[1] – Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, doses between 310 and 1500 mg/kg/day, and doses greater than 1500 mg/kg/day. Average doses in each pooled group were used in the analysis. [2]- Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, and doses between 310 and 1500 mg/kg/day. Average doses in each pooled group were used in the analysis.

Figure 5: Malignant lymphomas in male CD-1 mice poly-3 adjusted showing individual dose

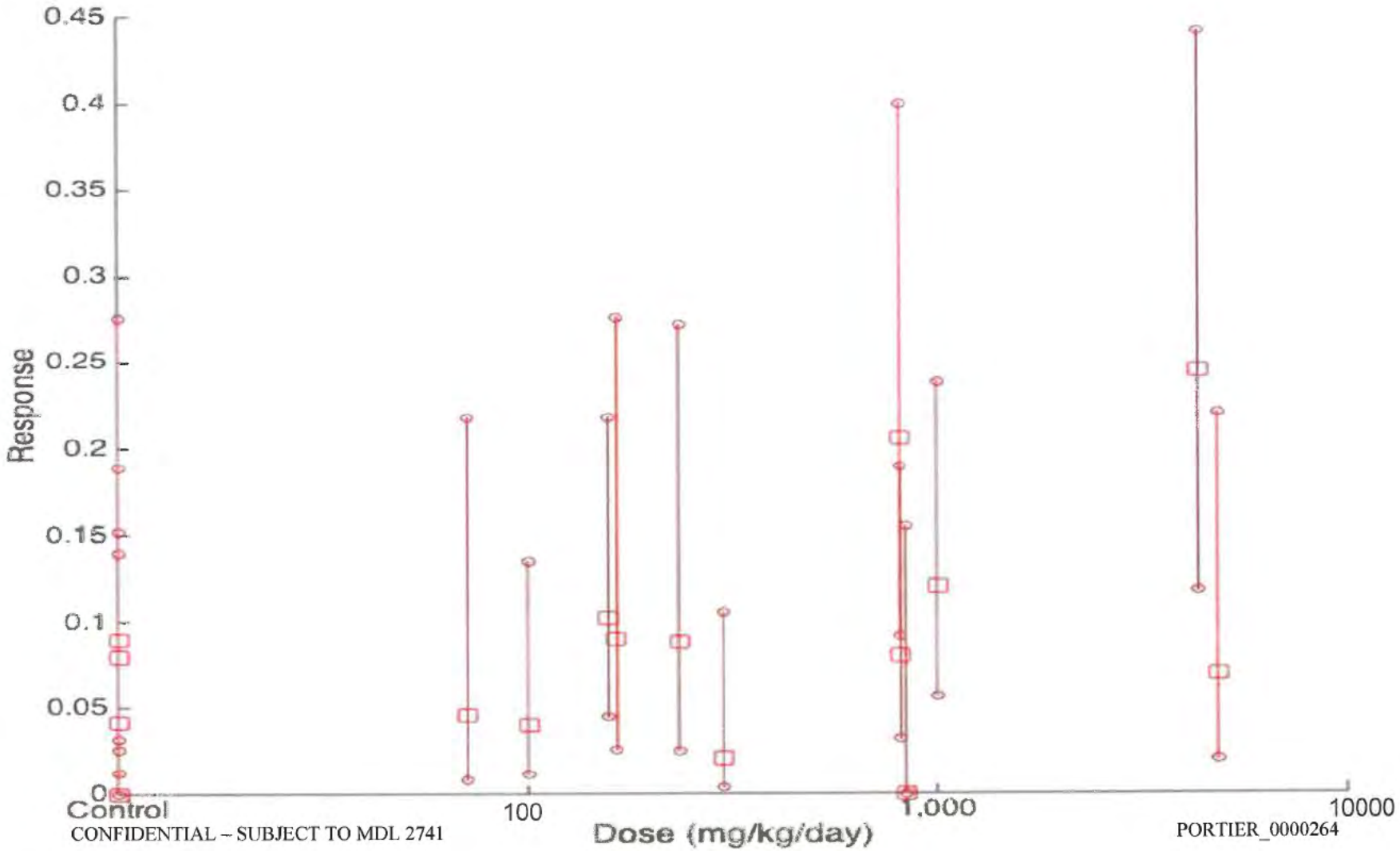


Figure 6: Malignant lymphomas in male CD-1mice poly-3 adjusted and clustered by similar doses

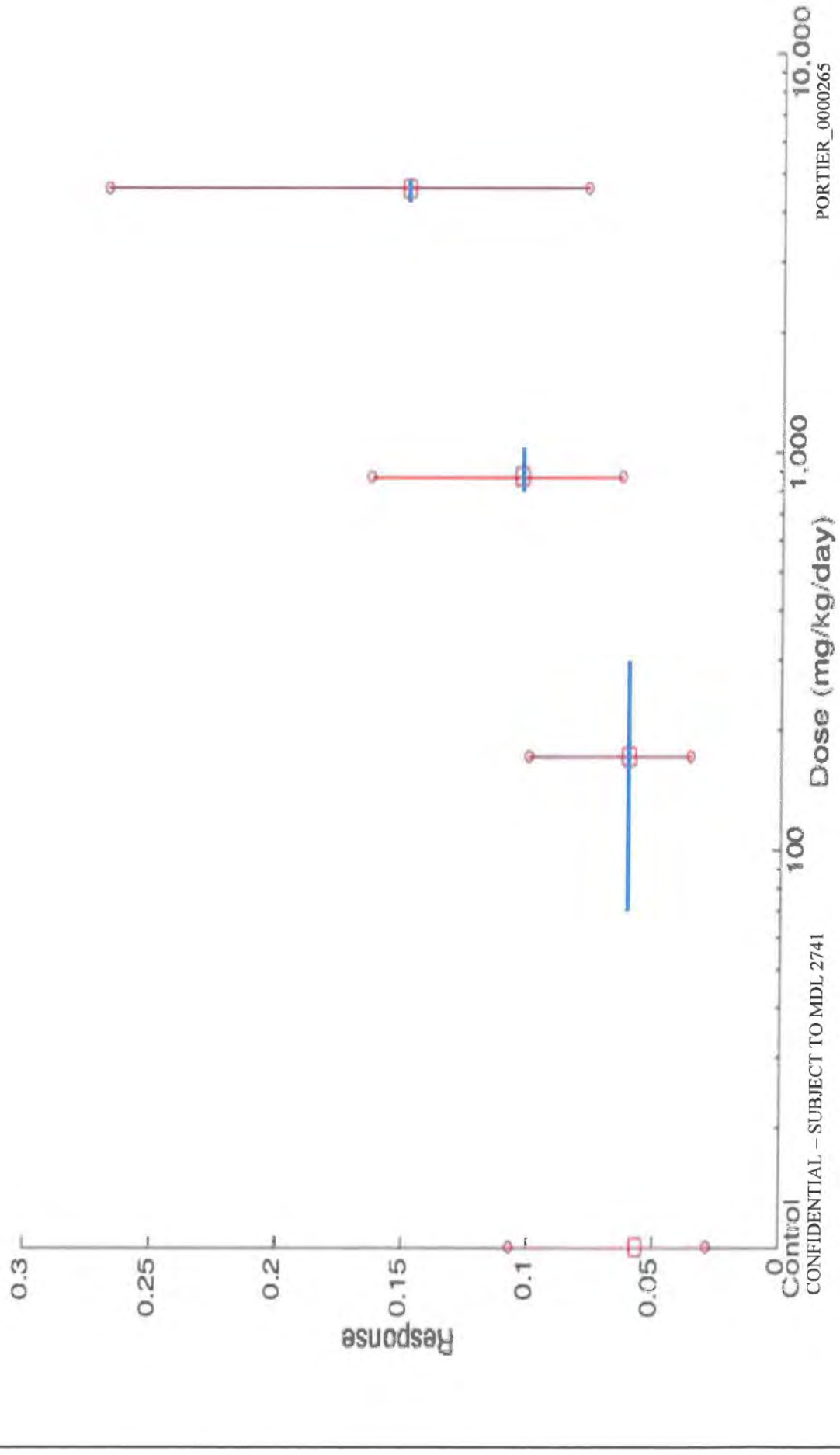


Table 8: Analysis of Male Mouse Hemangiosarcomas From the Individual

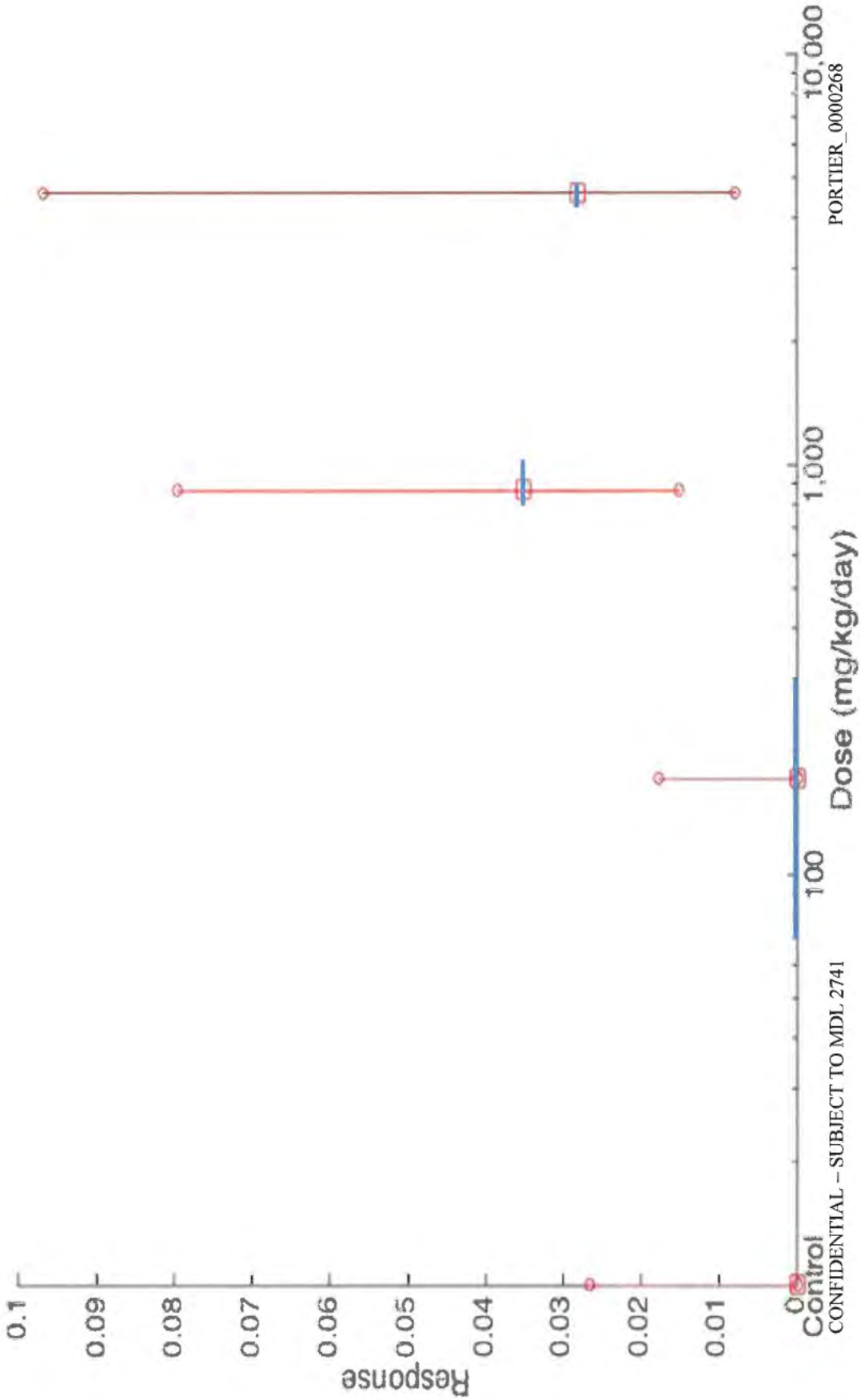
Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)
1983	Crl:CD-1	24	157, 814, 4841	0/50, 0/49, 1/50, 0/50	0.63 (0.63)
1993	?:CD-1	24	100, 300, 1000	0/50, 0/50, 0/50, 4/50	**0.0004 (0.0004)**
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	No Data	-
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51	-

Table 9: Pooled Analysis of Male Mouse Hemangiosarcomas

Year	Strain	p-Trend (p-poly3)
CD-1 Combined	CD-1	0.02 (0.03)
CD-1 Combined and Doses Pooled[1]	CD-1	0.02 (0.02)
CD-1 Combined, doses>1000 dropped	CD-1	<0.0001 (<0.0001)
CD-1 Combined, doses>1000 dropped and Doses Pooled[2]	CD-1	0.0003 (0.0003)

[1] – Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, doses between 310 and 1500 mg/kg/day, and doses greater than 1500 mg/kg/day. Average doses in each pooled group were used in the analysis. [2] – Doses were combined as follows: all controls, doses between 0 and 310 mg/kg/day, and doses between 310 and 1500 mg/kg/day. Average doses in each pooled group were used in the analysis.

Figure 8: Hemangiosarcomas in male CD-1 mice poly-3 adjusted and clustered by



Summary of Animal Cancer Data

- Sufficient Evidence
  - IARC, Portier et al.
- Insufficient Evidence
  - EFSA, ECHA, USEPA, WHO/JMPR
    - Dismissed high dose effects
    - Used historical controls inappropriately
    - Dismissed trend tests
    - Down-played or ignored consistency across mouse studies

EFSA/ECHA (draft) compared to IARC

- Agreed with the IARC on *limited evidence* in humans
  - dismissed the association as "insufficiently consistent" with no justification.
- Dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcoma in 2 mouse studies and malignant lymphoma in 2 mouse studies
  - Inappropriate historical control dataset used in an incorrect manner and ignoring established guidelines cited in their report
  - Trend test not convincing, Doses too high
- Down-weighted laboratory and human evidence of genotoxicity.
- Confirmed glyphosate induces oxidative stress
  - Not relevant for cancer because no other indications

EPA (draft) compared to IARC

- Disagreed with the IARC on *limited evidence* in humans
  - dismissed the association
- Dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcoma in 2 mouse studies and malignant lymphoma in 2 mouse studies
  - Inappropriate historical control dataset used in an incorrect manner and ignoring established guidelines cited in their report
  - Trend test not convincing, Doses too high
- Down-weighted laboratory and human evidence of DNA damage as a marker of genotoxicity
- Confirmed glyphosate induces oxidative stress
  - Not relevant for cancer because no other indications

What have we learned from these disagreements?

- Almost impossible to reproduce a regulatory decision
  - Lack of access to data
  - Subjective decisions made with little justification
  - Lack of strict adherence to guidelines
- Independent evaluations (like that done by IARC) are critical in order to keep all of the groups involved in regulatory decisions honest
- EC needs an outside set of experts, with no conflicts of interest, to review these types of risk assessments in an open forum

What needs to be done?

- Transparency of regulatory decisions needs to be re-evaluated
  - Authors and any conflicts need to be made public
  - Reviewers and any conflicts need to be made public
  - Literature used to make these decisions need to be made public
- Relationship between industry and regulatory communities needs to be carefully reviewed and guidelines put into place
- Scientific review and oversight of regulatory decisions needs to be done in an open and transparent fashion

Glyphosate Carcinogenicity

Christopher J. Portier, Ph.D.

Fachanlass: Pesticid-Zukunft Schweiz

28 September, 2016, Bern

Recent Cancer Assessments of Glyphosate

- IARC – March, 2015
  - Probable human carcinogen
- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- Portier et al. – January, 2016
  - Probable human carcinogen
- WHO/JMPR – March, 2016
  - unlikely to pose a carcinogenic risk to humans from exposure through the diet
- ECHA – May, 2016 (draft)
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment

Comparison Across Evaluations

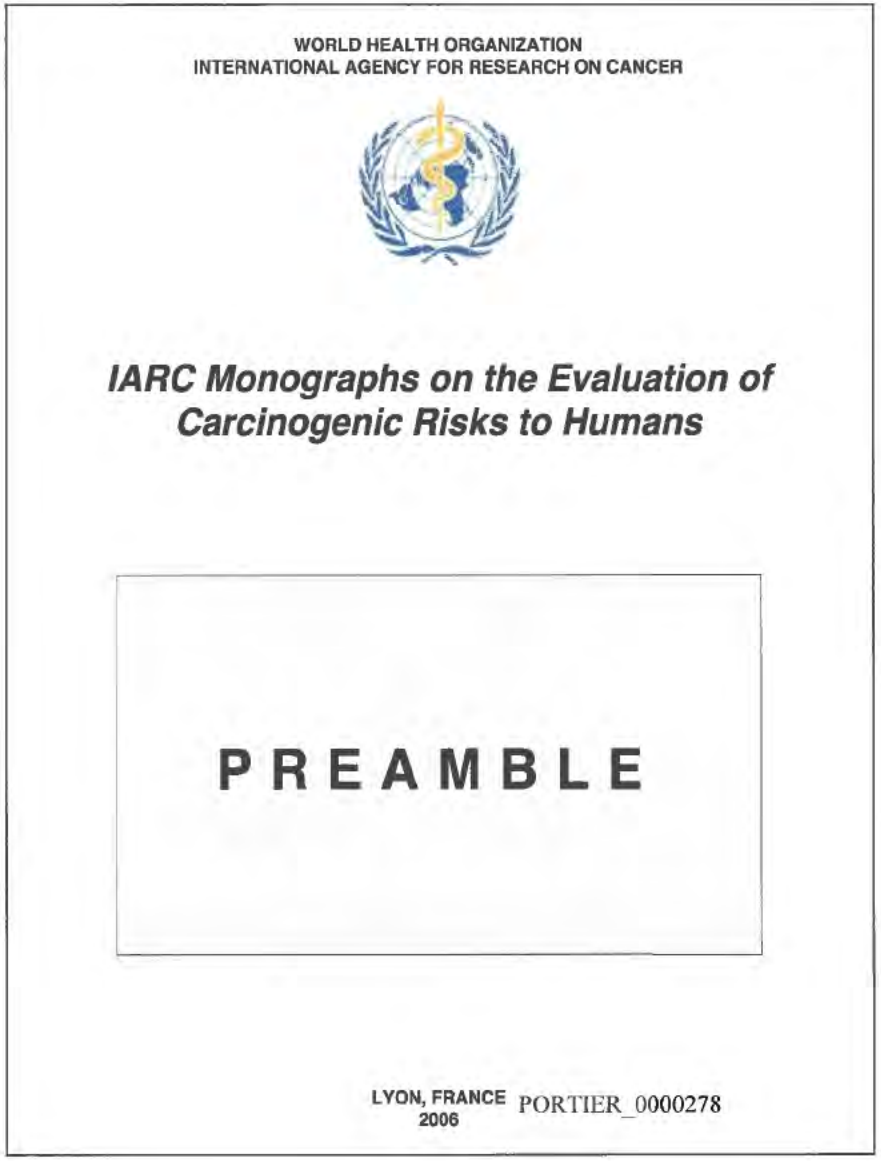
Study	Authors Known	COI Made Public	Proprietary Studies	Open Literature	Guidelines	Followed Guidelines	Evaluated Dose-Response
IARC	Yes	Yes	No	Yes	Yes	Yes	No
EFSA	No	No	Yes	Yes	Yes	No	No
Portier	Yes	Yes	Yes	Yes	Yes	Yes	No
JMPR	Yes	?	Yes	Yes	Yes	Yes	Yes
ECHA	No	No	Yes	Yes	Yes	No	No
EPA	?	Some	Yes	Yes	Yes	No	No

The IARC Monographs Program

- IARC Monographs Evaluate
  - Chemicals
  - Complex substances and mixtures
  - Occupational exposures
  - Physical and biological agents
  - Personal habits

IARC Monographs Process

- Written Guidelines
  - Public Document
  - Who? What? How?
  - Roles
  - Responsibilities
  - Instructions
    - Review
    - Summary of Evidence



IARC Monograph 112 Process

- Working Group Members
  - No real or apparent conflicts of interest
    - Formal process, written declarations of interest
  - Membership
    - Working Group members – review, evaluate
    - Invited Specialist – review only
    - Representatives – government, observe only
    - Observers – interested party, observe only
    - Secretariat – support the Working Group

IARC Monograph Timeline

- 1 year before Monograph Meeting
  - Meeting announced
  - Call for experts
  - Call for data
- 8 months before Monograph Meeting
  - Working Group membership selected
  - Request for observer status opened
  - Draft sections of Monograph developed by Working Group Members

IARC Monograph Timeline

- 1 month before Monograph Meeting
  - Call for data closed
  - Draft sections distributed to Working Group members for review and comment
- At Monograph Meeting
  - Finalize review of all literature
  - Evaluate the evidence in each category
  - Complete the overall evaluation

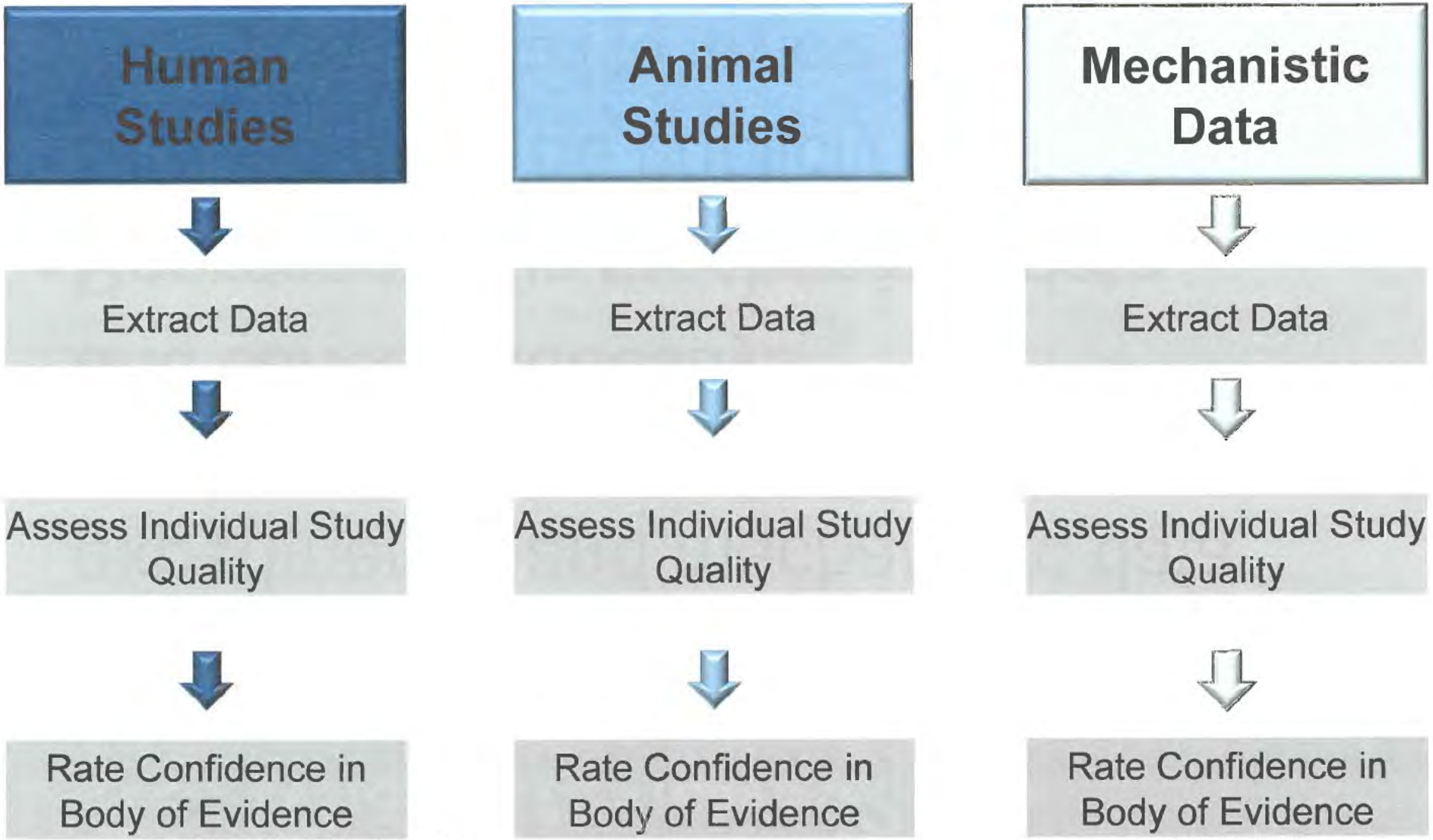
IARC Monograph Timeline

- 1-2 weeks after Monograph Meeting
  - Publish summary in Lancet Oncology
- 4-12 months after Monograph Meeting
  - Finalize Monograph and publish

IARC: What is reviewed?

- Systematic review of human, experimental and mechanistic data
- All pertinent epidemiological studies and cancer bioassays
- Representative mechanistic data
- Studies must be publicly available
  - Sufficient detail to review
  - Reviewers cannot have been associated with the study

IARC: Evidence Review



IARC: Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship is **established**
  - Chance, bias and confounding ruled out with reasonable confidence
- Limited Evidence
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence

IARC: Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Inadequate Evidence
  - Studies permit no conclusion regarding causality
- Evidence suggesting lack of carcinogenicity
  - Several strong studies showing consistent lack of positive association
  - Conclusion limited to cancer sites and conditions studied

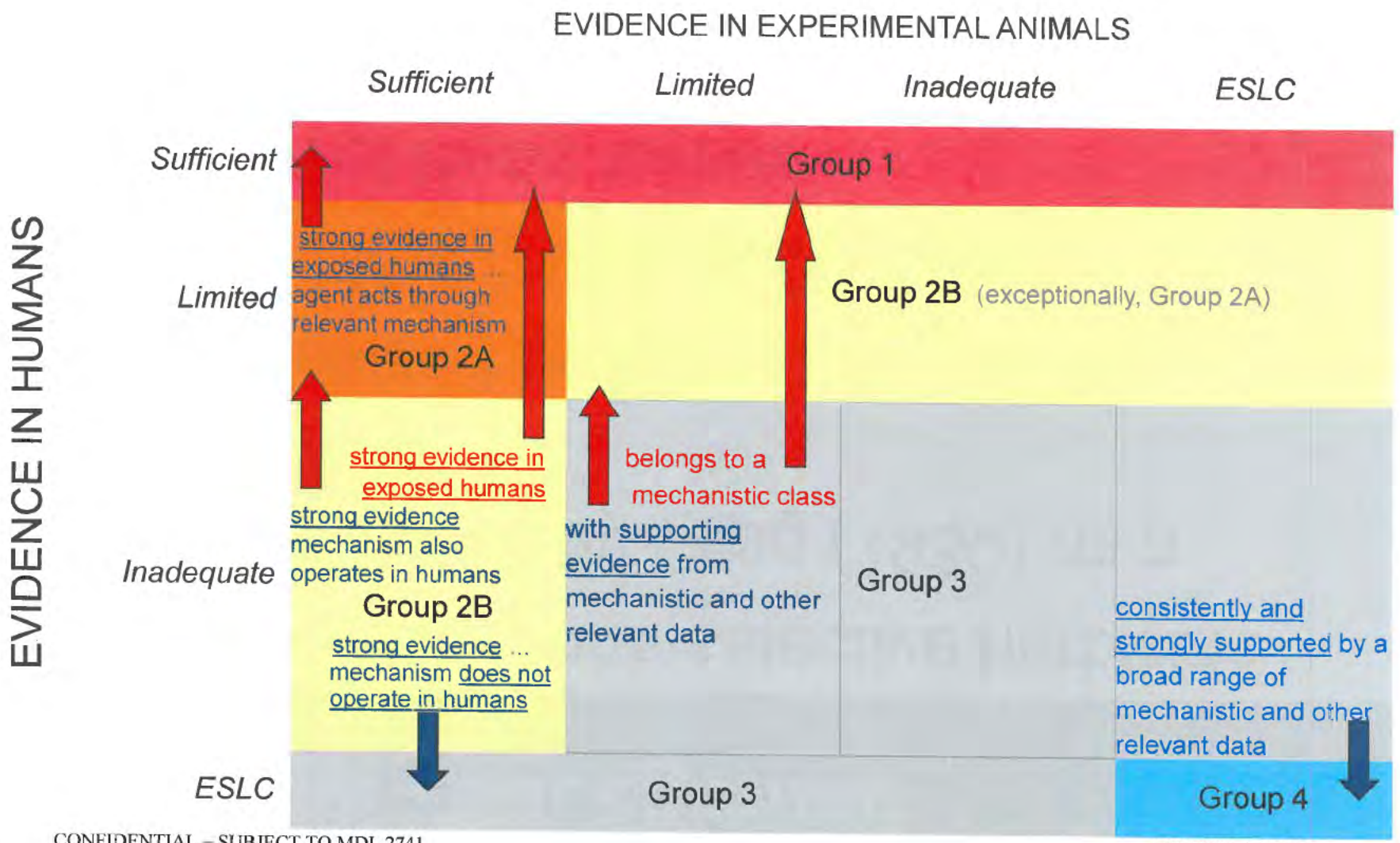
IARC: Evaluating Animal Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship established
  - Two or more species of animals or two or more studies
  - One study where malignant neoplasms occur to an unusual degree
    - Incidence (rare tumors)
    - Site (unusual tumors)
    - Age at onset
    - Strong findings at multiple sites

IARC: Evaluating Animal Evidence
Preamble Part B, Section 6(a)

- Limited Evidence
  - Single positive experiment
  - Unresolved questions about the studies
  - Only benign neoplasms
  - Only promoting activity demonstrated
- Inadequate evidence
- Evidence suggesting lack of carcinogenicity
  - All studies negative or inadequate
  - At least two well-conducted negative studies

IARC Overall Evaluation



Modified from Vincent Cogliano, IARC

Glyphosate - Background

- Broad-spectrum, non-selective herbicide
- First synthesized by Cilag (1950) as a possible drug
- Re-synthesized by Monsanto (1970)
- Patent expired [1991, 2000 (US)]
- Hundreds of trade names
- Approximately 91 producers in 20 countries

Glyphosate - Background

- Believed to be the most heavily used herbicide in the world
  - 2012 production volume > 700 million kg
- Production has increased sharply in recent years
  - Genetically modified glyphosate-resistant crop varieties
- Exposure pathways
  - Air (during spraying)
  - Water
  - Food

Glyphosate – Human Evidence

- Literature
  - US Agricultural Health Study (AHS)
  - Multiple independent case-control studies

Glyphosate – Human Evidence

- Epidemiological studies of cancer in humans
  - More than 2 studies
    - Non-Hodgkin Lymphoma (NHL)
    - Multiple Myeloma (MM)
  - Two studies
    - Leukemia, breast cancer, prostate cancer
  - One Study
    - Adult brain, oesophageal, stomach, prostate, soft-tissue sarcoma, lung, oral cavity, colorectal, pancreas, kidney, bladder, melanoma

Glyphosate – Key Epidemiology Studies for Non-Hodgkin Leukemia

Study	Type	Size
Agricultural Health Study *(Alavanja et al., 2003)*	Cohort – pesticide applicators and spouses	52 395 (+32 347 spouses), 92 cases, 4-8 years follow-up
US Midwest *(De Roos et al., 2003)*	Pooled analysis of 3 case-control studies	NHL: 650 cases, 1933 controls
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control	517 cases, 1506 controls
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)

IARC Glyphosate Evaluation
Human Evidence

- **Limited Evidence** for NHL
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence
- Basis
  - De Roos et al., 2003 (US), McDuffie et al., 2001 (Canada), Eriksson et al., 2008 (Sweden)
    - Positive association
    - Adjustment for other pesticides
  - Agricultural Health Study
    - No additional support for association, does not contradict
  - Positive meta-analysis

IARC Evidence in Experimental Animals

- 1 mouse feeding (glyphosate) study showed significant trend in the incidence of ***renal tubule adenoma or carcinoma*** (combined) in male mice; renal tubule carcinoma is a rare tumor
- 1 mouse feeding (glyphosate) study showed significant trend in the incidence of ***haemangiosarcoma*** in male mice
- 2 rat feeding (glyphosate) studies showed significant increase in the incidence of *pancreatic islet cell adenoma* (a benign tumor) in male rats
- 1 mouse study (GLY formulation) showed positive effect on *skin cancer* in an initiation-promotion study
- Several other oral feeding (glyphosate) and drinking water (glyphosate and glyphosate formulation) studies in rats showed no significant effects

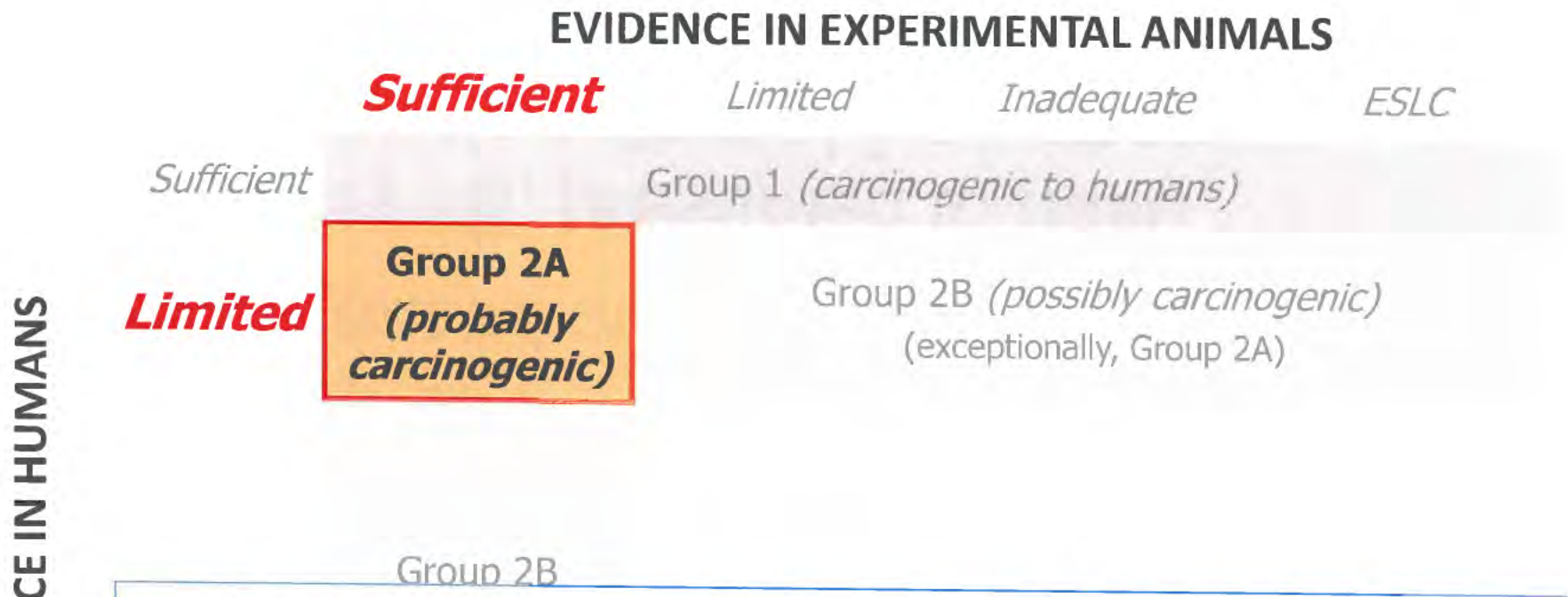
IARC Glyphosate Evaluation
Human Evidence

- **Sufficient Evidence** in experimental animals
  - More than two independent studies showing a significant, biologically relevant cancer finding

IARC Mechanistic Evidence

Key characteristic	Strength of Evidence
1. Electrophilic or ability to undergo metabolic activation	Glyphosate is ***not*** electrophilic
2. Genotoxic	Strong (G, GF)
3. Alters DNA repair or causes genomic instability	No data
4. Epigenetic Alterations	No data
5. Oxidative Stressor	Strong (G, GF and AMPA)
6. Induces chronic inflammation	No data
7. Immunosuppressant	Weak
8. Modulates receptor-mediated effects	Weak
9. Immortalization	No data
10. Alters cell proliferation, cell death, or nutrient supply	Weak

IARC Glyphosate Monograph
Overall Evidence



"*for […] glyphosate, the* ***mechanistic evidence provided independent support of the 2A classification*** *based on evidence of carcinogenicity in humans and experimental animals*"

(The Lancet Oncology; March 20, 2015)

CLP Guidance on Carcinogenicity

- Category 1: Known or presumed human carcinogens
  - Category 1A, known to have carcinogenic potential for humans, classification is largely based on human evidence
  - Category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence

Guidance on the Application of the CLP Criteria, ECHA (2015)

CLP Guidance on Carcinogenicity
(continued)

- The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:
  - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or
  - animal experiments for which there is sufficient (1) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).
- In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing **limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals**

Guidance on the Application of the CLP Criteria, ECHA (2015)

EFSA – What is reviewed for reassessment?

- All new data since the last review
- All endpoints
  - Including non-cancer endpoints
- Assessment is based upon
  - Reassessment document provided by industry
    - BfR and EFSA comment on document
    - Analysis of study results based upon submitted documents
  - All pertinent epidemiological studies and cancer bioassays
  - Representative mechanistic data
  - Studies may not be publicly available
  - Reviewers submit Declaration of Interests
    - Some of these are blank?

EFSA Glyphosate Review
Animal Carcinogenicity

Year	Strain	Length[1]	Top Dose[2]	Renal Tumors	Hemangio-sarcomas	Malignant Lymphoma
1983[5]	Crl:CD-1	24	4,841	+[3]		
1993[5]	?:CD-1	24	1,000		+	
1997	CrJ:CD-1	18	4,843	+	+	+
2001	SW	24	1,460	+		+/-[4]
2009	Crl:CD-1	18	810			+

1 – months; 2 – mg/kg bw/day; 3 - + indicates a p-value of <0.05 as calculated by BfR using the Armitage linear trend test in proportions; 4 – p=0.066; 5 – studies evaluated in IARC review

Historical Control Data used: collected 1987-96, 51 control groups from Crl:CD-1 mice from7 different research laboratories using mice from 3 different Charles River Laboratories production sites with sacrifice at ages 18-24 months

Renal Adenoma: 41 studies no tumors, 3 studies 1 tumor, 2 studies 2 tumors
Renal Carcinoma: 42 studies no tumors, 4 studies 1 tumor

EFSA compared to IARC

- Agreed with the IARC on *limited evidence* in humans
  - dismissed the association as "insufficiently consistent" with no justification.
- Dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcoma in 2 mouse studies and malignant lymphoma in 2 mouse studies
  - Inappropriate historical control dataset used in an incorrect manner and ignoring established guidelines cited in their report
  - Trend test not convincing, Doses too high
- Down-weighted laboratory and human evidence of genotoxicity.
- Confirmed glyphosate induces oxidative stress
  - Not relevant for cancer because no other indications

Carcinogenicity of Glyphosate
A Systematic Review of the Available Evidence

Christopher J. Portier, Ph.D.

21 November, 2016,

Recent Cancer Assessments of Glyphosate

- IARC – March, 2015
  - Probable human carcinogen
- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- Portier et al. – January, 2016
  - Probable human carcinogen
- FAO/WHO Joint Meeting on Pesticides Residue (JMPR) – March, 2016
  - Unlikely to pose a carcinogenic risk to humans from exposure through the diet
- CLP Proposal (Germany, BAuA, Federal Institute for Occupational Safety and Health) – May, 2016 (draft)
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment

Table 1: Human Epidemiology Studies

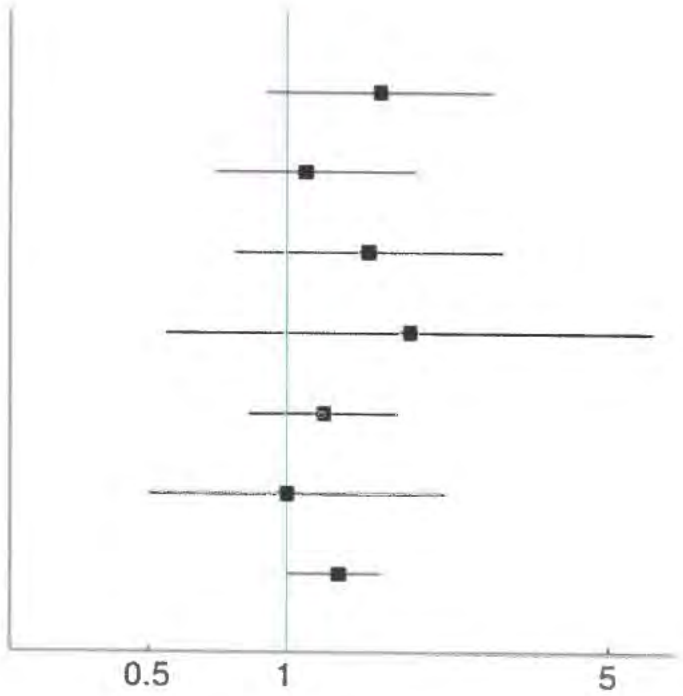
Study	Type	Size	Findings	Exposed Cases
Agricultural Health Study *(De Rooset al., 2005)*	Cohort – licensed pesticide applicators	52 395 (+32 347 spouses), 92 cases, 4-8 years follow-up	1.1 (0.7-1.9) C 0.7 (0.4-1.4) 21-56% tertile compared to <20% tertile 0.9 (0.5-1.6) 21-56% tertile compared to >57% tertile (31 cases no quantification of exposure)	73
US Midwest *(De Roos et al., 2003)*	Pooled analysis 3 case-control studies	NHL: 650 cases, 1933 controls	2.1 (1.1-4) U 1.6 (0.9-2.8) C	36 36
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control study	517 cases, 1506 controls	1.2 (0.83-1.74) U 1.0 (0.63-1.57) ≤2 d/Y 2.12 (1.2-3.73) >2 d/Y	51 28 23
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control	2.02 (1.1-3.71) U 1.51 (0.77-2.94) C 1.69 (0.7-4.07) ≤10 d/Y 2.36 (1.04-5.37) >10 d/Y 1.11 (0.24-5.08) ≤10 Y 2.26 (1.16-4.4) >10 Y	29 29 12 17 NR NR
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)	2.3 (0.4-13) U 5.8 (0.6-5.4) C (not specified)	4 NR
France Case-Control *(Orsi et al, 2009)*	Hospital-based case-control study	244 cases, 456 controls	1.0 (0.5-2.2) U	12
Swedish Case-Control Study *(Hardell et al., 2002)*	Population-based case-control study	515 cases, 1141 controls	3.04 (1.08-8.5) U 1.85 (0.55-6.2) C (not specified)	8 8
US Case-Control Study *(Lee et al., 2004)*	Population-based case-control study	872 cases, 2381controls	1.4 (0.98-2.1) U – no asthma 1.2 (0.4-3.3) U - asthma	53 6

Meta Analyses

Study	Included Studies	Findings
Schinasi and Leon, 2014	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.5 (1.1-2.0)
IARC Monograph Working Group	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.103-1.65) – used adjusted risk estimates from Hardell et al., 2003 and Eriksson et al., 2008
Chang and Delzell, 2016	McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003 and 2005; Eriksson et al., 2008; Orsi et al., 2009)	1.3 (1.0-1.6)

Tree Plot of Epidemiology Studies
(using analyses corrected for potential confounders)

Study	RR	Lower	Upper	Weight
De Roos et al. (2003)	1.600	0.900	2.800	16.2
De Roos et al. (2005)	1.100	0.700	1.900	21.0
Eriksson et al., (2008)	1.510	0.770	2.940	11.6
Hardell et al. (2002)	1.850	0.550	6.200	3.6
McDuffie et al. (2001)	1.200	0.830	1.740	38.1
Oris et al. (2009)	1.000	0.500	2.200	9.5
Meta-Analysis	1.300	1.000	1.600	100.0



Chang and Delzell (2016)

Summary of Human Evidence

- Limited Evidence in Humans
  - IARC, Portier et al.
- Insufficient evidence in humans
  - EFSA, CLP Proposal, EPA (draft)
- Definition of Limited Evidence (CLP Guidance, 2015; IARC 2006)
  - limited evidence of carcinogenicity: a positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence. (3.6.2.2.3.a)

Carcinogenicity Studies in Male Mice

Year	Strain	Length[1]	Top Dose[2]	Renal Tumors	Hemangio-sarcomas	Malignant Lymphoma
1983[5]	Crl:CD-1	24	4,841	+[3]		
1993[5]	?:CD-1	24	1,000		+	+/-[4]
1997	CrJ:CD-1	18	4,843	+	+	+
2001	SW	18	1,460	+		+/-[6]
2009	Crl:CD-1	18	810			+

1 – months; 2 – mg/kg bw/day; 3 - + indicates a p-value of <0.05 as calculated by BfR using the Armitage linear trend test in proportions; 4 – p=0.08; 5 – studies evaluated in IARC review; 6 – p=0.053

+ indicates studies evaluated by IARC

Table based on Table 5.3-1 in the EFSA Renewal Assessment Report, Addendum I (8/31/2015)

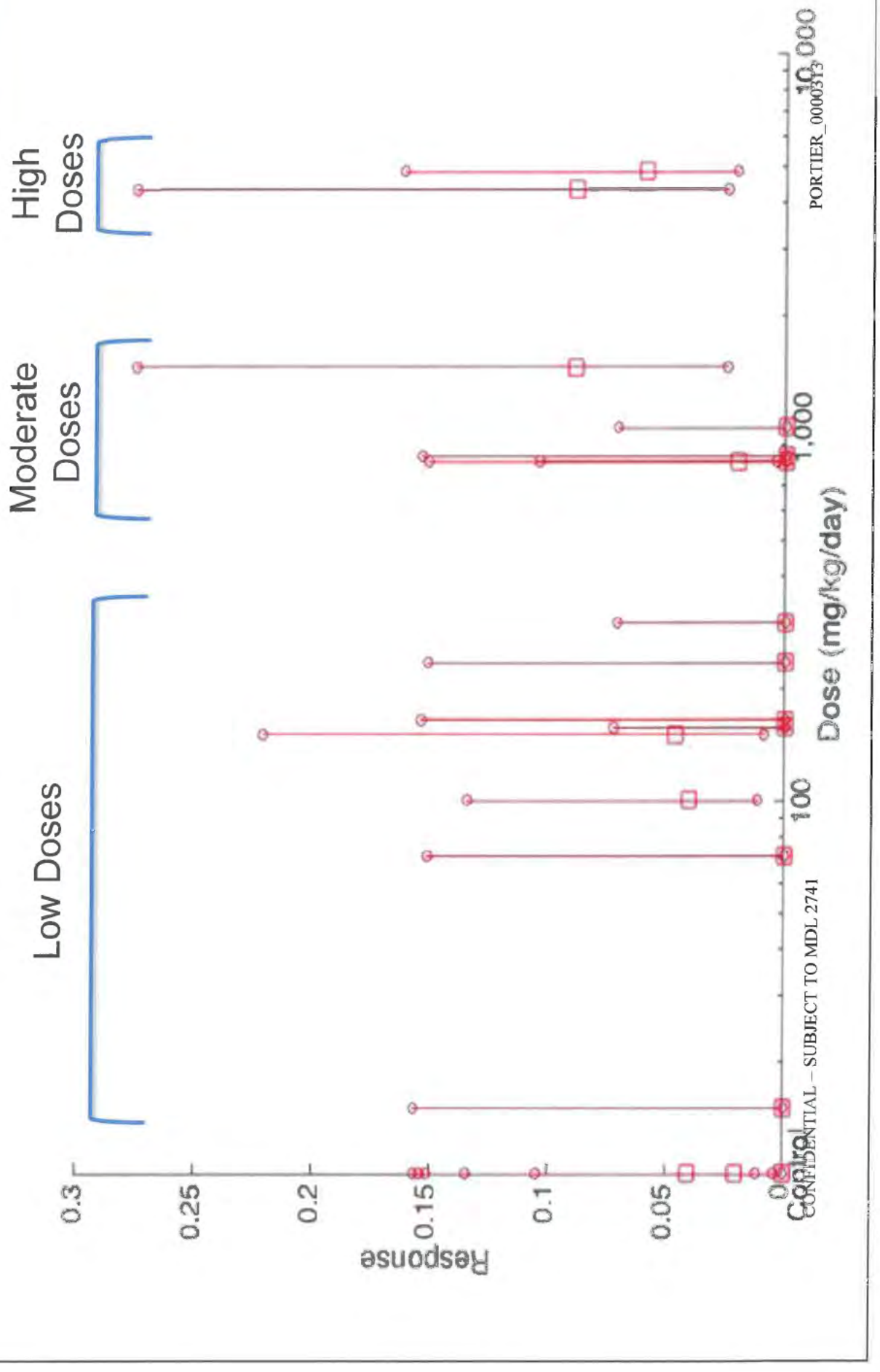
Analysis of Male Mouse Renal Tumors[1] From the Individual Studies

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[2]
1983	Crl:CD-1	24	157, 814, 4841	1/50, 0/49, 1/50, 3/50	**0.03 (0.03)**
1993	?:CD-1	24	100, 300, 1000	2/50, 2/50, 0/50, 0/50	0.94 (0.94)
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	0/49, 0/49, 1/50, 2/50	**0.04 (0.04)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51	-

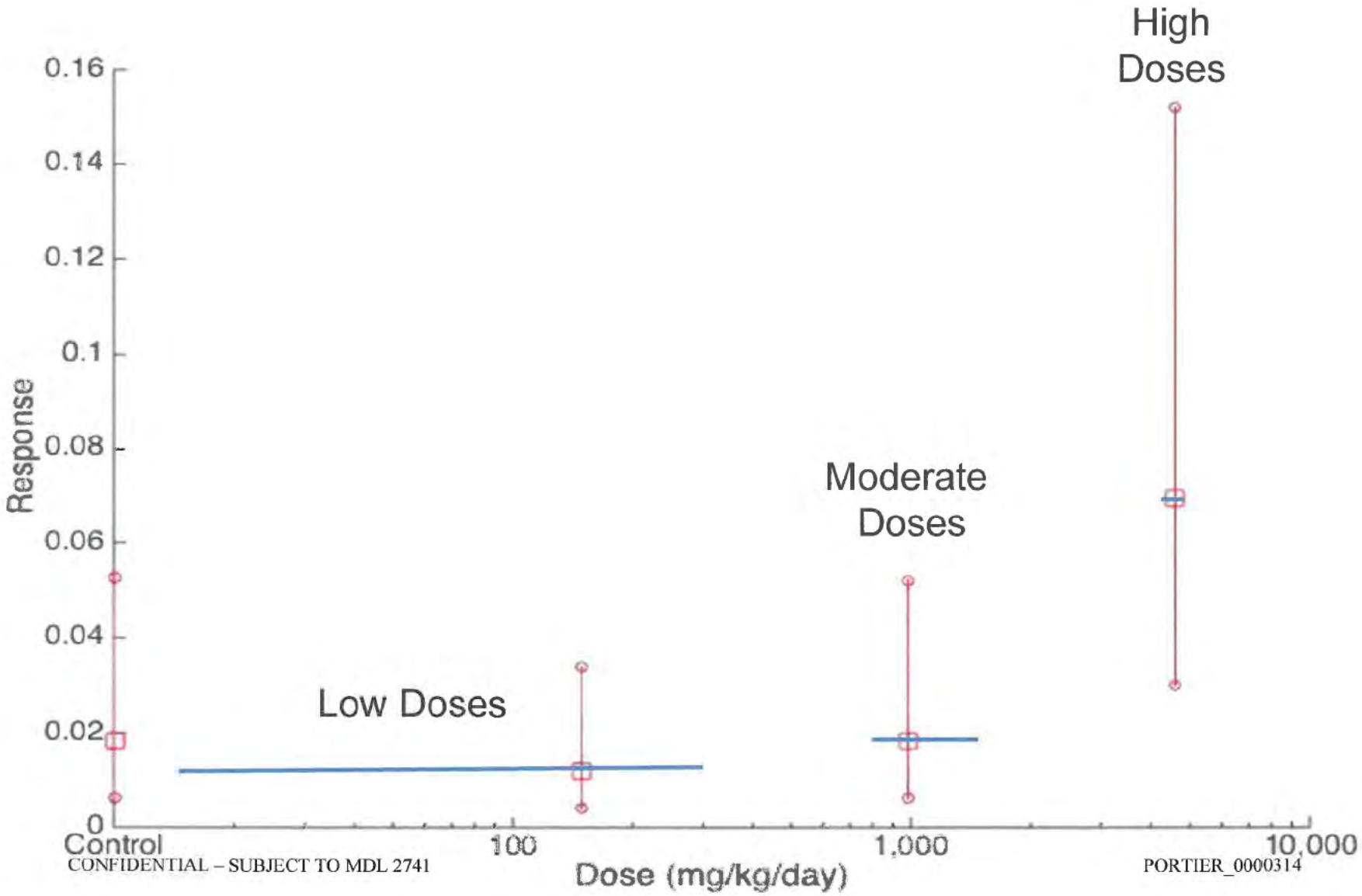
1 – Giknis and Clifford, 2005 historical control rate=0.0038, 43 of 52 studies had no tumors, 7 had 1 tumor and 2 had 2 tumors

2 – Poly-3 adjustment used to predict response at 24 months from response at 18 months; see Bailer and Portier (1988)

Renal tumors in male mice poly-3 adjusted showing individual dose groups



Renal tumors in male mice poly-3 adjusted and clustered by similar doses



Renal Tumors in Male Mice

Study	Approx. Trend	Exact Trend[1]	Historical Trend[2]
Knezevich and Hogan, 1983	0.033	0.063	0.009
Atkinson, 1993b	0.94	0.982	1
Sugimoto, 1997	0.008	0.061	0.009
Kumar, 2001	0.04	0.059	0.011
Wood et al., 2009b	0.5	1	0.629
All experiments combined	<0.001	0.003	0.004
All CD-1 Studies Combined	<0.001	0.005	0.008
All experiments combined, doses<1500	0.212	0.209	0.206
All CD-1 experiments combined, doses<1000	0.851	0.856	0.867

1 – Exact test is based upon a permutation test with fixed marginals.

2 - Historical trend test is based upon historical control data from Giknis and Clifford (2005)

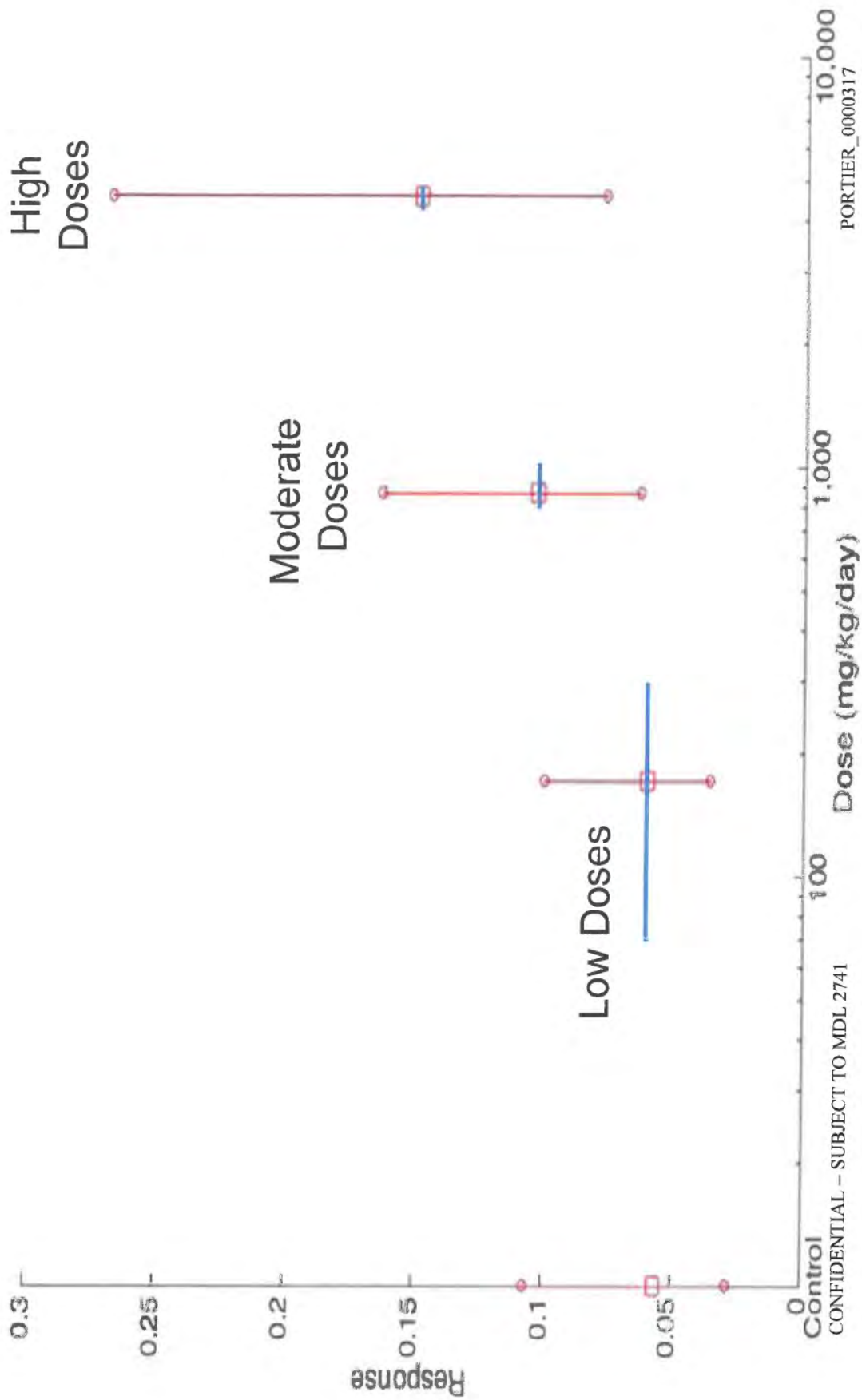
Analysis of Male Mouse Malignant Lymphoma From the Individual Studies

Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[2]
1983	Crl:CD-1	24	157, 814, 4841	2/50, 5/49, 4/50, 2/50	0.51 (0.51)
1993	?:CD-1	24	100, 300, 1000	4/50, 2/50, 1/50, 6/50	0.08 (0.08)
1997	CrJ:CD-1	18	165, 838, 4348	2/50, 2/50, 0/50, 6/50	**0.008 (0.012)**
2001	SW	18	15, 151, 1460	10/49, 15/49, 16/49, 19/49	**0.05 (0.09)**
2009	Crl:CD-1	18	71, 234, 810	0/51, 1/51, 2/51, 5/51	**0.004 (0.005)**

1 – Giknis and Clifford, 2005 historical control rate=0.045 (0.027 in 18 month and 0.06 in 24 month), 8 of 26 18-month studies had no tumors, 3 of 26 24-month studies had no tumors

2 – Poly-3 adjustment used to predict response at 24 months from response at 18 months, see Bailer and Portier (1988)

Malignant lymphomas in male CD-1mice poly-3 adjusted and clustered by similar doses



Malignant Lymphomas in Male Mice

Study	Approx. Trend	Exact Trend[1]	Historical Trend[2]
Knezevich and Hogan, 1983	0.515	0.736	0.484
Atkinson, 1993b	0.076	0.095	0.087
Sugimoto, 1997	0.008	0.02	0.013
Kumar, 2001	0.053	0.105	0.072
Wood et al., 2009b	0.004	0.008	0.007
All experiments combined	0.173	0.426	0.172
All CD-1 Studies Combined	0.015	0.084	0.021
All experiments combined, doses<1500	<0.001	0.002	0.001
All CD-1 experiments combined, doses<1000	0.031	0.036	0.039

1 – Exact test is based upon a permutation test with fixed marginals.
2 - Historical trend test is based upon historical control data from Giknis and Clifford (2005)

Analysis of Male Mouse Hemangiosarcomas[1] From the Individual Studies

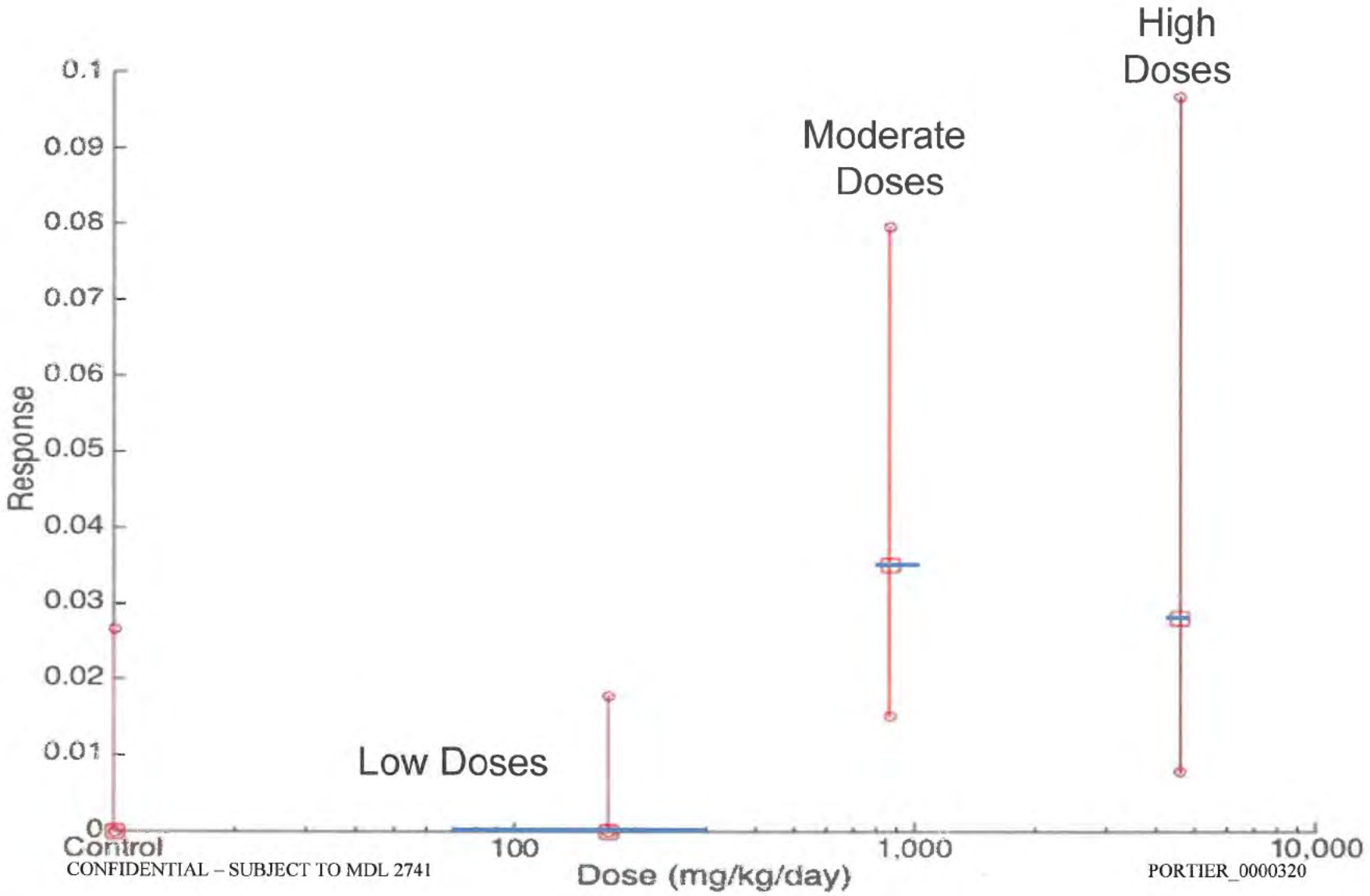
Year	Strain	Length	Doses (mg/kg/d)	Response	p-Trend (p-poly3)[2]
1983	Crl:CD-1	24	157, 814, 4841	0/50, 0/49, 1/50, 0/50	0.63 (0.63)
1993	?:CD-1	24	100, 300, 1000	0/50, 0/50, 0/50, 4/50	**0.0004 (0.0004)**
1997	CrJ:CD-1	18	165, 838, 4348	0/50, 0/50, 0/50, 2/50	**0.008 (0.009)**
2001	SW	18	15, 151, 1460	0/50, 0/50, 2/50, 0/50	0.724 (0.724)
2009	Crl:CD-1	18	71, 234, 810	0/51, 0/51, 0/51, 0/51[3]	0.5 (0.50

1 – Giknis and Clifford, 2005 historical control rate=0.01 (0 in 18 month and 0.018 in 24 month), all of 26 18-month studies had no tumors, 18 of 26 24-month studies had no tumors

2 – Poly-3 adjustment used to predict response at 24 months from response at 18 months; see Bailer and Portier (1988)

3 – CLP Proposal Table 42 lists tumor counts for this study of 2/51, 1/51, 2/51 and 1/51. However, these rates include hemangiomas from liver and kidney, making them different from the other studies and not applicable for the comparisons that follow

Hemangiosarcomas in male CD-1 mice poly-3 adjusted and clustered by similar



Hemangiosarcomas in Male Mice

Study	Approx. Trend	Exact Trend[1]	Historical Trend[2]
Knezevich and Hogan, 1983	0.628	0.5	0.592
Atkinson, 1993b	<0.001	0.004	<0.001
Sugimoto, 1997	0.008	0.061	0.021
Kumar, 2001	0.5	0.494	0.621
Wood et al., 2009b	0.5	1	0.49
All experiments combined	0.041	0.056	0.060
All CD-1 Studies Combined	0.024	0.044	0.041
All experiments combined, doses<1500	0.007	0.016	0.014
All CD-1 experiments combined, doses<1000	<0.001	<0.001	<0.001

1 – Exact test is based upon a permutation test with fixed marginals.
2 - Historical trend test is based upon historical control data from Giknis and Clifford (2005)

Carcinogenicity Studies in Rats

Year	Strain	Length[1]	Top Dose[2]	Finding
+Atkinson et al., 1993	SD	24	1000	none
+Lankas, 1981	SD	26	~32	inadequate dose, testicular tumors (M), pancreas islet cell aden. (M, weak)
+Stout & Ruecker, 1990	SD	24	1183	liver aden. (M), pancreas islet cell aden. (M), thyroid aden. (F)
Enemoto, 1997	SD	24	1127	none
Pavkov & Wyand, 1987	SD	24	41.8	inadequate dose and purity

1 – months; 2 – mg/kg bw/day;
+ indicates studies evaluated by IARC

Carcinogenicity Studies in Rats

Year	Strain	Length[1]	Top Dose[2]	Finding
+Seralini et al., 1993	SD	24	2250 mg/L in water	inadequate, mammary tumors
+Suresh, 1996	Wistar	24	886	none
Wood et al., 2004	Wistar	24	1229.7	mammary gland tumors (F)
Brammer, 2001	Wistar	24	1,498	Liver aden. (M)
+Chru-scielska et al., 2000	Wistar	24	2250 mg/L in water	inadequate documentation
+Syngenta , 1996	Wistar	12	1409	Inadequate length of study

1 – months; 2 – mg/kg bw/day;
+ indicates studies evaluated by IARC

Summary of Animal Cancer Data

- Sufficient Evidence
  - IARC, Portier et al.
- Insufficient Evidence
  - EFSA, CLP Proposal, USEPA, WHO/JMPR
- Definition of Sufficient Evidence (CLP Guidance, 2015; IARC, 2006)
  - sufficient evidence of carcinogenicity: 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.
  - A single study in one species and sex might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites

Glyphosate Monograph – Mechanistic and Other Considerations:

Key Characteristic of Carcinogens #2 (Genotoxic)

Agent	Strength of the evidence	Evidence base includes	Endpoints considered in the evaluation
Glyphosate	Strong	1. ***Largely positive*** studies: • in human cells *in vitro*, • in mammalian model systems *in vivo* and *in vitro*, • studies in other non-mammalian organisms 2. ***Generally positive*** studies in liver *in vivo* in mammals 3. ***Mixed*** results for kidney and bone marrow *in vivo* in mammals 4. ***Consistently negative*** results from tests in bacterial assays	• Biomarkers of DNA adducts • Biomarkers of various types of chromosomal damage
Glyphosate formulations	Strong	1. ***Evidence in exposed humans***: • three studies of genotoxicicity endpoints in community residents exposed to glyphosate formulations, two of which reported positive associations • one of these studies examined subjects before and after aerial spraying and found a significant increase in micronuclei after exposure in 3 of 4 different geographical areas 2. ***Largely positive*** studies: • in human cells *in vitro*, • in mammalian model systems *in vivo* and *in vitro*, • studies in other non-mammalian organisms 3. ***Generally negative*** results from tests in bacterial assays 4. The ***pattern*** of tissue specificity of genotoxicity endpoints observed with glyphosate formulations is similar to that observed with glyphosate alone	• Chromosomal damage (micronuclei) in circulating blood cells from humans • Biomarkers of DNA adducts • Biomarkers of various types of chromosomal damage
AMPA	Moderate	1. Two human *in vitro* studies 2. One mammalian *in vivo* study 3. One mammalian *in vitro* study 4. One study in eel	While the number of studies is not large, all of the studies were ***positive***

Glyphosate Monograph – Mechanistic and Other Considerations:

Key Characteristic of Carcinogens #5 (Oxidative Stressor)

Agent	Strength of the evidence	Evidence base includes	Endpoints considered in the evaluation
Glyphosate	Strong	1. Rodent studies *in vivo* (including similar effects observed in many tissues) 2. Rodent cells *in vitro* 3. Human cells *in vitro*	• Lipid peroxidation markers • Oxidative DNA adducts • Dysregulation of antioxidant enzymes • Some studies challenged this mechanism experimentally (*e.g.*, by co-administering antioxidants)
Glyphosate formulations	Strong		
AMPA	Strong		

Conclusions

- Glyphosate should be listed as a Category 1B Carcinogen
  - animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen)[1]
  - In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals[1]
  - In this case limited evidence in humans and sufficient in animals

1. Guidance on the Application of the CLP Criteria, Table 3.6.1 (2015)

IARC Monograph Review Process and Glyphosate

Christopher J. Portier, Ph.D.

December, 2015

The IARC Monographs Program

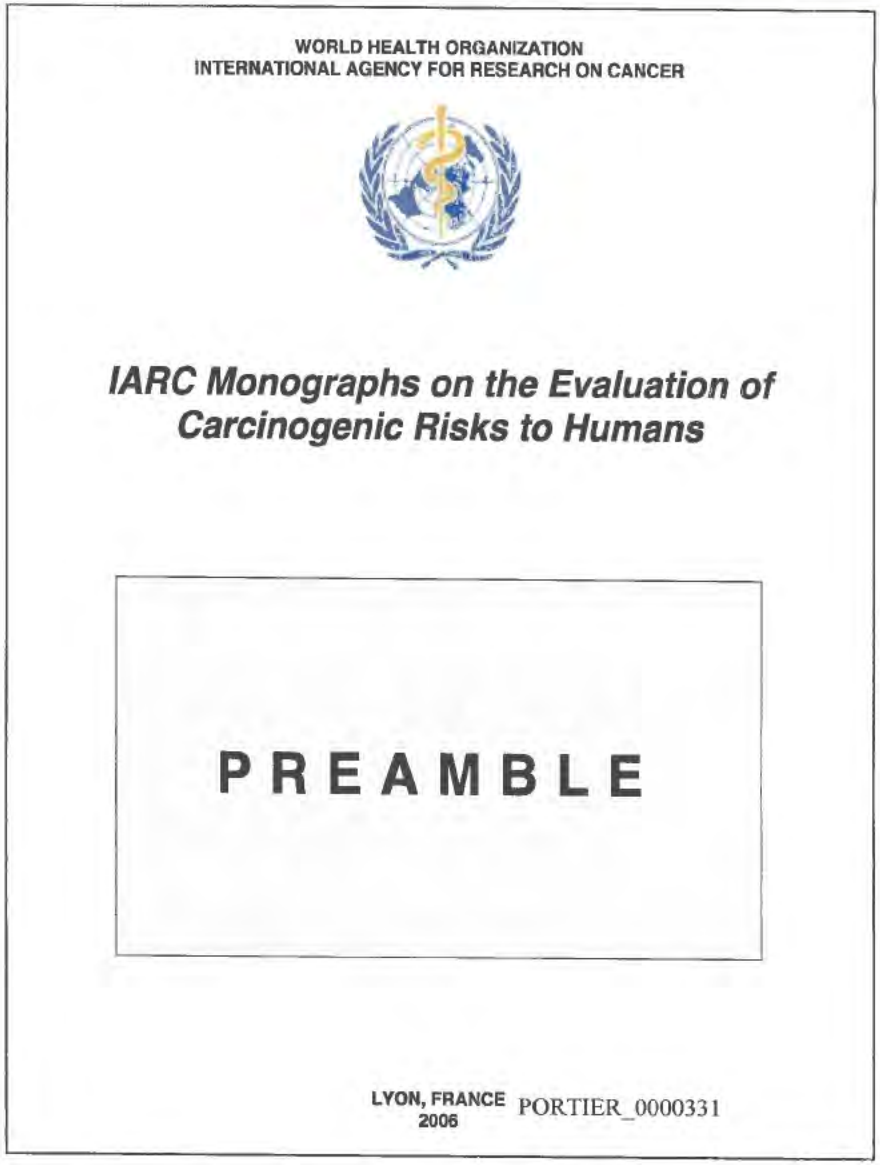
- IARC Monographs Evaluate
  - Chemicals
  - Complex substances and mixtures
  - Occupational exposures
  - Physical and biological agents
  - Personal habits

The IARC Monographs Program

- 980 Agents have been reviewed
  - 116 **known** human carcinogens
    - Group 1
  - 73 **probable** human carcinogens
    - Group 2A
  - 287 **possible** human carcinogens
    - Group 2B
  - 503 **not classifiable**
    - Group 3
  - 1 **probably not** carcinogenic

IARC Monographs Process

- Written Guidelines
  - Public Document
  - Who? What? How?
  - Roles
  - Responsibilities
  - Instructions
    - Review
    - Summary of Evidence



IARC Monograph 112 Process

- Working Group Members
  - No real or apparent conflicts of interest
    - Formal process, written declarations of interest
  - Membership
    - Working Group members – review, evaluate
    - Invited Specialist – review only
    - Representatives – government, observe only
    - Observers – interested party, observe only
    - Secretariat – support the Working Group

IARC Monograph Timeline

- 1 year before Monograph Meeting
  - Meeting announced
  - Call for experts
  - Call for data
- 8 months before Monograph Meeting
  - Working Group membership selected
  - Request for observer status opened
  - Draft sections of Monograph developed by Working Group Members

IARC Monograph Timeline

- 1 month before Monograph Meeting
  - Call for data closed
  - Draft sections distributed to Working Group members for review and comment
- At Monograph Meeting
  - Finalize review of all literature
  - Evaluate the evidence in each category
  - Complete the overall evaluation

IARC Monograph Timeline

- 1-2 weeks after Monograph Meeting
  - Publish summary in Lancet Oncology
- 4-12 months after Monograph Meeting
  - Finalize Monograph and publish

The IARC Monograph

Preamble

General Remarks

Several *Monographs* in one volume:

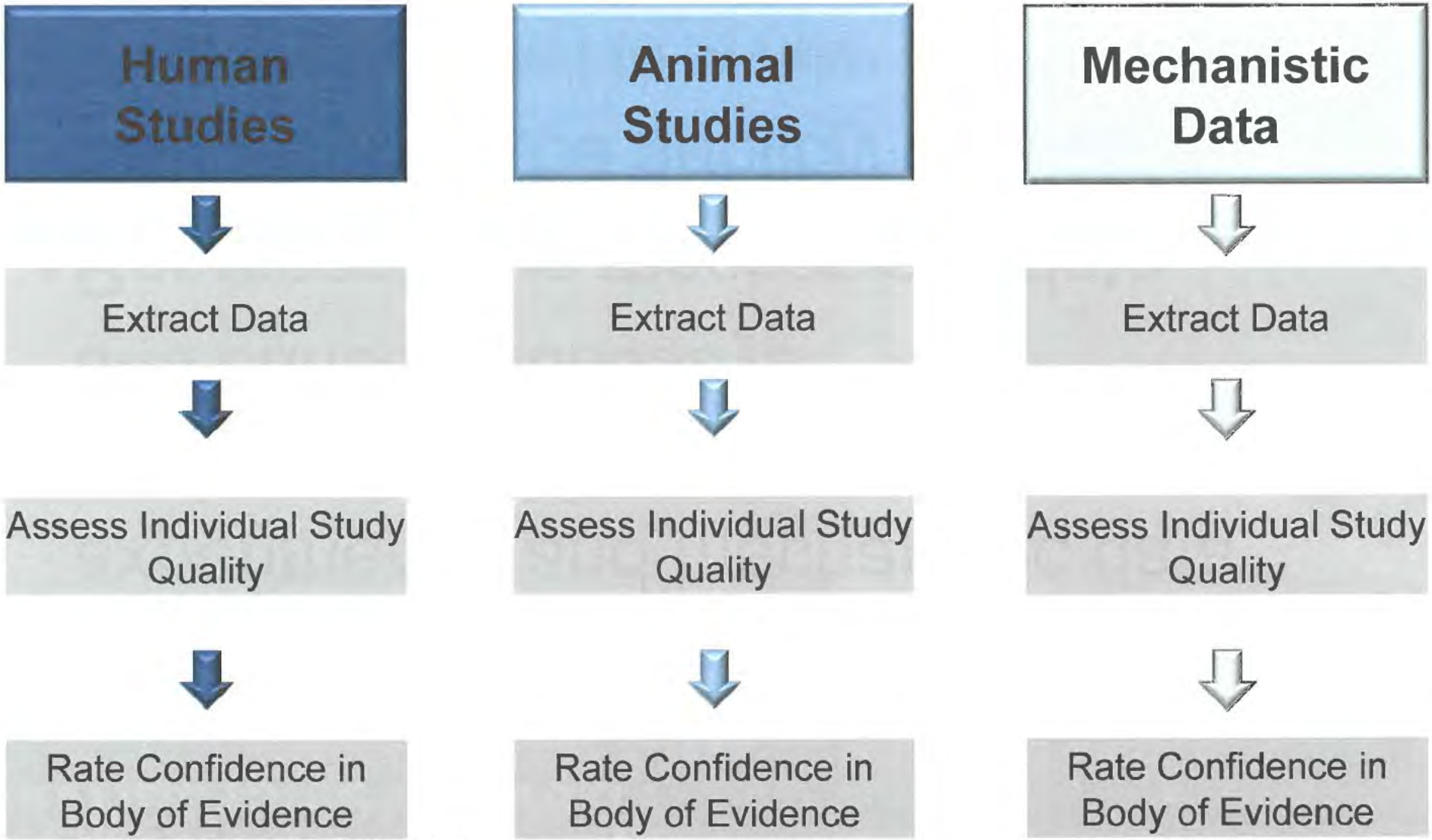
1. Exposure data
2. Cancer in humans
3. Cancer in animals
4. Mechanistic and other relevant data
5. Summary
6. Evaluation and rationale

References

What is reviewed?

- Systematic review of human, experimental and mechanistic data
- All pertinent epidemiological studies and cancer bioassays
- Representative mechanistic data
- Studies must be publicly available
  - Sufficient detail to review
  - Reviewers cannot have been associated with the study

Evidence Review



Glyphosate - Background

- Broad-spectrum, non-selective herbicide
- First synthesized by Cilag (1950) as a possible drug
- Re-synthesized by Monsanto (1970)
- Patent expired [1991, 2000 (US)]
- Hundreds of trade names
- Approximately 91 producers in 20 countries

Glyphosate - Background

- Believed to be the most heavily used herbicide in the world
  - 2012 production volume > 700 million kg
- Production has increased sharply in recent years
  - Genetically modified glyphosate-resistant crop varieties
- Exposure pathways
  - Air (during spraying)
  - Water
  - Food

Glyphosate – Human Evidence

- Literature
  - US Agricultural Health Study (AHS)
  - Multiple independent case-control studies

Glyphosate – Human Evidence

- Epidemiological studies of cancer in humans
  - More than 2 studies
    - Non-Hodgkin Lymphoma (NHL)
    - Multiple Myeloma (MM)
  - Two studies
    - Leukemia, breast cancer, prostate cancer
  - One Study
    - Adult brain, oesophageal, stomach, prostate, soft-tissue sarcoma, lung, oral cavity, colorectal, pancreas, kidney, bladder, melanoma

Glyphosate – Key Epidemiology Studies for Non-Hodgkin Leukemia

Study	Type	Size
Agricultural Health Study *(Alavanja et al., 2003)*	Cohort – pesticide applicators and spouses	52 395 (+32 347 spouses), 92 cases, 4-8 years follow-up
US Midwest *(De Roos et al., 2003)*	Pooled analysis of 3 case-control studies	NHL: 650 cases, 1933 controls
Cross-Canada *(McDuffie et al., 2001)*	Population-based case-control	517 cases, 1506 controls
Swedish Case-Control Study *(Eriksson et al., 2008)*	Population-based case-control study	910 cases, 1016 control
Swedish Case-Control Study *(Hardell et al., 1999)*	Population-based case-control study	404 cases, 741 control (limited power)

Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Sufficient Evidence
  - Causal relationship is **established**
  - Chance, bias and confounding ruled out with reasonable confidence
- Limited Evidence
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence

Evaluating Human Evidence
Preamble Part B, Section 6(a)

- Inadequate Evidence
  - Studies permit no conclusion regarding causality
- Evidence suggesting lack of carcinogenicity
  - Several strong studies showing consistent lack of positive association
  - Conclusion limited to cancer sites and conditions studied

Glyphosate Evaluation – Human Evidence

- **Limited Evidence** for NHL
  - Causal interpretation is **credible**
  - Chance, bias and confounding could not be ruled out with reasonable confidence
- Basis
  - De Roos et al., 2003 (US), McDuffie et al., 2001 (Canada), Eriksson et al., 2008 (Sweden)
    - Positive association
    - Adjustment for other pesticides
  - Agricultural Health Study
    - No additional support for association, does not contradict

Evidence in Experimental Animals

- 1 mouse feeding (glyphosate) study showed significant trend in the incidence of ***renal tubule adenoma or carcinoma*** (combined) in male mice; renal tubule carcinoma is a rare tumor
- 1 mouse feeding (glyphosate) study showed significant trend in the incidence of ***haemangiosarcoma*** in male mice
- 2 rat feeding (glyphosate) studies showed significant increase in the incidence of *pancreatic islet cell adenoma* (a benign tumor) in male rats
- 1 mouse study (GLY formulation) showed positive effect on *skin cancer* in an initiation-promotion study
- Several other oral feeding (glyphosate) and drinking water (glyphosate and glyphosate formulation) studies in rats showed no significant effects

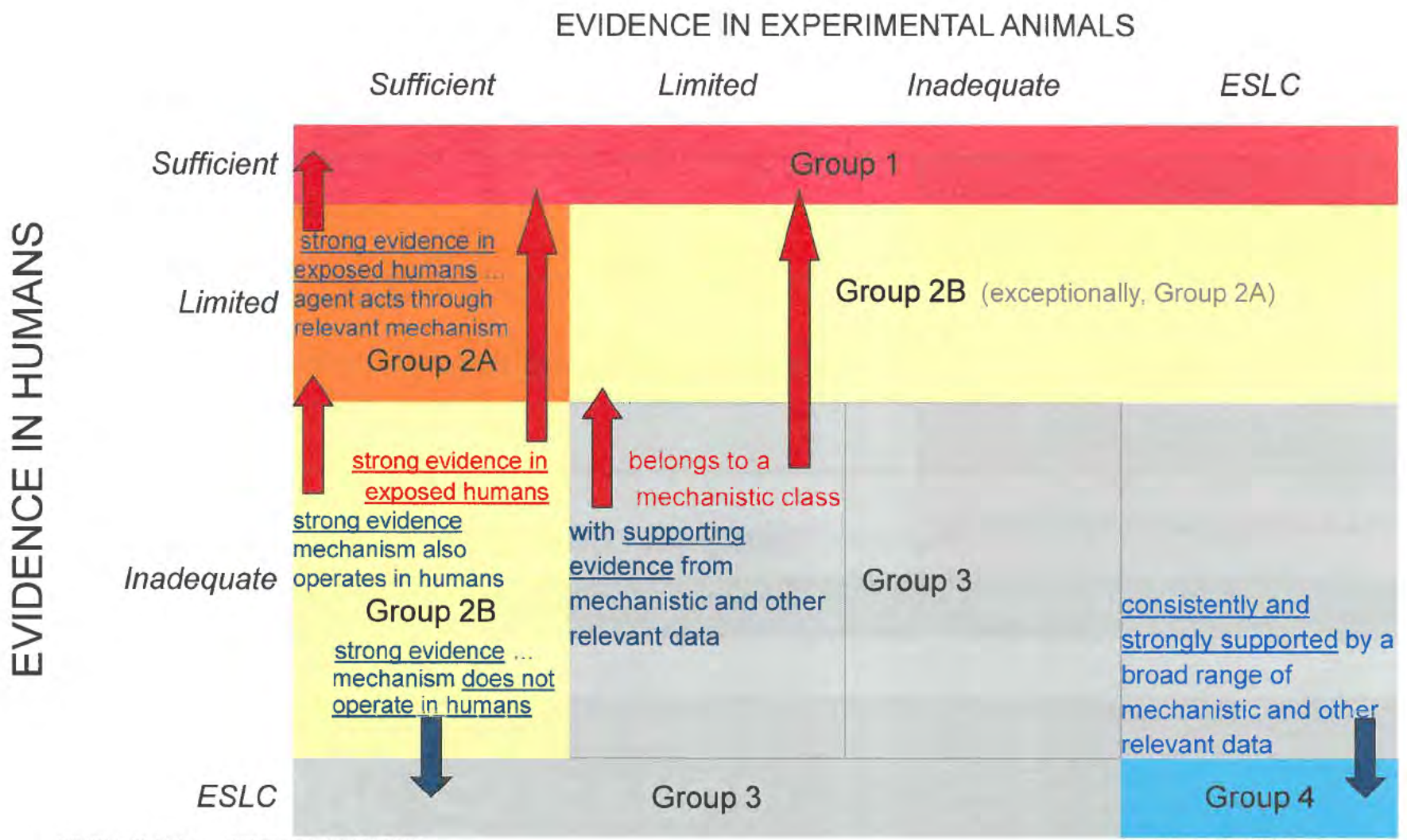
Glyphosate Evaluation – Human Evidence

- **Sufficient Evidence** in experimental animals
  - More than two independent studies showing a significant, biologically relevant cancer finding

Mechanistic Evidence

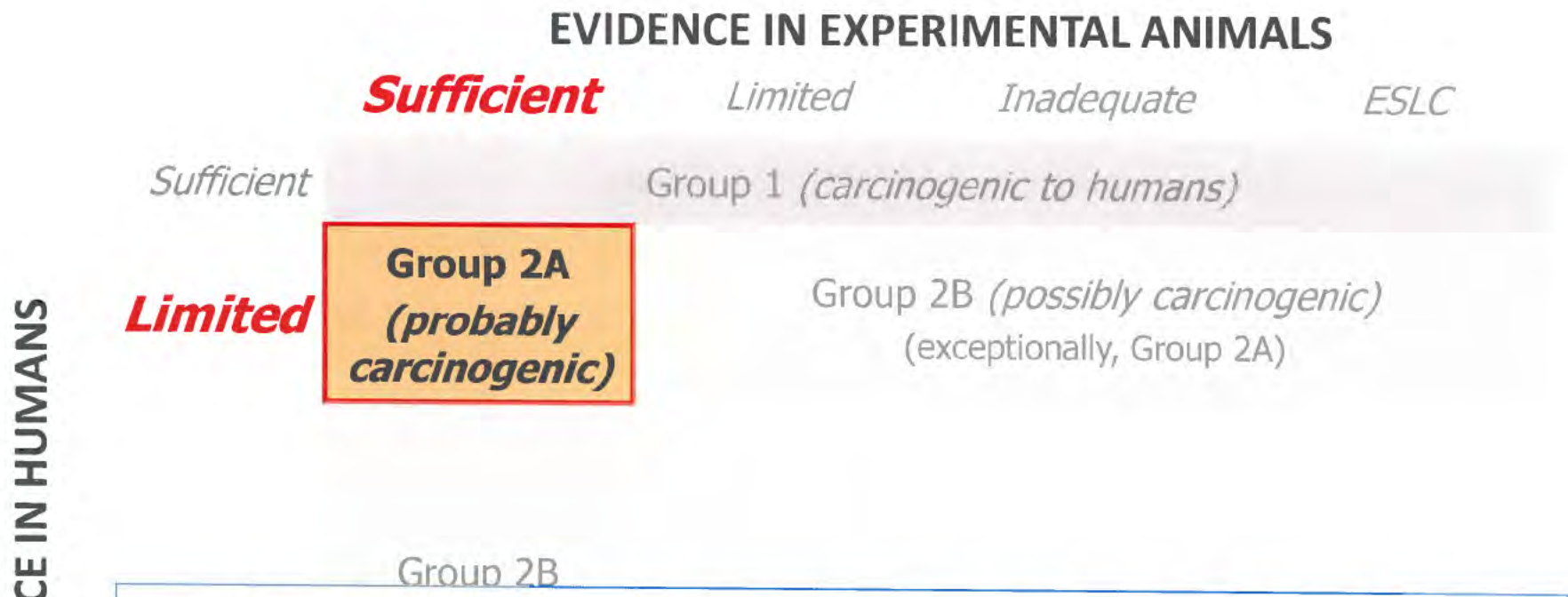
Key characteristic	Strength of Evidence
1. Electrophilic or ability to undergo metabolic activation	Glyphosate is ***not*** electrophilic
2. Genotoxic	Strong (G, GF)
3. Alters DNA repair or causes genomic instability	No data
4. Epigenetic Alterations	No data
5. Oxidative Stressor	Strong (G, GF and AMPA)
6. Induces chronic inflammation	No data
7. Immunosuppressant	Weak
8. Modulates receptor-mediated effects	Weak
9. Immortalization	No data
10. Alters cell proliferation, cell death, or nutrient supply	Weak

IARC Overall Evaluation



Modified from Vincent Cogliano, IARC

Glyphosate Monograph – Overall Evidence



"*for […] glyphosate, the* ***mechanistic evidence provided independent support of the 2A classification*** *based on evidence of carcinogenicity in humans and experimental animals*"

(The Lancet Oncology; March 20, 2015)

EFSA Glyphosate Review
Animal Carcinogenicity

Year	Strain	Length[1]	Top Dose[2]	Renal Tumors	Hemangio-sarcomas	Malignant Lymphoma
1983[5]	Crl:CD-1	24	4,841	+[3]		
1993[5]	?:CD-1	24	1,000		+	
1997	CrJ:CD-1	18	4,843	+	+	+
2001	SW	24	1,460	+		+/-[4]
2009	Crl:CD-1	18	810			+

1 – months; 2 – mg/kg bw/day; 3 - + indicates a p-value of <0.05 as calculated by BfR using the Armitage linear trend test in proportions; 4 – p=0.066; 5 – studies evaluated in IARC review

Historical Control Data used: collected 1987-96, 51 control groups from Crl:CD-1 mice from7 different research laboratories using mice from 3 different Charles River Laboratories production sites with sacrifice at ages 18-24 months

Renal Adenoma: 41 studies no tumors, 3 studies 1 tumor, 2 studies 2 tumors
Renal Carcinoma: 42 studies no tumors, 4 studies 1 tumor

EFSA compared to IARC

- Agreed with the IARC on *limited evidence* in humans
  - dismissed the association as "insufficiently consistent" with no justification.
- Dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcoma in 2 mouse studies and malignant lymphoma in 2 mouse studies
  - Inappropriate historical control dataset used in an incorrect manner and ignoring established guidelines cited in their report
  - Trend test not convincing, Doses too high
- Down-weighted laboratory and human evidence of genotoxicity.
- Confirmed glyphosate induces oxidative stress
  - Not relevant for cancer because no other indications

CLP Guidance on Carcinogenicity

- Category 1: Known or presumed human carcinogens
  - Category 1A, known to have carcinogenic potential for humans, classification is largely based on human evidence
  - Category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence

Guidance on the Application of the CLP Criteria, ECHA (2015)

CLP Guidance on Carcinogenicity
(continued)

- The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:
  - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or
  - animal experiments for which there is sufficient (1) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).
- In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing **limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals**

Guidance on the Application of the CLP Criteria, ECHA (2015)

Hide and Seek

Glyphosate Cancer Risks and the European Pesticide Regulatory Process

Christopher J. Portier, Ph.D.

11 May, 2017

Maastricht University

IARC Working Group Classifies Glyphosate as "Probably Carcinogenic to Humans"

NATURE | NEWS: EXPLAINER

Widely used herbicide linked to cancer

As the World Health Organization's research arm declares glyphosate a probable carcinogen, *Nature* looks at the evidence.

Roundup weedkiller 'probably' causes cancer, says WHO study

The Monsanto product – the world's most widely used herbicide – contains glyphosate, which may also be carcinogenic for non-Hodgkin's lymphoma

A Top Weedkiller Could Cause Cancer. Should We Be Scared?

ROUNDUP AND RISK ASSESSMENT

By Michael Specter April 10, 2015

A farmer sprays glyphosate across his cornfield.

Participants

Consolato Maria Sergi

Department of Laboratory Medicine and Pathology
University of Alberta
Edmonton, Alberta
Canada

Andrea 't Mannetje

Centre for Public Health Research
Massey University, Wellington Campus
Wellington
New Zealand

Lauren Zeise

Reproductive and Cancer Hazard Assessment
California Environmental Protection Agency
Oakland, CA
USA

Invited Specialist

Christopher J. Portier [retired] [3]

National Center for Environmental Health and Agency for Toxic Substances and Disease Registry
Centers for Disease Control and Prevention
Atlanta, GA
USA

Representatives

Amira Ben Amara [unable to attend] [4]

Agence Nationale de Contrôle Sanitaire et Environnementale des Produits (ANCSEP)
Montplaisir, Tunis
Tunisia

Catherine Eiden [unable to attend] [5]

Office of Pesticide Programs
United States Environmental Protection Agency
Washington, DC
USA

Marie-Estelle Gouze [6]

French Agency for Food, Environment and Occupational Health Safety (ANSES)
Maisons-Alfort
France

Jesudoss Rowland [7]

Office of Pesticide Programs
United States Environmental Protection Agency
Washington, DC
USA

[3] Christopher J. Portier receives a part-time salary from the Environmental Defense Fund, a United States–based non-profit environmental advocacy group.
[4] Amira Ben Amara attended as a representative of the National Agency of Sanitary and Environmental Control of Products, Tunisia.
[5] Catherine Eiden attended as a representative of the United States Environmental Protection Agency.
[6] Marie-Estelle Gouze attended as a representative of ANSES, France.
[7] Jesudoss Rowland attended as a representative of the United States Environmental Protection Agency.

Glyphosate - Background

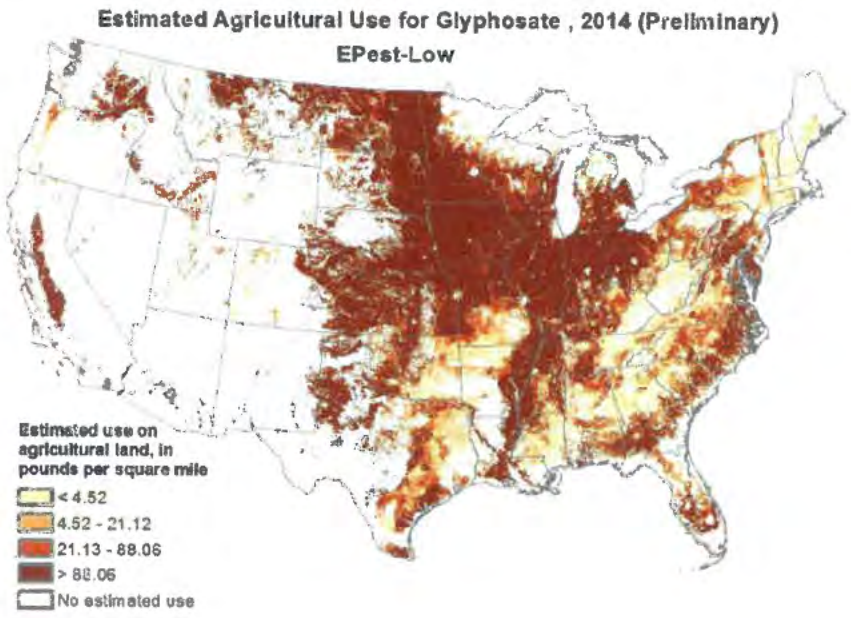
- Broad-spectrum, non-selective herbicide
- First synthesized by Cilag (1950) as a possible drug
- Re-synthesized by Monsanto (1970)
- Patent expired [1991, 2000 (US)]
- Hundreds of trade names
- Approximately 91 producers in 20 countries

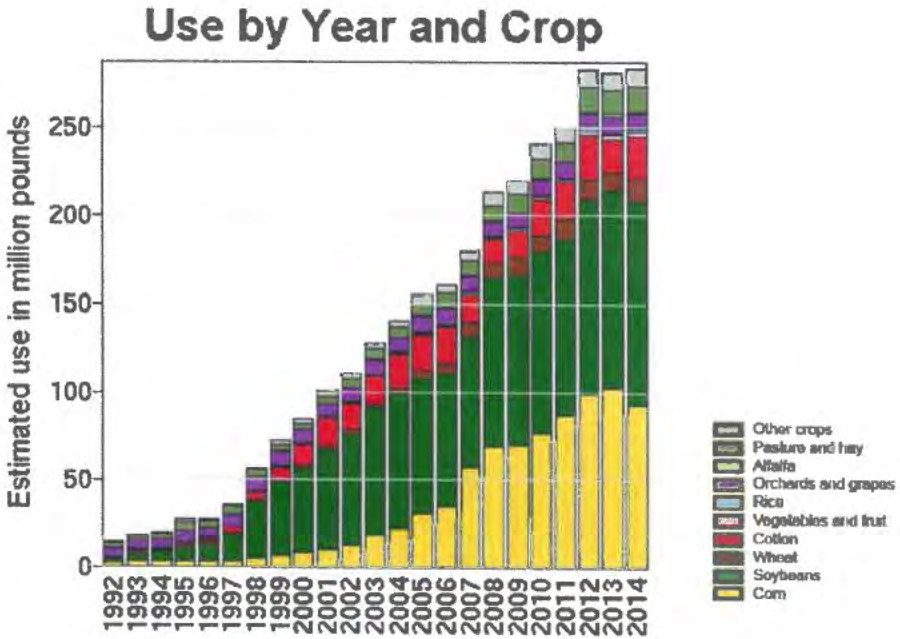
Glyphosate - Background

- Believed to be the most heavily used herbicide in the world
  - 2012 production volume > 700 million kg (approximately 3 times the adult human biomass population of The Netherlands[1])
- Production has increased sharply in recent years
  - Genetically modified glyphosate-resistant crop varieties
- Exposure pathways
  - Air (during spraying)
  - Water
  - Food

[1] "*The weight of nations: an estimation of adult human biomass*", Walpole et al., 2012, BMC Public Health, 12:439

US use of Glyphosate





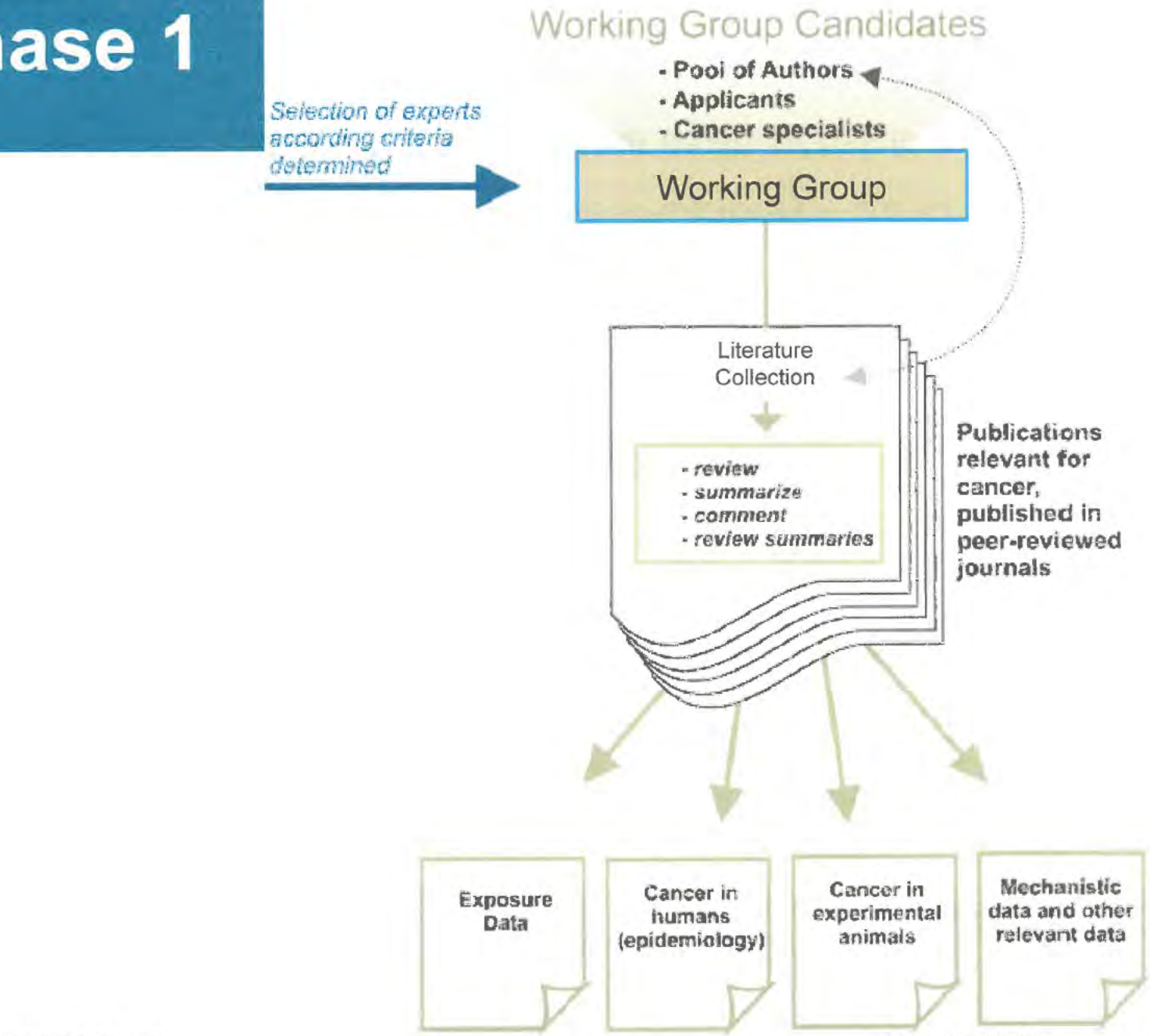
IARC Working Group Findings

- Consistent positive association for NHL but bias and confounding possible
- Renal tumors (1 study) and hemangiosarcomas (1 study) in mice (2 studies evaluated)
- Pancreas islet-cell tumors (2 studies), liver adenomas (1 study), Thyroid C-cell adenomas (1 study) in rats (5 studies evaluated)
- Genotoxicity and oxidative stress

Regulatory Authorities

- EFSA – November, 2015
  - Unlikely to pose a carcinogenic hazard to humans
- WHO/JMPR – March, 2016
  - Unlikely to pose a carcinogenic risk to humans from exposure through the diet
- ECHA – March, 2017
  - no hazard classification for carcinogenicity is warranted
- USEPA – September, 2016 (draft)
  - Not likely to be carcinogenic to humans at doses relevant to human health risk assessment
- Australia Pesticides and Veterinary Medicines Authority – 2015
  - the use of glyphosate in Australia does not pose a cancer risk to humans

IARC Phase 1

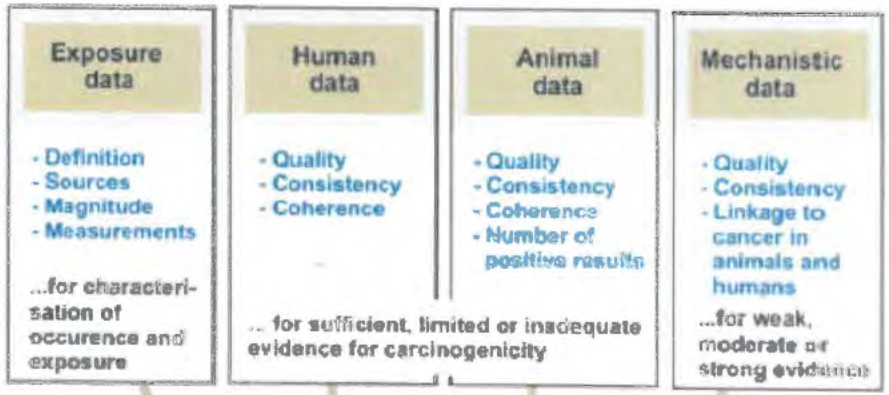


IARC Phase 2

Guidance on evaluating carcinogenicity

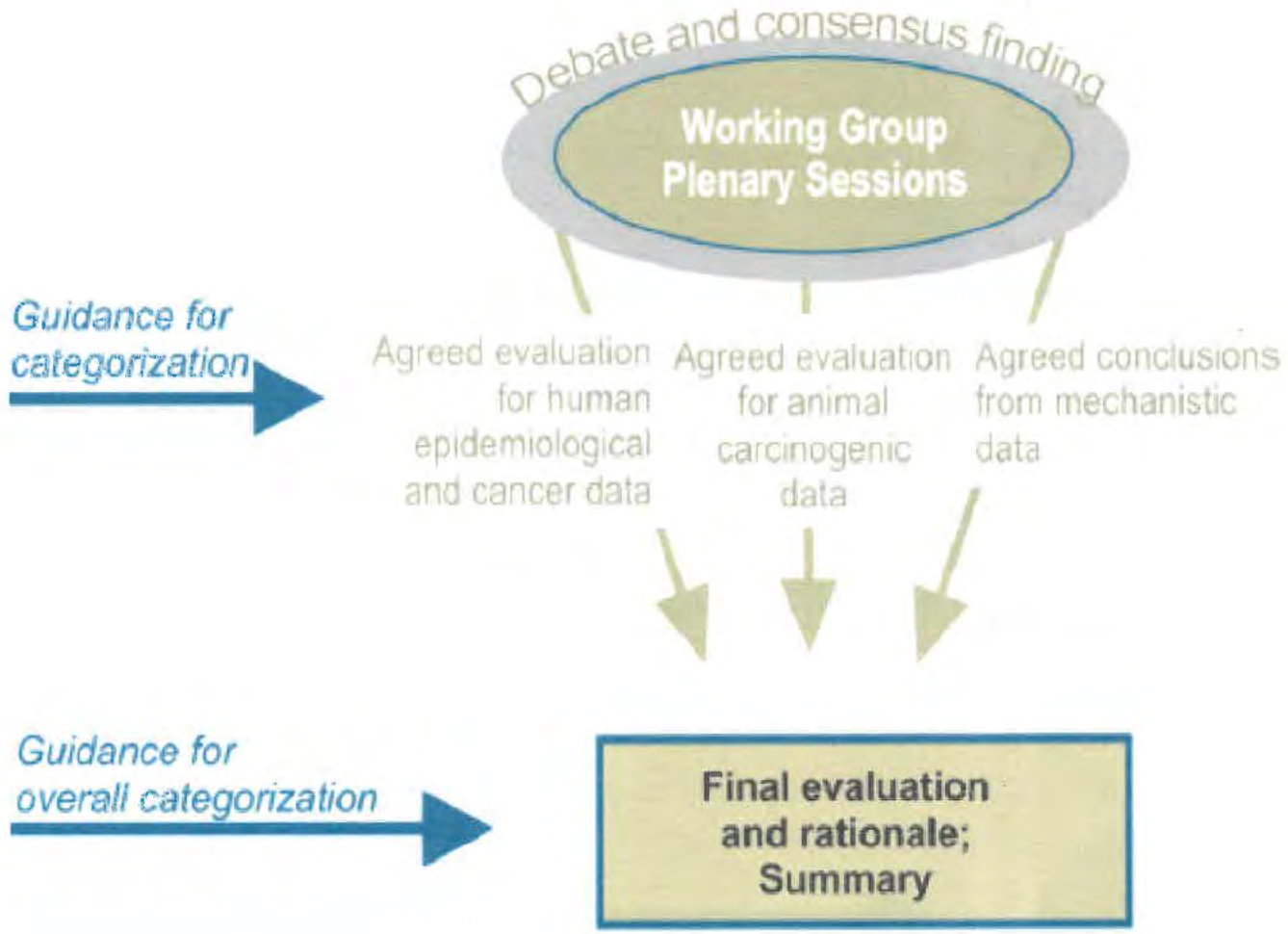
Work in Subgroups evaluating:

Evaluation Criteria



Wording and suggested evaluation | Wording and suggested evalutation | Wording and suggested mechanisms

IARC Final Phase



IS GLYPHOSATE PROBABLY CARCINOGENIC? PROBABLY NOT!

September 8, 2015 by James Gurney · in Blog Post, GMOs

THE LEAGUE OF NERDS

IARC S Ruling On Glyphosate Ignores The Science

The Risk-Monger

Monsanto Disagrees with IARC Classification for Glyphosate

WHAT THE IARC 2A RATING FOR GLYPHOSATE REALLY MEANS

Reuters attacks IARC over glyphosate cancer link

Claire Robinson reports on a hit piece titled "Who says bacon is bad?", which quotes industry-linked sources to smear the cancer agency that judged glyphosate a probable carcinogen

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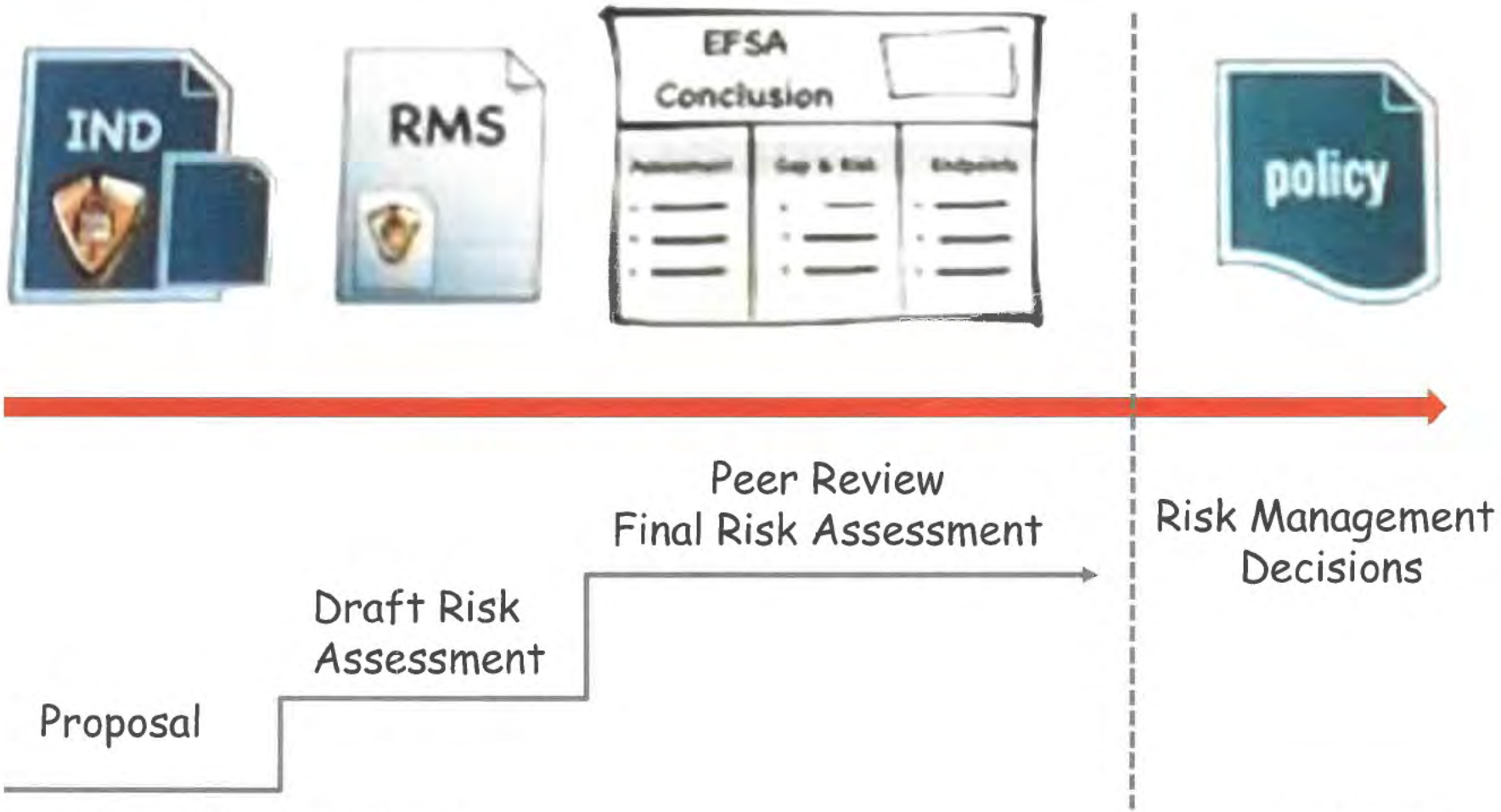
Pesticide Peer Review in the EU



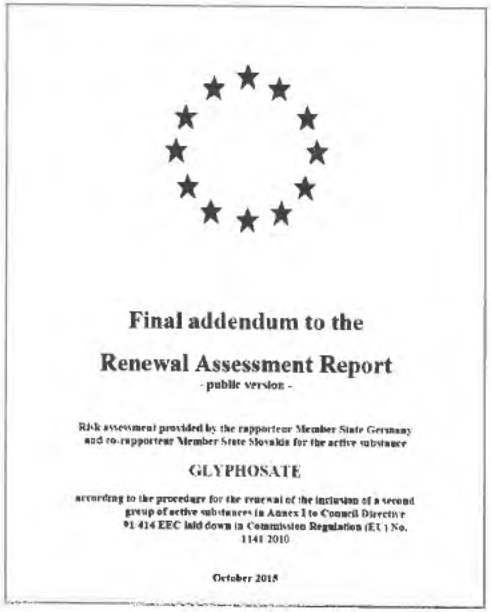
Modified from slide by J. Tarazona

Documents from EFSA Peer Review

Scientific Peer-Reviewed Literature

Industry Proprietary Research Reports

RMS → Comments → EFSA



Final addendum to the

Renewal Assessment Report

- public version -

Risk assessment provided by the rapporteur Member State Germany and co-rapporteur Member State Slovakia for the active substance

GLYPHOSATE

according to the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91-414 EEC laid down in Commission Regulation (EU) No. 1141 2010

October 2015

European Food Safety Authority

efsa

European Food Safety Authority

Peer Review Report on Glyphosate

- Comments on the assessment report and addendum 1
- Reporting tables and commenting table on addendum 1
- Pesticides peer review meeting reports
- Evaluation tables
- Comments on the additional information assessment
- Comments on the draft EFSA conclusion and updated EFSA conclusion

efsa

CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate

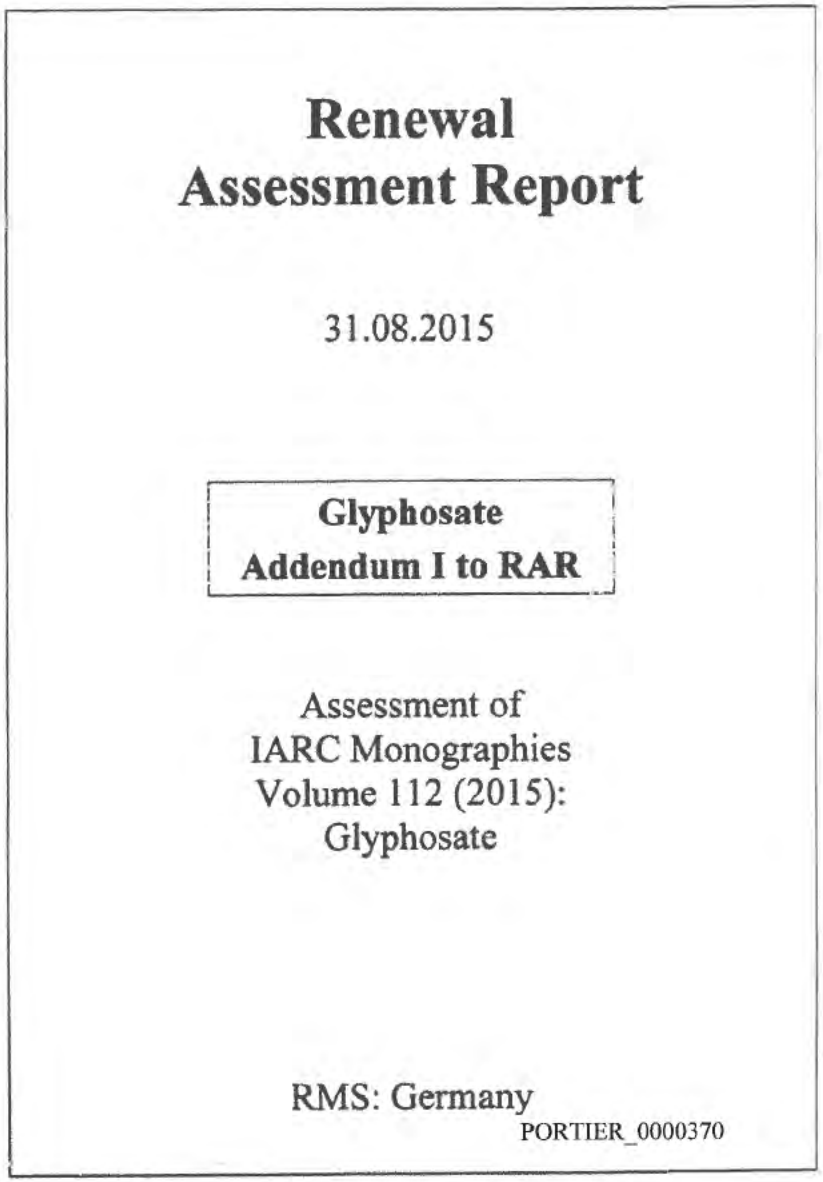
European Food Safety Authority (EFSA)

ABSTRACT

Modified from slide by J. Tarazona

Bundesinstitut für Risikobewertung (BfR)

- Responsible Member State (RMS)
- No consistent positive association in human data
- No indication of cancer risk in 7 rat and 5 mouse studies
- No mechanistic data to support finding
- IARC looked at fewer studies than BfR



Renewal Assessment Report

31.08.2015

Glyphosate
Addendum I to RAR

Assessment of
IARC Monographies
Volume 112 (2015):
Glyphosate

RMS: Germany

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Scientific Response (96 Scientists)

- BfR agreed on limited evidence in humans
  - dismissed the association as insufficiently consistent with no justification.
- BfR dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcomas in 2 mouse studies and malignant lymphomas in 2 mouse studies
  - inappropriate historical control dataset used in an incorrect manner and ignoring the OECD guidelines
  - BfR incorrectly discarded all of the glyphosate-induced carcinogenic findings in animals as chance occurrences.
- BfR ignored important laboratory and human evidence of genotoxicity
- BfR confirmed that glyphosate induces oxidative stress
  - dismissed this finding for lack of any other finding to support cancer causation because they had dismissed all of the other evidence


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

PORTIER_0000371

Response

EU scientists in row over safety of Glyphosate weedkiller

Dispute over possible carcinogenic effects of the widely used w
ahead of an EU decision on its continued use

SPECIAL REPORTS | Mon Apr 18, 2016 | 4:42pm EDT

Is your weed killer carcinogenic?

EFSA accuses world-class cancer experts of engaging in 'Facebook science'

Blogpost by **franziska achterberg** - December 8, 2015 at 14:06

Scientists take sides: Who's right about glyphosate?

The head of the EU's food safety body rips critics for 'Facebook science'

Posted Apr. 18th, 2016 *by* Kate Kelland

Questions you might ask

- Who wrote the original draft report?
  - European Glyphosate Task Force
    - a consortium of companies joining resources and efforts in order to renew the European glyphosate registration with a joint submission
    - ADAMA Agan Ltd., Agria S.A., Agro Trade GmbH, Albaugh UK Limited, Arysta Lifesciences SAS, Barclay Chemicals (Manufacturing) Ltd., Brokden SL, BROS Spółka z ograniczoną odpowiedzialnością spółka komandytowa, Cheminova A/S, Coromandel International Ltd, EXCEL CROP CARE(Europe) NV, Helm AG, Industrias Afrasa S.A., **Monsanto Europe S.A./N.V.,** Nufarm GmbH & Co KG, Rotam Agrochemical Europe Limited, Sapec Agro S.A., Sinon Corporation, Société Financière de Pontarlier, Syngenta Limited, United Phosphorus Ltd, Wynca UK Limited

Table B.2.9-6: Proposed risk mitigation measures for the achievement of an acceptable risk for non-target plants in off-field areas

~~Intended uses~~	~~Application rate (g a.s./ha)~~	~~Buffer strip (m) without drift reduction~~	~~Buffer strip (m) with x % drift reduction~~
~~Orchard crops, vine including citrus & tree nuts*~~	~~1 x 2880~~	~~10 m~~	~~1m 90%~~
	~~1 x 2160~~	~~10 m~~	~~1m 90%~~
	~~3 x 1440~~	~~10 m~~	~~1m 90%~~
~~All crops (all seeded and transplanted crops)~~	~~2 × 2160~~	~~trigger not reached~~	~~5m 75%~~
	~~2 × 1440~~	~~trigger not reached~~	~~5m 75%~~
	~~1 × 1440~~	~~10m~~	~~1m 90%~~
	~~1 × 1080~~	~~10m~~	~~1m 90%~~
~~Cereals, Oilseeds (pre-harvest) **~~	~~1 x 2160~~	~~trigger not reached~~	~~5m 90%~~
	~~1 × 1440~~	~~trigger not reached~~	~~5m 75%~~
	~~1 × 1080~~	~~trigger not reached~~	~~5m 75%~~
	~~1x 720 g~~	~~10 m~~	~~1m 90%~~
Intended uses	**Application rate (g a.s./ha)**	**Buffer strip (m) without drift reduction**	**Buffer strip (m) with x % drift reduction**
Orchard crops, vine including citrus & tree nuts*	1 x 2880	10 m	1 m-90%
	1 x 2160	10 m	1 m-90%
	3 x 1440	10 m	1 m-90%
All crops (all seeded and transplanted crops)	2 × 2160	trigger not reached	5m-75%
	2 × 1440	trigger not reached	5m-75%
	1 × 1440	10m	1 m-90%
	1 × 1080	10m	1 m-90%
Cereals, Oilseeds (pre-harvest) **	1 x 2160	trigger not reached	5m-75%
	1 × 1440	10m	1 m-90%
	1 × 1080	10m	1 m-90%
	1x 720 g	5m	1 m-75%

Sample comments in document

Conclusion by the Notifiers

Based on the study results the NOAEL in rats after chronic exposure to glyphosate acid for 24 month is 6000 ppm (corresponding to 361 mg/kg bw/day in males and 437 mg/kg bw/day in females). It is concluded that glyphosate technical is not carcinogenic in rats.

RMS comment:

The study is considered acceptable. We agree with the description of the study and its findings and support the conclusions including the NOAEL. It was surprising that the salivary gland findings reported by Milburn (1996, TOX2000-1998) were not confirmed although the study was run in the same laboratory employing rats of the same strain. No further remarks.

1st study: [redacted] 1981

Reference: IIA 5.5.2 05
Report: [redacted] (1981)
A Lifetime Feeding Study
of Glyphosate (ROUNDUP Technical) in Rats
[redacted]
Data owner: Monsanto
Study Project No.: 77-2062
Date: 1981-09-18
not published. TOX2000-595
Guidelines: Not stated: In general accordance with OECD 453 (1981)
Deviations: None
GLP: no
Acceptability: *See RMS comment*

Dates of experimental work: In-life: 1978-07-12 to 1980-09-04

Materials and methods

Test material:
Identification: Glyphosate acid (Round-up technical material)
Description: Fine White powder
Lot Batch #: XHJ-64
Purity: 98.7 % w/w
Stability of test compound: At least 45 days when stored at -20 °C.
Vehicle and/or positive control: Diet

Species: Rat
Strain: Sprague-Dawley CD
Source: [redacted]
Age: 28 days (on delivery). 41 days at initiation of delivery
Sex: Males and females
Weight at dosing: Males: 155.0 – 156.6 g (mean values); females: 136.0 – 138.4 g (mean values)
Acclimation period: 12 days.
Diet Food: Standard laboratory diet (Purina Lab Chow) *ad libitum*. Freshly prepared weekly
Water: Mains automated water system (Elizabethtown Water Company). *ad libitum*
Housing: Individually in elevated stainless steel cages.
Environmental conditions: Temperature: Monitored but values are not stated
Humidity: not stated
Air changes: not stated
12 hours light/dark cycle

In life dates: 12-07-1978 to 04-09-1980

Epidemiology Studies in RAR

2.2 Case–control studies on non-Hodgkin lymphoma, multiple myeloma, and leukaemia

16 studies have been reported in section 2.2 of the IARC monograph and are summarized including comments of the RMS in Table 2.2-1.

Two of these 16 studies did not mention glyphosate ([redacted] 2001, ASB2015-8037 and [redacted] 1990, ASB2013-11501).

Five studies reported no increased risk of non-Hodgkin lymphoma and/or leukaemia or multiple myeloma. ([redacted] 1990, TOX2003-999; [redacted] 1992, ASB2015-7885; [redacted] 2012, ASB2012-11865; [redacted] 2004a, ASB2015-8238, and [redacted] 2009, ASB2012-11985).

Some of the reported studies had according to the IARC assessment in agreement with the RMS assessment a limited or even very limited power to assess effects of glyphosate. In three studies only 4 exposed cases have been compared with 2, 3 or 5 control subjects ([redacted] 2013, ASB2014-7523; [redacted] 1999, ASB2012-11838; and [redacted] 1998, TOX1999-687).

Further studies reported different, contradictory results. Depending from the used method of statistical analysis the risk was increased in some cases or not increased in other cases.

The relevant studies on non-Hodgkin lymphoma have been selected by [redacted] (2014, ASB2014-4819) to perform a meta-analysis. For the analysis of an association between glyphosate and non-Hodgkin lymphoma the following studies have been used: [redacted] 2003, ASB2012-11606; [redacted] 2005a, ASB2012-11605; [redacted] 2008, ASB2012-11614; [redacted] 2002, ASB2012-11839; [redacted] 2001, ASB2011-364, and [redacted] 2009, ASB2012-11985.

Furthermore, for the analysis of an association between glyphosate and B cell lymphoma 2 studies have been used: [redacted] 2008, ASB2012-11614 and [redacted] 2013, ASB2014-7523.

2 of the 6 studies used for the analysis of non-Hodgkin lymphoma reported no increased risk of non-Hodgkin lymphoma ([redacted] 2005a, ASB2012-11605 and [redacted] 2009, ASB2012-11985).

3 of the above cited 7 studies were considered by IARC to have limited or even very limited power ([redacted] 2002, ASB2012-11839 and [redacted] 2013, ASB2014-7523) or a low participation rate ([redacted] 2001, ASB2011-364).

Finally, IARC referred in a publication in Lancet ([redacted] 2015, ASB2015-7076) to 3 studies ([redacted] 2003, ASB2012-11606; [redacted] 2001, ASB2011-364, and [redacted] 2008, ASB2012-11614) in context with the conclusion that there was limited evidence in humans for carcinogenicity of glyphosate. These 3 studies are discussed by RMS in Table 2.2-2.

Questions you might ask
(continued)

- Who reviewed the report at BfR?
  - Unknown
- Who reviewed the study for EFSA?
  - Partially known
  - COI unavailable on most reviewers

Glyphosate Back in the News – Regulation, Revolving Doors, Pesticides & Politics

Posted on 19 March, 2017 by Oliver Moore in Main stories // 1 Comment

By Oliver Moore

The chair of the ECHA committee, Tim Bowmer, worked for two consultancies in the chemical sector for 20 years, including as business development manager and senior account manager. His contract with the organisations ended the day before he started his employment as chair of ECHA's Risk Assessment Committee.

US Congressman Calls for DOJ Investigation into EPA-Monsanto Glyphosate Collusion

Posted on Mar 17 2017 - 3:20pm *by* Sustainable Pulse

« PREVIOUS | NEXT »

Categorized as
Breaking News
News
Sustainable

U.S. Congressman Ted Lieu issued a strongly worded statement this week regarding reports that unsealed court documents raise new
Monsanto weed killer Roundup and its chief ingred

UN/WHO panel in conflict of interest row over glyphosate cancer risk

Chairman of UN's joint meeting on pesticide residues co-runs scientific institute which received donation from Monsanto, which uses glyphosate

EPA Official Accused of Helping Monsanto 'Kill' Cancer Study

Joel Rosenblatt, Lydia Mulvany & Peter Waldman

March 14, 2017, 7:18 PM GMT+1 *Updated on* March 15, 2017, 1:44 AM GMT+1

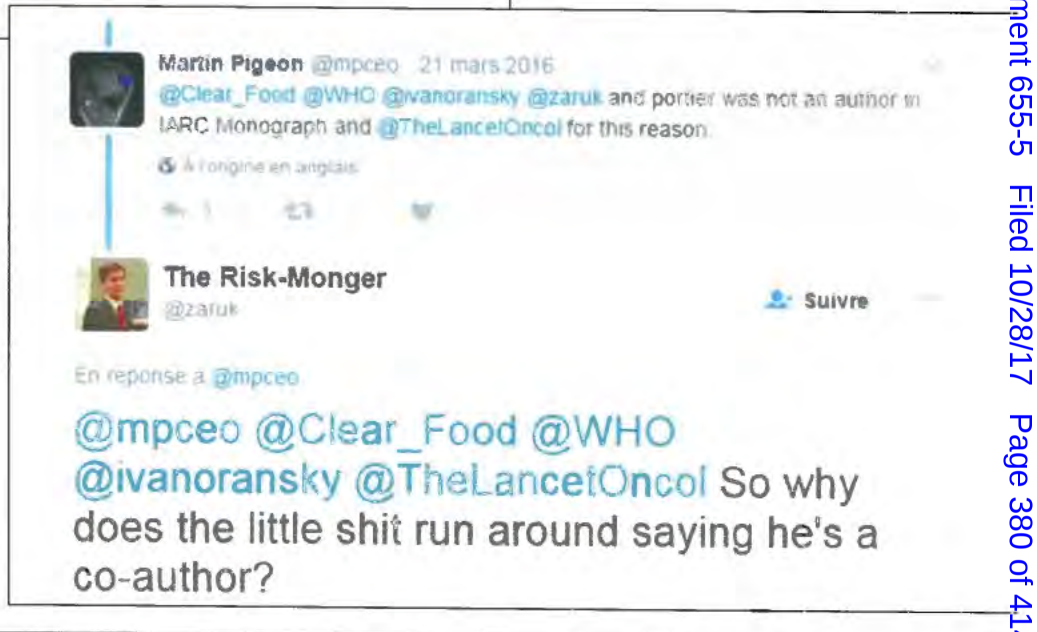
One activist scientist, Christopher Portier, squirreled his way onto an IARC Advisory Committee in 2014, which he then chaired and recommended an IARC study on glyphosate, and t
the technical adviser to that IARC Working Group
WG did what all IARC groups save one have done:
glyphosate was probably carcinogenic. All of this with IARC trying to hide that Portier was acting on behalf of the Washington-based anti-industry NGO – the Environmental Defense Fund.

LAWSUITS

Did Monsanto Hire Online Trolls to Attack Critics?

By Chris Crowley

EDF Official Position: "*Christopher Portier is a part time Senior Contributing Scientist with EDF. He also works on projects unrelated to the issues he works on for EDF. His work with EDF does not extend to glyphosate, and EDF's environmental health work does not focus on herbicides.*"



The Risk-Monger @zaruk · 8 févr.

How the hell did relentless little Chris Portier **worm** his way into ECHA's glyphosate consultation? youtube.com/watch?v=NBapbs... Worse than Waldo!

Questions you might ask

- What do the comments look like?

Experts' consultation 2.5 MSs to discuss the carcinogenicity of glyphosate. See reporting table public consultation 2(21)	**Background** **RAR:** **Vol. 3, B.6.5, Long term toxicity and carcinogenicity**, pp. 443-548 of the revised RAR **Vol. 1, 2.6.6 Summary of long term toxicity and carcinogenicity**, pp. 58-61 of the revised RAR – January 2015 Long-term toxicity and carcinogenicity of glyphosate were investigated in a large number of studies in rats and mice that were performed over the course of time on behalf of different notifiers. All studies previously evaluated in the EU were subject to rigorous re-evaluation for purposes of the RAR including an assessment of their quality and reliability according to current standards. For the new evaluation, five chronic or combined chronic toxicity/carcinogenicity studies in rats and three long-term studies in mice were additionally provided. There was no evidence of carcinogenicity of glyphosate in any of the rat studies. Chronic toxicity was confined to high dose levels in all the studies but remarkable differences became apparent in what was actually observed. In mice, the previously known studies did not provide evidence of carcinogenicity up to the high dose levels tested. The most recent 80-Week dietary mouse study conducted by [redacted] (2009, ASB2012-11492) can be considered very comprehensive with regard to histopathology. There were no adverse effects up to the highest dose level of 5000 ppm, that was equivalent to 810 or 1081 mg/kg bw per day in males and females, respectively. The carcinogenicity study in Swiss albino mice by [redacted] (2001, ASB2012-11491) revealed an increase in malignant lymphoma incidence (quite common in ageing mice) at the top dose level of around 1460 mg/kg bw per day. Malignant lymphoma accounted for 54.6 % of all tumours that were detected in all animals in the study by [redacted] (2001, ASB2012-11491). Malignant lymphoma incidence was significantly elevated as compared to the actual control groups in both sexes, was above the mean values of the (relatively small)	The experts (except BE expressing an uncertainty on this issue because of the lack of in-house HCD for the Wood study and exceedance of HCD in the [redacted] study) consider highly unlikely the carcinogenic potential of glyphosate. However, the background incidences of malignant lymphomas should be further elucidated for the Swiss albino mouse strain in a revised RAR. The reference values are considered to be protective with regard to the dose level where the malignant lymphomas occur. Open point: RMS to present the information available on the background incidences for the Swiss albino strain in a revised RAR.

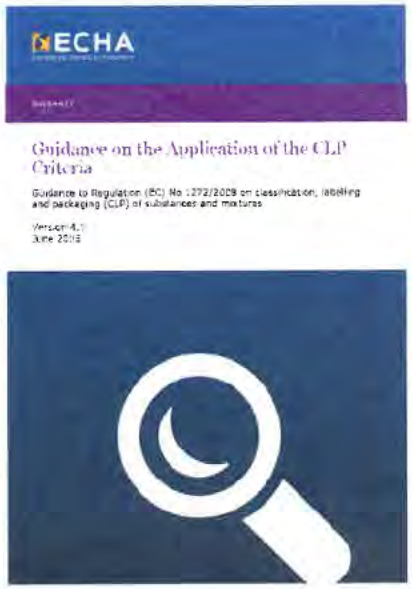
Comments of Norway

1. Cancer in experimental animals

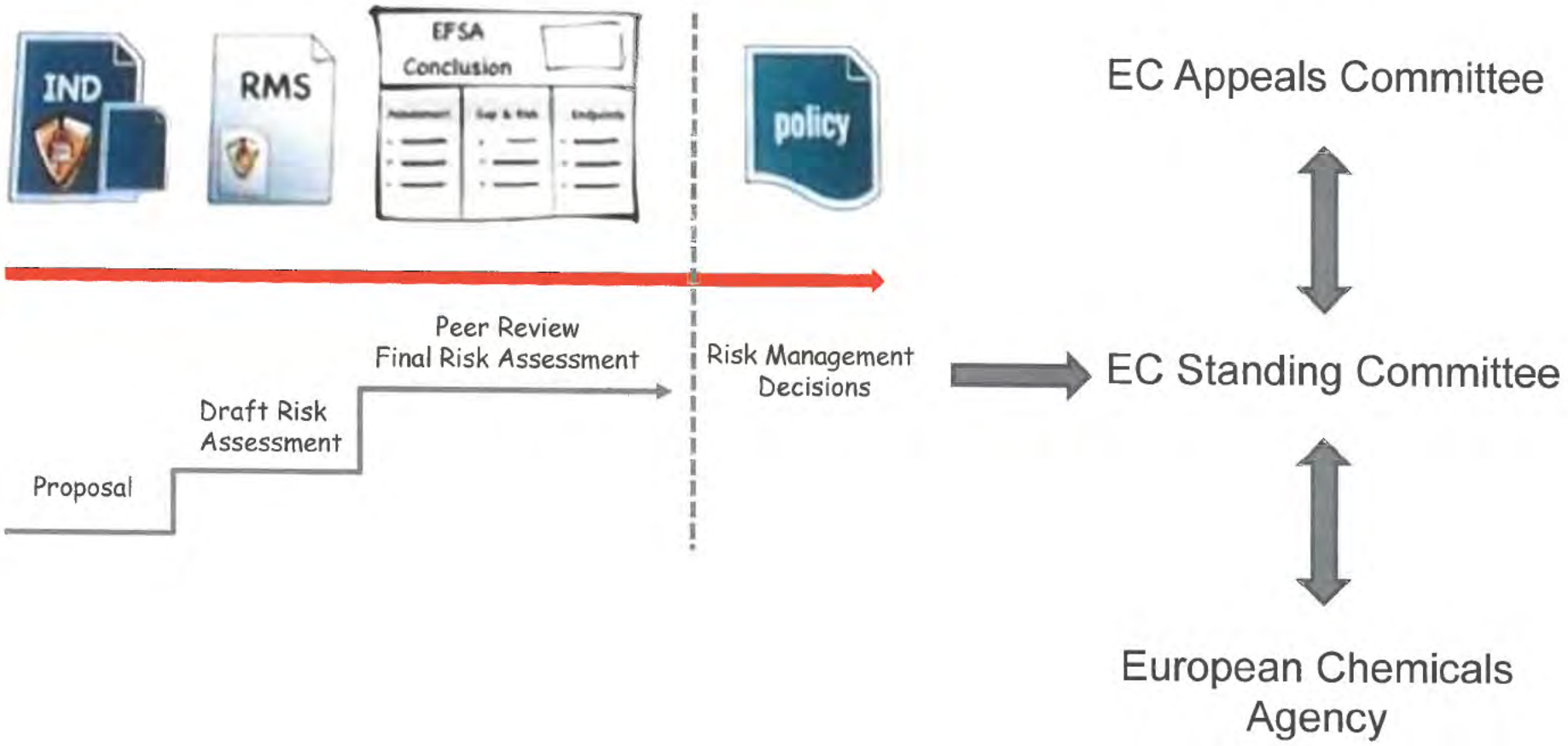
No.	Subject	Discussion Written Procedure	Conclusions Written Procedure
	Addendum 1 to RAR., Cancer in experimental animals, table 3-1	NO: Due to the application of different statistical approaches selected for the evaluation, IARC and RMS came to diverging conclusions. Why does the RMS consider the statistical evaluation provided with the study reports as more appropriate than the trend test used by IARC? According to the OECD guidance document on the conduct and design of chronic toxicity and carcinogenicity studies, significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result.	
	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, page 42	NO: It is stated on page 42 in the addendum that *"Since no consistent significant increase in any of the tumour types was originally reported in the available studies, the apparent effects were not considered sufficient for classification in the RAR."* However, we are of the opinion that effects do not necessarily have to appear in a consistent dose-dependent manner, in order to be considered as a treatment-related effect.	
	Addendum 1 to RAR., Cancer in experimental animals, point iii) differences in decision criteria, additional criteria CLP, page 43	NO: As stated in the addendum, the RMS has also taken into account additional criteria when evaluating the carcinogenic effects. To what extent should these additional criteria and the listed factors which may be taken into consideration, determine the conclusion with respect to a potential carcinogenic effect. In our opinion, too much weight is given to the factors "progression of lesions to malignancy" as well as "whether responses are in single or both sexes". This will for instance implicate that studies, in which a treatment-dependent increase in adenomas in male rats is demonstrated, will not be taken into consideration when evaluating the carcinogenic potential.	

Questions you might ask

- Why did the European Chemical Agency review glyphosate after EFSA?
  - EChA holds legal authority to classify products
  - EChA developed and maintains the guidelines used to evaluate data for carcinogenicity
  - Parliament asked for the review



Pesticide Peer Review in the EU



Glyphosate and Atrazine: EPA posts, then retracts, reports on top herbicide chemicals

Published time: 6 May, 2016 19:42

Get short URL

THE BLOG 05/02/2016 09:20 pm ET | Updated May 03, 2017

What Is Going On With Glyphosate? EPA's Odd Handling of Controversial Chemical

By Carey Gillam

EPA Magically Makes Glyphosate Safety Report Disappear

© Amr Abdallah Dalsh / Reuters

UNI

95% CI=1.03–1.65). Given the limitations of the studies used and uncertainty in the analytical methods, the CARC concluded that a different weighting scheme could have resulted in a different meta risk ratio. Thus, while epidemiologic literature to date does not support a direct causal association, the CARC recommends that the literature should continue to be monitored for studies related to glyphosate and risk of NHL.

MEMORANDUM

DATE: **October 1, 2015**

SUBJECT: **GLYPHOSATE:** Report of the Cancer Assessment Review Committee

Overall, the CARC concluded that there was no evidence of carcinogenicity in the eleven carcinogenicity studies conducted in Sprague Dawley or Wistar rats and CD-1 mice. There were no treatment-related increases in the occurrence of any tumor type in either sex of either species.

FROM: Jess Rowland,
Deputy Division Director
Chair, Cancer Assessment Review Committee
And
Karlyn Middleton, Co-Chair
Cancer Assessment Review Committee
Health Effects Division (7509P)

TO: Charles Smith, Chief,
Risk Assessment Branch I

Kirkland (2013) were not considered by IARC. The CARC, based on a weight-of-evidence of the *in vitro* and *in vivo* studies, concluded that there is no concern for genotoxicity or mutagenicity. Glyphosate was no mutagenic in bacterial reversion (Ames) assays or *in vitro* mammalian gene mutation assays. There is no convincing evidence that glyphosate induces micronuclei formation or chromosomal aberrations *in vitro* or *in vivo*.

O
E
Glyphosate in accordance with the *EPA's Final Guidelines for Carcinogen Risk Assessment* (March, 2005). Attached please find the final Cancer Assessment Document.

Questions you might ask (continued)

and organ/brain weight ratios faile
e administration of Glyphosate.

CONTAINS TRADE SECRET OR CTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY

- Can I see the studies?
  - All epidemiology and journal-published peer-reviewed studies are accessible
  - Industry supported studies only available through petition to EFSA
    - Considered proprietary material
    - You can only have the data tables, NO MATERIALS, NO METHODS, NO ANALYSIS, NO DISUCSSION, NO CONCLUSIONS
    - You cannot share the material, but you can cite it
    - Required the threat of a lawsuit by the Green Party in the European Parliament

CLP Guidance on Carcinogenicity

- Category 1: Known or presumed human carcinogens
  - Category 1A, known to have carcinogenic potential for humans, classification is largely based on human evidence
  - Category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence

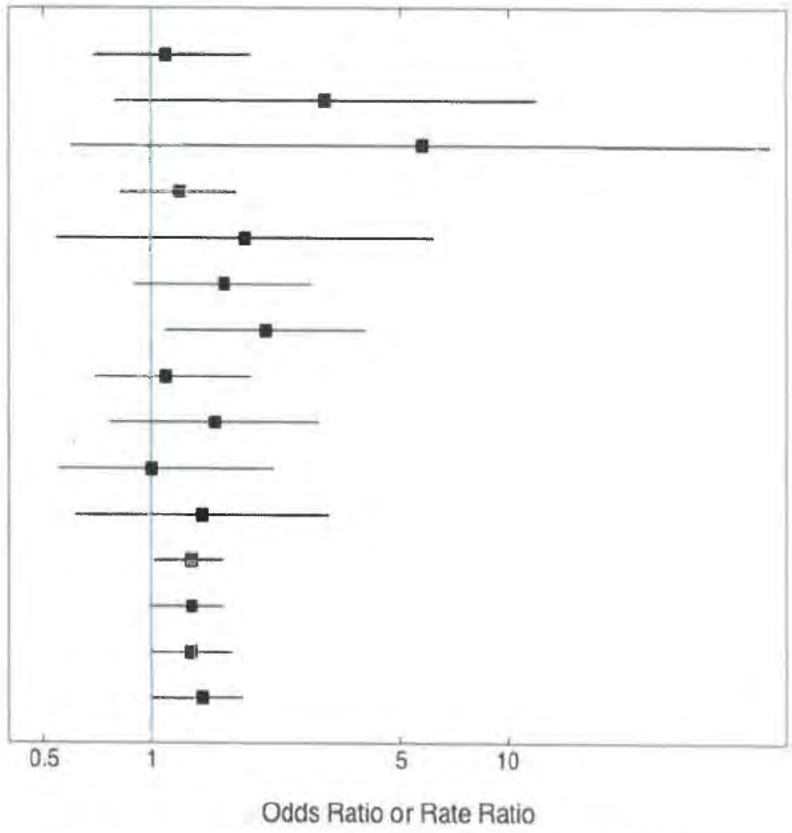
Guidance on the Application of the CLP Criteria, ECHA (2015)

CLP Guidance on Carcinogenicity
(continued)

- The classification in Category 1A and 1B is based on strength of evidence together with additional considerations (see section 3.6.2.2). Such evidence may be derived from:
  - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or
  - animal experiments for which there is sufficient (1) evidence to demonstrate animal carcinogenicity (presumed human carcinogen).
- In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing **limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals**

Epidemiology Data – Non-Hodgkin Lymphoma

Study	RR	Lower	Upper	Weight (Model 1)
Cantor et al. (1992)	1.10	0.70	1.90	0.0
Nordstrom et al. (1998)	3.10	0.80	12.00	0.0
Hardell and Eriksson (1999)	5.80	0.60	54.00	0.0
McDuffie et al. (2001)	1.20	0.83	1.74	38.1
Hardell et al. (2002)	1.85	0.55	6.20	3.6
De Roos et al. (2003)	1.60	0.90	2.80	16.2
logistic regression	2.10	1.10	4.00	0.0
De Roos et al. (2005)	1.10	0.70	1.90	21.0
Eriksson et al., (2008)	1.51	0.77	2.94	11.6
Orsi et al. (2009)	1.00	0.55	2.20	3.6
Hohenadel et al. (2011)	1.40	0.62	3.15	0.0
Meta-Analysis: Model 1	1.30	1.03	1.60	
Meta-Analysis: Model 2	1.30	1.00	1.60	
Meta-Analysis: Model 3	1.30	1.00	1.70	
Meta-Analysis: Model 4	1.40	1.00	1.80	



Limited Evidence of Carcinogenicity

- ECHA: a positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
- IARC: 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.

Human Data Conclusions

EFSA – very limited?

> From the wealth of epidemiological studies, the majority of experts concluded that there is very limited evidence for an association between glyphosate-based formulations and non-Hodgkin lymphoma, overall inconclusive for a causal or clear associative relationship between glyphosate and cancer in human studies. Minority views nevertheless were expressed that there was either inadequate or limited evidence of an association. No evidence of carcinogenicity was confirmed by the large

IARC Working Group – limited evidence

> There is *limited evidence* in humans for the carcinogenicity of glyphosate. A positive association has been observed for non-Hodgkin lymphoma.

Major Tumors in CD-1 Mice

Summary of significance tests for 5 tumors from 4 studies in CD-1 Mice

Study	Months on Study	Neoplasm				
		Hemangio-sarcoma (male)	Hemangi-sarcoma (female)	Malignant Lymphoma (male)	Kidney Tumor (male)	Lung Adeno-carcinoma (male)
Sugimoto 1997	18	+/+++[1]	+++/+++	++/++	+/+++	-/-
Wood 2009	18	-/-	-/-	+++/+++	-/-	++/++
Sugimoto & Wood Pooled		++/+++	+++/+++	+++/+++	++/+++	-/-
Atkinson 1993	24	+++/+++	-/-	+/+	-/-	-/-
Knezevich 1983	24	-/-	NA	-/-	+/++	-/-
Atkinson & Knezevich Pooled		-/-	NA	-/-	++/+	-/-
All CD-1 Studies Pooled		++/++	+++/+++	+/+	+++/+++	-/-

[1]entries are p_{Trend}/p_{Hist} with values: – p>0.1, + 0.1≥p>0.05, ++ 0.05≥p>0.01, +++ p≤0.01

Major Tumors in Rats

Table 8: Summary of significance tests for 5 tumors from 7 studies in Rats

Study	Strain	Neoplasm						
		Liver Adenomas (males)	Mammary Gland Tumors (females)	Thyroid C-Cell Tumors (females)	Thyroid C-Cell Tumors (males)	Thyroid Follicular Cell Tumors (males)	Testis Interstitial Cell Tumors (male)	Kidney Adenomas (males)
Brammer (2001)	Wistar	+++[1]	-					
Wood (2009)		-	+++					
Suresh (1996)		-	-					
Pooled Wistar Rats		++	++					
Lankas (1981)	Sprague Dawley	-		+	-	-	++	-
Enemoto (1997)		-		-	-	-	-	+++
Atkinson et al. (1993)		-		+	-	++	-	-
Stout and Ruecker (1990)		++		-	+	-	-	-
Pooled Sprague-Dawley Rats		++		-	++	-	-	++

[1]entries are p_{Trend}/p_{Hist} with values: – p>0.1, + 0.1≥p>0.05, ++ 0.05≥p>0.01, +++ p≤0.01

Summary

- 18 statistically significant trend tests
  - 11 with $p<0.01$
- 9 positive findings in 4 studies in CD-1 mice
  - 3 tumors seen in more than 1 study
  - 6 tumors with $p<0.01$
- Formal use of historical controls
  - Did not reverse any positive findings against concurrent controls
  - Moved two marginal findings in rare tumors to statistically significant

Sufficient Evidence in Animals

- ECHA
  - 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. A single study in one species and sex might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites
- IARC – exactly the same

Limited Evidence in Animals

- ECHA
  - the data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.
- IARC – exactly the same

Conclusions

EFSA

or limited evidence of an association. No evidence of carcinogenicity was confirmed by the large majority of the experts (with the exception of one minority view) in either rats or mice due to a lack of statistical significance in pair-wise comparison tests, lack of consistency in multiple animal studies and slightly increased incidences only at dose levels at or above the limit dose/MTD, lack of pre-neoplastic lesions and/or being within historical control range. The statistical significance found in trend analysis (but not in pair-wise comparison) *per se* was balanced against the former considerations. During the teleconference 117, the experts also agreed to the conclusion of the RMS.

IARC Working Group

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

So, what is EFSA's criteria for a causal finding in animals?

- Both the trend test and the pair-wise tests significant
- All studies showing the same thing
- Positive results at doses below 1000 mg/kg/day
- Clear dose-response for pre-malignant lesions
- The response must be outside of the historical control range

Is this reasonable?

Use of Historical Controls

- IARC Recommendations
  - Use a formal statistical method
  - *"Generally not appropriate to discount a tumor response that is statistically significantly increased in comparison to concurrent controls by arguing it falls within the range of concurrent controls"*
  - Can be used for rare tumors

Using Historical Control Range

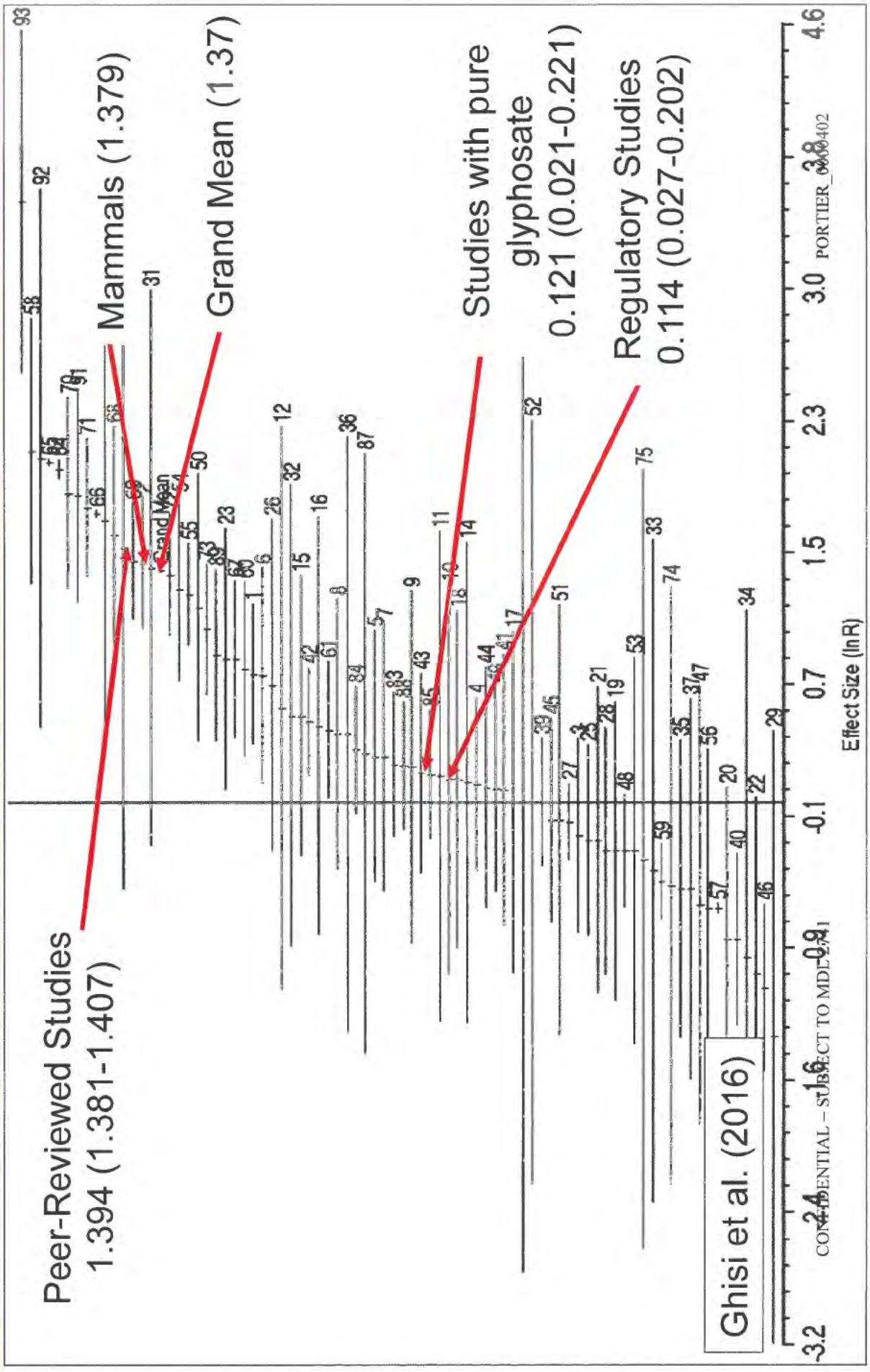
- Not a formal statistical test
- Range increases with number of historical control groups
- Animals in a cancer study are randomized to groups
  - Anything that would serve to alter concurrent control response also applies to treated groups

Summary of in vivo and in vitro genetox studies of glyphosate and glyphosate formulations in mammals[1]

In vivo or in vitro	Species	Cell type or tissue	Glyphosate[2]		Glyphosate Formulations	
			Number Positive	Number Negative	Number Positive	Number Negative
In vivo	Humans	Peripheral blood			2	1
in vitro	Humans	lymphocytes	5	2(1)	2	
		Hep 2	1			
		GM 38 HT1080	1			
		GM 5757	1			
		TR146	1		1	
In vivo	Swiss CD-1 Mouse	Liver/Kidney	1	1	2	
In vivo (micro-nucleus assay)	NMRI mouse	Erythrocytes		4(3)		2(1)
	Swiss CD-1 mouse		1		2	
	Balb C mouse		1			
	$B6C3F_1$ mouse			1		
	Swiss mouse		1(1)			3(2)
	CD-1 mouse		2(2)	1(1)	2 (2)	6 (6)
	Swiss albino mouse		1(1)	3(3)	1	
	C57BL mouse					1
	Mouse (not specified)				1	
	Rats (all)			2(1)		1(1)
In vitro	Mouse	L5178 lymphoma		2(2)		
	Chinese hamster	Lung		3(3)		
	Chinese hamster	ovary	1	1		
	Fischer rat	liver		1		
	Rat	Lymphocytes		1(1)		
	Bovine	Lymphocytes	1		2	

[1]each entry in the table corresponds to a single study where a study is positive if at least one valid positive finding emerged from the study $p<0.05$; entries in the table are only for studies where data was available to review including data from EFSA[88] and Kier and Kirkland (2000)[74]; [2]numbers are the total number of studies in this category, numbers in parentheses are the subset of studies that are regulatory studies

Forest Plot of Micronucleus Frequency



Green MEP: EFSA should release full glyphosate studies

By Nicole Sagener | EURACTIV.de | translated by Sam Morgan

May 2, 2017

Adverti

Is seeing the studies important?

Tumors with significant ($p<0.05$) trends in the carcinogenicity studies not cited in the EFSA and EChA Risk Assessments

Study (Species)	Tumor type Sex; Incidences	p-value (one-sided)	Test method
Sugimoto, 1997 (Mouse)	Total number of animals with malignant neoplasms	< 0.01	Pair-wise, Fisher's Exact Test (high dose)
	Males; 5/50, 5/50, 11/50, 16/50	0.004	Trend test
Wood et al., 2009 (Mouse)	Lung adenocarcinomas		
	Males; 5/51, 5/51, 7/51, 11/51	0.038	Trend test
Atkinson et al., 1993 (Rat)	Thyroid follicular cell adenomas and carcinomas	0.036	Trend test
	Males; 0/50, 0/21, 0/17, 2/21, 2/49		
Suresh, 1996 (Rat)	Thyroid c-cell Carcinomas		
	Females; 1/47, 0/49, 2/50, 6/47	0.003	Trend test
Enomoto, 1997 (Rat)	Kidney adenoma		
	Males; 0/50, 0/50, 0/50, 4/50	0.004	Trend test
Brammer, 2001 (Rat)	Hepatocellular Adenoma		
	Males; 0/52, 2/52, 0/52, 5/52	0.009	Trend test
Wood et al., 2009 (Rat)	Skin Keratocanthoma		
	Males; 2/51, 3/51, 0/51, 6/51	0.034	Trend test
Wood et al., 2009 (Rat)	Mammary gland adenocarcinomas		
	Males; 2/51, 3/51, 1/51, 6/51	0.046	Trend test

Current Events

Monsanto Weed Killer Roundup Faces New Doubts on Safety in Unsealed Documents

By DANNY HAKIM MARCH 14, 2017

The court documents included Monsanto's internal emails and email traffic between the company and federal regulators. The records suggested that Monsanto had ghostwritten research that was later attributed to academics and indicated that a senior official at the Environmental Protection Agency had worked to quash a review of Roundup's main ingredient, glyphosate, that was to have been conducted by the United States Department of Health and Human Services.

Go after the Funding

NIH needs public examination after giving millions to rogue UN agency

BY BRUCE M. CHASSY, CONTRIBUTOR - 10/24/16 12:32 PM EDT

POLITICS

Exclusive: U.S. lawmakers to investigate funding of WHO cancer agency

ACC begins campaign to change basis of UN cancer agency classifications

Current hazard-based approach 'misinforms policy making', says trade group

26 January 2017 / Toxicology, United States

The American Chemistry Council has launched a campaign aimed at reforming the monographs programme of the International Agency for Research on Cancer (Iarc) – a specialised agency of the World Health Organization.

International Agency for Research on Cancer

World Health Organization

The ACC describes its "campaign for accuracy in public health research" as "an initiative to promote credible, unbiased and transparent science as the basis of public policy decisions."

Take Home Messages

- Transparency is necessary
- Guidelines should be peer-reviewed and applied uniformly
- Proper statistical methods need to be applied and understood
- The format for the final evaluation needs better structure
- Data needs to be submitted electronically so re-analysis is possible
- Don't label me as a "Facebook Scientist" or a "little shit"

C. Portier Consultations

< 2015 >

Organisation not currently on the register; registration as it was on 21 Dec 2015

How to read and use (/how-to#data-cards) this data card.

This representative is currently not registered.

LOBBYING COSTS:

NO FIGURE AVAILABLE

Financial year: -

LOBBYISTS DECLARED:

0.25 FTE (1)

0.25

LOBBYISTS WITH EP ACCREDITATION: **0**

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Registration on EU Transparency Register

346450820048-50 (http://ec.europa.eu/transparencyregister/public/consultation/displaylobby id=346450820048-50) (First registered: 21 Dec 2015)

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Issues

Reregistration of the pesticide glyphosat

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Website development: nestor.coop (http://nestor.coop)

Growing Returns

A coalition of uncommon bedfellows is bringing sustainable agriculture to scale

By Suzy Friedman | Bio | Published: August 31, 2016

Today represents a huge advancement for sustainable agriculture, and a new era of food company collaboration. At the Farm Progress Show in Boone, Iowa, we are officially launching the Midwest Row Crop Collaborative (MRCC): a diverse coalition working to expand on-the-ground solutions to protect air and water quality, enhance soil health, and maintain high yields throughout the Upper Mississippi River Basin.

Founding members of the MRCC include Cargill, Environmental Defense Fund, General Mills, Kellogg Company, Monsanto, PepsiCo, The Nature Conservancy, Walmart, and World Wildlife Fund. The coalition will work directly with growers to help foster continuous improvement and implement conservation activities across three pilot states responsible for 44 percent of corn, soy, and wheat production in the United States: Illinois, Nebraska, and Iowa.

Clear goals and benefits

Along with a council of scientific and agronomic advisors, the MRCC has set the following goals:

- By 2025, 75 percent of row crop acres in the region will be engaged in sustainability measures that will advance Field to Market's Fieldprint Calculator analyses and improve soil health practices.
- By 2025, the region will reduce nutrient loading (primarily nitrogen and phosphorus) by 20 percent as a milestone to meet the Gulf of Mexico Hypoxia Task Force goal of a 45 percent reduction.
- By 2035, these three states will have met the 45 percent nutrient loss reduction goal and the Collaborative will be set up to expand across the Upper Mississippi River Basin.

Additionally, the MRCC will work to ensure that by 2025, 50 percent of all irrigation units used in Nebraska will maximize water conservation to reduce pressure on the Ogallala Aquifer.

Accomplishing these goals will result in clear environmental benefits: improved water quality, reduced eutrophication and greenhouse gas emissions, and restored groundwater in the Ogallala Aquifer, which provides water to about 20 percent of U.S. cattle, corn, cotton and wheat.

But the benefits expand to businesses and farmers, too, by improving yields, protecting against supply chain disruptions, and meeting consumer demand for sustainably grown ingredients.

Field to Market®
The Alliance for Sustainable Agriculture

Partnerships and measurements

Farmer organizations, environmental groups, food companies, state and local watershed organizations, and many others share these common goals – and much work is already underway to meet the MRCC's objectives.

That's why the Collaborative isn't reinventing any wheels. We're ramping up, leveraging and supporting the various technical and regional sustainability efforts already in place. Forging partnerships with farmers, who are at the core of MRCC, is absolutely essential to eliminate redundant efforts across various organizations and collaborators.

Some of the ongoing efforts to support farmers include:

- Collaborating with the National Corn Growers Association's Soil Health Partnership, which is identifying, testing and measuring farm management practices that improve soil health and benefit farmers.
- Establishing a Sustainable Agriculture Resource Center for farmers and trusted advisors that lays out the business advantages of sustainability – a key selling point for ag retailers, crop consultants, and farmers. Field to Market, The Alliance for Sustainable Agriculture, and the Agricultural Retailers Association will facilitate this initiative.
- Partnering with two existing Regional Conservation Partnership Program projects to improve the management of grower data and the metrics used to track environmental outcomes, as well as support conservation practices.

We're also applying the best available science and technologies to ensure that we're accurately measuring our on-the-ground environmental and yield benefits.

More work ahead

The MRCC is groundbreaking, since major companies have never before committed to ag sustainability at such a large scale. But it's also just a beginning. To keep momentum going for the MRCC and to make this effort a real success, we'll need many more partnerships with agribusinesses and trade groups, additional commitments from food companies, and we'll need every sector of the ag supply chain to get involved.

Related:

How Smithfield's landmark climate goal benefits farmers and the planet >>

Want to bring ag sustainability to scale? Collaboration, not confrontation. >>

GENETIC LITERACY PROJECT
SCIENCE TRUMPS IDEOLOGY
geneticliteracyproject.org

Monsanto joins Environmental Defense Fund, others in sustainable agriculture coalition

Suzy Friedman | September 1, 2016 | Environmental Defense Fund

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- By 2025, the region will reduce nutrient loading (primarily nitrogen and phosphorus) by 20 percent . . .

. . . .

Accomplishing these goals will result in . . . improved water quality, reduced eutrophication and greenhouse gas emissions, and restored groundwater in the Ogallala Aquifer. . .

The GLP aggregated and excerpted this blog/article to reflect the diversity of news, opinion and analysis. Read full, original post: A coalition of uncommon bedfellows is bringing sustainable agriculture to scale