

November 27, 2015

Mr. Vytenis Andriukaitis  
Commissioner Health & Food Safety  
European Commission  
Rue de la Loi / Wetstraat 200  
1049 Brussels  
Belgium

Cc: (email only)

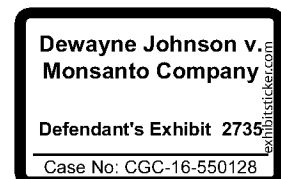
Mr. Phil Hogan, European Commissioner for Agriculture and Human  
Development  
Dr. Ladislav Miko, Deputy Director-General, DG Health & Food Safety  
Dr. Bernhard Url, Executive Director, EFSA  
Dr. Giovanni La Via, Chair, ENVI Committee  
EFSA Panel on Plant Protection Products and their Residues  
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

**Open letter: Review of the Carcinogenicity of Glyphosate by EFSA and BfR**

Dear Commissioner Andriukaitis,

We are a group of independent academic and governmental scientists from around the world who have dedicated our professional lives to understanding the role of environmental hazards on cancer risks and human health. 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<sup>[1]</sup> that the widely used herbicide, glyphosate “is unlikely to pose a carcinogenic hazard to humans.” We ask that you forward the letter to the representatives of all EU member states before the next meeting of the Standing Committee on Plants, Animals, Food and Feed (December 10/11).

The EFSA decision, based upon the Renewal Assessment Report<sup>[2]</sup> provided by the German Federal Institute for Risk Assessment (BfR), runs counter to the finding earlier this year by the International Agency for Research on Cancer (IARC), the highly respected cancer arm of the World Health Organization that glyphosate is a *probable human carcinogen*. This IARC classification is based on a comprehensive assessment of the peer-reviewed toxicologic and epidemiologic literature undertaken over a 12-month period by a Working Group of 17 independent expert scientists. The IARC review linked glyphosate to dose-related increases in malignant tumors at multiple anatomical sites in experimental animals and to an increased incidence of non-Hodgkin lymphoma in exposed humans.



We reviewed these two differing decisions on the human carcinogenicity of glyphosate and conclude that the IARC WG decision is by far the more credible. The IARC WG decision was reached relying on open and transparent procedures by independent scientists who completed thorough conflict-of-interest statements and were not affiliated or financially supported in any way by the chemical manufacturing industry. It is fully referenced and depends entirely on reports published in the open, peer-reviewed biomedical literature. It is part of a long tradition of deeply researched and highly credible reports on the carcinogenicity of hundreds of chemicals issued over the past four decades by IARC and used today by international agencies and regulatory bodies around the world as a basis for risk assessment, regulation and public health policy.

In contrast, the BfR decision is not credible because it is not supported by the evidence and it was not reached in an open and transparent manner.

Accordingly, we urge you and the European Commission to disregard the flawed EFSA finding on glyphosate in your formulation of glyphosate health and environmental policy for Europe and to call for a transparent, open and credible review of the scientific literature.

### **The IARC Working Group Decision**

The International Agency for Research on Cancer (IARC) Monographs Programme identifies environmental causes of cancer in humans and has evaluated more than 950 agents since 1971. The Monographs Programme evaluates chemicals, drugs, mixtures, occupational exposures, lifestyles and personal habits, physical agents and biological agents. Monographs are written by an ad hoc Working Group (WG) of international scientific experts over a period of about 12 months ending in an eight-day meeting. The WG evaluates all of the publically-available scientific literature on a given substance and, through a transparent and rigorous process<sup>[3]</sup>, reaches a decision on the degree to which the scientific evidence supports that substance's ability to cause or not cause cancer.

For Monograph 112<sup>[4]</sup>, 17 expert scientists evaluated the carcinogenic hazard for 4 insecticides and the herbicide glyphosate<sup>[5]</sup>. The WG concluded that the data for glyphosate meets the criteria to be identified as a *probable human carcinogen*. This finding stirred great debate globally on the safety of glyphosate and led to a careful evaluation by numerous agencies of the IARC monograph results when they became available on July 29, 2015.

### **The BfR Addendum**

In October, 2015, the EFSA reported<sup>[1]</sup> on their evaluation of the Renewal Assessment Report<sup>[2]</sup> (RAR) for glyphosate. EFSA concluded that "glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential". Addendum 1 (the BfR Addendum) of the RAR<sup>[2]</sup> discusses the scientific rationale for differing from the IARC WG conclusion.

We have serious concerns with regard to the scientific evaluation in the BfR Addendum and feel that it is misleading regarding the potential for a dose-dependent carcinogenic hazard from exposure to glyphosate. Since the BfR Addendum is the basis for the European Food Safety Agency (EFSA) conclusion<sup>[1]</sup>, it is critical that we express these concerns. We are also concerned about some of the implications of the BfR Addendum regarding the use of human data in identifying carcinogenic hazards.

Our comments to the BfR Addendum will focus on the human evidence, the animal laboratory evidence and the mechanistic evidence.

### **The Human Evidence**

The BfR agrees with the IARC WG that there is “*limited evidence* in humans for the carcinogenicity of glyphosate”. In the IARC review process, *limited evidence* is assigned if “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.”<sup>[3]</sup> The EFSA conclusion that “glyphosate is unlikely to pose a carcinogenic hazard to humans” is inappropriate when available data support the determination of *limited evidence* of carcinogenicity in humans. The BfR Addendum (p. ii) characterizes the IARC interpretation as “precautionary” and that the BfR takes a more “cautious view” of this classification because “no consistent positive association was observed”, “the most powerful study showed no effect” and that the studies “could not differentiate between the effects of glyphosate and the co-formulants”. We will consider the first two arguments here and discuss the third argument at the end of this letter.

The finding of *limited evidence* by the IARC WG was for non-Hodgkin lymphoma (NHL). High-quality cohort studies are particularly valuable for determining the carcinogenicity of an agent because their design can facilitate exposure assessment and reduce the potential for certain biases. The Agricultural Health Study<sup>[6]</sup> (AHS) was the only cohort study available providing information on the carcinogenicity of glyphosate. The study had a null finding for NHL (RR 1.1, 0.7-1.9) with no apparent exposure response in the results. The BfR refers to this study as “the most powerful study” and notes that it was “negative” for NHL.

Several potential limitations of case-control studies are laid out in epidemiology textbooks<sup>[7, 8]</sup>. The BfR uses these limitations to label all of the case-control studies as unreliable. This gives the impression that all of the studies are equal in quality and unusable for an overall evaluation. This is not the case: well-designed case-control studies are recognized as an efficient alternative to cohort studies<sup>[8]</sup>. An IARC WG carefully evaluates all of the available epidemiology data, looking at the study’s strengths and weaknesses. This is key to determining whether the positive associations seen in case-control studies are a reliable indication of an association or simply due to chance or methodological flaws. To provide a reasonable interpretation of the findings, an evaluation needs to properly weight studies according to their quality rather than simply count the number of positives and negatives. The meta-analyses cited in the IARC Monograph<sup>[9]</sup> and done by the WG

are excellent examples of an objective evaluation of the existence of a consistent positive association; both meta-analyses showed a statistically significant association. The BfR provided no justification for their evaluation of “no consistent positive association”. Finally, despite the potential advantages of prospective cohort studies versus case-control, there are fewer cases to include in analyses, depending on the follow-up time resulting in limited statistical power. There were only 92 NHL cases included in the AHS unadjusted analysis and fewer in adjusted analyses, compared to 650 in a pooled case-control analysis from the United States<sup>[10]</sup>.

The final BfR conclusion (p. 21) that “there was no unequivocal evidence for a clear and strong association of NHL with glyphosate” is misleading. IARC, like many other groups, uses three levels of evidence for human data<sup>[3]</sup>. *Sufficient evidence* means “that a causal relationship has been established” between glyphosate and NHL. IARC does not state that the evidence is *sufficient*. BfR concludes that the IARC designation of *limited evidence* was not applicable because there was not “an unequivocal and consistent excess”. In fact, that is the equivalent to the criteria for *sufficient evidence*, not *limited evidence*. Thus BfR’s conclusion is equivalent to concluding there is not *sufficient evidence*. Legitimate public health concerns arise when “causality is credible”, i.e., when there is *limited evidence*. BfR’s language is misleading and not internationally acceptable and thus fails to meet EC Guidelines.

### **Evidence from Animal Carcinogenicity Studies**

We find the conclusions of the BfR regarding the animal carcinogenicity data to be scientifically unacceptable. The IARC WG review found a significant positive trend for renal tumors in CD-1 mice<sup>[11]</sup>, a rare tumor although no comparisons of any individual exposure group to the control group were statistically significant. A significant positive trend means that the pattern seen in the data supports an increasing risk with increasing dose. The WG also identified a significant positive trend for hemangiosarcoma in male CD-1 mice<sup>[12]</sup>, again with no individual exposure group significantly different from controls. Finally, the WG also saw a significant increase in the incidence of pancreatic islet cell adenomas in two studies in Sprague-Dawley rats<sup>[13-15]</sup>. In one of these rat studies, thyroid gland adenomas in females and liver adenomas in males were also increased. Thus, glyphosate was positive for malignant tumors in both of the mouse studies examined and for benign tumors in two of the five rat studies examined. By the IARC review criteria<sup>[3]</sup>, the evidence in the mouse constitutes *sufficient evidence* in animals and the increased incidences of benign tumors constitutes additional support.

The BfR agreed, stating (p. 43) “it is obvious that IARC concludes on “*sufficient evidence* of carcinogenicity” because the above criteria for this conclusion are fully met.” The IARC WG reached this conclusion using data that were publicly available in sufficient detail for independent scientific evaluation (a requirement of the IARC Preamble<sup>[3]</sup>). Based on the BfR Addendum, it seems there were three additional mouse studies and two additional rat studies that were unpublished but available for review. BfR reported on two additional studies with a positive trend for renal tumors, one in CD-1 mice<sup>[16]</sup>, and one in Swiss-Webster mice<sup>[17]</sup>. One of these studies<sup>[16]</sup> also reported a positive trend for hemangiosarcoma. Moreover, BfR reported two studies in CD-1 mice showing significant trends for malignant

lymphoma<sup>[16,18]</sup>. For all of the mouse tumors described above, a positive trend was seen against the concurrent control.

However, in all studies in CD-1 mice, including those reviewed by the IARC, the BfR dismisses the observed trends in tumor incidence because there are no individual treatment groups that are significantly different from controls and because the maximum observed response is reportedly within the range of the historical control data (Table 5.3-1, p. 90). Care must be taken in using historical control data to evaluate animal carcinogenicity data. In virtually all guidelines<sup>[3,19]</sup>, scientific reports<sup>[20]</sup> and publications<sup>[21-23]</sup> on this issue, the recommended first choice is the use of the concurrent controls. For instance, the Preamble to the IARC Monographs states, "it is generally not appropriate to discount a tumor response that is significantly increased compared with concurrent controls by arguing that it falls within the range of historical controls...". When using historical control data, they should be from studies in the same timeframe, for the same exact animal strain, preferably from the same laboratory or the same supplier and preferably reviewed by the same pathologist<sup>[19]</sup>. This was not the case for the historical control database used by BfR. One of the mouse studies<sup>[11]</sup> was clearly done before this historical control database was developed, one study<sup>[16]</sup> used Crj:CD-1 mice rather than Crl:CD-1 mice, and one study<sup>[12]</sup> did not specify the substrain and was reported in 1993 (probably started prior to 1988); hence only a single study<sup>[18]</sup> used the same mouse strain as the historical controls, but was reported more than 10 years after the historical control dataset was developed. Interestingly, the historical control data used by the BfR<sup>[24]</sup> was from studies in seven laboratories using the Charles River Laboratory CD1 mice. It is important to note that there is a second report<sup>[25]</sup> by the same authors with a larger control database using the same mouse strain from 11 laboratories over the same time period (1987-2000) showing very different results. For example, the 2000 publication<sup>[24]</sup> shows five and four studies out of 46 with renal adenomas (no more than two in any one study) and renal adenocarcinomas (one in each study) respectively whereas the 2005 report<sup>[25]</sup> shows only one study each out of 54 studies with a single renal adenoma and a single renal adenocarcinoma; all other studies had no renal tumors.

Given this evidence, it is clear that BfR differed from standard scientific practices in order to reach their conclusions. BfR reported seven positive mouse studies with three studies showing increases in renal tumors, two with positive findings for hemangiosarcomas, and two with positive findings for malignant lymphomas. BfR additionally reported two positive findings for tumors in rats. Eliminating the inappropriate use of historical data, the unequivocal conclusion is that these are not negative studies, but in fact document the carcinogenicity of glyphosate in laboratory animals.

### **Mechanistic Information**

The BfR Addendum dismisses the WG finding that "there is strong evidence that glyphosate causes genotoxicity" by suggesting that unpublished evidence not seen by the IARC WG was overwhelmingly negative and that, since the studies that were reviewed were not done under guideline principles, they should get less weight. To maintain transparency, IARC reviews only publicly available data. Thus the use of confidential data submitted to the BfR makes it impossible for any scientist not associated with BfR to review this conclusion with scientific

confidence. Further skewing their interpretation, the BfR did not include evidence of chromosomal damage from exposed humans<sup>[24]</sup> that was highlighted in the IARC Monograph.

The BfR confirms (p. 79) that the studies evaluated by the IARC WG on oxidative stress were predominantly positive but does not agree that this is strong support for an oxidative stress mechanism. They minimize the significance of these findings predominantly because of a lack of positive controls in some studies and because many of the studies used glyphosate formulations and not pure glyphosate. The WG concluded that (p. 77) “Strong evidence exists that glyphosate, AMPA and glyphosate-based formulations can induce oxidative stress”. From a scientific perspective, these types of mechanistic studies can play a key role in distinguishing between the effects of mixtures, pure substances and metabolites and we encourage the BfR to carefully review this science.

Finally, we strongly disagree that data from studies published in the peer-reviewed literature should automatically receive less weight than guideline studies. Once a chemical or its formulations are on the market, the majority of the research done on these chemicals will be done by research laboratories using various models to address specific issues related to toxicity that will often not have testing guidelines associated with them. These peer-reviewed and published findings have great value in understanding mechanisms of carcinogenicity and should be given appropriate weight in an evaluation based on study quality and not just guideline rules.

### **General Comments**

Science moves forward based on data, careful evaluation of those data and a rigorous review of the findings and conclusions. One important aspect of this process is transparency and the ability to question or debate the findings of others. This ensures the validity of the results and provides a strong basis for decisions. Many of the aspects of transparency do not exist for the RAR<sup>[2]</sup> or the BfR Addendum. For example, citations for almost all of the references, even those from the open scientific literature, have been redacted from the document. The ability to objectively evaluate the findings of a scientific report requires a complete list of the cited supporting evidence. As another example, there are no authors or contributors listed for either document, a requirement for publication in virtually all scientific journals. This is in direct contrast to the IARC WG evaluation listing all authors, all publications and public disclosure of pertinent conflicts of interest prior to the WG meeting<sup>[26]</sup>.

A second important aspect of the scientific process is a careful evaluation and analysis of the facts. Several guidelines have been devised for analyzing carcinogenicity data, most after consultation with scientists from around the world. One of the most widely used guidelines is the OECD guidance on the conduct and design of chronic toxicity and carcinogenicity studies<sup>[19]</sup> which is cited in the BfR Addendum. This OECD guidance is in contradiction to the methods used by the BfR for both historical controls and for trend analysis; the two reasons given by the BfR for dismissing these data. Thus, BfR uses the

concept of testing guidelines to exclude substantive scientific evidence from their risk assessment and ignore OECD guidelines in addressing the important issues of historical controls and trend analyses.

Due to the potential public health implications of this extensively used pesticide it is essential that all scientific evidence be freely available, reviewed openly in an objective manner, and that financial support, conflicts of interest and affiliations of authors be fully disclosed. Many aspects of the evaluation conducted by the BfR and EFSA do not meet this fundamental objective criteria and raise significant questions of validity.

## Summary

The IARC WG concluded that glyphosate is a “probable human carcinogen” putting it into IARC category 2A due to *sufficient evidence* of carcinogenicity in animals, *limited evidence* of carcinogenicity in humans and *strong* mechanistic data.

- The IARC WG found an association between non-Hodgkin lymphoma and glyphosate based on the available human evidence.
- The IARC WG found significant carcinogenic effects in laboratory animals for two tumor types in two mouse studies and benign tumors in two rat studies.
- Finally, the IARC WG concluded strong evidence of genotoxicity and oxidative stress for glyphosate, entirely from publicly available research, including findings of DNA damage in the peripheral blood of exposed humans.

In their RAR, BfR concluded (Vol. 1, p. 160) “classification and labeling for carcinogenesis is not warranted” and “glyphosate is devoid of genotoxic potential”.

- BfR agreed with the IARC on *limited evidence* in humans but then dismissed the association as “insufficiently consistent” with no justification.
- Using an inappropriate historical control dataset in an incorrect manner and ignoring established OECD guidelines cited in their report, BfR dismissed evidence of renal tumors in 3 mouse studies, hemangiosarcoma in 2 mouse studies and malignant lymphoma in 2 mouse studies. Thus, BfR incorrectly discarded all of the glyphosate-induced carcinogenic findings in animals as chance occurrences.
- The BfR ignored important laboratory and human evidence of genotoxicity.
- The BfR confirmed that glyphosate induces oxidative stress and dismissed this finding for lack of any other finding because they had dismissed all of the other evidence.

The most parsimonious scientific explanation of the cancers seen in humans and laboratory animals supported by the mechanistic data is that glyphosate is a *probable* human carcinogen. On the basis of this conclusion and in the absence of

contrary evidence, it is reasonable to conclude that glyphosate formulations should also be considered probable human carcinogens.

We believe that the arguments promoted by the BfR to negate the human, animal and mechanistic evidence are fundamentally and scientifically flawed and should be rejected. We strongly object to the almost non-existent weight given to studies from the literature by the BfR and the strong reliance on non-publicly available data in a limited set of assays that define the minimum data necessary for the approval of a pesticide. We believe that the IARC WG evaluation of *probably carcinogenic to humans* accurately reflects the results of the published scientific literature on glyphosate and, on the face of it, the unpublished studies to which the BfR refers. Conversely, the BfR evaluation, and consequently the EFSA evaluation, do not reflect the available science.

Thus, repeating our earlier request, we urge you and the European Commission to disregard the flawed EFSA finding on glyphosate in your formulation of glyphosate health and environmental policy for Europe and to call for a transparent, open and credible review of the scientific literature.

**The views expressed in this letter are the opinion of the scientists who are listed below and DO NOT imply an endorsement or support for these opinions by any organizations to which they are affiliated.**

Sincerely,

Prof. Christopher J. Portier (Corresponding Author)  
Senior Contributing Scientist, Environmental Defense Fund, Washington, DC  
Visiting Professor, Maastricht University, Maastricht, The Netherlands  
Adjunct Professor, Emory University, Atlanta, Georgia, USA  
Honorary Professor, University of Queensland, Brisbane, Queensland, Australia  
Former Director, National Center for Environmental Health, Atlanta, USA  
Former Director, Agency for Toxic Substances and Disease Registry, Atlanta, USA  
Former Associate Director, US National Toxicology Program, RTP, NC, USA  
CH-3600 Thun, Switzerland



Bruce Armstrong MBBS, DPhil(Oxon), FFAPHM, FAA  
Emeritus Professor  
Sydney School of Public Health  
The University of Sydney, Australia

Distinguished Professor Bruce C Baguley  
Auckland Cancer Society Research Centre  
The University of Auckland  
Auckland, New Zealand

Prof. Dr. med. Xaver Baur  
Institute for Occupational Medicine



Charité University Medicine Berlin  
14195 Berlin , Germany

Igor Beliaev, PhD, DrSc  
Associate Professor of Genetic Toxicology  
Head, Laboratory of Radiobiology  
Cancer Research Institute  
Slovak Academy of Science  
Bratislava, Slovak Republic  
and  
Professor, Laboratory of Radiobiology  
Department of Ecological and Medical Problems  
Prokhorov General Physics Institute  
Russian Academy of Science  
Moscow, Russia

Professor Robert Bellé  
Laboratoire de Biologie intégrative des modèles marins (UMR 8227, CNRS-  
UPMC)  
Université Pierre et Marie Curie  
Station Biologique  
29680 Roscoff France

Dr. Fiorella Belpoggi  
Director  
Cesare Maltoni Cancer Research Center  
Ramazzini Institute  
40010 Bentivoglio (Bologna), Italy

Prof. Annibale Biggeri  
Director Biostatistics Unit  
Institute for Cancer Prevention and Research  
Department of Statistics Computer Science Applications "G. Parenti"  
University of Florence, Italy

Maarten C. Bosland, DVSc, PhD  
Professor of Pathology  
Department of Pathology  
College of Medicine  
University of Illinois at Chicago  
Chicago, IL 60612 USA

Prof. Paolo Bruzzi MD, MPH, PhD  
Director, Unit of Clinical Epidemiology  
National Cancer Research Institute  
San Martino – IST Hospital  
Genoa ITALY

Prof. Dr. Lygia Therese Budnik

University of Hamburg, Hamburg, Germany  
European Society for Environmental and Occupational Medicine.

Dr. Merete D. Bugge, PhD  
Senior Physician  
STAMI, National Institute of Occupational Health  
Oslo, Norway

Kathleen Burns, PhD  
Director  
Sciencecorps  
Lexington, MA, USA

Gloria M. Calaf Ph. D.  
Director, Instituto de Alta Investigación  
Universidad de Tarapacá  
Arica-Chile  
and  
Adjunct Associate Research Scientist  
Columbia University Medical Center  
Center for Radiological Research  
New York, New York USA

David O. Carpenter, M.D.  
Director, Institute for Health and the Environment University at Albany  
Rensselaer, NY 12144 USA

Hillary M. Carpenter, Ph.D., Toxicologist  
Minnesota Department of Health, Retired  
Maplewood MN 55109 USA

Lizbeth López-Carrillo  
Senior Researcher  
National Institute of Public Health  
Cuernavaca, Morelos, Mexico

Prof. Richard Clapp  
Professor Emeritus  
Boston University School of Public Health  
Boston, MA USA

Prof. Pierluigi Cocco, M.D., HonFFOM  
Chair, Occupational Medicine  
Department of Public Health, CLinical and Molecular Medicine  
University of Cagliari, Italy

Pietro Comba, PhD,  
Head , Unit of Environmental Epidemiology  
Department of Environment and Primary Prevention

Istituto Superiore di Sanità, Rome, Italy

Dr Dario Consonni, MD, MPH, PhD  
Occupational Physician and Epidemiologist  
Epidemiology Unit, Department of Preventive Medicine  
Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico  
Milan, Italy

Devra Davis, Md, PhD  
Visiting Professor, The Hebrew University, Hadassah Medical School, Jerusalem  
Visiting Professor, Ondukuz Mayıs University Medical School, Samsun, Turkey  
President, Environmental Health Trust  
Jackson Hole, WY USA

Anneclaire De Roos, MPH, PhD  
Associate Professor  
Environmental & Occupational Health  
Dornsife School of Public Health  
Drexel University  
Philadelphia, PA USA

Paul A. Demers, Ph.D.  
Director  
Occupational Cancer Research Centre, Cancer Care Ontario  
Professor  
Dalla Lana School of Public Health, University of Toronto  
Toronto, Canada

Dr. Jamie DeWitt  
Associate Professor of Pharmacology & Toxicology  
Brody School of Medicine, East Carolina University  
Greenville, NC, USA

Dr. Francesco Forastiere  
Director Etiological and Analytical Epidemiology  
Department of Epidemiology, Lazio Regional Health Service  
Rome, Italy

Dr. Jonathan H Freedman, Ph.D.  
Professor, Department of Pharmacology and Toxicology  
University of Louisville School of Medicine  
Louisville, Kentucky 40202 USA

Prof. Lin Fritschi  
School of Public Health, Curtin University  
Perth, Australia

Dr. Caroline Gaus Associate Professor  
Environmental Toxicology

The University of Queensland  
Brisbane, Australia

Julia M Gohlke, PhD  
Assistant Professor  
Department of Population Health Sciences  
Virginia-Maryland College of Veterinary Medicine  
Virginia Tech  
Blacksburg, VA 24061-0395, USA

Professor Marcel Goldberg  
Emeritus Professor of epidemiology  
Paris Descartes University  
Paris, France.

Prof. Eberhard Greiser  
Emeritus Professor of epidemiology and medical statistics  
Associate Professor, Center for Social Policy Research, Bremen University,  
CEO, Epi.Consult GmbH, Musweiler, Rhineland-Palatinate, Germany.

Prof. Per Gustavsson, MD  
Head of Unit of Occupational Medicine  
Institute of Environmental Medicine, Karolinska Institute  
Centre for Occupational and Environmental Medicine, Stockholm County Council  
Stockholm, Sweden

Dr. Johnni Hansen  
Senior Scientist  
Danish Cancer Society Research Center  
Copenhagen, Denmark

Dr. Lennart Hardell, MD, PhD  
Department of Oncology  
University Hospital  
Orebro, Sweden

Dr. Michael Hauptmann  
Head, Biostatistics Branch  
Netherlands Cancer Institute  
Amsterdam, The Netherlands

Wei Huang, ScD (HSPH 2003)  
Professor, Peking Univ School of Public Health  
Vice Director, Peking Univ Institute of Environmental Medicine  
Key Lab of Molecular Cardiovascular Research Ministry of Education  
Beijing, China, 100191

James Huff, PhD  
Formerly, Associate Director For Chemical Carcinogenesis

National Institute Of Environmental Health Sciences  
Research Triangle Park, North Carolina USA

Professor Margaret O. James  
Jack C. Massey Professor of Pharmacy, Professor of Medicinal Chemistry  
University of Florida  
Gainesville, Florida USA

C W Jameson, PhD  
CWJ Consulting, LLC  
Retired Director for the Report on Carcinogens  
National Toxicology Program/National Institute of Environmental Health  
Sciences  
National Institutes of Health  
Cape Coral, FL USA

Professor Andreas Kortenkamp  
Human Toxicology  
Institute of Environment, Health and Societies  
Brunel University London  
Uxbridge, UB8 3PH, United Kingdom

Prof. Dr. Annette Kopp-Schneider  
Head of Div. Biostatistics  
German Cancer Research Center  
69120 Heidelberg, Germany

Professor Hans Kromhout  
Chair in Exposure Assessment and Occupational Hygiene  
Chair in Epidemiology of Health Effects of Electromagnetic Fields  
Division of Environmental Epidemiology  
Institute for Risk Assessment Sciences  
Utrecht University  
Utrecht, The Netherlands

Prof. Marcelo L. Larramendy, Ph.D.  
Principal Researcher National Council of Scientific and Technological Research  
(CONICET)  
School of Natural Sciences and Museum  
National University of La Plata  
La Plata, Argentina

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  
New York, NY 10029 USA

Lawrence H. Lash, Ph.D.  
Professor and Associate Chair  
Department of Pharmacology  
Wayne State University School of Medicine  
Detroit, MI 48201 USA

Dariusz Leszczynski, PhD, DSc  
Adjunct Professor  
Department of Biosciences  
Division of Biochemistry & Biotechnology  
University of Helsinki, Finland

Prof. Charles F. Lynch, MD, PhD  
Department of Epidemiology  
College of Public Health  
University of Iowa  
Iowa City, IA, USA

Prof. Corrado Magnani MD  
Professor of Medical Statistics  
Head of the Cancer Epidemiology Unit  
University of Eastern Piedmont  
Novara, Italy

Daniele Mandrioli, MD  
Associate Director  
Cesare Maltoni Cancer Research Center  
Ramazzini Institute  
40010, Bentivoglio (Bologna), Italy

Francis L Martin  
Centre for Biophotonics, LEC, Bailrigg  
Lancaster University  
Lancaster LA1 4YQ, UK

Dr. Ron Melnick, PhD  
Ron Melnick Consulting, LLC  
Retired Senior Toxicologist  
National Toxicology Program/  
National Institute of Environmental Health Sciences  
National Institutes of Health  
Chapel Hill, NC USA

Dr. Enzo Merler, PhD  
Director  
Regional Registry on Mesothelioma, Veneto Region, Italy  
Department of Prevention, Occupational Health Unit  
National Health Service

Padua, Italy

Paola Michelozzi  
Director Environmental Epidemiology Unit  
Department of Epidemiology Lazio Region  
Rome, Italy

Dr. Lucia Miligi,  
Senior Epidemiologist,  
Occupational and Environmental Epidemiology Unit,  
ISPO-Cancer Prevention and Research Institute,  
Florence, Italy

Anthony B. Miller, MD  
Professor Emeritus  
Dalla Lana School of Public Health, University of Toronto  
Toronto, Canada

Dr. Dario Mirabelli  
Epidemiologist  
Unit of Cancer Epidemiology, University of Turin and CPO-Piemonte  
10126 Torino Italy

Franklin E. Mirer, PhD, CIH  
Professor, Environmental and Occupational Health Sciences  
City University of New York School of Public Health  
New York, NY 10035 USA

Michael M. Müller, PhD  
EUROTOX Registered Toxicologist  
Head of the Toxicological Laboratory Unit  
Department of Occupational, Social and Environmental Medicine  
University Medical Center Göttingen  
37073 Göttingen Germany

Dr Saloshni Naidoo (MBChB, FCPHM, MMed, PHD)  
Chief Specialist / Head of Discipline  
Public Health Medicine  
School of Nursing and Public Health  
University of KwaZulu-Natal  
Durben, South Africa

Prof. Melissa J. Perry, ScD, MHS, FACE  
Professor and Chair of Environmental and Occupational Health  
Professor of Epidemiology  
Milken Institute School of Public Health  
Professor of Biochemistry and Molecular Biology  
School of Medicine and Health Sciences  
The George Washington University

Washington, DC 20051 USA

Dr. Maria Grazia Petronio  
Head of Unit of Health and Environment-Department of Prevention  
Local Health Authority-Empoli, Florence, Italy  
Professor of Environmental Hygiene  
School of Specialization "Hygiene and Preventive Medicine  
University of Pisa, Italy  
Vice-President for Central Italy Area of International Society of Doctors for  
Environment, Italy

Dr Roberta Pirastu  
Researcher  
Department of Biology and Biotechnology "Charles Darwin"  
Sapienza Rome University, Italy

Prof. Miquel Porta, MD, MPH, PhD  
Professor and Senior Scientist, Hospital del Mar Institute of Medical Research  
(IMIM) and School of Medicine  
Universitat Autònoma de Barcelona  
Barcelona, Catalonia, Spain

Ralph J. Portier, PhD  
Distinguished Professor of Environmental Sciences  
Department of Environmental Sciences, School of the Coast & Environment  
Louisiana State University  
Baton Rouge, LA 70803 USA

Kenneth S Ramos, MD, PhD, PharmB  
Associate Vice President for Precision Health Sciences  
Professor of Medicine  
Director of Center for Applied Genetics and Genomic Medicine  
University of Arizona Health Sciences  
Tucson AZ. 85737 USA

Larry W. Robertson, MPH, PhD, ATS  
Professor and Director, Iowa Superfund Research Program and the  
Interdisciplinary  
Graduate Program in Human Toxicology  
The University of Iowa  
Iowa City, Iowa, USA

Martin Rössli, PhD  
Head of the Environmental Exposures and Health Unit  
Swiss Tropical and Public Health Institute  
Associated Institute of the University of Basel  
4002 Basel, Switzerland

Matt K. Ross, PhD



Associate Professor  
College of Veterinary Medicine  
Mississippi State University  
Mississippi State, MS 39762 USA

Prof. Deodutta Roy, MS, M.Phil., Ph.D.  
Department of Environmental and Occupational Health  
Robert Stempel College of Public Health and Social Work  
Florida International University  
Miami, FL 33199-0001 USA

Ivan Rusyn, MD, PhD  
Professor, Veterinary Integrative Biosciences Texas A&M University  
College Station, TX 77843-4458 USA

Paulo Saldiva, MD, PhD  
Professor of Pathology, Faculty of Medicine,  
University of São Paulo, Brazil  
Coordinator of the National Institute of Integrated Risk Assessment  
National Research Council, Brazil

Jennifer Sass, PhD  
Senior Scientist Natural Resources Defense Council and  
Professorial Lecturer, George Washington University  
Washington, DC USA

Kai Savolainen, MD, Ph.D., Research Professor  
Director, Nanosafety Research Centre  
Finnish Institute of Occupational Health  
Helsinki, Finland

Assoc Prof. Paul T.J. Scheepers, PhD, ERT  
Workgroup Leader and Head, Research Lab Molecular Epidemiology  
Radboud Institute for Health Sciences  
Radboud University Medical Center  
Nijmegen, The Netherlands

Prof. Dr. Consolato Sergi, MSc, MD, PhD, FRCPC  
Full Professor of Pathology and  
Full Professor of Pediatrics (Adjunct)  
University of Alberta,  
Edmonton, Alberta, Canada

Ellen K Silbergeld, PhD  
Professor, Environmental Health Sciences  
Johns Hopkins Bloomberg School of Public Health  
Baltimore MD 21205 USA

Prof. Martyn T. Smith

School of Public Health  
University of California, Berkeley  
Berkeley, CA USA

Prof. Bernard W. Stewart  
Faculty of Medicine, University of New South Wales  
Head, Cancer Control Program South East Sydney Public Health Unit  
Randwick NSW 2031 Australia

Patrice Sutton, MPH  
Research Scientist  
University of California, San Francisco, Program on Reproductive Health and the  
Environment  
San Francisco, USA

Dr. Fabio Tateo  
Researcher  
Istituto di Geosceinze e Georisorse (CNR)  
35131 Padova, Italy

Prof. Benedetto Terracini  
Professor of Cancer Epidemiology (retired)  
University of Torino  
Torino, Italy

Prof. Dr. med. Dr. rer. nat. Heinz W. Thielmann  
Former Division Head at the German Cancer Research Center, Heidelberg  
Retired Prof. of Biochemistry, Faculty of Pharmacy, Heidelberg University  
Member of Committee on Health Hazards of Chemicals of the Deutsche  
Forschungsgemeinschaft  
Germany

David B. Thomas, MD, DrPH  
Prof Emeritus, School of Public Health and Community Medicine  
University of Washington  
and  
Member, Fred Hutchinson Cancer Research Center  
Seattle, WA, U.S.A.

Prof. Harri Vainio  
Professor of Environmental and Occupational Health  
Dean-Elect  
Faculty of Public Health, Kuwait University, Kuwait  
Kuwait City, Kuwait

John E. Vena, Ph.D.  
Professor and Founding Chair  
Department of Public Health Sciences  
Medical University of South Carolina

Charleston SC 29425 USA

Professor Paolo Vineis  
Chair in Environmental Epidemiology  
Imperial College London, UK

Professor Elisabete Weiderpass, M.D., M.Sc., Ph.D.  
Head - Department of Research  
Head - Group of Etiological Cancer Research  
Institute of Population Based Cancer Research  
Cancer Registry of Norway, Oslo, Norway  
Department of Community Medicine, Faculty of Health Sciences  
University of Tromsø, The Arctic University of Norway, Tromsø, Norway  
Department of Medical Epidemiology and Biostatistics  
Karolinska Institutet, Stockholm, Sweden  
Genetic Epidemiology Group  
Folkhälsan Research Center, Helsinki, Finland

Dennis D. Weisenburger, M.D.  
Professor/Chair, Department of Pathology  
City of Hope Medical Center  
Duarte, CA 91010 USA

Professor Tracey J. Woodruff, PhD, MPH  
Director  
University of California, San Francisco, Program on Reproductive Health and the  
Environment  
San Francisco, USA

Prof. Dr. rer. nat. Irene Witte (retired)  
Institute for Biology and Environmental Sciences  
University of Oldenburg  
Germany

Dr. Takashi Yorifuji  
Associate Professor  
Okayama University  
Okayama, Japan

Il Je Yu, PhD, Professor  
Director, Institute of Nanoproduct Safety Reserch  
Hoseo Universtiy,  
Asan, Korea

Dr. Paola Zambon  
Past Director Veneto Tumor Registry  
University of Padua  
Padova Italy

Prof. Dr. Hajo Zeeb  
Head, Department of Prevention and Evaluation, Leibniz-Institute for  
Prevention Research and Epidemiology - BIPS  
Bremen, Germany

Prof. Shu-Feng Zhou, MD, PhD  
Associate Dean for International Research and Chair  
College of Pharmacy  
University of South Florida  
Tampa, Florida, USA

---

## References

1. European Food Safety Authority, *Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate*. EFSA Journal, 2015. **13**(11): p. 4302.
2. European Food Safety Authority. *Final Addendum to the Renewal Assessment Report*. 2015; Available from: <http://registerofquestions.efsa.europa.eu/roqFrontend/outputLoader?output=ON-4302>.
3. IARC. *PREAMBLE TO THE IARC MONOGRAPHS* 2006; Available from: <http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf>.
4. Guyton, K.Z., et al., *Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate*. Lancet Oncol, 2015. **16**(5): p. 490-1.
5. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, *Glyphosate, in IARC Monogr Eval Carcinog Risks Hum*, I.M. Program, Editor. 2015. p. 1-92.
6. De Roos, A.J., et al., *Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study*. Environ Health Perspect, 2005. **113**(1): p. 49-54.
7. Checkoway, H., N. Pearce, and D. Kriebel, *Research methods in occupational epidemiology*. 2nd ed. Monographs in epidemiology and biostatistics. 2004, New York: Oxford University Press. xiv, 372 p.
8. Rothman, K.J., S. Greenland, and T.L. Lash, *Modern epidemiology*. 3rd ed. 2008, Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. x, 758 p.
9. Schinasi, L. and M.E. Leon, *Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and meta-analysis*. Int J Environ Res Public Health, 2014. **11**(4): p. 4449-527.
10. De Roos, A.J., et al., *Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men*. Occup Environ Med, 2003. **60**(9): p. E11.
11. Epa, *Glyphosate; EPA Reg. # 524-308; mouse oncogenicity study*, B. William Dykstra. Toxicology, Editor. 1985.
12. JCF, *Evaluation of certain food additives and contaminants: Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives*. 1999, Joint Committee on Food Additives (including C. Portier), World Health Organization/Food and Agriculture Organization: Geneva. p. 96.
13. Epa, *Second peer review of Glyphosate*. 1991. p. 1-19.
14. Epa, *Glyphosate - EPA Registration No. 524-308 - 2-Year Chronic Feeding/Oncogenicity Study in Rats with Technical Glyphosate*, I. William Dykstra. Toxicology Branch, Editor. 1991.
15. Epa, *Glyphosate; 2-Year Combined Chronic Toxicity/ Carcinogenicity Study in Sprague-Dawley Rats - List A Pesticide for Reregistration*, B. William Dykstra. Toxicology, Editor. 1991. p. 1-29.
16. Sugimoto, *18-Month Oral Oncogenicity Study in Mice*. Unpublished, designated ASB2012-11493 in BfR RAR, 1997.

17. Unknown, *A chronic feeding study of glyphosate (roundup technical) in mice*. unpublished, designated ABS2012-11491 in BfR RAR, 2001.
18. Unknown, *Glyphosate Technical: Dietary Carcinogenicity Study in the Mouse*. Unpublished, designated ABS2012-11492 in BfR RAR, 2009.
19. OECD, *Guidance Document 116 on the Conduct and Design of Chronic Toxicity and Carcinogenicity Studies*, H.a.S.P. Environment, Editor. 2012, OECD: Paris.
20. NRC Committee to Review the Styrene Assessment in the National Toxicology Program 12th Report on Carcinogens, in *Review of the Styrene Assessment in the National Toxicology Program 12th Report on Carcinogens: Workshop Summary*. 2014, National Academies Press: Washington (DC).
21. Keenan, C., et al., *Best practices for use of historical control data of proliferative rodent lesions*. *Toxicol Pathol*, 2009. **37**(5): p. 679-93.
22. Haseman, J.K., G.A. Boorman, and J. Huff, *Value of historical control data and other issues related to the evaluation of long-term rodent carcinogenicity studies*. *Toxicol Pathol*, 1997. **25**(5): p. 524-7.
23. Greim, H., et al., *Evaluation of historical control data in carcinogenicity studies*. *Hum Exp Toxicol*, 2003. **22**(10): p. 541-9.
24. Giknis, M. and C. Clifford, *Spontaneous Neoplastic Lesions in the CrI:CD-1(ICR)BR Mouse*. 2000, Charles River Laboratories.
25. Giknis, M. and C. Clifford, *Spontaneous Neoplastic Lesions in the CrI:CD-1(ICR)BR Mouse in Control Groups from 18 Month to 2 year Studies*. 2005, Charles River Laboratories.
26. IARC Monograph 112. *List of Working Group Participants*. IARC Monogr Eval Carcinog Risks Hum 2015 26 March, 2015 [cited 2015 24 November]; Available from: <http://monographs.iarc.fr/ENG/Meetings/vol112-participants.pdf>.