PUBLIC HEALTH CONCERN:

WHY DID THE NZ EPA IGNORE THE WORLD AUTHORITY ON CANCER?

AN ASSESSMENT OF THE AUGUST 2016 ENVIRONMENTAL PROTECTION AUTHORITY REVIEW OF GLYPHOSATE AND CANCER

A FAILURE OF GOVERNMENT AGENCIES TO MEET STATUTORY OBLIGATIONS

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Foreword

This paper examines and assesses a New Zealand Environmental Protection Authority (NZ EPA) commissioned paper, *Review of the Evidence Relating to Glyphosate and Carcinogenicity*[1] for its consideration of international scientific evidence to protect public health.

Governments around the world are responding to evidence that glyphosate products are carcinogenic. However, New Zealand authorities appear to be ignoring the evidence, which raises serious questions about government systems and risk assessment processes. Does the NZ EPA report on glyphosate constitute a legal breach of the purpose of the Hazardous Substances and New Organisms Act (HSNO) and the statutory functions of the NZ EPA? This paper brings together the thinking and research findings of a range of scientists and public health advocates to answer that question.

At a time when people around the world are looking to governments to use their power in the best interests of citizens and the environment, we should expect authorities tasked with regulating harmful products to take account of the best science, such as findings by the International Agency for Research on Cancer (IARC). The IARC is the world's leading authority on cancer, which the NZ EPA cites as an authority.

The IARC has determined that glyphosate products are a probable human carcinogen (Group 2A). The IARC Working Group consisted of 17 experts[2] from 11 countries, drawing on independent peer-reviewed science.

Despite the new IARC determination, the NZ EPA has found that glyphosate does not require classification as a carcinogen or mutagen. The Terms of Reference (ToR) for the Review of the evidence appear not to have been followed fully by the principal author, or, as suggested by Official Information, the NZ EPA Review was significantly edited by NZ EPA and Ministry for Primary Industries (MPI) staff.

The NZ EPA has said it evaluated the 'relevant data' concerning glyphosate and reviewed the quality of evidence in order to identify the likelihood of glyphosate being genotoxic or carcinogenic. This Review included communications with Monsanto, the Ministry for Primary Industries (MPI), overseas regulatory authorities, and public concern about previous usage and how to best control future usage in Aotearoa New Zealand.

How the NZ EPA classifies products influences the actions of consumers, such as Territorial Local Authorities (TLAs) who frequently request guidance

[1] 'Review of the evidence relating to Glyphosate and Carcinogenicity' by Dr Wayne Temple. August 2016 http://www.epa.govt.nz/Publications/EPA_glyphosate_review.pdf

[2] IARC Monographs: List of participants. http://monographs.iarc.fr/ENG/Meetings/vol112-participants.pdf See also Appendix VI

on the risks of glyphosate-based herbicides (GBH) for use in public places such as streets and parks. For this reason, it's important that NZ EPA advice is derived from rigorous assessment.

Instead, the NZ EPA appears to rely excessively on protocols and guidelines that are described in the scientific literature as outdated and 'restrictive to the point that regulators could be underestimating the risks posed by exposures to low doses of mixtures of chemicals.'[3] The NZ EPA Review also appears to ignore key requirements within its own manual that include the requirement that the NZ EPA consider formulation synergies[4], which alter the impact of chemicals in combination.

This paper concludes that the science and opinion primarily relied on by the NZ EPA was supplied by industry and based on unpublished data, rather than the independent peer-reviewed science informing the IARC classification.

This paper recommends that the NZ EPA immediately withdraw its Review and adopt the IARC determinations. It also recommends a full investigation by the Ombudsman into NZ EPA systems and processes, including the role of the Ministry for Primary Industries (MPI), and the Ministry for the Environment (MFE) in meeting statutory obligations and acting in the best interests of the public.

This paper also recommends that Parliament notes the conclusions and recommendations in this paper, and pursues an inquiry into the adequacy or otherwise of the NZ EPA's approach to regulating chemical toxicity risks to the public.

Further recommendations, including for Local Territorial Authorities (LTAs), are outlined in Section 8.2.

In light of new scientific knowledge that much lower, hormonally relevant, exposure levels to glyphosate-based herbicides may be harmful, the NZ EPA Review appears outdated.

The significant issues outlined in this paper show that current risk assessment systems are unable, or unwilling, to grasp the complexities and challenges that must be addressed when we acknowledge science that shows chemical mixtures harm us at much lower levels than previously estimated.

> The exercise of a discretionary power, even for a proper purpose, may be invalid if the decision-maker fails to take into account relevant

[3] Goodson, W. H., L. Lowe, D. O. Carpenter, M. Gilbertson, A. Manaf Ali, A. Lopez de Cerain Salsamendi, A. Lasfar, et al. 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead. Carcinogenesis 36 (Suppl 1): S254-S296. doi:10.1093/carcin/bgv039. http://dx.doi.org/10.1093/carcin/bgv039.

[4] Synergy occurs when the effect of a mixture of chemicals is greater than the sum of the individual effects.

> considerations, or is influenced by considerations that are legally irrelevant.[5]

The IARC Working Group's Monograph remains the primary authoritative document relating to glyphosate, glyphosate-based herbicides, and their potential for carcinogenicity.

The failure of New Zealand authorities to draw on the IARC finding and protect New Zealanders from chemicals with probable carcinogenic properties signals a need to investigate the functioning of the NZ EPA, MPI, and MfE.

We should be able to rely on these government agencies to ensure public health.

Steffan Browning MP commissioned this assessment and assisted in its writing.

[5] Ibid. P.948

Authors

Steffan Browning is a Green Party MP (2011 – 2017) who has specialised in regulatory aspects of pesticides, food safety, biosecurity, organics, and genetic-engineering portfolios. Steffan's experience with pesticides issues started in 2003. He entered Parliament as an MP in 2011.

For the Soil & Health Association of New Zealand, he has held various roles including Co-chair and spokesperson, researcher and advocate. He has been associated with many assessments of the regulatory conduct of the Environmental Risk Management Authority (ERMA) and the NZ EPA covering such topics as pesticides, bio-controls, and genetically engineered organisms.

Steffan has served on the New Zealand Food Safety Authority's Consumer Forum, and within various organic sector bodies, including organic standards and certification committees. He has concerns about industrial farming causing adverse ecosystem effects and monitors such issues closely through his reading and attendance at relevant international conferences.

J.I. Bruning (B.Bus.Agribusiness), Principal researcher and author. New Zealand-based career writer and researcher, Jodie Bruning developed RITE, www.rite-demands.org, an informative international online platform dedicated to continuous improvement in toxicological pesticides risk assessment with the public interest at the forefront of policy and decision-making.

Dedicated research within the conventional regulatory risk assessment framework has ignited a drive to support increased transparency and resources in regulatory toxicity assessment, with a particular focus on addressing risk relating to complex chemical exposures and infant and child health.

Further Acknowledgements:

Dr Heli Matilainen, PhD in Biotechnology, MSc in Molecular Biology, has scientific experience in cancer research with a career stretching across Finland, the United States, and New Zealand. She has worked in a research team of Dr Ruoslahti, a world-renowned expert in the cancer research and molecular mechanisms of cancer. She is currently focusing on the molecular effects of chemicals and cancer prevention. Dr Matilainen is an organic technical expert providing scientific and technical support to growers and operators while assisting them to obtain and safeguard their organic certification.

B. Maskell
A machinery-of-government specialist and a consulting strategist, who made contributions to authors of the paper on relevant principles that lawful government in New Zealand is supposed to observe in order to protect the public interest and the trust of the NZ public – particularly matters of proper statutory interpretation and fundamentals of public law associated with administrative regulatory conduct.

M. Watts PhD
Senior Technical Advisor to PAN Asia Pacific (PANAP), Coordinator Pesticide Action Network (PAN) Aotearoa New Zealand, Co-Chair Persistent Organic Pollutants (POPs) Pesticide Working Group for IPEN (International POPs Elimination Network).

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5. **Professor Jack Heinemann**
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1. Professor Jeroen Douwes (1)**, Associate Professor Andrea 't Mannetje**(2)**, Dr Dave McLean**(3)**, Professor John Potter**(4).

Centre for Public Health Research, Massey University

‘Professor Jacqueline Rowarth recently commented that “the EPA’s role is to uphold and explain standards that can be defended rigorously, while explaining the reason for decisions that have been made in a manner that is appropriate for and understandable by the audience – those affected.” (AGCARM Newsletter, May 2017). She also appropriately highlights the need for good science to underpin policy decisions and quotes Sir Peter Gluckman who stated that “the proper use of science and technology is essential to our economic, social, and environmental health”.

It seems that the EPA, who recently appointed Professor Jacqueline Rowarth as Chief Scientist, do not adhere to these same principles. In particular, as described in this report, the EPA questions the scientific validity of a recent International Agency on Research on Cancer (IARC) report on glyphosate – a comprehensive report underpinned by clear and standardised criteria written by leading and independent international scientists, involving careful consideration of all available evidence including peer reviewed data on human exposure, epidemiological studies, animals studies, toxicokinetics and mechanism(s) of carcinogenesis, and published by the foremost authority (IARC) on evaluating cancer risk. Instead of relying on the best available evidence as presented in the IARC report, the EPA commissioned their own report involving a single New Zealand author with limited expertise in this specific area, with editing by EPA and MPI staff.

The reasons for commissioning another report are unclear, but may be related to a recent European Food Safety Authority (EFSA) report which concluded that “glyphosate is unlikely to pose a carcinogenic hazard to humans”, in contrast to IARC’s report which concluded that the data for glyphosate meet the criteria for classification as a “probable human carcinogen”.

However, it is worth pointing out that the EFSA report, unlike the IARC report, included findings from studies that had not undergone objective peer-review as well as studies directly funded by the pesticide-producing industry. This is not best practice (as it likely results in bias and risks misleading the public) and will go some way to explain the different conclusions between the IARC and EFSA evaluations and EPA’s own evaluation.

This is of concern and raises the question as to what motivated the EPA (and EFSA), and whether it had the public's best interest in mind when deciding to go against IARC's assessment. It also raises important questions about the processes employed by the EPA in evaluating risk and (to use the words of Sir Peter Gluckman) "the proper use of science".'

Professor Jeroen Douwes (1), Associate Professor Andrea 't Mannetje (2), Dr Dave McLean (3), Professor John Potter (4).

Centre for Public Health Research, Massey University

(1) Member of steering committee of the International Agricultural Cohort Consortium. International Agency for Research on Cancer (IARC), 2007 – present.

(2) Member of the IARC Working Group on the evaluation of carcinogenic risk to humans, Volume 112: evaluation of five organophosphate insecticides and herbicides (which included glyphosate).

(3) Member of the IARC Working Group on the evaluation of carcinogenic risk to humans, Volume 117: evaluation of the carcinogenicity of pentachlorophenol and some related compounds.

(4) US Representative, Science Council, IARC, 2001-2006; Vice-Chair, Science Council, IARC, 2004; Chair, Science Council, IARC, 2005 – 2006

2. Professor Alistair Woodward

MB BS, MMedSci, PhD, FNZCPHM

Head of Epidemiology and Biostatistics at the University of Auckland

'This is an important issue. Not just the status of glyphosate, though that certainly matters given the widespread use of the chemical in New Zealand; even more important is the process by which reviews are carried out and conclusions reached on the safety of potentially hazardous substances.

How the EPA thought it could match the IARC process of assessing carcinogenicity, I don't know. This is pretty much the gold standard, internationally, for hazard identification for cancer, and it is costly, drawing on the knowledge of large numbers of scientists in a wide range of relevant disciplines. Another strength of the IARC reports is the open, explicit, robust procedure that is applied to manage conflicts of interest and reduce the chance of a biased assessment.

And anyway, why should the NZ EPA even attempt to replicate such effort? Not only the IARC judgement, but also the advice of our own Ministry of

Health was apparently put to one side. Why and how these decisions were taken surely deserves close attention.'

(Professor Woodward was a member of the external Panel in early 2017 that reviewed the work of the Environment and Radiation Section of the International Agency for Research on Cancer, as part of the standard quality assessment process at IARC.)

3. Christopher J. Portier, PhD

Director, US National Center for Environmental Health, Retired

'Two of the strongest aspects of the scientific reviews done by the International Agency for Research on Cancer (IARC) are the transparency of their process and their rigorous evaluation of the available scientific evidence. Using multiple scientists with knowledge of epidemiology, toxicology and statistics, and focusing only on studies that are publicly available, has resulted in the most trusted cancer-hazard evaluation program in the world. There is simply no way in which an evaluation done by a single scientist can be as thorough and scientifically defendable as the IARC review.

The use of only publicly available scientific data allows other scientists to review the same data as the IARC and, if they disagree, openly discuss why they disagree. Globally, studies of pesticides conducted by industry and provided to regulatory authorities have been considered proprietary information and have not been openly shared with other scientists.

One of the major criticisms of the IARC review has been that they did not review this proprietary data. However, in recent months, these data have been made available to outside researchers by the European Food Safety Agency (EFSA) and a careful review of these data has shown multiple errors in EFSA's review and stronger support for the IARC hazard classification.

If the NZ-EPA is going to disagree with the findings of the IARC review, it should be done in an open and transparent fashion, with all of the available data, analyses and conclusions provided to the broader scientific community for comparison, criticism and discussion. Only in this way will the regulatory authorities be able to argue that the high quality and trusted reviews by the IARC should be replaced with the reviews done by regulatory authorities.'

4. Professor Philip A Joseph LLD

LLB (Hons), LLM (Br Col), LLD (Canterbury), Barrister and Solicitor of the High Court of New Zealand. Professor of Law at the University of Canterbury.

This comprehensive inquiry into the EPA-sponsored review of glyphosate-based product is necessary in the public interest, and I commend the authors for their endeavours. However, as a lawyer and not a scientist, I confine my endorsement to those parts of the report – but principally chapter 7 – that address the applicable administrative law principles relevant to the authors' inquiry. I am happy to report that they have encapsulated well those principles from which they draw their conclusions on the discharge (or lack of discharge) of the EPA's statutory functions. The authors' report serves an important public interest in ventilating the processes affecting the decision-making around the use of glyphosate.'

(Professor Joseph is the author of Constitutional and Administrative Law in New Zealand (4th Edition, Thomson Reuters, Wellington, 2014) and has published widely in his field.)

5. Professor Jack Heinemann

Ph.D. University of Oregon, USA. BSc (Honours) University of Wisconsin, USA

Genetics and molecular biology, School of Biological Sciences, University of Canterbury

'This report on the EPA sponsored review of glyphosate-based products echoes international concerns about how regulators choose the evidence upon which they make life and death decisions for the public. It is important for public agencies to champion the public interest.

Instead of dismissing uncertainties in the science, they should be doggedly identifying uncertainties and insist that those gaps in understanding be closed. The public does not demand to live in a risk-free world. However, members of the public reasonably expect that agencies of government will balance the power between them and industry, especially an industry the size of the agrochemical giants. Agencies must do more than use what they consider to be the best available science. They must judge whether or not the best available science is enough to conclude that a product can and will be used safely. Regardless of whether the NZ EPA conclusions on glyphosate herbicides are proven in time to be right, how it got to these conclusions should build public confidence. The existence of this report is evidence that at least in this regard NZ EPA failed.'

6. Dist Prof Bruce C Baguley

MSc (Hons), PhD, ONZM

Co-Director at the Auckland Cancer Society Research Centre, University of Auckland

"I think that the document is a well-prepared and honest attempt to provide a balanced view on glyphosate risk. I cannot claim to be an expert in the area, but on the basis of my personal experience on IARC committees, firmly support the research methodology that they have used and the conclusions they have reached".

7. Dr Jane Goodall DBE

Founder of the Jane Goodall Institute and UN Messenger of Peace

'Glyphosate-based herbicide, such as that used by Monsanto's Roundup, has been relentlessly promoted around the world, ostensibly to increase the amount of food that can be produced to feed our growing populations. Yet everywhere there are those voicing concerns about the risks posed by these chemicals to environmental and human health. This assessment by Jodie Bruning and Steffan Browning is a useful analysis and an example of how EPA regulators appear to be dominated by science that was funded by the agrichemical industry, while independent research linking glyphosate use to cancer in humans and other animals is widely ignored by the agricultural and agrichemical industry. In my book, *Harvest for Hope: A Guide to Mindful Eating*, I postulated, "Someday we shall look back on this dark era of agriculture and shake our heads. How could we have ever believed that it was a good idea to grow our food with poisons?" Today, I find myself wondering how we might hold regulators to account when they appear to be failing in their duty of protecting people and the environment.'

8. Physicians and Scientists for Global Responsibility (PSGR)

'PSGR is a not-for-profit, non-aligned charitable trust whose members are science and medical professionals. Since the recommendations of the Royal Commission on Genetic Modification (RCGM) to proceed with caution, we have maintained a watching brief on the scientific developments in genetic engineering (also referred to as genetic modification) and related issues.

PSGR is in support in general of Steffan Browning's assessment of the New Zealand Environmental Protection Authority (NZ EPA) commissioned paper, which disagreed with the findings of the World Health Organisation

International Agency for Research on Cancer (IARC) that glyphosate was "probably carcinogenic to humans". (Category 2A). [1]

That assessment is a thorough study, in large part reiterating our own several statements on glyphosate [2], the PAN Monograph on glyphosate [3], the 2017 CHEM Trust report (buff.ly/2mAtWpV) [4] and the Consensus report of J P Myers et al (doi.1086/s 12940-066-0117-0) [5].

The findings can be summarised by the fact that a European Parliament workshop stated, "The criteria used by the IARC for Group 2A are comparable to those for Category 1A in Regulation (EC) No.1272/2008." The European Parliament has legislation that requires that if a plant protection product receives (EU) classification of 1A or 1B, they cannot be approved for sale for use where residues exceed 0.01 mg/kg (as is the case with glyphosate).

The NZ EPA has apparently not bothered to monitor for toxic residues from glyphosate-based herbicides (GBH) and now apparently seems content to set aside the IARC findings on the basis of its one-person report that strangely seems to conclude that IARC's finding of a probable material risk to people, animals and the environment from use of 'glyphosate-based herbicide products' can be ignored. Thus, the EPA report is arguably irrelevant because its focus is on literature searches on glyphosate – and not on glyphosate-based herbicides that are actually sold and used.

It is arguably material that GBHs contain other toxic substances (e.g. POEA) that also raise questions of toxic synergy, but that factor seems to have been given no due consideration in the EPA paper.

The other relevant matter apparently not considered by the NZ EPA is that glyphosate is a known bactericide – a factor that has profound significance for probable soil and gut microbiota. And alterations to gut microbiota must have a high probability of damaging immune functions and causing inflammation that is one of the bedrocks for cancer.

In summary, the toxicity of the GBH combinations that are sold to the market are arguably a most relevant consideration for a regulator to address.

Therefore, the EPA report is arguably unfit to be used for asserting regulatory powers, and the IARC findings remain unchallenged for the purposes of public policy review and considerations of the public interest.’

[1] http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-09.pdf

[2] http://www.psgr.org.nz/glyphosate

[3] http://www.psgr.org.nz/glyphosate/finish/10-glyphosate/36-glyphosate-pan-mongraph

[4] http://www.chemtrust.org.uk/tag/glyphosate/

[5] https://www.ncbi.nlm.nih.gov/pubmed/26883814

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Contents

ABBREVIATIONS

ADI	acceptable daily intake
AMPA	aminomethylphosphonic acid
ARfD	acute reference dose
AC	Auckland Council
AT	Auckland Transport
BfR	German Federal Institute for Risk Assessment
bw	body weight
DWSNZ	Drinking water standards for New Zealand
EFSA	European Food Safety Authority
EFSA Peer Review	EFSA (European Food Safety Authority), 2015. Peer review of glyphosate. doi:10.2903/j.efsa.2015.4302. https://echa.europa.eu/documents/10162/13626/efsa_glyphosate_conclusion_en.pdf
FAO	Food and Agriculture Organisation
Final Addendum	Addendum 1 to the RAR Assessment of IARC Monographs, 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. August 31 First Draft of Addendum 1.
GBH	Glyphosate Based Herbicides
GHS of Chemicals	Globally Harmonised System for Classification and Labelling
GLP	good laboratory practice
HSNO	Hazardous Substances and New Organisms Act
IARC	International Agency for Research on Cancer – the specialised cancer agency of the World Health Organisation
IARC Monograph	IARC, Volume 112 (2015) Some Organophosphate Insecticides and Herbicides: Diazinon, Glyphosate, Malathion, Parathion, and Tetrachlorvinphos.

	http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf
IARC Working Group	IARC Working Group of 17 experts who carried out detailed assessments which are published as Volume 112 of the IARC Monographs, March 2015
IEDI	international estimated daily intake
IESTI	international estimate of short-term dietary intake
JMPR	World Health Organisation – Food and Agricultural Organisation (WHO-FAO) Joint Meeting on Pesticides Residues
JMPR 2006	(Referred to by IARC as 'JMPR 2006'and NZ EPA as 'WHO 2006') Glyphosate. Joint FAO-WHO Meeting on Pesticide Residues. Pesticide residues in food – 2004: Part II toxicological evaluations. Report No. WHO/ PCS/06.1. Geneva. ISBN 978 92 4 166520 9. WHO published 2006 http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf
JMPR 2016	Pesticide residues in food – 2016: Part II toxicological evaluations / Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva. 9–13 May 2016. Glyphosate ISBN 978-92-4-165532-3 (Page 89 onwards) http://apps.who.int/iris/bitstream/10665/255000/1/9789241655323-eng.pdf?ua=1
MAV	maximum acceptable value
MfE	Ministry for the Environment
mg/kg bw/day	milligrams per kilogram body weight per day
MRL	maximum residue limit
NOAEL	no-observed-adverse-effect level
NZ EPA	New Zealand Environmental Protection Authority
NZ EPA Review 'Review of the evidence relating to Glyphosate and Carcinogenicity'	Dr Wayne Temple. August 2016. http://www.epa.govt.nz/Publications/EPA_glyphosate_review.pdf
OECD	Organisation for Economic Co-operation and Development
OPP	US EPA Office of Pesticide Programs (OPP)
PDE	potential daily exposure value

POEA	polyoxyethylene amine or polyoxyethylene tallowamine
Ppb	parts per billion
Ppm	parts per million
RAR BfR)	Renewal Assessment Report for glyphosate (provided by
RfD	Reference dose
TEL	tolerable exposure limit
TLA	Territorial Local Authorities
ToR	terms of reference
US EPA	United States Environmental Protection Agency

US EPA 1993 EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014. Washington (DC): Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, United States Environmental Protection Agency. https://www3.epa.gov/pesticides/endanger/litstatus/effects/glyphosate-red.pdf accessed 9/5/2017

WHO	World Health Organization

Sections 1.0 – 8.0

1.0 Summary

In August 2016, the New Zealand Environmental Protection Authority (NZ EPA) released a paper *Review of the Evidence relating to Glyphosate and Carcinogenicity*[6] (NZ EPA Review) authored by retired toxicologist Dr Wayne Temple. The NZ EPA Review did not classify glyphosate products as a carcinogen or mutagen in contrast with a recent decision by the International Agency for Research on Cancer (IARC) to classify these products as a Group 2A carcinogen, 'probably carcinogenic'.

Having assessed the NZ EPA Review and the information on which it is based, we have concluded that the Review:

- relies on predominantly industry science
- discounts relevant independent science
- uses outdated guidelines
- does not consider glyphosate in mixtures or formulations as actually used
- appears to exclude new data from toxicology and cancer biology
- is contrary to Ministry of Health advice
- challenges a finding by a key authority (IARC) to EPA and the Ministry of Health
- is not peer reviewed by a public expert in carcinogenicity
- appears to be heavily influenced by Ministry of Primary Industries (MPI)

We therefore recommend that the NZ EPA Review:

- be removed as a regulatory guide for decision-makers such as Territorial Local Authorities (TLAs)
- should be subject to an independent Parliamentary or Ombudsman's inquiry as to the intent and consequences of its finding.

Further recommendations in Section 8.2 include:

- that the IARC retains its status as the NZ EPA authority on cancer that glyphosate-based herbicides are urgently reassessed, removed from use in public spaces and from use on food

[6] Dr Wayne Temple. Review of the Evidence Relating to Glyphosate and Carcinogenicity. Environmental Protection Authority. August 2016

- that future risk assessment evaluations prioritise the use of published and peer reviewed data and base risk assessment on the toxicity of pesticide formulations
- that the EPA more closely align with overseas jurisdictions who utilise the precautionary principle in decision-making and are required to consider full formulation toxicity
- that authorities rapidly adopt regular screening of glyphosate and its metabolites in New Zealand in food and water
- an independent inquiry is conducted into the agencies involved in the Review to investigate the relationships between industry, MPI, NZ EPA, and MfE to ensure they meet the purposes of the Hazardous Substances and New Organisms Act, and protect public health and the environment

The NZ EPA Review implies that it is a carcinogenicity review, that it is a review scrutinising 'relevant data' concerning glyphosate's potential to cause cancer. The introduction section of the NZ EPA Review indicates that it focuses solely on the main active herbicide ingredient, glyphosate, and its potential on its own to cause cancer.

By contrast, the issue of greatest public interest is the more complex chemistry of the full formulation of the glyphosate-based herbicides as used such as Monsanto's Roundup formulations that the public is exposed to.

The narrow interpretation of the available science renders the NZ EPA Review inadequate for the purposes of formulating and implementing policy to protect public health and the environment.

The NZ EPA Review considers that the narrow glyphosate chemistry (ignoring the broader chemistry of the herbicide formulations used) does not require classification as a carcinogen or mutagen under the Hazardous Substances and New Organisms Act 1996 (HSNO Act).[7] The narrow 'weight of evidence' finding appears to have given undue weight to unpublished studies that are not peer reviewed and are encapsulated within outdated regulatory assessments.

The NZ EPA Review also relies on outdated, industry-developed policy guidelines (reference needed) to exclude studies (limiting the 'weight of evidence') that might otherwise shift glyphosate into a more harmful carcinogen and/or mutagen classification.

Principles of administrative law arguably render the NZ EPA Review unfit to have any lawful influence on policy formulation or policy review by the Environmental Protection Authority.

The NZ EPA Review acknowledges the inadequate 'weight of evidence' and 'poor quality and reliability of the available data'. However, the

[7] *Hazardous Substances and New Organisms Act 1996*. Reprint as at 1 July 2016

absence of evidence about scientific safety is not evidence of safety, nor is the evidence absent.

NZ EPA's approach appears to selectively prefer industry-sponsored research, which is increasingly being exposed throughout the world in other industry-regulator collusions.[8] Similarly, NZ EPA's reliance on industry science that 'glyphosate is unlikely to be genotoxic or carcinogenic to humans' carries very little, if any, weight and should be independently verified.

The NZ EPA Review was not authored by a specialist in cancer and carcinogenicity, yet it challenges the June 2015 Monograph[9] despite the recognised authority[10] of the IARC.

Seventeen expert scientists (the Working Group) were engaged in producing that IARC Monograph. Their considerations included full-formulation studies of glyphosate-based herbicides.

The IARC Monograph declared glyphosate 'probably carcinogenic to humans' (Group 2A). The classification is based on 'limited evidence for the carcinogenicity of glyphosate in humans' and 'sufficient evidence in experimental animals for the carcinogenicity of glyphosate' as well as 'strong evidence that glyphosate can operate through two key characteristics of known human carcinogens', namely genotoxicity and the ability to induce oxidative stress, and that these 'can be operative in humans'.

The IARC Monograph concluded that:

> 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.
>
> There is strong evidence that glyphosate, glyphosate-based formulations and aminomethylphosphonic acid can act to induce oxidative stress, based on studies in experimental animals, and in studies in humans in vitro.

Glyphosate, when broken down by microbial degradation, forms the breakdown product (metabolite) aminomethylphosphonic acid (AMPA), which has been found to persist in the environment for years.[11]

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[8] Glyphosate and cancer: Authorities systematically breach regulations. How industry strategized (and regulators colluded) in an attempt to save the world's most widely used herbicide from a ban. Dr. Peter Clausing. *PAN Europe*. http://www.pan-europe.info/sites/pan-europe.info/files/public/resources/reports/20170713_Glyphosate_Report_Global2000_EN.pdf

[9] IARC Working Group. Glyphosate. In: Some organophosphate insecticides and herbicides: diazinon, glyphosate, malathion, parathion, and tetrachlorvinphos. Vol 112. *IARC Monograph Program* 2015:1–92. http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf (accessed 4.10.17)

[10] Thresholds and Classifications under the HSNO Act 1996. 2012 EPA0109 Page 126. Table 9.15: Information sources for toxicity – carcinogens http://www.epa.govt.nz/Publications/ER-UG-03-2.pdf

[11] Watts MA et al 2016. Glyphosate Monograph. PAN International. Page 6 http://pan-international.org/wp-content/uploads/Glyphosate-monograph.pdf

The Working Group considered studies that were published in the public domain and were publicly available. A commentary published in June 2015, with epidemiologist Professor Neal Pearce as lead author, concluded that recent criticisms of IARC evaluations were 'unconvincing', that the procedures used by the Working Group provided a 'balanced evaluation' and that:

> IARC Monographs have made, and continue to make, major contributions to the scientific underpinning for societal actions to improve the public's health.[12]

The NZ EPA Review heading and introduction implies that the paper is a carcinogenicity review of a single active ingredient. However, the terms of reference (ToR), as advised by the office of Hon Dr Nick Smith on 19 September 2016 suggests the NZ EPA paper was supposed to directly address the IARC Monograph and its referenced documents.

The terms of reference were as follows:

> A detailed toxicological review of the International Agency for Research on Cancer (IARC) Monograph on glyphosate published in 2015 will be undertaken. A report will address the basis for the IARC's conclusions and the strengths and weaknesses in the conclusions reached. A draft report will be prepared for review by experts selected by the EPA and then a final report taking into account the reviewers' comments received will be provided.
>
> I am advised that before the final review was received, EPA staff ensured that the review would take into account the referenced documents used by IARC, and relevant European Food Safety Authority's documents.

There was arguably no NZ EPA ToR requirement to consider the sole chemistry of glyphosate on its own. To do so would have had no relevance to the NZ EPA statutory requirement to consider what is (or could be) authorised for application in New Zealand.

The NZ EPA's stated ToR for the Review of Evidence has apparently been overlooked by the NZ EPA Review's author and peer reviewers, who appear to ignore the predominant weighting given to glyphosate formulations by the Working Group.

The NZ EPA Review does not appear to make use of information that addresses the complexity of twenty-first-century scientific understanding of cancer within the widely accepted 'Hallmarks of Cancer' framework.[13] In 2011 the framework was updated to include the role of the immune system,

[12] Pearce N et al. (2015). IARC Monographs: 40 years of evaluating carcinogenic hazards to humans. *Environmental Health Perspectives* 123(6): 507-514

[13] D.A.Hanahan & R.A.Weinberg. Review: The Hallmarks of Cancer. *Cell.* Vol. 100, pp57–70, 2000 http://dx.doi.org/10.1016/S0092-8674(00)81683-9

inflammation, and metabolism as mechanisms of carcinogenesis, bringing into focus important new considerations.[14]

These modern considerations of cancer hallmarks appear to be largely ignored in the NZ EPA Review. In 2011, New Zealand Prime Minister's Chief Science Advisor Professor Peter Gluckman explained in *Towards better use of evidence in policy formation: a discussion paper:*

> For most of the past 200 years science has largely been conducted in a linear manner. The general pattern has been that a problem or question is identified, a scientific investigation is undertaken to directly address the problem and in turn, assuming the problem is properly identified and understood, the knowledge is applied. There is a general presumption in such a model of binary outcomes that science brings precision to the answer. But increasingly, science is being applied to systems that are complex, non-linear and dynamic…This type of science almost never produces absolute answers, but serves to elucidate interactions and reduce uncertainties. Precision is not the outcome, rather an assessment of probabilities…There can be a danger of scientists claiming greater certainty than can be justified.[15]

It seems reasonable to be concerned that the NZ EPA Review indicates significant inadequacies in the manner in which the NZ EPA approaches formulation of policies and controls in the carrying out of its statutory obligations. It appears in its Review, that the NZ EPA has ignored relevant considerations including full formulation effects and new scientific knowledge. Ignoring relevant considerations and giving undue weight to industry representations and claims can undermine the public trust in a government's administration of its statutory obligations to protect the safety of the public and the environment.

This may expose the departments responsible for risk assessment in New Zealand to regulatory or judicial review. Responsible decision-makers and legislators may be persuaded to ask: 'Has something gone wrong? Have the decision-makers in question acted illegally?'[16] (See Section 7)

The NZ EPA Review appears to draw on the European Food Safety Authority (EFSA) peer review of the pesticide risk assessment of the active substance glyphosate.[17] Members of EFSA have so far declined to declare

[14] Hanahan D., et al. (2011) Hallmarks of cancer: the next generation. *Cell,* 144, 646–674. doi: 10.1016/j.cell.2011.02.013

[15] Professor Sir Peter Gluckman. Office of the Prime Minister's Science Advisory Committee. Towards better use of evidence in policy formation: a discussion paper. 2011 http://www.pmcsa.org.nz/wp-content/uploads/Towards-better-use-of-evidence-in-policy-formation.pdf

[16] The Judge over your shoulder. A guide to judicial review of administrative decisions. *Crown Law Office*. ISBN 0-478-04451-8.

[17] EFSA (European Food Safety Authority), 2015. Peer review of the pesticide risk assessment of the active substance glyphosate. *EFSA Journal* 2015;13(11):4302, 107 pp. doi:10.2903/j.efsa.2015.4302. October 2015

industry affiliations, yet the authors of the IARC Monograph fully declared their affiliations.[18]

In September 2015, former industry toxicologist Dr Peter Clausing analysed the March 2015 draft European Renewal Assessment Report (RAR). Dr Clausing, who has authored some 30 scientific papers in peer-reviewed journals, noted that European regulators minimise or dismiss evidence in order to arrive at a 'weight of evidence' conclusion.

> The denial of genotoxicity, the neglect of oxidative stress as a mechanism, and the strange way of looking at the data from carcinogenicity studies in the RAR gives the impression of a purposeful separation and, thereby, weakening of evidence.[19]

Dr Clausing heavily criticised the EFSA October 2015 Peer Review in a December 2015 paper.

> The weight of evidence points to the opposite direction and that EFSA's Conclusion has no scientific basis.[20]

The decision-making stratagem by which regulators, including EFSA and the NZ EPA, arrive at a 'weight of evidence' conclusion, demonstrates an inability or reluctance to consider complex interrelationships between the cancer studies, epidemiological studies, and the mechanistic evidence that act to build a profile of risk.

As an example, the Working Group considered the consistency of studies showing the same type of cancer (e.g. Lymphoma). Their conclusion was supported by strong mechanistic evidence (genotoxic effects and oxidative effects).

The NZ EPA does not appear to have consulted with New Zealand or internationally based public health specialists in carcinogenicity and cancer, outside of regulatory confines. Peer review of the NZ EPA Review concerning glyphosate and carcinogenicity was predominantly conducted by staff within MPI and NZ EPA itself.

The NZ EPA Review appears not to have weighed risk in terms of the toxicity of a major metabolite of glyphosate, AMPA. In contrast, the IARC concluded that AMPA induced oxidative stress. This finding formed an integral part of the hazard profile that led to the IARC conclusion.

The NZ EPA Review and NZ EPA's position on glyphosate has informed decision-making on using glyphosate-based herbicides (GBH) in Auckland

[18] IARC Working Group List of Participants. http://monographs.iarc.fr/ENG/Meetings/vol112-participants.pdf. Posted on 26 January 2015, updated 19 October 2016
[19] Dr. P. Clausing. The Glyphosate Renewal assessment Report: An Analysis of Gaps and Deficiencies. *PAN Germany.*
[20] Dr P. Clausing. The EFSA Conclusion on the Peer Review of the Glyphosate Risk Assessment A Reality Check. *PAN Germany.* Hamburg December 2015 http://www.pan-germany.org/download/Analysis_EFSA-Conclusion_151201.pdf

and other TLAs throughout New Zealand, and in the continued use of GBH in the food supply through pre-harvest treatments on food crops.

NZ EPA's position directly impacts decision-making by the Ministry of Health (MoH). To date, the MoH does not require drinking-water suppliers to monitor glyphosate and its metabolite, even though the herbicide is applied along drains and beside surface waters.

The NZ EPA review appears to have disregarded many 'relevant considerations' that the Working Group has taken into consideration, and has used apparently outdated protocols and guidelines not as a guide, but as a command*.* [21]

Professor Philip Joseph noted in the authoritative text on public law in New Zealand 'Constitutional and Administrative Law' that:

> The exercise of a discretionary power, even for a proper purpose, may be invalid if the decision-maker fails to take into account relevant considerations, or is influenced by considerations that are legally irrelevant.[22]

Yet when the relevant Acts and regulations are consulted to understand which legislative instruments would apply – should glyphosate and its formulations be declared a 'probable' (or in New Zealand, 'presumed') carcinogen – it appears that *discretion* by public servants working under the authority of the relevant legislation is a principal mechanism for decision-making. This includes whether to reassess such a chemical considered a 'probable' carcinogen.

The NZ EPA has a significant fiduciary obligation to the public. As a statutory administrator, it has a relationship of considerable trust with the New Zealand public who cannot be reasonably expected to have the specialist competencies needed to protect its health or the safety of the environment.

To appear to abuse that trust and not take due care with the exercise of its statutory powers threatens to dismantle public trust in the country's machinery of government.

The IARC finding needs to be applied to New Zealand regulatory application of the HSNO Act. The NZ EPA has avoided adopting a determination of its own trusted authority, IARC.

The deliberate approach of the NZ EPA to challenge IARC and bypass its own statutory purpose, indicates a need for a robust inquiry into its actions.

An inquiry should consider the relationships between industry, MPI, NZ EPA, and MfE. It would either investigate the ability of the agencies to meet

[21] Constitutional and Administrative Law in New Zealand, 4th Ed., Philip A Joseph*, Thomson Reuters* 2014. 23.3.2 (1) P.965
[22] Ibid. 23.2.3 (1) P.948

the purposes of HSNO, or recommend how a full and independent inquiry should investigate the ability of NZ EPA and MPI to function independently and protect the health of the community and environment.

Further recommendations are covered in Section 8.2.

'We have a moral responsibility to act when there is a doubt, not when victims emerge, laws change and loopholes close.'[23]

2.0 Materiality of herbicide formulations v. glyphosate as a singular active ingredient

2.1 Technical acid salt used to evaluate toxicity is not the product used in commercial formulations

Regulatory carcinogenicity studies to date have limited scrutiny to technical, or pure glyphosate N-(phosphonomethyl)glycine (purity 95% – 99%), an acid. Due to the acid nature of the molecule, glyphosate is commonly formulated as a salt.

The glyphosate salts isopropylamine (IPA), ammonium, sodium, potassium and glyphosate trimesium (trimethylsulfonium) commonly form the active ingredient used in glyphosate formulations.

Glyphosate is formulated in its salt forms to further increase the water solubility. The order of water solubility is glyphosate << ammonium salt < sodium salt < potassium salt < isopropylammonium salt < trimesium salt, the solubility of the trimesium salt being two orders of magnitude higher than that of glyphosate.[24]

Scientists have criticised use of glyphosate technical acid to evaluate toxicity.

> However, studies on effects of glyphosate technical acid are not relevant for assessing the potential effects of the glyphosate active ingredient in

[23] **Opening remarks of the 2017 Conferences of the Parties to the Basel, Rotterdam, and Stockholm Conventions (Geneva). Ibrahim Thibaw, Deputy Executive Director, UN Environment. 24 April 2016. New Approach to Chemical Management.**
http://www.brsmeas.org/Implementation/MediaResources/SpeechesandInterviews/Openingremarksofthe2017COPsIbrahim/tabid/5911/language/en-US/Default.aspxof

[24] András Székács and Béla Darvas (2012). Forty Years with Glyphosate, Herbicides - Properties, Synthesis and
Control of Weeds Dr. Mohammed Nagib Hasaneen (Ed.), ISBN: 978-953-307-803-8, *InTech,*
https://www.intechopen.com/books/herbicides-properties-synthesis-and-control-of-weeds/forty-years-with-glyphosate

> herbicides. We argue that this is a possible explanation for the contradictory published results in specific species of test- animals and specific test-systems, presenting EC50 values which span several orders of magnitude.[25]

The difference in solubility of the acid versus the various salt formulations in the final formulation (and the implications for early studies submitted for registration of glyphosate that prove relative safety of the chemical[26]) should be an important consideration in moving to risk assessment of complete pesticide formulations.

Furthermore, when comparing different formulations, it is important to compare the concentrations of free acid form of glyphosate, e.g. acid equivalent, as the different salt formulations will have different molecular masses.[27]

2.2 Adjuvants enhance formulation performance

There is evidence that the glyphosate formulations that the population and the environment are exposed to can be many times more harmful (formulations include other ingredients, referred to as 'adjuvants'[28]) than the active ingredient glyphosate on its own.[29] This is not new information: a ten-year-old paper advised:

> Demonstrations of important impacts of inert ingredients have not been limited to particular classes of pesticides, types of formulations, or toxicity end points. Instead, it appears that the effects of inert ingredients may be both common and far-reaching.[30]

In the USA, mixture synergies are an important part of patent applications.

> 72 percent of the patent applications that claimed or demonstrated synergy involved some of the most highly used pesticides in the United States, including glyphosate, atrazine, 2,4-D, dicamba and the controversial neonicotinoids thiamethoxam, imidacloprid and clothianidin, among others, indicating that potential impacts could be widespread.

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[25] Cuhra et al 2016. Review Glyphosate: Too Much of a Good Thing? *Front. Environ. Sci.* http://dx.doi.org/10.3389/fenvs.2016.00028

[26] Cuhra, M. (2015c). Glyphosate nontoxicity: the genesis of a scientific fact. *J. Biol. Phys. Chem*. 15, 89–96. doi: 10.4024/08CU15A.jbpc.15.03

[27] András Székács and Béla Darvas (2012). Forty Years with Glyphosate, Herbicides - Properties, Synthesis and Control of Weeds. *InTech*

[28] Adjuvants are added to enhance the physical properties of the active ingredients and hence enhance performance of the end product. They can include (but are not limited to) spreaders, stickers, surfactants, oils, compatibility agents, defoaming agents, soil or plant penetrants, drift control agents, and thickeners.

[29] Mesnage et al 2014. Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. Article ID 179691 *Biomed Res Int.* DOI: 10.1155/2014/179691

[30] C.Cox & M.Surgan. 2006. Unidentified Inert Ingredients in Pesticides: Implications for Human and Environmental Health. *Environ Health Perspect* 114:1803–1806 (2006). doi:10.1289/ehp.9374

> This suggests that synergistic action between pesticide active ingredients is much better documented and more common than current EPA pesticide assessments would indicate.[31]

Adjuvants are generally considered inert by regulators. Adjuvants are not considered to pose risk, and unless an adjuvant is listed as an active ingredient, there will be no daily exposure rates set. If this is the case, crops will not be tested to understand adjuvant residue levels. An adjuvant can be applied to different food crops (e.g. Tween 80 – polysorbate 80). Yet, as the adjuvant is assumed safe, there will be no dietary monitoring to understand total population exposures. The result is there is no knowledge of whether the individual adjuvant or synergies arising from adjuvants presents harm to the population, and particularly vulnerable groups.

Concern is not limited to the toxicity of ingredients considered inert and therefore undeclared, as there are synergies between active ingredients which may be in the retail formulation or in a tank mix, combined by the applicator after the product purchase. New Zealand does not consider synergies from formulation mixtures using different salts that may combine as the active ingredient.[32] Many labels recommend applicators tank mix a GBH with an herbicide and/or insecticide pre-application.[33] The increased toxicity from these synergies is not considered by regulators despite being permitted.

Adverse effects from synergies exerted by salts and adjuvants do not so far seem to have been publicly considered by regulators; yet these risks have been demonstrated to be greater than the sum of the separate risks of the elements in a formulation. [34] Adjuvants in GBHs have been found to pose material toxicity and safety concerns.

As an example, Mesnage and colleagues (2014)[35] studied nine glyphosate-based formulations. The researchers considered glyphosate alone, the formulation without glyphosate and used, as a control, a major adjuvant (polyethoxylated tallowamine). The paper demonstrated that all formulations were more toxic than the active ingredient, glyphosate.

A related paper declared:

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[31] Dr.N. Donley. Toxic Concoction: How the EPA ignores the dangers of pesticide cocktails. Center for Biological Diversity. July 2016.
http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/Toxic_concoctions.pdf
[32] Eg. Nufarm Weedmaster TS470 uses a 'twin salt' formulation of potassium and ammonium salts
[33] Eg. Titan Glyphosate 450 Herbicide
http://www.titanag.com.au/Products/Labels/TITAN_Glyphosate_450_PM.pdf
[34] Mesnage et al 2014. Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. Article ID 179691 *Biomed Res Int*. DOI: 10.1155/2014/179691
[35] Mesnage R., Defarge N., Vendomois, J. S., Seralini G-E. (2014) Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. BioMed Research International. Vol 2014, Article ID 179691.

> Since pesticides are always used with adjuvants that could change their toxicity, the necessity to assess their whole formulations as mixtures becomes obvious.[36]

Responsible regulators have since taken action to remove the toxic ingredient, as this study revealed that POEA was significantly more toxic than glyphosate alone, but also more toxic than formulations that did not contain POEA.

The European Commission recently recommended minimising the use of the substance in public parks, public playgrounds, and gardens and banning the co-formulant POE-tallowamine. [37]

However, New Zealand has not assessed POEA for risk, nor required POEA to be listed on labels, nor moved to ban the adjuvant. POEA is included in most products marketed in New Zealand.

OIA material revealed that the NZ EPA and MPI know of and allow some POEA-containing products in use in New Zealand not to be registered. OIA material also showed that a draft NZ EPA Review was suggesting that a minority of GBHs contained POEA, until Green MP Steffan Browning asked officially for the names of all GBHs in New Zealand and which of those contained POEA. The NZ EPA found that over 75% of New Zealand GBH products contained POEA, which the EU is banning, and had their commissioned report writer delete "used in a minority of products"[38] from its Review. The NZ EPA still fails to allow the public, including farmers, to know which products are free from POEA.

Formulation ingredients (e.g. POEA) are kept secret via commercial confidentiality agreements, and are not disclosed in New Zealand. The Minister for the Environment stated in a response to a Question for Written Answer,

> I am advised that the EPA is not prepared to release the names of the 69 glyphosate-based herbicides containing POEA, because the composition of the formulations is commercial-in-confidence information.[39]

While local councils might act to minimise use of harmful substances in public places, they, like farmers, are unable to easily avoid the unlisted toxic co-formulant POE-tallowamine (POEA) which is present in 69 of the 91 (75%) glyphosate-based-herbicide formulations currently available in New Zealand. [40]

[36] Mesnage et al 2013. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity.
[37] European Commission - Fact Sheet. FAQs: Glyphosate. Brussels, 29 June 2016
[38] Email to Wayne Temple August 2 2016 - titled 'additional wording proposal' see Appendix 1b (iv)
[39] Appendix Ib Question for Written Answer Nick Smith to Steffan Browning 10 August 2016
[40] Appendix Ib. Question for Written Answer Nick Smith to Steffan Browning 10 August 2016

Italy has disclosed products that contain POEA. This includes but is not limited to Roundup, Rodeo, and Touchdown. [41]

Substitutes replacing toxic chemicals are intended to be safer than the replaced toxic adjuvant or additive. However, replacing toxic adjuvants or chemical additives, may not automatically decrease or eliminate the risks. Nevertheless, there have been occasions that replacements have been found to be toxic themselves. This is not limited to pesticides.

> The BPA substitute, BPS, is now shown to have endocrine-disrupting activity on par with BPA in experimental studies.[42]

Consideration of full formulation adverse effects should form a necessary part of New Zealand risk assessment. The NZ EPA Threshold and Classifications Manual advises:

> 9.3.1. Synergistic and antagonistic effects: If there is information about possible synergistic effects that may enhance the toxicity of the substance as a mixture, this must be considered when classifying the substance.[43]

The IARC Working Group included full-formulation studies for its evaluations for glyphosate carcinogenicity. However, in contrast, the NZ EPA Review, using a 'weight of evidence' rational and regulatory convention, placed less emphasis on full formulation results.

This 'weight of evidence finding' seems to depend on manufacturers being able to withhold information from regulators about full-formulation toxicity – manufacturers select the studies submitted for risk assessment – even though judging from the industry term 'acid equivalent,' industry acceptance of full-formulation toxicity is well established.

The NZ EPA review (similar to EFSA) puts weight on, or favours, active ingredient only studies, largely ignoring the results from publications using full glyphosate formulas.

2.3 A 'detailed toxicological review'

The ToR for its review stated that the study was to undertake, 'a detailed toxicological review of the International Agency for Research on Cancer (IARC) Monograph on glyphosate published in 2015 …", that did consider risks from full formulations of glyphosate-based herbicides.

[41] Watts MA et al 2016. Glyphosate Monograph. PAN International. Page 10 http://pan-international.org/wp-content/uploads/Glyphosate-monograph.pdf
[42] Gore AC et al 2015. Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine Reviews, 2015: 36(6):593– 602. http://press.endocrine.org/doi/10.1210/er.2015-1093
[43] Thresholds and Classifications under the HSNO Act 1996. 2012 EPA0109 Page 115.

A 'detailed toxicological review' would be expected to objectively review all the available evidence, including the publications regarding full-glyphosate formulas contained in the IARC monograph.

A global taskforce of 174 scientists from leading research centres across 28 countries studied the link between mixtures of commonly encountered chemicals and the development of cancer at much lower doses than are considered by regulators.[44]

The research paper *'Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead'* was published in June 2015, after the IARC Monograph. That taskforce advised:

> So dominant has the focus been on single chemicals, that combinations of chemicals are rarely tested or even considered. For example, although IARC (authors note, conventionally) has focused on extensive monographs of the carcinogenic nature of individual chemicals, little has been done to evaluate the possibility of carcinogenic effects attributable to chemical mixtures.[45]

2.4 Regulators responsible for public safety dismiss commercial formulation toxicity

The NZ EPA Review limited consideration of full formulation effects, and chose instead to defer to the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung - BfR) stating on page 8.

> The BfR considered that generally testing of formulations should not be used for the toxicological evaluation of active substances because co-formulants may extensively alter the outcome.

Germany-based BfR (as the Rapporteur Member State – RMS) provided the Renewal Assessment Report (RAR) for glyphosate to the European Food Safety Authority (EFSA) December 20, 2013. EFSA forwarded this to the Member States and the applicants of the European Glyphosate Task Force, (represented by Monsanto Europe S.A.) for peer review. The EFSA conclusion was published October 2015.[46]

Critics may be cautious regarding comments from the BfR report as the pesticide industry lobby group Glyphosate Task Force provided the description on which BfR based their evaluations.

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[44] Global taskforce calls for research into everyday chemicals that may cause cancer. Brunel University London

[45] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead. Carcinogenesis. 2015 Jun;36 Suppl 1:S254-96. doi: 10.1093/carcin/bgv039

[46] Peer review of the pesticide risk assessment of the active substance glyphosate. EFSA Journal 2015;13(11):4302

There was a change in tone between the BfR and the final EFSA conclusion, as the NZ EPA paper noted.

> EFSA concluded that the genotoxic potential of such complete formulations should be further assessed.

European Commission approval periods for reviews of agrichemicals are for fifteen years.

EFSA, with the regulatory responsibility for reviewing carcinogenicity of glyphosate, has ignored full-formulation effects while also acknowledging and recommending further assessment of full formulations – at some stage, in the future.

The World Health Organisation (WHO) – Food and Agricultural Organisation (FAO) – Joint Meeting on Pesticide Residues (JMPR) taskforce traditionally uses a narrower range of primarily industry-supplied data to arrive at critical endpoints in their toxicological evaluations. The JMPR evaluated the IARC Working Group findings and acknowledged in August 2015 that:

> The databases for IARC and JMPR monographs for glyphosate, malathion and diazinon were significantly different and that many studies, mainly from the published peer reviewed scientific literature that had not been evaluated by JMPR were available to the IARC Monographs working group.[47]

The JMPR task force noted that the:

> IARC Monographs working group considered studies of active substance, commercial formulations and primary metabolites and that such information is useful to the overall evaluation.[48]

A JMPR Special Session[49] was convened to evaluate glyphosate in May 2016 (JMPR 2016. See 4.5.1) for the WHO and FAO. It effectively ignored full-formulation toxicity and concluded that 'glyphosate is unlikely to pose a carcinogenic risk to humans from exposure through the diet.'[50]

In April 2017 the JMPR Monograph (JMPR 2016), following the May 2016 meeting on diazinon, glyphosate and malathion, was published on-line. It included all the toxicological references.[51]

Contradictions and questions of relevance appear as regulators avoid assessing the full formulation while concurrently increasing scientific

[47] Main findings and recommendations of the WHO Core Assessment Group on Pesticides. Expert task force on Diazinon, Glyphosate and Malathion. http://www.who.int/foodsafety/areas_work/chemical-risks/main_findings_and_recommendations.pdf?ua=1
[48] Ibid
[49] Special Session of the Joint FAO/WHO Meeting on Pesticide Residues: ISSN-2515. Glyphosate 158. www.fao.org/3/a-i5693e.pdf
[50] JMPR toxicological monographs. WHO Evaluations Part II: Toxicology. List of publications in chronological order http://www.who.int/foodsafety/publications/jmpr-monographs/en/
[51] Pesticide residues in food - 2016 evaluations. Part II - Toxicological. World Health Organization, 2017 Page 89 onwards http://apps.who.int/iris/bitstream/10665/255000/1/9789241655323-eng.pdf?ua=1

evidence points towards the fact that full formulation of many pesticides can act synergistically and may exert greater toxicity than the active ingredient.[52] [53] [54] Public sector scientists are working to unravel the chemical mixtures that industry considers subject to commercial confidentiality.

(Appendix I lists a selection of published research demonstrating greater toxicity of the full formulation of glyphosate based herbicides.)

The regulatory position that formulation ingredients should evade scrutiny represents questionable delay and prevarication on the part of the regulators, and appears illogical from a scientific perspective and unconscionable from a public health perspective.

A Consensus Statement[55] by highly regarded expert scientists on the risks associated with glyphosate exposures that was published in 2016 noted:

> The distinction in regulatory review and decision processes between 'active' and 'inert' ingredients has no toxicological justification, given increasing evidence that several so-called 'inert' adjuvants are toxic in their own right.[56]

Regulators have a duty to evaluate risk and toxicity, and this is outlined in the legislation under which regulators operate.

2.5 New Zealand Ministry of Health questioned the EPA challenge to the authority of IARC

The IARC has established a precedent in considering toxicity of full formulation.

The EPA recognises the IARC as a leading authority on cancer, so this consideration should now be understood as relevant to a mandatory consideration for all intents and purposes in law.

There is an inherent contradiction that a government agency responsible for health-based decisions should act to dismiss an IARC decision. This is evident in an email (contained within Appendix VI) dated 12 January 2016,

[52] Mesnage R, Bernay B, Seralini GE. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology. 2013;313(2–3):122–8.
[53] Tsui MT, Chu LM. Aquatic toxicity of glyphosate-based formulations: comparison between different organisms and the effects of environmental factors. Chemosphere. 2003;52(7):1189–97
[54] Folmar LC, Sanders HO, Julin AM. Toxicity of the herbicide glyphosphate and several of its formulations to fish and aquatic invertebrates. Arch Environ Contam Toxicol. 1979;8(3):269–78.
[55] Myers J P et al (2016). Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environmental Health 15(19). DOI 10.1186/s12940-016-0117-0. https://ehjournal.biomedcentral.com/articles/10.1186/s12940-016-0117-0
[56] Mesnage et al 2013. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity.

which demonstrates the reluctance of New Zealand Ministry of Health officials to support the NZ EPA Review.

> Given the international standing of IARC and the expertise and methodology used to undertake these classifications, the Ministry of Health would be reluctant to criticise any classification based on the review of one individual. This would also be seen as a precedent for other classifications and other advice from WHO and its supporting organisations. If the EPA wishes to review or challenge the IARC classification, this would need to be carefully considered, with a detailed methodology and undertaken by an appropriate range of experts recognised in their relevant fields.[57]

The Ministry of Health response is appropriately cautious. The MoH stated that any challenges to an IARC classification should be 'undertaken by an appropriate range of experts recognised in their relevant fields', that is, experts in carcinogenicity.

2.6 Subordinate legislation must be consistent with the purpose of an Act

2.6.1 HSNO Act

The Hazardous Substances and New Organisms Act (HSNO Act) was established to manage the 'risks that hazardous substances and new organisms pose to the health and safety of people and communities and the New Zealand environment'. The purpose of the HSNO Act is to:

> …protect the environment, and the health and safety of people and communities, by preventing or managing the adverse effects of hazardous substances and new organisms.[58]

The NZ EPA focuses on assessment of the active chemical, yet the HSNO Act requires that adverse effects of 'substances' are considered. The HSNO Act's interpretation of 'substance' does not limit a 'substance' to a single active ingredient.

> (a) any element, defined mixture of elements, compounds, or defined mixture of compounds, either naturally occurring or produced synthetically, or any mixtures thereof.[59]

Lower order 'subordinate' legislation includes regulations, thresholds, controls and obligations initiated by government decision-makers operating under an Act. Subordinate legislation must be consistent with the Act's

[57] OIA October 4 2016 to Tim Onnes, Office of Steffan Browning, from Dr Allan Freeth Chief Executive, EPA. File Ref. ENQ-30321-W5D4Q7. Copy inserted into Appendix VI
[58] Hazardous Substances and New Organisms Act. Part 2. Purpose of Act. Sn 4. http://www.legislation.govt.nz/act/public/1996/0030/latest/DLM381222.html
[59] Hazardous Substances and New Organisms Act. Part 1. Preliminary Sn 2 Interpretation

purpose and intent. In this case, the HSNO Act specifies that substances include 'mixtures' and that the overriding purpose of the Act is to protect the environment and the public.

Requirement of the NZ EPA to further consider synergies is contained within the EPA's Thresholds and Classifications manual: *9.3.1. Synergistic and antagonistic effects.*

However, studies supplied to regulators solely research the active ingredient. A formulation may have several active ingredients in addition to adjuvants which express varying toxicity.[60]

Regulators have made no effort to demand studies of full formulation for risk assessment. For example, the WHO – FAO recommended data requirements for registration of technical materials focus on testing of the technical-grade active ingredient (TGAI).[61]

Protocols within the WHO – FAO or OECD should not preclude the NZ EPA from considering the substance the public is exposed to in order to protect health. Issues of constitutional and administrative law are considered in Part 7 *'Has something gone wrong?'*

2.6.2 ACVM Act

The Ministry for Primary Industries (MPI) has responsibilities, functions, duties and powers under the ACVM Act to ensure agricultural compounds (which may be hazardous and fall under the HSNO Act), sold and used in New Zealand, are managed safely.

Lower regulations appear at variance with the purpose of the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM)[62] that hazardous substances must not constitute a risk to public health.

The Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011 exempt adjuvants from registration.[63] As discussed, adjuvants increase the 'performance' or toxicity of the formulation, and individual adjuvants have been demonstrated to be toxic in their own right (e.g. POEA).

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[60] Myers J P et al (2016). Glyphosate Consensus Statement. DOI 10.1186/s12940-016-0117-0.
[61] International Code of Conduct on the Distribution and Use of Pesticides Guidelines on data requirements for the registration of pesticides http://www.who.int/whopes/recommendations/FAO_WHO_Guidelines_Data_Requirement_Registration.pdf
[62] **Agricultural Compounds and Veterinary Medicines Act 1997** http://www.legislation.govt.nz/act/public/1997/0087/latest/whole.html#DLM414583
[63] Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. Schedule 2. Part C. Exemptions for agricultural compounds used to manage plants or plant production (28) http://www.legislation.govt.nz/regulation/public/2011/0327/latest/DLM3982848.html

A pesticide will come under the ACVM Act if it falls within the definition of an 'agricultural compound.'[64] A Ministry of Primary Industry email noted that not all glyphosate products require an ACVM registration and that some home garden products are exempted from the ACVM Act as they may fall into the exempt from registration and out of scope categories. The correspondent suggested that 80% of glyphosate products available in New Zealand would be registered under the ACVM Act.[65]

POEA is contained in 75% of registered GBH products and presumably is in at least some of the potentially 20% of GBH products that are not registered through the ACVM Act. POEA is one example of an adjuvant that is known to be highly toxic and, as such, is subject to bans throughout Europe.

Lower-order legislation exempts adjuvants for consideration of toxicity. There are other surfactants, wetting agents and safeners used in formulations in New Zealand whose toxicity is not being appropriately or transparently assessed.

Downstream implications include lack of screening for these adjuvants in food, groundwater and drinking water as the products are undeclared and rarely known outside the EPA and MPI.

Subordinate legislation that enables regulators to avoid consideration of the toxicity of synergies within the full formulation (substance), and exempts adjuvants from consideration of toxicity, demonstrably fails to meet the purposes of both the HSNO and ACVM Acts.

[64] Agricultural Compounds and Veterinary Medicines Act 1997 http://www.legislation.govt.nz/act/public/1997/0087/latest/whole.html#DLM414583 Sn 2 Interpretation.

[65] APPENDIX 1 (c) 20% GBH products exempt from ACVM Act Registration

3.0 IARC and NZ EPA conclusions: carcinogenic risk

3.1 Oxidative stress, chronic inflammation and carcinogenicity

The IARC Working Group included full-formulation studies of glyphosate-based herbicides as part of their evaluation for IARC Monograph on Glyphosate. When evaluating the mechanistic evidence, specifically oxidative stress, to support the carcinogenic risk of glyphosate to humans they concluded that:

> …there is strong evidence that glyphosate, glyphosate-based formulations, and aminomethylphosphonic acid can act to induce oxidative stress based on studies in experimental animals, and in studies in humans in vitro.[66]

Oxidative stress causing chronic inflammation is a well-established mechanism for pre-disposing development of cancer:

> Cancer is a multistage process defined by at least three stages: initiation, promotion, and progression. Oxidative stress interacts with all three stages of this process.[67] [68]

The general evidence seems to indicate that regulators are slow to accommodate within guidelines and protocols the role of oxidative stress in relation to cancer development. This is a relevant and mandatory consideration when understanding the potential toxicity of a product.

Science regarding the significance of oxidative stress and inflammation has exploded in the last two decades. Yet, regulators seem to persist with a view that oxidative stress and inflammation is of no consequence to evaluations of safety and toxicity of chemical formulations.

Perhaps that reluctance is directed by established industry-derived guidelines that have remained (inappropriately and unlawfully according to New Zealand constitutional and administrative law) unquestioned by regulators (see Section 4.0).

The NZ EPA ignored the IARC findings of oxidative stress, referring to methodological issues, such as exposure routes, that they considered to be not relevant to human exposure. The NZ EPA critique is irrelevant, as the

[66] IARC, Volume 112 (2015) Some Organophosphate Insecticides and Herbicides: Diazinon, Glyphosate, Malathion, Parathion, and Tetrachlorvinphos. http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf
[67] D.A.Hanahan & R.A.Weinberg. Review: The Hallmarks of Cancer. Cell. Vol. 100, pp57–70, 2000 http://dx.doi.org/10.1016/S0092-8674(00)81683-9 Cell
[68] Reuter et al 2010. Oxidative stress, inflammation, and cancer: How are they linked? Free Radical Biology and Medicine Vol. 49, 1 December 2010, Pp 1603–1616. http://dx.doi.org/10.1016/j.freeradbiomed.2010.09.006

IARC Working Group based its findings on the following conclusions on page 79 of the IARC Monograph:

> There is strong evidence that glyphosate, glyphosate-based formulations, and aminomethylphosphonic acid can act to induce oxidative stress based on studies in experimental animals, and in studies in humans in vitro. This mechanism has been challenged experimentally by administering antioxidants, which abrogated the effects of glyphosate on oxidative stress. Studies in aquatic species provide additional evidence for glyphosate-induced oxidative stress.

NZ EPA commented that most evidence towards oxidative stress was seen with whole glyphosate formulations, and referring to EFSA review, they concluded:

> EFSA considered that generally testing of formulations should not be used for the toxicological evaluation of active substances because co-formulants may extensively alter the outcome. Thus any effects found cannot then be attributed to the glyphosate active ingredient present.[69]

In contrast to NZ EPA comments, the October 2015 Final Addendum[70] to the RAR (a response to the IARC Monograph) by EFSA acknowledged that studies demonstrated glyphosate induced oxidative stress.

> From the available data on glyphosate there is some indication of induction of oxidative stress from testing in human cell cultures and in mammalian (in vivo) experimental systems. In particular, the IARC statement that there are indications of oxidative stress in the blood plasma, liver, brain and kidney of rats upon exposure to glyphosate can be supported.

The Final Addendum went on to conclude:

> However, from the sole observation of oxidative stress and the existence of a plausible mechanism for induction of oxidative stress through uncoupling of mitochondrial oxidative phosphorylation alone, genotoxic or carcinogenic activity in humans cannot be deduced for glyphosate and glyphosate-based formulations.*[71]*

In a scientific commentary on the *Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA),*'[72] Dr Christopher Portier and 93 fellow scientists commented on the inconsistent actions of EFSA, pointing out that:

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[69] NZ EPA Review P.13

[70] Addendum 1 to the RAR Assessment of IARC Monographs, 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. August 31 First Draft of Addendum 1. Page 4248.

[71] Ibid. Page 4160

[72] Portier CJ et al 2016. Commentary. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). *J Epidemiol Community* Health 2016:0:1–5. Published Online First: March 3, 2016. doi:10.1136/jech-2015-207005 Page 3.

> EFSA confirmed that glyphosate induces oxidative stress but then, having dismissed all other findings of possible carcinogenicity, dismissed this finding on the grounds that oxidative stress alone is not sufficient for carcinogen labelling.[73]

The JMPR 2016 assessment avoided discussing oxidative stress in their glyphosate review and does not appear to include recently published papers on the topic of oxidative stress and inflammation.[74]

Perhaps by evading discussion of full formulation effects, international regulators can avoid the questions that are created when risk assessment considers realistic pesticide exposures.

The ubiquitous and large-scale use of glyphosate-based herbicides places an additional obligation on regulators to undertake particularly careful and precautionary-based risk assessments that are based on 'reasonable probability' of harm. Precautionary risk assessment is required by section 7 of the HSNO Act.

3.2 Genotoxicity

In discussion of glyphosate genotoxicity, the IARC Working Group states in the IARC Monograph Rationale that:

> 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.
>
> There were three studies of genotoxicity end-points in community residents exposed to glyphosate-based formulations two of which reported positive associations.

Genotoxic substances damage DNA, and this can lead to cancer and birth defects (Phillips and Volker 2009[75], Williams 1989[76]).

The IARC Working Group noted on page 77 of the IARC Monograph:

> Additional evidence came from studies that gave largely positive results in human cells in vitro, in mammalian model systems in vivo and in vitro, and studies in other non-mammalian organisms.

Yet the NZ EPA Review places weight on potentially biased studies by Kier and Kirkland (2013) (paid consultants of Monsanto Company), EFSA (Glyphosate Task Force) and Kier (paid consultants of Monsanto

[73] Ibid Page 3.
[74] Pesticide residues in food - 2016 evaluations. Part II - Toxicological. *World Health Organization*, 2017
[75] Phillips, D., and Volker, M. (2009) Genotoxicity: damage to DNA and its consequences. *Molecular, Clinical and Environmental Toxicology.* Vol 1: Molecular Toxicology, Birkhauser Verlag/Switzerland.
[76] Williams, G. (1989) Methods for evaluating chemical genotoxicity. *Annu. Rev. Pharmacol.Toxicol.* 29:189-211.

Company) to play down the importance of the studies considered to demonstrate evidence of genotoxicity of glyphosate.

There are problems within the publications preferred by the NZ EPA Review; for example, the industry-paid Kier and Kirkland (2013) review referred to bacterial test systems.

> An overwhelming preponderance of negative results in well-conducted bacterial reversion...assays indicates that glyphosate and typical GBFs are not genotoxic...in these core assays.[77]

(Author note: glyphosate-based formulations (GBFs)).

However:

> Bacterial test systems are scientifically flawed for the assessment of compounds with antibiotic properties. Glyphosate has been patented as a broad-spectrum antibiotic (US patent number 7771736) and then again as an "antimicrobial agent" (US patent number 20040077608 A1).[78]

It is not difficult to estimate the ramifications to the glyphosate industry should a chemical be declared genotoxic. For example, once a pesticide is declared genotoxic, it can no longer be approved for use as a pesticide in Europe.[79] European best practice may inspire competitive importers to implement similar standards.

3.3 Glyphosate: Evidence of carcinogenicity

The key evidence concerning glyphosate carcinogenicity for IARC Working Group originates from the studies conducted using experimental animals. The IARC Monograph concluded (page 78) that there was 'sufficient evidence in experimental animals for the carcinogenicity of glyphosate'.

The assessment process and criteria that IARC uses when evaluating the carcinogenic capacity of the substances for the purpose of Monographs is described in the Preamble to the IARC Monographs. The first sentences of the Preamble describe its purpose as follows:

> The Preamble to the IARC Monographs describes the objective and scope of the programme, the scientific principles and procedures used in developing a Monograph, the types of evidence considered and the scientific criteria that guide the evaluations.[80]

[77] Kier LD, Kirkland DJ (2013). Review of genotoxicity studies of glyphosate and glyphosate based formulations. *Crit Rev Toxicol*. 43(4):283–315.
[78] PAN Germany. PAN Germany: Comments on EChA's CLH-Report regarding Genotoxicity. July 2016
[79] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32009R1107
[80] WHO IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Preamble. Lyon 2006. http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf, accessed January 2017. Page 1.

According to the Preamble, the IARC Working Group uses data that is publicly available in sufficient detail in order to conduct an independent scientific evaluation.

3.3.1 Animal studies

When evaluating the carcinogenicity of glyphosate for IARC Monograph, IARC Working Group reviewed dietary administration studies of glyphosate testing for carcinogenicity, two studies that were conducted in male and female mice (US EPA 1985a[81], followed by later pathology reports concerning the original 1985 study: 1985b[82], 1986[83], in addition to study JMPR 2006[84]) and five studies in male and female rats (JMPR 2006[85], US EPA 1991a[86], b[87], c[88], d[89]). There was one glyphosate drinking-water carcinogenicity study using rats (Chruscielska et al. (2000)[90].

[81] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/ chemical/foia/cleared-reviews/reviews/103601/103601183.pdf, accessed January 2017

[82] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. Document No. 004855. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/ chemical/foia/cleared-reviews/reviews/103601/103601206.pdf, accessed January 2017

[83] EPA (1986). Glyphosate; EPA Registration No. 524–308; Roundup; additional histopathological evaluations of kidneys in the chronic feeding study of glyphosate in mice. Document No. 005590. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/ chemicalsearch/chemical/foia/cleared-reviews/reviews/103601/103601-211.pdf, accessed 10 March 2015.

[84] JMPR (2006). Glyphosate. In: Joint FAO/WHO Meeting on Pesticide Residues. Pesticide residues in food – 2004: toxicological evaluations. Report No. WHO/ PCS/06.1. Geneva: World Health Organization; pp. 95–169. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf Accessed 9/5/2017 (NB NZ EPA refers to this paper as WHO 2006)

[85] JMPR (2006). Glyphosate. In: Joint FAO/WHO Meeting on Pesticide Residues. Pesticide residues in food – 2004: toxicological evaluations. Report No. WHO/ PCS/06.1. Geneva: World Health Organization; pp. 95–169. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf Accessed 9/5/2017 (NB NZ EPA refers to this paper as WHO 2006)

[86] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/ chemical/foia/cleared-reviews/reviews/103601/103601265.pdf, accessed January 2017

[87] EPA (1991b). Glyphosate; 2-year combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats - List A pesticide for reregistration. Document No. 008390. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/chemical/foia/clearedreviews/reviews/103601/103601-263.pdf, accessed June 2015; see also http://www.epa.gov/pesticides/ chemicalsearch/chemical/foia/cleared-reviews/reviews/103601/103601-268.pdf, accessed January 2017

[88] EPA (1991c). Peer review on glyphosate. Document No. 008527. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency.

[89] EPA (1991d). Glyphosate – EPA registration No. 524–308 – 2-year chronic feeding/oncogenicity study in rats with technical glyphosate. Document No. 008897. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/chemical/foia/clearedreviews/reviews/103601/103601-268.pdf, accessed 10 March 2015.

[90] Chruscielska K, Brzezinski J, Kita K, Kalhorn D, Kita I, Graffstein B et al. (2000). Glyphosate - Evaluation of chronic activity and possible far-reaching effects. Part 1. Studies on chronic toxicity. Pestycydy (Warsaw), 3–4:11–20.

Glyphosate-based formulations were tested in drinking water in male and female rats (Seralini et al. 2014[91]). Additionally, a tumour initiation-promotion study using male mice was assessed (George et al. 2010[92]).

The IARC Working Group reported major findings in animal studies, including a positive trend in renal tubule carcinoma in male CD-1 mice (US EPA 1985a[93], b[94], 1986[95]), as well as 'a significant positive trend in the incidence of haemangiosarcoma in male CD-1 mice' (JMPR 2006[96]), both results from feeding studies using glyphosate. A significant increase in the incidence of pancreatic islet cell adenoma in males, was reported in two feeding studies using the Sprague-Dawley rat strain (US EPA 1991a[97], b[98], c[99], d[100]).

> One of these two studies also showed a significant positive trend in the incidences (sic) of hepatocellular adenoma in males and of thyroid C-cell adenoma in females.

Additionally, two studies (one in Wistar rats, one in Sprague-Dawley rats) evaluatedd, did not report significant increase in tumor incidence (JMPR 2006[101]). Another rat feeding study was found to be inadequate due to short duration of exposure (JMPR 2006[102]). No significant increase in tumour incidence was found in the study in Wistar rats who were given drinking water containing glyphosate (Chruscielska et al. 2000[103]). The drinking water study using glyphosate-based formula was noted as inadequate for evaluation (Seralini et al. 2014[104]).

The IARC Working Group found evidence of a positive trend in the incidence of renal tubule carcinoma and of renal tubule adenoma or

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[91] Séralini GE, Clair E, Mesnage R, Gress S, Defarge N, Manuela Malatesta M et al. (2014). Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Environmental Sciences Europe, 26(1):1–14. doi:10.1186/ s12302-014-0014-5

[92] George J, Prasad S, Mahmood Z, Shukla Y (2010). Studies on glyphosate-induced carcinogenicity in mouse skin: a proteomic approach. J Proteomics, 73(5):951–64. doi:10.1016/j.jprot.2009.12.008 PMID:20045496

[93] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.

[94] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.

[95] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.

[96] JMPR (2006). Glyphosate. In: Joint FAO/WHO Meeting on Pesticide Residues. 2004: toxicological evaluations.

[97] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances

[98] EPA (1991b). Glyphosate; 2-year combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats No. 008390.

[99] EPA (1991c). Peer review on glyphosate. Document No. 008527.

[100] EPA (1991d). Glyphosate 2-year chronic feeding/oncogenicity study in rats with technical glyphosate. No. 008897.

[101] JMPR (2006). Glyphosate. 2004: toxicological evaluations. (NB NZ EPA refers to this paper as WHO 2006)

[102] Ibid.

[103] Chruscielska K, Brzezinski J, Kita K, Kalhorn D, Kita I, Graffstein B et al. (2000). Glyphosate - Evaluation of chronic activity and possible far-reaching effects. Part 1. Studies on chronic toxicity. Pestycydy (Warsaw), 3–4:11–20.

[104] Séralini GE et al 2014. Republished study:long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Environmental Sciences Europe, 26(1):1–14. doi:10.1186/ s12302-014-0014-5

carcinoma (combined) in males in a feeding study in CD-1 mice (US EPA 1985a[105], b[106], 1986[107]). This was a 24-month feeding study with groups of 50 male and 50 female CD-1 mice. Animals were given glyphosate at a concentration of 0, 1000, 5000, or 30 000 ppm, ad libitum as part of feed.

US EPA describes this study in some later memorandums with variable experimental setup details, e.g. duration of the experiment being 18 months instead of 24 months (US EPA 1991a[108]).

Additionally, some reports outline the dosing regime (and duration) being 0, 150, 750 or 4500 mg/kg/day of glyphosate for 18 months (US EPA 1993[109]) while the actual results of the study stay exactly the same. Due to these inconsistencies and that there is no universal study identification (at least in the documents referred to) to verify the origin of study or to ensure that the separate US EPA documents do refer to the same original study, it is challenging to actually review the situation. As the results are identical, we have assumed that the later US EPA reports (US EPA 1991[110] and 1993[111]) do refer to pathological evaluations US EPA 1985a[112], b[113], 1986[114], with inaccurate experimental set up details.

The IARC Working Group noted that after the second pathological evaluation (US EPA 1986[115]) of the original study (US EPA 1985a[116], 1985b[117]), requested by US EPA and conducted by a pathology working group, the:

> incidence of carcinoma of the renal tubule was 0/49, 0/49, 1/50 (2%), 2/50 (4%) [P = 0.037, trend test for carcinoma]; and the incidence of adenoma or carcinoma (combined) of the renal tubule was 1/49 (2%), 0/49, 1/50 (2%), 3/50 (6%) [P = 0.034, trend test for combined].

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[105] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[106] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[107] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.
[108] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances
[109] EPA (1993a). Knezevich, A.; Hogan, G. A chronic feeding study of glyphosate (Roundup technical) in mice. Unpublished Report no. BDN-77420,project no. 77-2061, 1983, submitted to U.S. Environmental Protection Agency by Monsanto Company, prepared by BioDynamics, Inc.
Reregistration Eligibility Decision (RED) Glyphosate; EPA-738-F-93-011; U. S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1993. MRID 00130406 (Later pathology report produced of this paper McConnel, R. A chronic feeding study of glyphosate (Roundup technical) in mice: pathology report on additional kidney sections. Unpublished project no. 77-2061A, 1985) Page 14. See also Appendix III for reference terms used by regulatory authorities.
[110] EPA (1991a). Second peer review of glyphosate.
[111] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014.
[112] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[113] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[114] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.
[115] Ibid
[116] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[117] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.

> IARC Working Group considered that this second evaluation indicated a significant increase in the incidence of rare tumours, with a dose-related trend, which could be attributed to glyphosate.

A United States Environmental Protection Agency (US EPA) Consensus Review originally in 1985 classified glyphosate as a '*category C oncogen'* (Authors note: 'oncogen' is not a generally recognised or used term in the area of cancer research. Word *'oncogene'* refers to gene that has potential to cause cancer, however, glyphosate is not a nucleic acid and therefore not a gene or any kind of epigene. The correct word to use for a substance that has the ability to cause cancer is 'carcinogen'), based on an increased incidence of renal tubular adenomas in male mice'.[118]

A later US EPA Second Peer Review 1991 Memorandum[119] noted in their summary that the 1985 decision was based on the conclusion that:

> the tumor is rare, it occurred in a dose-related manner, and the incidence was outside the reported historical control range.

After a re-evaluation of this particular mouse study (reporting increased incidence of renal tubular adenomas in male mice), and taking into consideration other animal studies available (two rat dietary studies), the US EPA changed its classification to 'evidence of non-carcinogenicity for humans' (Group E) in 1991.[120]

When commenting on the re-evaluation of the mouse study reporting increased incidence of renal tubular adenomas in male mice, the US EPA Second Peer Review 1991 Memorandum does admit that:

> No statistically significant pairwise differences existed, although the trend was significant. [121]

It also states that:

> Although comparison of these findings to historical control incidences yielded a statistically significant result, this finding did not override the lack of pairwise significance of comparisons to concurrent controls.

(Author's note: US EPA Second Peer Review 1991 Memorandum outlines inconsistent duration for the apparently same study (US EPA 1985a[122], b[123], 1986[124]), e.g. 18 months instead of 24 months).

The New Zealand EPA Glyphosate review on page 7 states:

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[118] March 04, 1985. Memorandum. 4 Page(s). Theodore Farber. Toxicology Branch. Consensus Review of Glyphosate. Caswell No. 661A.
https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/103601/103601-171.pdf
[119] US EPA Second Peer Review of glyphosate June 29 1991 (Memorandum dated Oct 30 1991.)
https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/pdf/103601/103601-265.pdf
[120] Ibid.
[121] US EPA Second Peer Review of glyphosate 1991 Memorandum. Page 14
[122] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[123] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[124] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.

> This finding [the IARC Monograph reporting significant increase in incidence of carcinoma of the renal tubule] is at variance with the US EPA (1993), which reported in their glyphosate review that the occurrence of these adenomas was spontaneous rather than compound-induced because the incidence of renal tubular adenomas in males was not statistically significantly different when compared with the concurrent controls.

When discussing this US EPA 1985a[125], b[126], 1986[127] study, the NZ EPA actually refers to the US EPA 1993[128] reregistration document, which outlines inconsistent duration and dosing regimes for this study ('0, 150, 750 or 4500 mg/kg/day of glyphosate for 18 months), when compared to the original reports.

This US EPA conclusion refers to the original studies that compared proportions of the animals affected, as well as the original linear trend analysis (the details of which are not outlined) which, according to US EPA, did not show significant increase in incidence[129]. In contrast to this statement, a later US EPA 1991 Memorandum[130] states that 'no statistically significant pairwise differences existed, although the trend was significant'.

When The IARC Working group analysed the data from this specific study (e.g. US EPA 1985a[131], b[132], 1986[133]) using the trend tests, specifically testing for linear trend in proportions, this again resulted in significant findings. Trend tests are more powerful statistical test methods particularly for rare tumours, with low incidence rates, and these were the preferred statistical tests for these specific experimental conditions chosen by the IARC Working Group according to guidance as per IARC Preamble.[134]

The IARC Working Group reported that a second feeding study (JMPR 2006[135]) had 'a significant positive trend in the incidence of haemangiosarcoma in male CD-1 mice'. This study had been reported to the Joint FAO – WHO Meeting on Pesticide Residues (JMPR). It had

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[125] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[126] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[127] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.
[128] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014. Washington (DC): Office of Prevention, Pesticides And Toxic Substances, Office of Pesticide Programs, United States Environmental Protection Agency.
https://www3.epa.gov/pesticides/endanger/litstatus/effects/glyphosate-red.pdf accessed 9/5/2017
[129] EPA (1986). Glyphosate; EPA Registration No. 524–308; Roundup; additional histopathological evaluations of kidneys in the chronic feeding study of glyphosate in mice. Document No. 005590.
[130] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances
[131] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[132] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[133] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.
[134] WHO IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Preamble. Lyon 2006. http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf, accessed January 2017.
[135] Atkinson et al 1993a. JMPR (2006). Glyphosate. In: Joint FAO/WHO Meeting on Pesticide Residues. P.122. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf Accessed 9/5/2017

groups of 50 male and 50 female CD-1 mice, who were given glyphosate 'doses of 0, 100, 300, or 1000 mg/kg bw, ad libitum, for 104 weeks'. The Working Group reported 'an increase in the incidence of haemangiosarcoma in males – 0/50, 0/50, 0/50, 4/50 (8%) [P < 0.001, Cochran–Armitage trend test]'. The Working Group considered this study to be adequately reported.

New Zealand EPA Review ignored the IARC reported significant positive trend found in this particular JMPR 2006 study[136], referring to JMPR 2006[137] analysis.

> JMPR (WHO 2006) found that owing to the lack of a dose-response relationship, the lack of statistical significance and the fact that the incidences recorded in this study fell within the historical ranges for controls, these changes were not considered to be caused by administration of glyphosate. They concluded administration of glyphosate to CD-1 mice for 104 weeks produced no signs of carcinogenic potential at any dose.[138]

Regarding the statistical significance, a later US EPA October 1 2015 Memorandum, *Report of the Cancer Assessment Review Committee (CARC)* [139] discusses:

> The IARC attributed the hemangiosarcomas observed in male CD-1 mice at the high dose in separate feeding study (MRID No. 49631702) to treatment due to the positive trend (P<0.001) in a Cochran-Armitage trend test. As shown in Table 16, the agency's statistical analyses also showed a positive trend (P=0.00296) in the trend test. In the Fisher's exact test, there was no pairwise significance when compared to controls.*[140]*

The trend test, specifically Cochran-Armitage trend test was, again in line with the criteria in the IARC Preamble[141], selected by the Working Group as the correct test in these specific circumstances. This test identified a significant positive trend for hemangiosarcoma in male CD-1 mice, in line with *Cancer Assessment Review Committee (CARC) Memorandum* results.[142]

(The CARC memorandum, *Final Report* signed by senior US EPA staff, was posted online by the EPA on April 29, then retracted. The EPA advised they were 'inadvertently posted'.)[143]

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[136] Ibid P.122
[137] Ibid P.122
[138] NZ EPA Review Page 8. Quote from JMPR 2006 Page 122.
[139] US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee (CARC) P.76 http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/EPA-HQ-OPP-2009-0361-0057.pdf Accessed 10/5/2017
[140] Ibid P.76
[141] Ibid
[142] Ibid.
[143] What Is Going On With Glyphosate? EPA's Odd Handling of Controversial Chemical. C.Gillam. *The Huffington Post Blog.* http://www.huffingtonpost.com/carey-gillam/what-is-going-on-with-gly_b_9825326.html

In summary, based on the findings of the animal carcinogenicity studies, the Working Group assessed 'a positive trend in the incidence of renal tubule carcinoma and of renal tubule adenoma or carcinoma (combined)' in male CD-1 mice (US EPA 1985a[144], b[145], 1986[146]). They also assessed 'a significant increase in the incidence of pancreatic islet cell adenoma' in two male Sprague-Dawley rats studies (US EPA 1991a[147], b[148], c[149], d[150]) and 'a significant positive trend in the incidences of hepatocellular adenoma in males and of thyroid C-cell adenoma' in female Sprague-Dawley rats (US EPA1991a[151], b[152], c[153], d[154]), as well as 'a significant positive trend in the incidence of haemangiosarcoma in male CD-1 mice' (JMPR 2006[155]). The Working Group concluded, 'There is sufficient evidence in experimental animals for the carcinogenicity of glyphosate.'

3.3.2 Malignant lymphoma

The IARC Working Group stated that an increase in incidence of lymphoma was reported in three animal studies summarised in the review study by Greim et al. (2015)[156]. However, the IARC Working Group was unable to evaluate these studies, due to insufficient data sets being available.

The three studies named Study 12, 13 and 14 reported by Greim et al. (2015) are briefly summarised below.

Study 12, 1997a reported groups of 50 male and 50 female CD-1 mice, who were given glyphosate as part of their diets at a concentration of 0, 1600, 8000, or 40,000 ppm for the time period of 18 months. A nonsignificant increase in the incidence of lymphoma among other (nonsignificant) findings in males and females was reported.

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[144] EPA (1985a). Glyphosate; EPA Reg.#: 524–308; Mouse oncogenicity study. Document No. 004370.
[145] EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. No. 004855.
[146] EPA (1986). Glyphosate; EPA Registration No. 524–308; histopathological evaluations of kidneys. No. 005590.
[147] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances
[148] EPA (1991b). Glyphosate; 2-year combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats No. 008390
[149] EPA (1991c). Peer review on glyphosate. Document No. 008527.
[150] EPA (1991d). Glyphosate 2-year chronic feeding/oncogenicity study in rats with technical glyphosate. No. 008897.
[151] EPA (1991a). Second peer review of glyphosate. Washington (DC): Office of Pesticides and Toxic Substances
[152] EPA (1991b). Glyphosate; 2-year combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats No. 008390
[153] EPA (1991c). Peer review on glyphosate. Document No. 008527.
[154] EPA (1991d). Glyphosate 2-year chronic feeding/oncogenicity study in rats with technical glyphosate. No. 008897.
[155] JMPR (2006). Glyphosate. In: Joint FAO/WHO Meeting on Pesticide Residues. 2004: toxicological evaluations.
[156] Greim H, Saltmiras D, Mostert V, Strupp C (2015). Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/carcinogenicity rodent studies. Crit Rev Toxicol, 45(3):185–208. doi:10.3109/10408444.2014 .1003423 PMID:25716480

Study 13, 2001 had groups of 50 male and 50 female Swiss albino mice receiving diets that contained glyphosate at a concentration of 0 (control), 100, 1000 or 10,000 ppm for the duration of 18 months. The IARC Working Group concluded that the authors of this study reported 'a statistically significant increase in the incidence of malignant lymphoma (not otherwise specified, NOS) in males at the highest dose: 10/50 (20%), 15/50 (30%), 16/50 (32%), 19/50 (38%; $P < 0.05$; pairwise test); and in females at the highest dose: 18/50 (36%), 20/50 (40%), 19/50 (38%), 25/50 (50%; $P < 0.05$; pairwise test)'.

> *Study 14, 2009a* had 51 male and 51 female CD-1 mice, who were given glyphosate through diet at concentrations of 0, 500, 1500 or 5000 ppm for the duration of 18 months. Incidences of a number of adenomas as well as carcinomas were reported, including malignant lymphoma. The Working Group concluded that according to the authors of the study, there was 'a significant positive trend in the incidence of...malignant lymphoma (0/51, 1/51, 2/51, 5/51)'. The statistical tests were not specified.[157]

Study 14 2009a, reviewed by the IARC Working Group, was featured additionally as Nufarm 2009b, (Author's note: Greim et al 2015 have apparently made a mistake as they are referring to the original Nufarm 2009b mouse study as Nufarm 2009a) when summarised in the US EPA October 1 2015 Memorandum, *Report of the Cancer Assessment Review Committee*[158] in the following way:

> In male mice at the high dose (5000 ppm) there were increases in the incidences of...malignant lymphomas...For the malignant lymphomas, there was a trend and pairwise significance.
>
> There was a dose-dependent and statistically significant increase in the incidence of malignant lymphomas in male mice (Nufarm, 2009b[159],). The incidence was: 0/51 (0%; trend P=0.006633), 1/51 (2%), 2/51 (4%) and 5/51 (10%; P=0.02820) at the 0, 85, 267 or 946 mg/kg/day groups, respectively.[160]

US EPA Glyphosate Final Report continues its discussion:

> The malignant lymphomas were not considered to be treatment-related since the 0% incidence of this lesion in the concurrent control for male mice was lower than the historical control mean (4.5%) and range (1.5–21.7%) in this strain and age of mice...Therefore, the apparent statistical significance of the pairwise comparisons of the high dose male groups with the concurrent control might have been attributable to this factor and not to actual carcinogenic response.[161]

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[157] IARC Working Group.35
[158] US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee P.73 http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/EPA-HQ-OPP-2009-0361-0057.pdf Accessed 10/5/2017
[159] Cited in Greim et al., 2015
[160] US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee P.73
[161] US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee P.57

Historical control data should be used cautiously when evaluating carcinogenicity data. The OECD Guidance Document 116 on the Conduct and Design of Chronic Toxicity and Carcinogenicity Studies[162] states in its historical control consideration that:

> In any discussion about historical control data, it should be stressed that the concurrent control group is always the most important consideration in the testing for increased tumour rates.

In the event of using the historical control data, this should be from the same timeframe, animal strain, preferably from the same laboratory or supplier and the pathologist should preferably be the same.[163]

Therefore, the statistically significant increase of malignant melanoma in *Study 14, Nufarm 2009a*, summarised in the *Cancer Assessment Review Committee October 2015 Memorandum,* should be considered treatment-related as the increase in the incidence of these tumours compared to the concurrent controls is significant by both pairwise statistical comparison and by using trend test.

Although not evaluated by the IARC Working Group, the above reported findings of malignant lymphoma are consistent with, and further support, the IARC Working Group findings of 'sufficient evidence in experimental animals for the carcinogenicity of glyphosate.' as well as ‘limited evidence for the carcinogenicity of glyphosate in humans', ie non-Hodgkin’s lymphoma.

The NZ EPA Review adopts the mode of action apparent in the European BfR Final Addendum of the Renewal Assessment Report (RAR) and Glyphosate Issue Paper: Evaluation of Carcinogenic Potential[164] discussion of the IARC Working Group, where occurrence of malignant lymphoma was dismissed.

NZ EPA Review uses the conclusions from the latter EFSA peer review[165] to dismiss mouse studies indicating evidence of malignant lymphoma. EFSA accepted only one as having a carcinogenic effect and then questioned the validity of that study due to the presence of a viral infection.

[162] OECD Guidance Document 116 on the Conduct and Design of Chronic Toxicity and Carcinogenicity Studies, Supporting Test Guidelines 451, 452 and 453 *Second edition.* 4.22 Historical control considerations 398. Page 135.
[163] Ibid.
[164] Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. EPA’s Office of Pesticide Programs September 12, 2016 . https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf
[165] EFSA (European Food Safety Authority), 2015. Peer review of glyphosate. doi:10.2903/j.efsa.2015.4302. https://echa.europa.eu/documents/10162/13626/efsa_glyphosate_conclusion_en.pdf

Dr Clausing notes that there was no viral infection in this 2001 study. The 31 March RAR had merely discussed (on page 63) that viruses *could* be present.[166] This study has attracted controversy. (See Section 4.2.1)

As is evident, the 'experimental animal studies' are a central part of this debate and so deserve greater public health consideration outside of the narrow confines of the regulatory environment.

New Zealand EPA Glyphosate report heavily relies on the European Food Safety Authority (EFSA) Glyphosate peer review[167] findings.

The European approach has been heavily criticised. An expert scientific Commentary responding to the release of the RAR *Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)*, Dr. Portier and colleagues criticised EFSA for dismissing evidence of cancer.

> Ignoring established guidelines cited in their report, EFSA dismissed evidence of renal tumours in three mouse studies, hemangiosarcoma in two mouse studies and malignant lymphoma in two mouse studies. Thus, EFSA incorrectly discarded all findings of glyphosate-induced cancer in animals as chance occurrences.*[168]*

In a 'state of science' review of glyphosate, released October 2016, PAN International addressed deficits within the RAR evaluation.

> Of particular concern is the BfR's refusal to acknowledge the toxicological significance of an increase in malignant lymphoma observed in male mice of 3 different mouse studies, where the top dose of 2 of the studies was close to or even below the dose of 1,000 mg/kg body weight (considered as a "limit dose" by the BfR, though a questionable limitation from a guideline perspective). The finding of malignant lymphoma was clearly supported by historical control data (HCD) in one study (Kumar 2001), while HCD did not contradict the result of the second study (Sugimoto 1997), and no valid HCD were available for the third one (Wood et al 2009). Two more mouse carcinogenicity studies were available which did not show a significant increase in malignant lymphoma. Although not spelled out, these studies were obviously used by the BfR to claim lack of reproducibility. However, the BfR ignored the fact that with regard to malignant lymphoma one of these studies was invalid and the other one equivocal. For a more extended discussion see PAN Germany (2016)*[169]*

[166] Dr P. Clausing. The EFSA Conclusion on the Peer Review of the Glyphosate Risk Assessment A Reality Check. PAN Germany. Hamburg December 2015 http://www.pan-germany.org/download/Analysis_EFSA-Conclusion_151201.pdf
[167] EFSA (European Food Safety Authority), 2015. Peer review of glyphosate.
[168] Portier CJ et al 2016. Commentary. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). *J Epidemiol Community* Health 2016:0:1–5. Published Online First: March 3, 2016. doi:10.1136/jech-2015-207005
[169] Watts MA et al 2016. Glyphosate Monograph. PAN International. Page 22

Dr Peter Clausing and PAN Germany heavily criticised the European Peer Review in the December EFSA *Conclusion on the Peer Review of the Glyphosate Risk Assessment: A Reality Check*:

> Clear evidence for carcinogenic effects in animal experiments is dismissed by the use of unfounded statements and distortion of facts. Significant increases of the incidence of one or more tumour types have been shown in all five mouse studies. The studies themselves are considered valid by the EFSA and the RMS.[170]

Dr Clausing, a former industry toxicologist claims that same tumour type is evidence of consistency, the trend test (Cochran-Armitage) demonstrating statistically significant findings should be accepted as evidence, and that the concept put forward of a maximum tolerated dose is false.

Similar criticism is faced by regulators in the United States. Comment on the US EPA Issue Paper on glyphosate by the US Centre for Food Safety (CFS) found the former lacked rigour.

> EPA has failed to report several statistically significant tumor findings. When these are considered, the animal data are much more persuasive than suggested in EPA's discussion (EPA 2016, pp. 95-96). Malignant lymphomas were among the strongest findings in animal studies, while epidemiology suggests glyphosate exposure is a risk factor for malignant lymphomas in humans.[171]

The CFS considered the USA EPA criteria for classifying glyphosate.

> This classification system (e.g. likely or not likely to be carcinogenic) is based purely on the hazard assessment, prior to the consideration of dose-response or human exposure levels required for a full risk assessment. On this basis, "likely to be carcinogenic to humans" best fits the evidence. Criteria for assignment of this descriptor include "an agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans" or "a 28 positive tumor study that is strengthened by other lines of evidence, for example…plausible (but not definitively causal) association between human exposure and cancer" (EPA 2005, 2-55).

3.3.3 Human studies: Non-Hodgkin's Lymphoma

In addition to finding 'sufficient evidence in experimental animals for the carcinogenicity of glyphosate', the IARC Working Group concluded that 'there is limited evidence in humans for the carcinogenicity of glyphosate'.

[170] Dr. P. Clausing The EFSA Conclusion on the Peer Review of the Glyphosate - A Reality Check. PAN P.7

[171] Centre for Food Safety. OPP Docket- US EPA. Docket EPA-HQ-OPP-2016-0385. October 12, 2016. Page 26. http://www.centerforfoodsafety.org/files/sap-glyphosate-cancer-comments--cfs-20161_35863.pdf

In particular, they reported 'a positive association has been observed for non-Hodgkin's lymphoma' (NHL) and advised:

> In summary, case–control studies in the USA, Canada, and Sweden reported increased risks for NHL associated with exposure to glyphosate.

A 2016 Commentary published by 96 scientists, *Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)* considered that:

> The finding of limited evidence by the IARC WG was for NHL, based on high-quality case–control studies, which are particularly valuable for determining the carcinogenicity of an agent because their design facilitates exposure assessment and reduces the potential for certain biases.[172]

However, 'limited evidence' may be interpreted in many ways. EFSA established:

> Limited evidence for an association between glyphosate-based formulations and non-Hodgkin lymphoma (NHL), overall inconclusive for a causal or clear associative relationship between glyphosate and cancer in human studies.[173]

The NZ EPA Review appears to ignore consistently positive findings identified by the IARC Working Group which display various levels of statistical significance, and downplays risk of NHL and states on page fifteen:

> Given the lack of confirmation of the small number of positive findings from case-control studies in the more powerful cohort study, the epidemiological support for the conclusion "limited evidence" in humans is not convincing.

Contrast this with the IARC monograph conclusion of 'limited evidence in humans for the carcinogenicity of glyphosate', in particular a positive association for non-Hodgkin's lymphoma (NHL), which was:

> based on high-quality case–control studies, which are particularly valuable for determining the carcinogenicity of an agent because their design facilitates exposure assessment and reduces the potential for certain biases.

Portier et al (2016) criticised the methods by which EFSA weighted studies and expressed frustration at regulators' more linear approach:

> To provide a reasonable interpretation of the findings, an evaluation needs to properly weight studies according to quality rather than simply count the number of positives and negatives. The two meta-analyses cited in the

[172] Portier CJ et al 2016. Commentary. doi:10.1136/jech-2015-207005
[173] EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. *EFSA Journal* 2015;13(11):4302, 107 pp. doi:10.2903/j.efsa.2015.4302

> IARC Monograph are excellent examples of objective evaluations and show a consistent positive association between glyphosate and NHL…Finally, we strongly disagree that data from studies published in the peer-reviewed literature should automatically receive less weight than guideline studies.[174]

The PAN International Monograph throws some light on the situation to discuss the difference between the IARC Monograph and the European position:

> Both institutions come to the same conclusion, i.e. that there is "limited evidence" in humans for the carcinogenicity of glyphosate, but they use this conclusion for opposite ends. The IARC considers the observed association between glyphosate use and NHL as supportive of the sufficient evidence in experimental animals (with main effects on the lymphatic system), while the BfR adopts – according to its own words – "a more cautious view since no consistent positive association is observed" (RMS Germany 2015b, p.90).
>
> To provide a reasonable interpretation of the findings, an evaluation needs to properly weight studies according to quality rather than simply count the number of positives and negatives. The two meta-analyses cited in the IARC Monograph are excellent examples of objective evaluations and show a consistent positive association between glyphosate and NHL…[175]

The IARC Working Group considered that the available human evidence was sufficient to demonstrate an association with NHL and glyphosate; this was elaborated upon by Portier et al 2016.

> Sufficient evidence means 'that a causal relationship has been established' between glyphosate and NHL...Legitimate public health concerns arise when 'causality is credible', that is, when there is limited evidence of carcinogenicity.[176]

Responsible decision-makers may consider that the IARC conclusion is, at a minimum, consistent with the 'probable harm' (ie a probability greater than 50 per cent) that is the reasonable benchmark for invoking the 'precautionary principle' in matters of responsible government policy-making and regulatory conduct where evidence of harm is 'scientifically plausible but uncertain.'[177]

> The precautionary principle is about avoidance of harm, and it also is about avoidance of uncertain harm. [178]

[174] Portier CJ et al 2016. Commentary. doi:10.1136/jech-2015-207005
[175] Watts et al 2016. Glyphosate Monograph. Sept 2016 PAN International Page 23
[176] Portier CJ et al 2016. Commentary. doi:10.1136/jech-2015-207005
[177] UNESCO. March 2005. The Precautionary Principle. World Commission on the Ethics of Scientific Knowledge and Technology (COMEST)
[178] Pesticide Action Network Handbook. *PAN Germany* 2003 http://www.pan-germany.org/download/pan_action_handbook.pdf

3.4 Reliance on outdated scientific understanding

Prof Ian Shaw, Professor of Toxicology, University of Canterbury, commented on the requirement to reduce exposure to glyphosate in light of new evidence.

> In addition to glyphosate's carcinogenicity, it has recently been shown (in a single study) to be an endocrine disruptor (ie it interferes with the action of hormones; in glyphosate's case, the female hormone estradiol). This is a surprising result, but means that there might be long term environmental implications because of the large amounts used in agriculture. And, of course the risk to humans might not only relate to cancer, but also hormone related issues.
>
> All of these changes to our understanding of the toxicity of glyphosate underline the need to review its use. This does not mean that we should ban glyphosate outright, but that we should look at ways of significantly reducing its use as a means of reducing human exposure.[179]

3.4.1 Endocrine disruption

IARC and EFSA did not consider the endocrine action of GBHs and had they done so, the case for the carcinogenicity of glyphosate may have been strengthened. Endocrine-disrupting compounds may disrupt homeostasis and influence the development or progression of some cancers. Children are highly susceptible to endocrine disruptors.

Cancer can occur via multiple routes and the endocrine (hormone) system can play a significant part in cancer establishment.

> Endocrine disruptors (EDCs) are the hundreds or more 'exogenous chemical(s) or mixtures of chemicals that interfere with any aspect of hormone action.[180]

Glyphosate-based formulations have been linked to endocrine disruption in recent papers.[181] [182]

Glyphosate-based herbicides are known to be estrogenic at low concentrations and may act to induce breast cancer cell growth.[183]

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[179] Glyphosate weedkiller: what's the risk? – Expert reaction Science Media Centre. January 20th, 2016. https://www.sciencemediacentre.co.nz/2016/01/20/glyphosate-weedkiller-whats-the-risk-expert-reaction/
[180] Gore AC et al 2015. Endocrine Society's Second Scientific Statement. DOI:10.1210/er.2015-1093
[181] Richard, S., Moslemi, S., Sipahutar, H., Benachour, N., Séralini, G-E. 2005. Differential effects of glyphosate and Roundup on human placental cells and aromatase. Env.Health Perspectives 113: 716–20.
[182] Gasnier, C., Dumont, C., Benachour, N., Clair, E., Chagnon, M.C., Seralini, G.E., 2009. 499 Glyphosate-based herbicides are toxic and endocrine disruptors in human cell 500 lines. Toxicology 262, 184 -191.
[183] Thongprakaisang S. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol. 2013 Sep; 59:129-36. doi: 10.1016/j.fct.2013.05.057

Hormone-sensitive cancers (for example breast, endometrial, ovarian, prostrate) are increasing.[184] [185] For example:

> A weak xeno-estrogen can stimulate the production of estradiol, a potent endogenous carcinogen or alter the receptors with which a cell will respond to estrogen.[186]

Regulatory risk assessment frameworks have not addressed new scientific understanding of the impacts of endocrine disruption (and the more toxic interplay of formulation mixtures), and they resist considering the role of endocrine disruptors in cancer development.

Regulatory protocols do not stretch to consideration of these often delicate and difficult-to-establish linkages. It can be easy to dismiss (arguably inappropriately) endocrine effects that may precede or facilitate cancer development.

Endocrine effects resulting from chemical exposures that contribute to cancer establishment have been understood for 20 years. In 1993, Dr Theo Colburn and colleagues stated for the first time:

> Low-level exposure to endocrine disrupting chemicals (EDCs) especially during early development, leads to both transient and permanent changes to endocrine systems. This results in impaired reproduction, thyroid function, and metabolism, and increased incidence and progression of hormone-sensitive cancers.[187]

The U.S. 2008 – 9 President's Cancer Panel noted:

> Some chemicals indirectly increase cancer risk by contributing to immune and endocrine dysfunction.[188]

The panel acknowledged:

> These substances typically are not listed as carcinogens by regulatory agencies, but the body of evidence linking EDCs to breast and other cancers is growing.

Pollutant chemicals rarely have boundaries and the placental and blood brain barrier of the foetus, previously assumed to act as a safeguard, is permeable in the early months of life. The panel stated in 2009:

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[184] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures P.598

[185] March 2012. Study Finds Prostate Cancer Increasing in Most Countries. WHO IARC. Press Release No.209.

[186] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures

[187] Colborn T, vom Saal FS, Soto AM (October 1993). "Developmental effects of endocrine-disrupting chemicals in wildlife and humans". Environ. Health Perspect. 101 (5): 37884. doi:10.2307/3431890 http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1519860&blobtype=pdf (Accessed 4.10.2017)

[188] 2008–2009 Annual Report. President's Cancer Panel. REDUCING ENVIRONMENTAL CANCER RISK What We Can Do Now Suzanne H. Reuben for The President's Cancer Panel April 2010.

> Numerous environmental contaminants can cross the placental barrier; to a disturbing extent, babies are born "pre-polluted.*"*

Endocrine effects may not follow a typical dose-response curve that dominates regulatory protocol and guideline requirements which insist that increasingly adverse effects should be observed at higher dose levels. However, established science (but not regulators) acknowledge that in addition these effects can occur at exceedingly low levels not studied by regulators; and they can occur as a result of synergistic responses between different chemicals (which further suggests the irrelevance of 'active-ingredient-only' risk assessment).

> Part of the complexity of the EDC field is that exogenous chemicals are being added on top of the endogenous hormonal milieu, such that complex mixtures, dose additivity, and synergism between and among hormones and chemicals are the norm.*[189]*

The existing regulatory paradigm that depends on 'silo-ised' responses to single chemicals tested in isolation, fails to address complexities of the endocrine system to disruption and the consequences of lifelong disruption.

It is profoundly important that responsible government and the health sector comprehend the implications of lifelong exposure to environmental stressors that operate at extraordinarily low dose levels and scientific knowledge that:

> …demonstrates first that even "weak" estrogens can significantly alter estrogen action, and second, that there is no obvious threshold of effect.*[190]*

The economic costs of 'externalities' associated with chemical use and endocrine disruption have been documented. European researchers have analysed costs associated with endocrine disruption and advised it is 'likely to contribute substantially to disease and dysfunction across the life course with costs in the hundreds of billions of Euros per year'.[191] [192] [193]

A recent paper researching the costs of exposure to endocrine-disrupting chemicals in the USA concluded that 'disease costs of EDCs were much higher in the USA than in Europe ($340 billion [2·33% of GDP] vs $217 billion [1·28%])*'.[194]*

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[189] Gore AC et al 2015. Endocrine Society's Second Scientific Statement. DOI:10.1210/er.2015-1093
[190] Ibid.
[191] Health Costs in the EU: How much is related to EDCs? Health and Environment Alliance (HEAL) June 2014
[192] Trasande et al 2016. Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. Andrology. 2016 Jul;4(4):565-72. doi: 10.1111/andr.12178. 2016 Mar 22.
[193] Rijk et al 2016 Health cost that may be associated with Endocrine Disrupting Chemicals. IRAS 2016
[194] Exposure to endocrine-disrupting chemicals in the USA: a population-based disease burden and cost analysis
Attina, Teresa M et al. The Lancet Diabetes & Endocrinology , Volume 4 , Issue 12 , 996 – 1003. http://www.thelancet.com/journals/landia/article/PIIS2213-8587(16)30275-3/fulltext

3.4.2 Dose response curve and non-linear curve effects

Conventional science understands that the endocrine effects from chemical toxicity do not occur in a traditional dose response manner. Regulatory pesticide risk assessment is yet to 'accept' non-monotonic (non-linear) dose-response curves, which may resemble a U (even an inverted U).

HSNO regulations include an uninformed and outdated requirement that values must be consistent with a dose-response curve:

> (a) the shape and slope of the dose response curve for the substance based on the dose of the substance and the significant adverse biological effects or toxic effects of the substance.[195]

NZ EPA's User Guide for Thresholds and Classifications synchronises with these HSNO regulations:

> …evidence of dose–time–response relationships; that is, an increased cancer incidence associated with higher exposure levels or with increasing exposure duration.[196]

The NZ EPA Review dismissed carcinogenic effects in laboratory animals, due to lack of dose response, the fact that tumours only occurred at high levels, that cancers fell within the range of normal, and that effects were not similar in all studies.

Modern mainstream medicine acknowledges non-linear curve effects at hormonally relevant levels. For example, low doses of hormonally active drugs Lupron and tamoxifen stimulate disease, while high doses inhibit disease.[197]

Medicines do not go through clinical trials as 'active ingredients' but as formulations. These are the best models of pesticide safety testing because it is the formulation and not the active ingredient to which we are exposed.

Benchmark dosages, relied on for public policy formulation, should include endocrine-sensitive disease endpoints that are focused upon biological health outcomes that are material to both humans and the environment as a whole.[198]

Vandenberg and colleagues in a 2012 review that considered low dose and non-monotonicity in endocrine studies, outlined the problems with regulatory protocols and the practice of using high doses to predict low dose responses:

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[195] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001 Section 18 (3) (a)
[196] Thresholds and Classifications under the HSNO Act 1996. 2012 EPA0109. http://www.epa.govt.nz/Publications/ER-UG-03-2.pdf Page 223.
[197] Myers et al 2009b. A Clash of Old and New Scientific Concepts in Toxicity, with Important Implications for Public Health. Environ Health Perspect. 2009 Nov; 117(11): 1652–1655.
[198] Gore AC et al 2015. Endocrine Society's Second Scientific Statement. DOI:10.1210/er.2015-1093

> In the standard practice of regulatory toxicology, the calculated safe dose, also called a reference dose, is rarely tested. In a system that is responding non-monotonically, it is not appropriate to use a high-dose test to predict low-dose effects. Unfortunately, all regulatory testing for the effects of chemical exposures assume that this is possible. All current exposure standards employed by government agencies around the world, including the FDA and EPA, have been developed using an assumption of monotonicity. The low-dose range, which presumably is what the general public normally experiences, is rarely, if ever, tested directly.
>
> The standard procedure for regulatory testing typically involves a series of tests to establish the lowest dose at which an effect is observable (the LOAEL), then a dose beneath that at which no effect is observable (the NOAEL). Then a series of calculations are used to acknowledge uncertainty in the data, species differences, age differences, etc., and those calculations, beginning with the LOAEL or the NOAEL, produce a reference dose that is presumed to be a safe exposure for humans. Typically, the reference dose is 3- to 1000-fold lower than the NOAEL. That reference dose then becomes the allowable exposure and is deemed safe, even when it is never examined directly. For chemicals with monotonic linear dose-response curves, this may be appropriate. But for chemicals that display non-monotonic patterns, it is likely to lead to false negatives, i.e. concluding that exposure to the reference dose is safe when in fact it is not.[199]

Chemical regulators are yet to adopt transparent protocols and incorporate a specific science-based approach to assess substances with endocrine-disrupting properties in risk assessment. It can be done.[200]

3.4.3 Synergies that arise from chemical mixtures

If the HSNO Act requires that government employees and agencies consider the adverse effects of 'hazardous substances,' then the failure to consider the 'substance' or mixture is deeply inconsistent, and in direct conflict with the statutory requirements established by the HSNO Act.

When applying for a patent, companies note new pesticide formulations and the benefit from mixture synergies. The US EPA Office of Inspector General recently released a paper that called for consideration of synergies to help reduce uncertainties as studies of mixture synergies are not requested during the registration or risk assessment process. The paper cited a 2016 research paper published by the Center for Biological

[199] Vandenberg, LN, Colborn, T, Hayes, TB et al 2012. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012; 33: 378–455
[200] Niemann et al 2014. Assessment of three approaches for regulatory decision making on pesticides with endocrine disrupting properties. Regul Toxicol Pharmacol. 2014 Dec;70(3):590-604. doi: 10.1016/j.yrtph.2014.09.001.

Diversity, which reviewed the US EPA's pesticide mixture approval process:[201]

> The research paper reported that there was evidence of synergy in the patent application of nearly 70 percent of multi-ingredient pesticide products (including herbicides, insecticides, and fungicides/nematicides) approved by the EPA in the last 6 years, and from four major agricultural companies. The report found 140 products with at least two active ingredients were registered between June 2010 and June 2016. Some of the most frequently used herbicides in the United States (e.g., glyphosate; atrazine; 2,4-D; Dicamba; and neonicotinoids) were present in the majority of these patent applications.

Within the NZ EPA framework there is a sole, and therefore possibly misleading, focus on safety issues arising from high-dosage levels of a single 'active' ingredient in a formulation.

> Unfortunately, risk assessment practices that are currently used to assess the carcinogenic potential of chemicals have changed very little. Without a way to anticipate the carcinogenicity of complex mixtures, an important gap in capability exists and it creates a significant weakness in current risk assessment practices. [202]

A wide body of literature accepts the potential harm from mixtures of chemicals that may not be individually carcinogenic (and may be structurally dissimilar) but can contribute to instigation of carcinogenesis by, amongst other things, environmentally relevant chronic low-dose exposures; synergies that act via dissimilar sequences and processes; reflect the probability that mixtures will target different cancer-relevant body systems; and therefore carcinogenic effects that might be second-order or third-order from disruption of such body systems.

It seems that traditional regulatory guidelines ignore formulation synergies, and claim that there must be a common toxic endpoint, and that each chemical must be a carcinogen before it can be a possible contributor to a carcinogenic formulation, or mixture.

> However, it is now evident that not every pro-carcinogenic action resulting from a chemical exposure must be the result of a chemical that is a carcinogen itself. Continued focus on individual carcinogens reflects a lingering paradigm that overlooks the examples of synergies.[203]

NZ EPA does not seem to have guidelines inclusive of synergies arising from mixtures of chemicals – for example, chemical clusters that disrupt endocrine function where, for further example, those effects may lead at first, second or third-order steps which increase carcinogenicity risk.

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[201] N. Donley. "Toxic Concoctions: How the EPA Ignores the Danger of Pesticide Cocktails," Center for Biological Diversity. July 2016. http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/Toxic_concoctions.pdf

[202] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures.

[203] Gore AC et al 2015. Executive Summary to EDC-2

If New Zealand regulators were to consult regularly with endocrinologists and oncologists, as either academics or practicing professionals from the health sector, this would perhaps commence an informed era in NZ EPA risk assessment – and transition from sixteenth-century science (single ingredient, dose makes the poison science), and from apparently close industry ties that seem to eclipse the public interest and the precautionary principle that are supposed to be the bedrock principle of responsible and trustworthy government.

The Halifax Project Taskforce comprised 174 scientists from 28 countries and focused on 'Assessing the Carcinogenic Potential of Low Dose Exposures to Chemical Mixtures in the Environment.'[204] This group considered that common environmental chemicals assumed to be safe at low doses may act separately or together to disrupt human tissues in ways that eventually lead to cancer.[205] The paper was critical of regulators that neglect to adopt or account for emerging scientific factors that likely require regulatory caution in decision-making. The Taskforce noted:

> Advances in our understanding of the complexity of cancer biology have resulted in serious critiques of current risk assessment practices related to exogenous exposures along with calls for an expanded focus on research that will allow us to evaluate the (potentially carcinogenic) effects of in-utero exposures and low-level exposures to combinations of chemicals that occur throughout our lifetime.[206]

This paper is one of many calls for better risk assessment.

A 2016 scientific Consensus Statement found that:

> Regulatory estimates of tolerable daily intakes for glyphosate in the United States and European Union are based on outdated science.[207]

The paper expressed concern that the effects of GBH may be in part due to endocrine disrupting activities and called for more research. Another key paper discussing endocrine disruption and the adequacy of current risk assessment stated:

> Unless and until regulatory agencies incorporate modern endocrinologic principles into their risk assessment paradigms, they will continue to provide false assurances of "safety" and fail to recognize the actual health risks posed by chronic low-level exposure to an increasing number of chemicals found in commonly used products.[208]

[204] Getting to know cancer. http://www.gettingtoknowcancer.org/taskforce_environment.php
[205] Common chemicals may act together to increase cancer risk, study finds. *Science Daily*. July 21 2015. https://www.sciencedaily.com/releases/2015/07/150721091751.htm
[206] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures.
[207] Myers J P et al (2016). Glyphosate Consensus Statement. DOI 10.1186/s12940-016-0117-0.
[208] Myers et al 2009b. A Clash of Old and New Scientific Concepts in Toxicity.

The US EPA recently called for increased scrutiny of formulation synergies and chemical pathways (mechanism of action) as part of a series of recommendations to address herbicide resistance.

Debate within the IARC Working Group was not about whether glyphosate was probably carcinogenic or not: the debate centred on the concern as to whether glyphosate should be declared a dangerous carcinogen, or less harmful but still dangerous 'probable carcinogen' – the finding the scientists eventually agreed to.

3.4.4 Low-dose effects from mixtures of endocrine disruptors

There is evidence that synthetic chemicals introduced into the environment – even at claimed 'low levels' – can play a significant role in harmful endocrine (hormone) disruption.

Low-dose effects of glyphosate-based herbicides in relation to first, second and third-order links to cancer development and cancer progression do not appear to have been studied. However, there is reason to act with caution. The Halifax Project taskforce advised that:

> The known effects for chemicals examined in isolation and at higher concentrations cannot be readily extrapolated to effects at lower concentrations.[209]
>
> When the potential for non-linear dose-response relationships is combined with the possibility of synergism between and amongst low doses of mixtures of individual chemicals in the environment, it appears plausible that chemicals that are not individually carcinogenic may be capable of producing carcinogenic synergies that would be missed using current risk assessment practices.[210]

Regulators resist assessing chemicals at low, sub-lethal dose levels; rather they seem to assume that high-dose testing (parts per million) can be used to predict responses at lower doses. Hormones circulate at parts per billion and parts per trillion concentrations.

However, the popular 16th century observation 'the dose makes the poison' has been found recently to not apply to every poison in the same way. While dose response may still apply, a dose may exhibit a different effect at high and at very low doses.

[209] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures.
[210] Ibid.

Therefore, it seems that regulators have a bias to remain ignorant of what happens when individuals are exposed to low-level and long-term dosing of glyphosate-based herbicides.

Now that glyphosate is permitted by regulators to be used on food crops and is increasingly used for pre-sowing pasture, in crop and lawn treatment, is heavily used understory in horticulture and is extensively used for roadside and drainage vegetation management, residues have been detected in groundwater in Canada, Austria, Belgium, Denmark, Germany, Ireland, Spain, Sweden, Switzerland, Netherlands, UK, Sri Lanka, and USA.[211] Such uses and outcomes should require a less complacent approach by regulators to the issue of low-level and cumulative effects of glyphosate-based herbicide ingredients.

It seems that established regulatory approaches to risk assessment of pesticides place people and the environment at serious risk of harm. It also seems strange that studies that demonstrate harm at these 'low levels' appear to be excluded from regulatory assessment.

Drs Vandenberg, Colborn, Hayes, et al recommended:

> …that low-dose testing, followed by regulatory action to minimize or eliminate human exposures to EDCs, could significantly benefit human health.[212]

3.5 Vulnerable subpopulations (including prenatal / childhood exposure) and the problem with dietary studies

The NZ EPA Review does not appear to have consulted neonatal, paediatric or adolescent health experts in carcinogenicity in order to assess risk to vulnerable subpopulations from chronic glyphosate exposure.

Distinguished Professor Bruce Baguley Co-Director of the Auckland Cancer Society Research Centre at the University of Auckland was invited to two of the IARC meetings.[213] [214]Professor Baguley noted that there is a greater risk for children:

> The IARC decision that glyphosate is a “probable carcinogen” means that the product cannot be guaranteed not to cause cancer. Because very large

[211] Watts MA et al 2016. Glyphosate Monograph. PAN International. Page 10 http://pan-international.org/wp-content/uploads/Glyphosate-monograph.pdf
[212] Vandenberg, LN, Colborn, T, Hayes, TB et al 2012. Hormones and endocrine-disrupting chemicals.
[213] The results of these meetings were published as volumes 100a and 108. Orakei Board 8 Dec 2016.
[214] Professor Baguley also invited to join the Commentary paper Portier et al 2016

> populations are exposed worldwide to Roundup, even a small effect would lead to a large number of cancer cases.
>
> The IARC decision was made on the basis of several criteria, including high quality published analyses that demonstrate an association between the use of glyphosate and an increased incidence of cancer of the lymph nodes.

Professor Baguley's opinion is that:

> New Zealand should follow the Netherland's example in banning the use of Roundup for the control of weeds on municipal areas such as footpaths. These pose a particular exposure risk for children.

Regulators internationally claim they allow for children, but do not take into account prenatal or childhood risk when setting exposures. Simply put, children consume more per bodyweight, and the developing foetus, infants, children and adolescents have windows of vulnerability that increase risk of disease. Risk assessment is undertaken within an agricultural and trade focused environment with peer review by colleagues in toxicity, rather than pursued via a health-based ministerial portfolio with peer review by experts in paediatrics, endocrinology and childhood cancer.

The WHO – FAO 2006 risk assessment assumed glyphosate was fully excreted and did not consider biologically relevant, lifetime exposure from conception until death.[215] The JMPR 2016 assessment[216] notes that in many studies the 'majority' is excreted - but does not discuss lifetime effects resulting from chronic exposure through the daily diet.

Children, the developing foetus, the aged, and cancer patients in remission form a part of the community who may be more vulnerable to carcinogenesis. A 2008 World Health Organization report noted that foetuses and babies 'are not little adults' and have age-specific periods of susceptibility, known as 'critical windows of exposure,' and 'critical windows of development'.[217]

This is not new science, as endocrine disruptors have been known to cause neonatal damage for over 20 years. In 1993, Dr Colborn and colleagues noted that:

> Many of these chemicals can disturb development of the endocrine system and of the organs that respond to endocrine signals in organisms indirectly exposed during prenatal and/or early postnatal life; effects of exposure during development are permanent and irreversible.[218]

[215] WHO-FAO JMPR Pesticide residues in food: 2004 : toxicological evaluations : part II
[216] Pesticide residues in food – 2016: Part II toxicological evaluations / Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 9–13 May 2016 Glyphosate ISBN 978-92-4-165532-3 (Page 89 onwards) http://apps.who.int/iris/bitstream/10665/255000/1/9789241655323-eng.pdf?ua=1
[217] Children are not little adults. Children's Health & the Environment, WHO Training Package for the Health Sector World Health Organization July 2008.
[218] Colborn et al 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans

This early paper retains its authority and relevance, noting:

> Low-level exposure to endocrine disrupting chemicals (EDCs) especially during early development, lead to both transient and permanent changes to endocrine systems. This results in impaired reproduction, thyroid function, and metabolism, and increased incidence and progression of hormone-sensitive cancers.[219]

Risk assessment does not consider exposure and the hormone system during adolescence, yet:

> …reproductive developmental periods, especially prenatal and early postnatal life and puberty, are vulnerable periods for high sensitivity to EDC exposures.[220]

New Zealand considers the WHO – FAO JMPR evaluations the authoritative agency for information on toxicological safety of pesticides. JMPR 2016 was released in April 2017 and included an evaluation of glyphosate.[221]

To all appearances, this is their first complete glyphosate toxicological evaluation since 2004, and as such, the 2016 evaluation is an important evaluation for New Zealand policy and glyphosate 'safety.'

The 2016 JMPR comment relating to children indicated that existing studies were satisfactory to evaluate neonatal and childhood risk:

> The Meeting concluded that the existing database on glyphosate was adequate to characterize the potential hazards to the general population, including fetuses, infants and children. [222]

(Concerns with the JMPR 2016 glyphosate evaluation are outlined in Section 4.)

The JMPR 2016 toxicological evaluations do not consider the special vulnerabilities specific to prenatal, neonatal, childhood or adolescent exposure; nor does it address the potential for harm from full formulation effects via endocrine and/or epigenetic pathways. If taken in context of modern science and population risk, the JMPR 2016 paper is outdated before release.

This paper has discussed the failure of the current regulatory model of risk assessment – that scientists critical of current regulatory methods point out that regulators are avoiding testing at environmentally relevant levels (parts per billion (Ppb) and parts per trillion (Ppt)) that may affect public health at an epigenetic and/or endocrine relevant level.

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[219] Ibid.
[220] Gore AC et al 2015. Endocrine Society's Second Scientific Statement. DOI:10.1210/er.2015-1093
[221] Glyphosate. Joint FAO/WHO Meeting on Pesticide Residues. Pesticide residues in food – 2004: toxicological evaluations. Report No. WHO/ PCS/06.1. Geneva: World Health Organization; pp. 95–169. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf
[222] WHO 2016 Page 257

Authors Vandenberg et al have joined the chorus of scientists who advise that current risk assessment is unsafe and unsuitable because it does not address critical windows of vulnerability:

> The weight of the available evidence suggests that EDCs affect a wide range of human health endpoints that manifest at different stages of life, from neonatal and infant periods to the aging adult.[223]

This leads to the conclusion by the same authors that:

> Assumptions used in chemical risk assessments to estimate a threshold dose below which daily exposure to a chemical is estimated to be safe are false for EDCs.[224]

Formulation of population daily exposures to a given chemical, referred to as the acceptable daily intake (ADI), are considered the safe doses to consume daily for a lifetime. These ADIs are established from industry-selected and supplied studies, and based on parts per million evaluations that are not environmentally relevant or realistic models of population exposures. ADI determinations never delve into the environmentally relevant levels of ppb or ppt.

The risk during infancy and childhood was outlined in May 2014 to a New Zealand Parliamentary Select Committee. Petition 2011/112 requested the New Zealand Parliament put in place regulations for zero tolerance of pesticides in baby food.[225]

The Petitioner asked specifically that 'New Zealand match the European Union directives that processed infant and young children's food must no[t] contain individual pesticide residues greater than 0.01 ppm (mg/kg).' Government Members of Parliament, with Ministry for Primary Industries advice, declined the petition.

The transcript of petitioner Alison White and Dr Meriel Watts' presentation to the Primary Production Select Committee explaining childhood risk is available.[226] [227]

A curious person may wonder at the intransigence, or rigidity of a system that necessitates that a petitioner request an agricultural department, as the primary decision-maker responsible for analysing risk and 'adverse effects' of agrichemicals from conception, through infancy and childhood health (following over 4,000 submissions) rather than a department that prioritises population health.

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[223] Vandenberg, LN, Colborn, T, Hayes, TB et al 2012. Hormones and endocrine-disrupting chemicals.
[224] Ibid.
[225] Petition 2011/112 of Alison White and 4,276 others. NZ House of Representatives. Report of the Primary Production Committee https://www.parliament.nz/resource/en-nz/51DBSCH_SCR63100_1/ff5afe121ae1cf2075afd9de7f9e2d7aac5bc411
[226] Parliament Today. https://www.youtube.com/watch?v=QMzMI4307CY&list=UU3A_NzK_nFHkFmJu-TLHUFg
[227] Written transcript: http://www.rite-demands.org/make-it-safer-blog/2014/12/submission-to-urge-the-new-zealand-government-to-put-in-place-regulations-for-zero-tolerance-for-pesticides-in-baby-food

3.5.1 Total Diet Studies (TDS)

Most regulators rely on dietary studies to claim or demonstrate that population dietary intakes are well below the ADI, and therefore of no risk.

The setting of maximum residue levels (MRL) in food, which affect the quantity and timing of pesticide applications permitted on food and feed crops per acre or hectare, are recommended after crop trials. The chemical in question is sprayed at the industry-recommended application level per acre/hectare. [228]

The crops are then tested to evaluate the amount of residue per kilogram contained in the product that is harvested. The MRLs are usually then set above the highest residue levels found in the trials, first by the WHO – FAO , then for example at a later stage, by Codex Alimentarius[229] or the US EPA.[230]

Total Diet Studies (TDS) are undertaken to assess population exposures to a particular chemical based on average consumption across food groups – they involve different calculations to estimate for short term or long term dietary intakes. The International estimated daily intake (IEDI) is a prediction of long-term intake of a pesticide residue, but frequently, IESTI, international estimated short-term intake, is used as a generic term for both. The FAO has recently released the 'Submission and Evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed.'[231]

In order to assess exposure to children, the international default, established by the WHO – FAO, and used in total dietary studies to understand exposure of chemical residues in food, considers children 6 and under to weigh the equivalent of a 15kg adult. Children over that age are considered to be 60kg (55kg in Asia). This is based on a 1999 WHO ad hoc meeting.[232]

For example, an ADI of 0.1mg for each kilogram of bodyweight per day would translate x60 for an adult, and x15 for a child. Dietary exposure estimates are then calculated (roughly, by multiplying highest-serving portion reported of a particular food by highest residues found from crop

[228] For example: 'Pesticide Residues in Food 2005, Plant Production & Protection Paper' Glyphosate 158 P.133.
[229] International Food Standards. Codex Pesticides Residues in Food Online Database Glyphosate No.158
[230] US EPA Electronic code of federal regulations: Title 40: Protection of the environment. PART 180—TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD specific tolerances: Glyphosate tolerances for residues: S 180.364
[231] Paper 225. Submission and Evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. 3rd Ed. FAO. Rome 2016.
[232] Plant and protection paper 197. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. 2009 Rome. 2nd Ed. FAO P.131 http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/FAO_manual2nded_Oct07.pdf

trials, then dividing the sum by bodyweight[233]), and usually found to be far beneath the ADI. These calculations do not take into account that toxicity needs to be assessed at environmentally relevant levels, which may be significantly lower than the ADI.

Europe has established a body weight of children of 11.9 kg for 1–3 years and 23 kg for 3–10 years for dietary studies purposes.[234]

(Europe and the FAO and WHO are moving towards a harmonised approach.[235])

Using TDS or IESTIs to extrapolate exposure based on MRLs and to confirm that population exposure is below the ADI threshold appears to be a distractive process that maintains an illusion of safety rather than measuring real risk.

The ADI is set artificially high without assessment of chronic environmental (low dose) exposures, so risk assessment at parts per million that result in the ADI will usually be above consumption levels, ie low-dose exposure, at parts per billion or trillion.

The agrichemical industry initially set the recommended levels of application, which then following crop trials, often become the permitted residue level.

When related to toxicity and risk from chemical exposures, total diet studies may be considered by childhood health experts a misleading 'smoke and mirrors' process, and in light of twenty-first century science, rather disingenuous; a process undertaken by government agencies that may act solely to confirm the establishment of predetermined MRLs, doing nothing to protect or prevent harm.

The national TDS programme will not test a chemical if the agricultural (rather than health) department overseeing the TDS does not consider the chemical likely to cause adverse effects.

In October 2015, a New Zealand Total Diet Study (NZTDS) Consultation paper was released for public consultation. Many submitters requested that the MPI monitoring programme include glyphosate, specifically citing the IARC Monograph. The response by the NZ Ministry of Primary Industries to the submissions noted that the IARC Monograph was hazard classification only, cited the EFSA review and noted the responsibility for risk assessment internationally lay with the WHO, and advised there had been limited detection in other regulatory programmes.

> Glyphosate was assessed for inclusion into the NZTDS, but has not been included, primarily because there are currently other, more comprehensive,

[233] Paper 225. Submission and Evaluation of pesticide residues data for the estimation of MRLs in food & feed.
[234] The EFSA Comprehensive European Food Consumption Database, EFSA, 2011
[235] Towards a harmonised total diet study approach: a guidance document. 2011 EFSA FAO WHO

> MPI monitoring programmes that will be targeting glyphosate to determine compliance with regulatory limits.[236]

For discussion of problems with the WHO evaluations, see: 4.5.1 World Health Organisation (WHO) and Food and Agriculture Organisation (FAO) Joint Meeting on Pesticides Residues (JMPR) May 2016.

Dietary studies are equations concerned with understanding exposure levels of a single 'active ingredient' – chemical – which do not consider exposures from multiple chemicals in a formulation, nor with the multiple chemicals applied to a food crop over a single growing period, and rarely the combination in single meals.

As cited earlier, foetuses and babies 'are not little adults' and have age-specific periods of susceptibility, known as 'critical windows of exposure', and 'critical windows of development.'[237]

Reinforcing also that chemicals that act as endocrine disruptors can exert harm during:

> prenatal and/or early postnatal life; effects of exposure during development are permanent and irreversible.[238]

Children are exposed to chemicals from conception as many chemicals cross the placental 'barrier'. The placenta is a 'key endocrine organ in pregnancy'[239] and low-dose exposures are known to be responsible for adverse outcomes in children.

Woodruff et al 2011[240] noted that pregnant women test positive for multiple (including banned) chemicals. The study noted that the chemical levels found in the body have been associated with negative effects in children.

Dr Meriel Watts discussed 'Children's Special Vulnerability' in Section 3 of the book Poisoning our Future: Children and Pesticides. The book discussed the impact of pesticides on the endocrine system, increasing awareness of harm via epigenetic alterations, vulnerability of metabolic pathways; of immune, respiratory and nervous systems, and noted that children are more likely than adults to accumulate chemicals in their bodies. Dr Watts advised that:

> Despite the general lack of understanding, multiple contaminants and stressors are always at play, and so multiple and cumulative risks must always be taken into account when considering the effects of pesticides on

[236] New Zealand Total Diet Study 2015/16 Response to submissions on the Study Proposal Consultation. ISBN No: 978-1-77665-139-9. December 2015. https://www.mpi.govt.nz/news-and-resources/publications.aspx
[237] Children are not little adults. Children's Health & the Environment, WHO Training Package for the Health Sector World Health Organization July 2008. http://www.who.int/ceh/capacity/Children_are_not_little_adults.pdf
[238] Colborn et al 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans
[239] Placenta Power. Nov 8 2016. Chemicalwatch.com. Emma Davies.
[240] Tracey J. Woodruff, Ami R. Zota, Jackie M. Schwartz. Environmental Chemicals in Pregnant Women in the US: NHANES 2003-2004. Environmental Health Perspectives, 2011; DOI: 10.1289/ehp.1002727

> children. In the absence of complete knowledge, a precautionary approach must be taken to exposure of pregnant women and children to hazardous pesticides.[241]

Environmental exposures are directly linked to disease, but the vast majority of toxins cannot change the DNA sequence. They cannot mutate DNA – the DNA sequence is extremely stable. Mutagens are very rare. Science is unravelling the role of environmental agents (including pesticides) to influence DNA epigenetically.[242]

The challenge for health-based policymakers and legislators is to understand that the considerable increase in disease, including childhood cancer over the last few decades, is environmental in origin, and that effects may happen via multiple chemicals using multiple mechanisms, influencing multiple pathways and cause multiple adverse effects.

Mohammad Shahidehnia discussed this emerging understanding in the 2016 paper *Epigenetic Effects of Endocrine Disrupting Chemicals*:

> A few years ago we thought that our life starts with the DNA we receive from our parents, but currents studies have shown that we receive more than just DNA from our parents…Environmental exposure to EDCs during early development and pregnancy can modify epigenomes and induce trans-generationally asthma, autism, cancer, cardiovascular dysfunctions, diabetes, obesity, schizophrenia, infertility, reproductive diseases and dysfunction later in life. There is evidence showing that EDCs can induce epigenetic gene alterations by which these altered genes can be transferred into subsequent generations.[243]

Increasing evidence indicates that early environmental exposures can affect people epigenetically and then later in life, promote disease. Regulators do not consider the implications of 'non-genetic inheritance' – the role of epigenetic mechanisms to confer heritable traits. Chemicals have the ability to adversely affect not just the generation in question, but great grandchildren, by epigenetic influences that do not directly damage the gene.[244]

It is critical that public health experts, including paediatricians, endocrinologists and specialists in childhood disease, understand the profound and dismaying deficit that may have the most impact on New Zealand babies and children.

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[241] Poisoning our Future: Children and Pesticides. Pesticide Action Network Asia and the Pacific, 2013. P.48 http://www.pananz.net/wp-content/uploads/2013/04/2013-PAN-AP-POISONING-OUR-FUTURE-Children-and-Pesticides-Book-v8-WEB-lo-res.pdf

[242] Environmentally induced epigenetic transgenerational inheritance of reproductive disease. Michael K. Skinner, Ph.D. Washington State University. https://sbs.wsu.edu/faculty/?faculty/155 Accessed 5/5/2017

[243] 2016: Epigenetic Effects of Endocrine Disrupting Chemicals. Shahidehnia, M. J Environ Anal Toxicol 2016, 6:4 http://dx.doi.org/10.4172/2161-0525.1000381

[244] Skinner. M. 2014 Forum: Epigenetic Transgenerational Actions of Endocrine Disruptors on Reproduction & Disease. https://www.youtube.com/watch?v=yeG72CMS1vU&t=1089s

a) Failure to assess risk to vulnerable populations of chemical formulations at relevant levels of population exposure within toxicological evaluations and risk assessment;

b) Questionable effectiveness of Total Diet Surveys (TDS) as ADI are always set above exposure levels;

c) Delay by risk assessment regulators in adoption of new science of EDC and epigenetics and reliance on outdated science; and

d) The current separation of food safety and public health risk assessment by agricultural departments and EPA from the expert practitioners with a vested public health interest in health-based decision-making.

4.0 Bias in risk assessment

> The test for apparent bias reflects the standards of the fair-minded lay observer: would the lay observer, having been fully informed of the facts, reasonably suspect that the decision maker may have been biased?[245]

NZ EPA appears to have adopted a long-standing and pre-determined position about the 'safety' of glyphosate formulations: online EPA information 'Learn about glyphosate' page, there is a heading *'The **safety*** (emphasis added) ***of glyphosate.'***[246] Note that the side-heading implies that the EPA has a long-standing position that it has no concern of any material dangers to human or environmental toxicities of GBHs.

It appears that where there is doubt, the NZ EPA consistently moves to imply that there is no evidence of adverse harm. As The Guardian asked in relation to the European assessment:

> We might reasonably want to ask how have the choice-laden aspects of those assessments been exercised: in ways that resolve ambiguities and uncertainties in favour of public health, or in favour of agribusiness?[247]

Current risk assessment protocols and guidelines which favour industry selected science, could be considered a form of 'regulatory arbitrage,' a common term used to criticise banking regulation.

> Regulatory arbitrage is a practice whereby firms capitalize on loopholes in regulatory systems in order to circumvent unfavourable regulation. [248]

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[245] P.A. Joseph Constitutional and Administrative Law in New Zealand, 4th Ed. P.1076
[246] Learn about glyphosate August 2016 http://www.epa.govt.nz/hazardous-substances/pop_hs_topics/glyphosate_learn/Pages/default.aspx Accessed 4.10.17
[247] Chemical reactions: glyphosate and the politics of chemical safety. *The Guardian* May 2015, P.van Zwanenberg.
[248] http://www.investopedia.com/terms/r/regulatory-arbitrage.asp

Professor Jane Kelsey has referred to regulatory arbitrage as a ‘race to the bottom’.[249] Skewed decision-making by regulators that work closely with industry to ensure industry will economically benefit from new chemical technology, may result in decision-making that ignores and overrides public sector interests, and may result in incomplete consideration of downstream risk including accumulation in water sources.

Perhaps NZ EPA has a long-standing position that causes bias in its approach to terms of reference for literature reviews like that of the review that is the subject matter of this paper.

New Zealand is not alone in this problem. The UN Special Rapporteur on the Right to Food, Hilal Elver in her report to the UN Human Rights Council in January 2017, drew attention to the influence of industry on governments and their regulatory agencies.

> The pesticide industry is dominated by a few transnational corporations that wield extraordinary power over global agrochemical research, legislative initiatives and regulatory agendas.[250]

4.1 Regulatory assessment

New Zealand has joined several high-profile regulators that have drawn on glyphosate industry-paid and industry-provided science to downplay the IARC Working Group conclusion of a probable linkage between glyphosate-based herbicides and carcinogenicity.

Regulatory agencies have long been observed to be vulnerable to 'regulatory capture.' Special interest groups representing industry hold high stakes in the policy outcomes from regulatory agencies. They have long exerted influence.

> Commissions have proved to be more susceptible to private pressures, to manipulation for private purposes, and to administrative and public apathy than other types of governmental organization. They have lacked an affirmative concept of public interest; they have failed to meet the test of political responsibility in a democratic society; and they tend to define the interest of the regulated groups as the public interest.[251]

[249] J.Kelsey. The Fire Economy. *Bridget Williams Books & the New Zealand Law Foundation*. 2015
[250] UN General Assembly. Human Rights Council Thirty-fourth session. Report of the Special Rapporteur on the right to food A/HRC/34/48 https://documents-dds-ny.un.org/doc/UNDOC/GEN/G17/017/85/PDF/G1701785.pdf?OpenElement
[251] Regulating Business by Independent Commission M. H. Bernstein, *Princeton University Press* 296

The tendency of institutions to adopt policies contrary to voter preferences, but preferred by powerful interest groups is recognised as 'interest group distortion.'

Strangely, the NZ EPA Review consistently dismisses several studies that appear to indicate 'limited evidence of carcinogenicity'. Instead the NZ EPA seems to revert to older evaluations, e.g. JMPR 2006, US Environmental Protection Agency 1993[252],that depend on unpublished industry-paid and industry-provided science to arrive at critical and material conclusions for public policy formulation and public policy reviews.

Such apparently biased assessments may be judged unlawful if they are found to have ignored relevant considerations (see Section 6).

Individuals, from the Director of Public Health to the layperson, may be unaware that a narrow range of studies are traditionally relied on by agrichemical regulators to approve and establish population exposure levels (ADI) of chemicals, and in 2015 and 2016 to arrive at 'limited evidence,' and/or 'weight of evidence,' conclusions on cancer to rebut the IARC Working Group.

Regulators do not appear to consider that the absence of evidence about public and environmental safety is not evidence of safety.

Regulators historical culture of dependency on industry-paid and industry-supplied unpublished science to form the backbone of risk assessment may be perceived as a form of regulatory capture.

Long-term and dependent relationships between contracted parties appear to build in bias towards 'approval friendly' results that tend to lead regulators to conclude that a chemical product can pass a risk evaluation.

A recent editorial by NZ EPA's new Chief Scientist Jacqueline Rowarth in the May 2017 Agcarm industry newsletter discussed the problem of public trust in regulatory function, and the need for effective communication to address this problem. However, it did not discuss the obligation for New Zealand's hazardous substance risk assessment regulator to keep 'at arm's length' from the industry it regulates.[253]

The NZ EPA's Chief Scientist in a July 7 2017 NBR opinion piece[254], championed parts of an apparently biased Reuters reporter's selective approach to some unpublished industry research not being considered in the IARC process.[255] The Reuters article[256] appeared to target IARC and

[252] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014.
[253] AgCarm Newslatter May 2017. Role to Change Public Perception. J.Rowarth. http://agcarm.co.nz/wp-content/uploads/inputmay2017.pdf
[254] Heartland: Regulators heed facts despite public fear of herbicide, Jacqueline Rowarth. July 7, 2017. National Business Review. https://www.nbr.co.nz/article/heartland-regulators-heed-facts-despite-public-fear-herbicide-204784
[255] Monsanto Spin Doctors Target Cancer Scientist In Flawed Reuters Story. C.Gillam. Huffington Post. 16 June 2017. http://www.huffingtonpost.com/entry/monsanto-spin-doctors-target-cancer-scientist-in-flawed_us_594449eae4b0940f84fe2e57

misrepresent some scientists involved. It is not the first Reuters article (extensively quoting pro-industry sources) authored by Kelland to attack the IARC.[257] The NZ EPA Chief Scientist's approach confirms the NZ EPA's selectivity of data and industry spin, and continuation of industry-favoured outcomes, rather than a precautionary approach that may better protect the community and environment.

The IARC follows clear criteria contained within the IARC Preamble: 'reports that have been published or accepted for publication in the openly available scientific literature are reviewed'. It is surprising that NZ EPA's Chief Scientist writes so dismissively of this process.

IARC responded to the Reuters article (which also discussed the problem of Monsanto funding one of the scientists quoted in that article), stating the IARC criteria is 'based on the systematic assembly and review of all publicly available and pertinent scientific studies, by independent experts, free from vested interests'. [258]

Industry influence and lobbying keeps charges for approvals at an affordable 'industry-friendly' level. Demands for evaluation of new products restricts regulators' ability to commit resources to reassessment of older off patent products (that do not appear to be charged for).

The new position of Chief Scientist, by all appearances an effort to improve communications between the public and the EPA, may not address institutional short-comings within the New Zealand regulatory environment.

Regulatory capture is discussed in Section 6.4.

4.1.1 NZ EPA – HSNO risk assessment restricted by a limited budget

The NZ EPA has scarce resources to conduct its own research on each new application for registration and primarily relies on studies supplied by the registrant. Many new applications are processed each year. Significantly greater resources should be dedicated to assessing the safety of older products, particularly those that come off-patent and may have any mix of toxic ingredients, but this is limited by the EPA budget.

The current NZ EPA Chief Executive Dr Allan Freeth, and Board Chair, Ms Kerry Prendergast, met with Parliament's Local Government and

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[256] Cancer agency left in the dark over glyphosate evidence. K.Kelland. June 14 2017. *Reuters.* http://www.reuters.com/investigates/special-report/glyphosate-cancer-data/

[257] Industry fingerprints all over Reuters' attack on IARC over glyphosate and cancer Claire Robinson 21st April 2016. *The Ecologist* http://www.theecologist.org/News/news_analysis/2987591/industry_fingerprints_all_over_reuters_attack_on_iarc_over_glyphosate_and_cancer.html

[258] IARC responds to Reuters article of 14 June 2017 http://governance.iarc.fr/ENG/Docs/IARC_responds_to_Reuters_15_June_2017.pdf

Environment Select Committee on 8 December 2016 to respond to questions during the Annual Review 2015/16 Environmental Protection Authority (Appendix VII):

The NZ EPA Board Chair at the Annual Review hearing, discussed the appointment of a Chief Scientist to:

> ...help us drive Kiwi excitement around science and discovery, contributing to a better understanding of the work we undertake, and the way in which our decisions are made via robust risk-management framework, underpinned by precautionary principle and a clear understanding of Mātauranga Māori.
>
> This work is particularly relevant when it comes to addressing community concerns around chemicals such as glyphosate and triclosan. These can quickly become emotive and sensitive issues in the face of incomplete or misrepresented information.

Dr Freeth outlined the magnitude of reassessing existing substances including pesticides of concern.

> There are around 150,000 substances in New Zealand, made up of 28,000 chemicals that are on the registry. That's divided into 210 group standards based on hazard or on use.
>
> Of those 150,000, 330 have been identified as of substances of concern, that we're concerned about, and they are rated according to risk. We're just doing the review now on the basis of toxicity, use, volumes, and the geographic aspect of it. We had a budget, originally, of $300,000 per annum to do a number of reassessments. We're in the process of appointing through cost-savings internally from baseline, one senior scientist and one analyst to begin to form a reassessment plan to begin a new program of reassessments.[259]

He acknowledged, 'However, that will be limited.'

Dr Freeth continued on page 16:

> The Minister has encouraged us to talk in the new NRS round for a Budget bid for further money for reassessments to take that through. The reassessment process, which people misunderstand. There are two stages to it: grounds for assessment, which is a very low threshold, easy to get through. So I have a number of chemicals that have grounds for reassessment that I can tell you we won't reassess probably in the next 5 years.

To a question about the Chief Executive Initiated Reassessment List, Dr Freeth responded:

> We're changing that list as we speak because the list was based on pesticides, 30 very bad pesticides, that we're concerned about. So someone gets grounds, like triclosan, for reassessment. I then look at that

[259] Transcript: 2015/2016 Annual Review Environmental Protection Agency. Pages 15 and 16.

> and ask the scientists to give me a risk profile relative to everything else in the list. And that's why we say we're not going to get to it – relatively, it's of a very low risk for us, compared to all the others in front of us. One of the issues that we're talking to the Minister about is changing some amendments to the Act so we can rely on overseas jurisdictions, because it won't take 100 years to get through 300 substances.

The Chief Executive has acknowledged the NZ EPA does not have the capacity to reassess many compounds and has relegated glyphosate low in his reassessment priorities.

In full knowledge of the budgetary limitations imposed on NZ EPA scientists, it could appear incongruous and inconsistent that this under-resourced agency would resist a decision of the IARC. The Ministry of Health was unwilling to challenge IARC authority and questioned the merits of the NZ EPA doing so. (See Section 2.5)

4.1.2 Ghosts from the past: decades old reviews help decision-makers frame 2017 decisions

New agrichemical products rarely have independent toxicity analysis performed on mixture ingredients, and data concerning formulation is subject to commercial confidentiality clauses. There is little independent research available when a new product is registered.

This acts to ensure the primary source of data comes from industry. As long as the full formulation is not considered within risk assessment, independent researchers' hands are tied. Regulators' greater dependency on industry-provided information can lead to serious questions of conflicts of interest.[260]

The chemical industry may claim that its information is derived from independently-contracted and therefore 'independent laboratories.' There are many examples where scientific fraud is claimed to have arisen within 'independent laboratories'.[261] [262]

The NZ EPA review commences with a comment that world regulatory bodies consider glyphosate to have *'no carcinogenic potential.'*

[260] Robinson C, Holland N, Leloup D, et al.2013. Conflicts of interest at the European Food Safety Authority erode public confidence. J Epidemiol Community Health doi:10.1136/jech-2012-202185
[261] Cuhra, M. 2015c. Glyphosate nontoxicity: the genesis of a scientific fact. J. Biol. Phys. Chem. 15, 89–96. doi: 10.4024/08CU15A.jbpc.15.03 P.93
[262] The Scandal in Chemical Testing. Opinion. New York Times, May 16 1983 http://www.nytimes.com/1983/05/16/opinion/the-scandal-in-chemical-testing.html

The review then cites the US Environmental Protection Agency (US EPA) classification as a Group E carcinogen – 'evidence of non-carcinogenicity for humans.'[263]

The NZ EPA Review fails to acknowledge the (a) age of the US EPA 1993 Glyphosate Reregistration Eligibility Decision[264] data (the primary study that derived the most critical endpoint was a 1981 study); (b) limited carcinogenicity data the US EPA reregistration drew upon; and (c) focus on glyphosate as a single ingredient rather than the formulations of an increasing current range of glyphosate-based herbicides.

The carcinogenicity data in the 1993 US reregistration consisted of three unpublished Monsanto studies that were apparently not subject to public peer review.[265]

The NZ EPA review fails to mention that the current US EPA re-registration, which commenced in 2009, is mired in controversy and remains incomplete nearly seven years later.

The NZ EPA review refers to JMPR 2006[266] as an authority. The carcinogenicity studies contained in the JMPR 2006 evaluation consisted of five studies, two provided by Cheminova, one by Syngenta, and one by Monsanto. [267]

Reference to older, superseded, unpublished evaluations are misleading.

Risk of conflicts of interest and bias arise when regulators seem to rely, for policy-making and exercise of statutory decision-making, on unpublished papers selected by industry.

Older, private, unpublished studies may demonstrate harm at levels currently considered safe, and may become critical endpoints used in assessment, but are unavailable for peer review or comment in the public domain. (See Case Study: Lankas & Hogan 1981, Appendix II.)

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[263] US EPA Second Peer Review of glyphosate June 29 1991 (Memorandum dated Oct 30 1991.)
[264] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014.
[265] Ibid. Pages 13 and 14. Lankas, G.R.; Hogan, G.K. (1981) A Lifetime Feeding Study of Glyphosate MRID 00093879; Stout, L.; Ruecker, F. (1990) MRID 41643801; McConnel, R. (1985) A Chronic Feeding Study of Glyphosate (Roundup Technical in Mice): Pathology Report on Additional Kidney Sections MRID 00150564
[266] Glyphosate. Joint FAO/WHO Meeting on Pesticide Residues. Pesticide residues in food – 2004: toxicological evaluations. Report No. WHO/ PCS/06.1. Geneva: World Health Organization; pp. 95–169. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf Accessed 10/5/2017
[267] JMPR 2006 .Pages 121-132. (1) Atkinson, C., Martin, T., Hudson, P. & Robb, D. (1993a) Glyphosate: 104 week dietary carcinogenicity study in mice. Unpublished report No. 7793 (Cheminova); (2) Milburn, G.M. (1996) Glyphosate acid: one year dietary toxicity study in rats. Unpublished report No CTL/P/5143 (Syngenta); (3) Stout, L.; Ruecker, F. (1990) Chronic Study of Glyphosate Administered in Feed to Albino Rats: Lab Project Number: MSL- 10495: R.D. 1014. Unpublished study prepared by Monsanto Agricultural Co. 2175 p.MRID 41643801; (4) Atkinson, C., Strutt, A.V., Henderson, W., Finch, J. & Hudson, P. (1993b) Glyphosate: 104 week combined chronic feeding/oncogenicity study in rats with 52 week interim kill (results after 104 weeks.). Unpublished report No. 7867, IRI project No. 438623; (5) Brammer, A. (2001) Glyphosate acid: two year dietary toxicity and oncogenicity study in rats. Unpublished report No. CTL/PR1111 (Syngenta).

The European Commission's European Food Safety Authority (EFSA) evaluation of glyphosate is controversial. EFSA predominantly relied on industry provided data and analysis. (See Section 4.5.2)

Media noted that the European Commission included studies that weren't in the IARC Monograph. NGO GMWatch advised:

> EFSA says it considered more studies than the IARC, as if that made its report more authoritative. Yes, it did consider studies that IARC didn't. But what EFSA omits to mention is that the extra studies were done by industry. That means they are not peer-reviewed or published and are kept secret from the public and scientists. IARC only took into consideration published studies – a policy that ensures transparency for the public and the scientific community.[268]

4.2 Industry-paid and published reviews

Published industry-paid reviews of unpublished industry research prove an effective mechanism to transition unpublished, hidden studies into the literature without the original studies undergoing public peer review from scientists separate from industry. The conflicts that may arise resulting from use of industry-sponsored published data from a public health perspective can be significant.

4.2.1 Bias as an emerging issue.

Professor Gluckman discussed emerging issues regarding government (and regulator) dependence on advisory experts or expert groups/committees, and commented that issues are likely to develop, cautioning that:

> Steps need to be taken early on to ensure that the scientific advice is:
>
> • focused on the data and its appropriate interpretation
>
> • unbiased with respect to its use of data
>
> • open about what is known and not known
>
> • able to communicate in terms of probabilities and magnitude of effect
>
> • free from conflicts of interest, provided apolitically and independent of any particular end-user perspective.[269]

[268] Glyphosate not a carcinogen, says EFSA (of course). *GMWatch* November 2015. http://gmwatch.org/news/latest-news/16530-glyphosate-not-a-carcinogen-says-efsa-of-course
[269] P. Gluckman. Towards better use of evidence in policy formation: a discussion paper. 2011 P.14

Unpublished studies inserted within published industry-paid reviews (with the peer review, of the review, undertaken by industry-paid reviewers) prevent public-domain scientists from scrutinising important facets of the research.

A recent paper by Mesnage et al 2015 stated:

> Carcinogenicity of glyphosate is a complex and controversial issue. In order to support glyphosate re-approval, several reviews have been published by paid consultants of Monsanto Company (Kier, 2015; Kier and Kirkland, 2013; Mink et al., 2012) or by the glyphosate task force (Greim et al., 2015).[270]

It is many of the above study authors that NZ EPA Review has turned to, in addition to claimed scientific studies encapsulated within outdated regulatory assessments, to downplay the many epidemiological studies demonstrating harm, considered by the IARC Working Group.

Indeed, many of the industry-paid published reviews used within the NZ EPA Review represent a significant conflict of interest. For example, the authors of the Williams et al 2000[271] paper worked closely with Monsanto.

4.2.2 Court documents disclose 'inappropriately close' relationship between EPA scientist and Monsanto

Court documents reveal that the Williams paper was ghost written by Monsanto. [272] This paper is at the centre of an international controversy where Monsanto is alleged to have ghost written studies used for regulatory decision-making.[273]

The New York Times reported on the US court action brought about by claimants[274] alleging their non-Hodgkin's lymphomas are the result of exposure to glyphosate:

> The records suggested that Monsanto had ghost-written 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

[270] Mesnage et al 2015 Potential toxic effects of glyphosate below regulatory limits, *Food & Chem Tox.*
[271] Williams GM, Kroes R, Munro IC (2000). Safety Evaluation and Risk Assessment of the Herbicide Roundup and its active ingredient, glyphosate, for humans. Regulatory Toxicology and Pharmacology 31: 117-165.
[272] Patients: Roundup gave us cancer as EPA official helped the company. H.Yan May 15 2017. *CNN* http://edition.cnn.com/2017/05/15/health/roundup-herbicide-cancer-allegations/index.html
[273] Monsanto Weed Killer Roundup Faces New Doubts on Safety in Unsealed Documents. D.Hakim. March 14 2017 *New York Times*. https://www.nytimes.com/2017/03/14/business/monsanto-roundup-safety-lawsuit.html
[274] According to CNN the Miller Firm represents around 500 claimants. https://millerfirmllc.com/current-litigations/roundup-non-hodgkins-lymphoma-multiple-myeloma/

> Roundup's main ingredient, glyphosate, that was to have been conducted by the United States Department of Health and Human Services. [275]

The Plaintiff's attorney, Thomas Litzenburg, said the court documents 'seem to show an inappropriately close relationship' between Monsanto and the former EPA official.*[276]*

The documents revealed that senior US EPA scientist Jess Rowland, told Dan Jenkins, Monsanto U.S. Agency Lead, Regulatory Affairs that 'no coordination is going on and he wanted to establish some saying 'If I can kill this I should get a medal*'.[277]*

The apparent circle of influence of Jess Rowland has expanded to include European regulatory decision-making. A study[278] that revealed an increase in malignant lymphoma was dismissed by EFSA after a communication between EFSA and former US EPA scientist Jess Rowland. The Kumar study 'was reconsidered during the second experts' teleconference as not acceptable due to viral infections'. [279]

As noted in Part 3.3.1, the earlier European RAR had merely noted that viruses *could* be present. The RAR had limited comments to (page 63) the fact that the mice were 'prone to developing lymphoreticular tumours'.

Inclusion of this study would have effectively tipped EFSA into having to ban glyphosate.

Claire Robinson, a European researcher who has authored several papers on glyphosate, stated:

> According to the European legislation, evidence for carcinogenicity in at least two separate studies is "sufficient evidence" to label a compound as carcinogenic (category 1B). That would mean an automatic ban. Thus, in Dr Clausing's view, the Kumar study "presented an obstacle" to EFSA's apparent intention to declare glyphosate as non-carcinogenic:
>
> That's why the exclusion of this particular study from further consideration was so important*. [280]*

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[275] Monsanto Weed Killer Roundup Faces New Doubts on Safety in Unsealed Documents. D.Hakim. March 14 2017 *New York Times*. https://www.nytimes.com/2017/03/14/business/monsanto-roundup-safety-lawsuit.html

[276] CNN Ibid.

[277] Roundup products liability litigation. Case 3:16-md-02741-VC Document 189 Filed 03/14/17 http://i2.cdn.turner.com/cnn/2017/images/04/10/doc.189.-.docs.mentioning.epa.jess.rowland.pdf

[278]2001, ASB2012-11491 *also referred to as* Kumar, D.P.S. 2001 Carcinogenicity Study with Glyphosate Technical in Swiss Albino Mice TOXI: 1559.CARCI-M FSG GLP: Y, published: N 2309396 / ASB2012-11491 FSG (Feinchemie Schwebda GmbH). *also referred to as* Feinchemie Schwebda . Carcinogenicity Study with Glyphosate Technical in Swiss Albino Mice. Bangalore, India: Rallis India, Ltd; (2001) *also referred to* Greim et al as Study 13.
ASB2012-11491

[279] EU declared Monsanto weedkiller safe after intervention from controversial US official. A Neslen, May 24 2017 *The Guardian* https://www.theguardian.com/environment/2017/may/24/eu-declared-monsanto-weedkiller-safe-after-intervention-from-controversial-us-official

[280] Did former US EPA man influence EFSA verdict on glyphosate? C. Robinson. May 24, 2017. http://gmwatch.org/en/news/latest-news/17639-did-former-us-epa-man-influence-efsa-verdict-on-glyphosate

Industry is firmly established in the culture of risk assessment today, in the form of influential industry lobby groups (e.g. Crop Life and the Glyphosate Task Force) that attend, for example WHO – FAO JMPR meetings, and influential lobby group members (See:4.5.1) who may even chair these same meetings, and industry-paid published reviews and papers.

The idea of the study being unacceptable due to a 'viral infection' was introduced in the industry paper Greim et al 2015, who downgraded it to 'Klimisch 2 for reliability, based on speculation of a viral infection within the colony'.

The risk-tolerant disclosure-based model[281] used by regulators enables studies to be selected by industry rather than a model which would:

> (a) Require a full literature review and industry disclosure of all relevant science produced (or contracted separately) by industry; and/or
>
> (b) Require industry to pay a fee that would cover research costs of required studies.

Regulators (or an international health-based organisation) with budgets, authority and agility would transform risk assessment and set a significantly higher bar to match twenty-first century demands.

Conflicts of interest regarding regulator and industry are further outlined in '4.5 Regulators risk-tolerant disclosure-based model lacks transparency.'

4.3 Weight of evidence: playing down carcinogenicity associations between glyphosate and cancer

The IARC Working Group consistently observed studies that indicate or demonstrate an association of glyphosate with cancer and this compounded to establish a finding of 'probable carcinogen.'

By contrast the NZ EPA Review seems to generalise, marginalise and minimise the work of the WHO's cancer arm IARC, without advancing the required reasoning to support that treatment.

Carcinogenic patterns of effects appear to be downplayed by the NZ EPA Review. Similarly, there appears to be no appropriate weight given to evidence of genotoxic effects and oxidative stress effects.

[281] J.Kelsey. The Fire Economy. Bridget Williams Books & the New Zealand Law Foundation. 2015

Such apparent exclusion of appropriate weight for relevant considerations appears to have enabled the NZ EPA Review to reach a conclusion that glyphosate is 'unlikely to be genotoxic or carcinogenic to humans and does not require classification under HSNO as a carcinogen or mutagen'.

As an example; the IARC Working Group identified a positive trend in renal tumours in male CD-1 mice, within the unpublished Monsanto paid and produced chronic feeding study, Knezevich & Hogan 1983 (referred to by the IARC Working Group as 'EPA (1983)'.[282]

In contrast, the NZ EPA review found the IARC finding at 'variance' with the US EPA, directly citing page 14 of the 1993 US EPA glyphosate reregistration that the:

> …occurrence of these adenomas was spontaneous rather than compound-induced because the incidence of renal tubular adenomas in males was not statistically significant when compared with the concurrent controls.[283]

This feeding study was discussed at length in Section 3.3 Glyphosate: Evidence of carcinogenicity. Monsanto's Knezevich & Hogan study is confusingly referenced throughout regulatory papers and may appear to be several studies when it is a single study. Appendix III identifies the various references used by different regulators.

This has always been an extremely contentious study – the tumour was exceptionally rare and so of concern. The NZ EPA review does not discuss the controversial background to this study. The March 1985 Consensus Review considered that the renal tubular adenomas were related to compound administration and considered that glyphosate should be classified as a Category C oncogene.[284] The 1986 Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) acknowledged 'three neoplasms in high dose male mice is unusual and using historical controls is statistically significant'.[285]

The IARC Working Group observed a significant positive trend for renal tumours. The discussion and caution observed by the IARC due to the rarity of this tumour, on page 33 of the Monograph, is worth observing.

The New Zealand regulator (as with the US EPA and Europe) dismisses evidence as 'spontaneous' reflecting early comments from Monsanto

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[282] Hogan, G.K. (1983). A chronic feeding study of glyphosate in mice. Unpublished report prepared by Bio/Dynamics Inc., dated July 21, 1983. Report No. 77-2061. EPA Acc. Nos. 251007-251009, and 251014.
Also referred to as: Knezevich, A.L. and Hogan, G.K. (1983) A Chronic Feeding Study of Glyphosate (Roundup technical) in Mice: Project No. 77-2061. (Unpublished study received Aug. 17, 1983 under 524-308; prepared by Bio/dynamics, Inc., submitted by Monsanto Co. Accession #251007-251014 MRID 130406. See also Appendix III

[283] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014.

[284] March 04, 1985. Memorandum. 4 Page(s). Theodore Farber. Toxicology Branch. Consensus Review of Glyphosate. Caswell No. 661A.
https://archive.epa.gov/pesticides/chemicalsearch/chemical/foia/web/html/103601.html

[285] US EPA FIFRA Scientific Advisory Panel report Feb 1986. Report of the SAP recommendations.

employee, Dr. R.Squire in 1985.[286] Regulators dismissing this study may not have assessed historical control data from the original laboratory to understand tumour incidence. A February 26, 1985 US EPA Memorandum discussing 'Use of historical data in determining the weight of evidence from kidney tumor incidence' was confident that the Monsanto claim that tumours were 'unrelated to treatment' was incorrect and that the registrant's interpretation of statistical significance missed important points.

The claims surrounding this study highlight many issues that are of public health concern. Policymakers must act cautiously. Good science must be replicable to be reliable, the data transparently available and free of bias. Yet this private study (likely not guideline) where regulators dismiss tumours as 'spontaneous' relies on private pathology reports provided by the industry that is seeking approval to continue selling the product.

The US Environmental Protection Agency (US EPA) 1993 Glyphosate Reregistration Eligibility Decision considered glyphosate as a Group E carcinogen, having 'evidence of non-carcinogenicity for humans' which was based on, as the NZ EPA review notes in the second paragraph, 'a lack of convincing evidence of carcinogenicity in adequate studies with two animal species, rat and mouse'.[287]

The carcinogenicity data in the US EPA 1993 consisted of three unpublished Monsanto studies that have never been subject to public peer review.

In a second example of the NZ EPA Review appearing to claim that the IARC Working Group conclusion about probable carcinogenicity of glyphosate-based herbicide formulations was not relevant, is the NZ EPA Review discussing the unpublished Cheminova study - Atkinson et al 1993a:

> The IWG reviewed a second feeding study reported to the FAO/WHO Joint Meeting on Pesticide Residues (JMPR), and found there was a significant positive trend in the incidence of hemangiosarcoma in male CD-1 mice.

The NZ EPA Review chose to contrast this, and advises that the JMPR 2006:

> …found that owing to the lack of a dose-response relationship, the lack of statistical significance and the fact that the incidences recorded in this study fell within the historical ranges for controls, these changes were not considered to be caused by administration of glyphosate.

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[286] US EPA Memorandum from William Dykstra 3-11-86 005590 Glyphosate Reregistration No. 524-308

[287] EPA (1993a). Reregistration Eligibility Decision (RED): Glyphosate. EPA 738-R-93–014. Washington (DC): Office of Prevention, Pesticides And Toxic Substances, Office of Pesticide Programs, United States Environmental Protection Agency. Page 13-14. https://www3.epa.gov/pesticides/endanger/litstatus/effects/glyphosate-red.pdf accessed 9/5/2017. Lankas, G.R. ; Hogan, G.K. (1981) (Monsanto); Stout, L.; Ruecker, F. (1990); McConnel, R. (1985) (Monsanto).

(See: 4.4.3 Reliance on industry-derived historical control data to dismiss tumorigenic responses as normal.)

There does in fact appear to be a dose-response relationship in the study.

> Haemangiosarcoma was evident in 4/50 males at the highest dose, in 2/50 females at the lowest dose, and in 1/50 females at the highest dose, but in none of the 50 animals of the control group.[288]

The NZ EPA review appears to follow similar processes of evaluation followed by EFSA.

Portier et al's 2016 commentary paper criticised the processes by which EFSA dismissed evidence of carcinogenicity. There are remarkable similarities between the NZ EPA methodologies and EFSA's:

> Ignoring established guidelines cited in their report, EFSA dismissed evidence of renal tumours in three mouse studies, hemangiosarcoma in two mouse studies and malignant lymphoma in two mouse studies. Thus, EFSA incorrectly discarded all findings of glyphosate-induced cancer in animals as chance occurrences. [289]

It is evident that regulators internationally have moved in unison to dismiss many of the studies considered within the IARC Monograph, creating a rearrangement of the 'weight of evidence.'

Independent scientists have criticised European regulatory claims. Toxicologist Dr Peter Clausing admonished the European Renewal Assessment Report (RAR) for gaps and errors, stating:

> Specifically consideration of mechanistic evidence for glyphosate's carcinogenic effects, i.e. oxidative stress and genotoxicity is missing or insufficient. The report remains mute about oxidative stress as related to genotoxicity and almost one third of the scientific literature on genotoxicity is missing. In addition at least one important study on genotoxicity received a false and distorted description by the BfR. Furthermore, the handling of an important mouse carcinogenicity study by industry (i.e. not applying state-of- the-art statistical methods and wrong claims about historical control data) give the impression that this was done deliberately.[290]

In May of 2017, Dr Christopher Portier (an invited specialist to the IARC review) wrote an open letter[291] to the president of the European Commission, Jean Claude Junker, explaining the possible failure of EFSA and EChA to identify all the statistically significant cancer findings in the chronic rodent carcinogenicity studies.

Dr Portier had been able to review a portion of the raw data that was released in December 2016 as a result of an access to documents

[288] WHO 2006 Glyphosate. Pesticide residues in food – 2004: toxicological evaluations. Atkinson et al., 1993a Page 122.
[289] Portier CJ et al 2016. Commentary. doi:10.1136/jech-2015-207005
[290] Dr. Peter Clausing The Glyphosate Renewal Assessment Report. An Analysis of Gaps and Deficiencies P.2
[291] PDF https://corporateeurope.org/sites/default/files/attachments/letterjuncker28may2017.pdf

request.[292] Dr Portier identified a further eight additional positive tumour findings from reviewing raw data. His open letter addressed the concern that other EFSA may have had inadequate evaluations and queried why scientists were unable to identify tumours in the original data. The letter reiterated the concerns that are considered not to have been adequately addressed in the EFSA and EChA assessments:

- The classification of the human evidence as "very limited" is not a valid characterization under the CLP guidelines and fails to properly address the strength of the available evidence;
- Both EFSA and EChA dismissed positive findings because they fell inside of the range of the historical controls (this is an improper use of historical control evidence);
- Both EFSA and EChA compared findings across different strains and different study durations to conclude that studies were inconsistent (this is not scientifically justifiable)
- Both EFSA and EChA characterize the evidence for genotoxicity as negative, yet a careful review of the evidence released by EFSA and the open scientific literature suggest there are many guideline and non-guideline studies demonstrating genotoxicity.

4.4 Regulators including the NZ EPA use narrow criteria formulated via industry agreed test guidelines.

Health and public expectation that risk assessment should grow to embrace the dynamic interface between the complex chemical environment and the complex biological environment, (in the face of increasing public criticism) may persuade policymakers to:

> …acknowledge that scientific knowledge is multidimensional and cannot be arranged in only one hierarchical system.[293]

As with the procedure evident within the NZ EPA Review, regulators by convention dismiss and exclude data that is not supplied by laboratories who defer to industry developed ‘Good Laboratory Practice’ (GLP) and OECD guidelines protocols.

These ‘guidelines’ therefore have the effect of constraining the proper exercise of regulatory discretion in the public interest. This could be interpreted as the administration of regulatory powers being effectively 'captured' by third parties – an 'illegality' in terms of generally-accepted principles of administrative law.

[292] Scientist writes to Juncker: new tumor evidence found in confidential glyphosate data Corporate Europe Observatory. May 29 2017. https://corporateeurope.org/food-and-agriculture/2017/05/scientist-writes-juncker-new-tumor-evidence-found-confidential
[293] Fernandez et al 2015. Evidence-based medicine: is it a bridge too far? DOI: 10.1186/s12961-015-0057-0

GLP protocols (a laboratory management system) and OECD test guidelines (which use insensitive methods) are not considered to provide critical, sensitive results and so independent research scientists choose to not follow these recommendations in their own research.

It is common regulatory practice to exclude studies - many independent papers were omitted in the recent RAR, where 31 publications were restricted due to ‘deficiencies’ based on guidelines and protocols.

For example, the NZ EPA Review notes that:

> All studies done according to internationally agreed test guidelines did not find evidence of a genotoxic (damaging to DNA) effect of glyphosate.

Independent scientists and researchers contend that ‘Good Laboratory Practice’ and OECD guidelines do ‘not guarantee validity and relevance of the study design, statistical rigour and attention to sources of bias', yet these parameters are used by regulators and employees to dismiss published and peer reviewed literature.

4.4.1 Good Laboratory Practice

Many scientists experienced in the field of toxicology and genetics acknowledge that current test guidelines are outdated and exclude delicate and important responses. The Good Laboratory Practice (GLP) system is an (expensive) laboratory management system. A 2009 scientific commentary concerning guidelines and public health, regarding the debate on Bisphenol A discussed the problems with GLP:

> The GLP outlines basic guidelines for conducting scientific research, including the care and feeding of laboratory animals, standards for facility maintenance, calibration and care of equipment, personnel requirements, inspections, study protocols, and collection and storage of raw data. [294]

These GLP regulations were developed in response to widespread misconduct by private research companies. This misconduct was possible because their data usually do not go through the rigorous, multi-stage scientific review that is normal for academic data publicly funded and published in the peer-reviewed literature. The lack of these safeguards from academic science had enabled fraud.

A May 2012 letter addressed to European Commissioner for Health and Consumer Policy and the Scientific Committees Management Officer (DG SANCO) stated:

[294] Goldman D. Chemical aspects of compliance with Good Laboratory Practices. In: Garner WY, Barge SB, editors. Good Laboratory Practices: An Agrochemical Perspective. *American Chemical Soc.;* 1988. pp. 13–23.

> GLP is not a hallmark of good or reliable science: it is a laboratory management system invented for the purpose of preventing fraud in industry studies conducted for regulatory purposes. Researchers operating independently of industry consider GLP to be irrelevant to their research – and thus too expensive in terms of labour hours to implement without good reason. Crucially, at no point have regulators informed independent scientists that their study is considered unreliable for not using GLP. [295]

The NZ EPA's thresholds and classifications manual advises that:

> Data from internationally harmonised test methods are preferred…Data should preferably be derived using the OECD test guidelines or equivalent, according to the principles of Good Laboratory Practice. [296]

Of public interest concern is the scientific acknowledgement that GLP guidelines make it more difficult for scientists to detect low-dose, endocrine disrupting effects. The guidelines do not ensure the methods used are modern, nor whether the research being conducted is effective.

Critically, a published study, subject to peer review must be replicable – repeatable – and therefore reliable. This is 'good science.' A private study, submitted confidentially to regulators evades this scrutiny.

A final caution might come from a 2009 scientific commentary concerning guidelines and public health, regarding the debate on Bisphenol A:

> GLP is not considered a guarantee of reliable or valid science…Public health decisions should be based on studies using appropriate protocols and the most sensitive assays. They should not be based on criteria that include or exclude data depending on whether or not the studies use GLP. Simply meeting GLP requirements is insufficient to guarantee scientific reliability and validity.[297]

4.4.2 OECD Guidelines

A June 2015 taskforce 'Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment' advised that:

> Populations worldwide are continually exposed to a wide range of chemicals, so keeping the precautionary principle in mind, there is a need to take the risks related to the cumulative effects of these chemicals seriously. Of primary concern is the fact that WHO IPCS mode of action framework and the OECD guidelines for risk assessment are restrictive to

[295] Myers JP, Vom Saal FS. et al 2009. Good Laboratory Practice: The case of bisphenol A.
[296] *Thresholds and Classifications under the HSNO Act 1996*. 2012 EPA0109 p.221
[297] Myers JP, Vom Saal FS. et al 2009. Good Laboratory Practice: The case of bisphenol A.

> the point that regulators could be underestimating the risks posed by exposures to low doses of mixtures of chemicals.[298]

Problems and concerns with outdated and narrowly defined industry developed guidelines are well-outlined in the published literature. A recent commentary by 96 scientists, 'Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA),' explained the situation clearly:

> We strongly disagree that data from studies published in the peer-reviewed literature should automatically receive less weight than guideline studies. Compliance with guidelines and Good Laboratory Practice does not guarantee validity and relevance of the study design, statistical rigour and attention to sources of bias. The majority of research after the initial marketing approval, including epidemiology studies, will be conducted in research laboratories using various models to address specific issues related to toxicity, often with no testing guidelines available. 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, not just on compliance with guideline rules. [299]

There are concerning inconsistencies. Porter et al note that in regards to guidelines used in Europe:

> OECD guidance on the conduct and design of chronic toxicity and carcinogenicity studies and the European Chemicals Agency Guidance on Commission Regulation (EU) No 286/2011; both are cited in the RAR. The methods used for historical controls and trend analysis are inconsistent with these guidelines.[300]

Tony Tweedale, Brussels-based independent consultant to NGOs, expressed concern that the OECD guidelines are antiquated and that studies conforming to guidelines:

> …test a narrow and unrealistic portion of the dose–response curve and relatively few end points, mostly fail to test toxicity during vulnerable development, and kill the animals being tested before most diseases develop (a human equivalent of ~ 60 years). Society should not accept that the OECD GLP protocols are better than those developed by independent, curious academics. [301]

Privately held research data contained within papers such as Williams et al, discussed earlier, is frequently old, and studies incorporated in these industry paid reviews can quietly fall outside of the Good Laboratory

[298] Goodson et al 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures
[299] Portier CJ et al 2016. Commentary. doi:10.1136/jech-2015-207005
[300] Ibid.
[301] Tweedale 2011. Enhancing Credibility of Chemical Safety Studies: No Consensus. *Environ Health Perspect.* 2011 Dec; 119(12): a507–a508.doi: 10.1289/ehp.1104130

Practice (GLP) and OECD guidelines used by regulators to exclude modern studies showing effects at low levels.

> Decision-makers do not operate in administrative vacuums. They may adopt policy rules, provided they leave room for judgement and discretion. [302]

In summary, the NZ EPA Review seems to adopt guideline protocols or 'policy rules' understood to be irrelevant by expert scientists; it also appears to rebalance 'weight of evidence' while downplaying evidence considered by the IARC Monograph giving significant weight to glyphosate-based formulations exerting carcinogenic and/or genotoxic effects.

The NZ EPA Review may be considered misleading and deceptive because it does not appear to incorporate and therefore give due weight to studies indicating harm that occurs outside of narrow and antiquated industry parameters and 'inappropriately restrictive' guidelines.

4.4.3 Reliance on industry-derived historical control data to dismiss tumorigenic responses as normal

Use of (frequently unpublished) 'historical control data' to dismiss findings is relatively common in regulatory reviews. This practice may potentially enable the author or regulator to dismiss statistically significant findings and claim that a harmful effect is 'within the range of normal'.

OECD Guidelines are cautious regarding the use of historical control data, for example requiring that:

> Historical control data should be from studies in the same time frame, for the same animal strain, preferably from the same laboratory or the same supplier and preferably reviewed by the same pathologist. [303]

When evaluating increased incidence in laboratory studies:

> It should be stressed that the concurrent control group is always the most important consideration in the testing for increased tumour rates… only be used if the concurrent control data are appreciably 'out of line' with recent previous studies and that only historical data collected over the last 5 years should be used. [304]

Most guidelines prefer to rely on use of concurrent controls and trend tests.

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[302] *Constitutional and Administrative Law in New Zealand, 4th* Ed., P.A Joseph,P.966
[303] OECD. Guidance Document 116 on the Conduct and Design of Chronic Toxicity and Carcinogenicity Studies, H.a.S.P. Environment, Editor. Paris: OECD, 2012. European Chemicals Agency. Guidance on the Application of the CLP Criteria: Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Helsinki, Finland: European Chemicals Agency, 2015.
[304] Guidance No. 116 (OECD 2012). P.135

The US EPA 2005 Guidelines for Carcinogen Risk Assessment advise:

> When historical control data are used, the discussion should address several issues that affect comparability of historical and concurrent control data, such as genetic drift in the laboratory strains, differences in pathology examination at different times and in different laboratories (e.g., in criteria for evaluating lesions; variations in the techniques for the preparation or reading of tissue samples among laboratories), and comparability of animals from different suppliers. The most relevant historical data come from the same laboratory and the same supplier and are gathered within 2 or 3 years one way or the other of the study under review; other data should be used only with extreme caution. [305]

Portier et al's IARC Monograph commentary noted there were inconsistencies in the use of historical controls and trend analysis within the German RAR.[306]

The December 2015 paper 'EFSA Conclusion on the Peer Review of the Glyphosate Risk Assessment: A Reality Check'[307] by Dr Peter Clausing discussed reliance of EFSA on use of historical incidence data.

The NZ EPA Review relies on a different statistical test from the IARC, using pair-wise comparison (rather than trend analysis) to dismiss studies. Dr. Clausing discussed different statistical methods and the importance of significance in the Reality Check paper:

> The EFSA Conclusion gives the impression that a pair-wise comparison is the most relevant statistical method, which is not in line with applicable guidance. The European Union uses the OECD…guidance No. 116 (OECD 2012)…explicitly and unequivocally points to the Cochran-ArmitageTrend test as the method of choice for the analysis of tumour incidences. In this decision tree pair-wise comparisons are not even mentioned for the assessment of tumour rates. Unlike the pairwise test that compares each exposure group to the control, the Cochran-ArmitageTrend test detects a linear trend, which, if significant, indicates an increasing risk of carcinogenicity with increasing exposure. In addition, for pair-wise comparisons and trend tests in general, both Guidance No. 116 (OECD 2012, p. 116) as well as Guidance No. 35 (OECD 2002, p. 62) state: "Significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result." [308]

As Dr Clausing states:

[305] US Environmental Protection Agency (EPA). Guidelines for Carcinogen Risk Assessment. U.S. Environmental Protection Agency, Washington, DC (2005) EPA/630/P-03/001F
[306] Portier CJ et al 2016 Commentary. doi:10.1136/jech-2015-207005.
[307] Dr P. Clausing. The EFSA Conclusion on the Peer Review of the Glyphosate Risk Assessment A Reality Check. PAN Germany.
[308] Ibid. P.5

> Therefore, the claim of "(n)o evidence of carcinogenicity…due to lack of statistical significance in pair-wise comparison tests" (EFSA 2015, p.11) has no scientific basis.[309]

In contrast to the IARC Working Group, the questionable approach of the NZ EPA review has been to place considerable reliance on the historical ranges for controls, counter with claims of a spontaneous tumour, questions of statistical significance which enable the review to dismiss elevated tumour incidence (hemangiosarcoma, carcinoma, hepatocellular adenomas) within the papers discussed, repeating the actions of other regulatory bodies.

4.5 Regulators risk-tolerant disclosure-based model lacks transparency

Questions of accountability and integrity are not limited to risk assessment of glyphosate.

Whether in use by scientific advisors to heads of state, or by a contractor to the New Zealand Environmental Protection Authority, transparency and accountability of 'evidence-based science' used in development of scientific advice or policy has never been more important.

In a Declaration following the World Science Forum (WSF) in Budapest in 2015 discussing scientific advice, delegates called for:

> …the need to define the principles, processes and application of science advice and to address the theoretical and practical questions regarding the independence, transparency, visibility and accountability of those who receive and provide advice has never been more important…We call for concerted action of scientists and policy-makers to define and promulgate universal principles for developing and communicating science to inform and evaluate policy based on responsibility, integrity, independence, and accountability.

Risk assessment of glyphosate is mired in controversy, in large part because of the dependence on industry to select the studies for disclosure for scientific evidence and analysis.

The cost of long-term ill health from low dose exposures to environmental chemicals are yet to be researched in New Zealand. Early indicators demonstrate that these costs place a significant burden on our economy, tax payers and the individual alike. [310]

[309] Ibid. P.5

[310] Trasande et al 2014. Estimating burden and disease costs of exposure to endocrine-disrupting chemicals in the European Union. *J Clin Endocrinol Metab.* 2015 Apr;100(4):1245-55. doi: 10.1210/jc.2014-4324. Epub 2015

The EFSA glyphosate RAR evaluation has faced sustained criticism for lack transparency. The Portier et al commentary discussed:

> Many of the elements of transparency do not exist for the RAR. For example, citations for almost all references, even those from the open scientific literature, have been redacted…there are no authors or contributors listed for either document, a requirement for publication in virtually all scientific journals where financial support, conflicts of interest and affiliations of authors are fully disclosed. 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.[311]

Under a 'disclosure based model' the studies submitted for analysis within risk assessment are selected and supplied directly by industry. There is no requirement for disclosure of industry laboratory studies that may have resulted in less successful outcomes.

The opacity of risk assessment has been challenged in Europe. In a landmark European Court of Justice 23 November 2016 ruling, the court ruled:

> Safety tests conducted by the chemical industry and used by regulators to assess the dangers of pesticides must be disclosed. It argued that such research falls under "information on emissions into the environment", as defined under the Aarhus Convention and the EU law implementing this Convention. [312]

Groups, including Greenpeace and Pesticide Network Action Europe, have called for EFSA scientific opinions to be based on publicly available scientific evidence.

The IARC Monograph (page 45) advises criteria for data inclusion is laid out in the Preamble to the IARC Monographs:

> Reports that have been published or accepted for publication in the openly available scientific literature' and 'data from governmental reports that are publicly available. [313]

Little has been done to disconnect regulatory risk assessment from the industry that depends on it to ensure robust sales. It is of critical urgency that governments build in 'at arm's-length' policy (and financial budgets) to ensure risk assessment is separate from bias and influence and protocols and methodologies are developed in the best interest of the public.

The 'revolving door of industry and government' is an established practice in the banking and pharmaceutical and agrichemical-biotech sectors. Cash-strapped regulators are reliant on systems that ensure international

[311] Portier CJ et al 2016 Commentary. doi:10.1136/jech-2015-207005.
[312] Landmark ECJ ruling: research on dangers of pesticides must be made public. Press release. 23 November 2016. Greenpeace
[313] WHO IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Preamble. Lyon 2006. http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf, accessed January 2017.

industry-friendly opaque agrichemical evaluations to facilitate pesticides sales.

Central to the European debate has been lack of data transparency. Unpublished raw data critical to the evaluation has remained inaccessible to the public. In 2016 EFSA committed to share the raw data from the glyphosate risk assessment.[314] The data, when supplied (not to the public, rather to the organisations who made the request), was not in machine readable format, and critical sections were redacted (including summary, methodology and conclusions).

Expert scientists noted that the data was provided in a form that was impossible to process. Consequently, any work to understand how the Glyphosate Task Force analysed and interpreted the raw data into the RAR document would be 'titanic', and that as long as the data had to remain private it could not be cited and published, and so it could not be publicly considered.[315]

Transparency regarding raw data and associated literature would enable better informed risk assessment; replace controversy with greater certainty, and as a result, expedite informed decision-making.

4.5.1 World Health Organization (WHO) and Food and Agriculture Organisation (FAO) Joint Meeting on Pesticides Residues (JMPR) May 2016

The Joint Meeting on Pesticides Residues (JMPR), as the group that assemble to conduct WHO and FAO evaluations, relies heavily on unpublished industry selected studies (rather than published and peer reviewed science) to arrive at endpoints critical for establishing whether an active ingredient is toxic, or, as glyphosate is currently considered by JMPR 2016[316], of 'low toxicity'.

Conflicts of interest permeate regulatory authorities:

> Problems inherent with reliance on GLP as the standard for choosing data are compounded by the process used by federal agencies to determine membership on science advisory panels. Leading experts qualified by

[314] Glyphosate: EFSA shares raw data from risk assessment. *EFSA.* December 2016. http://www.efsa.europa.eu/en/press/news/161209

[315] Glyphosate specialists: EFSA's data disclosure better than nothing, but of little help. *CEO.* April 27 2017. https://corporateeurope.org/efsa/2017/04/glyphosate-specialists-efsa-data-disclosure-better-nothing-little-help

[316] Pesticide residues in food – 2016: Part II toxicological evaluations / Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 9–13 May 2016 Glyphosate ISBN 978-92-4-165532-3 (Page 89 onwards) http://apps.who.int/iris/bitstream/10665/255000/1/9789241655323-eng.pdf?ua=1 Accessed 10/5/2017

> specific experience on the chemical or end points under consideration are often specifically excluded from membership. [317]

The JMPR committee responsible for the most recent 2016 May glyphosate evaluation are closely aligned with industry. The Guardian reported:

> Professor Alan Boobis, who chaired the UN's joint FAO/WHO meeting on glyphosate, also works as the vice-president of the International Life Science Institute (ILSI) Europe. The co-chair of the sessions was Professor Angelo Moretto, a board member of ILSI's Health and Environmental Services Institute, and of its Risk21 steering group too, which Boobis also co-chairs.
>
> In 2012, the ILSI group took a $500,000 (£344,234) donation from Monsanto and a $528,500 donation from the industry group Croplife International, which represents Monsanto, Dow, Syngenta and others, according to documents obtained by the US right to know campaign. [318]

Professor Boobis has also spent time on the EFSA Panel on Plant Protection Products and their Residues (PPR).[319]

The Centre for Media and Democracy's SourceWatch advises:

> Today the ILSI specialises in lobbying national and international agencies such as the Food and Agriculture Organization (FAO) and the World Health Organisation (WHO). Its membership consists of 400 of 'the world's leading manufacturers of food and food ingredients, chemicals, pharmaceuticals and other consumer products. [320]

SourceWatch notes that ILSI has over 400 companies listed as members, including Dow Agrosciences/Dow Chemical, Monsanto, DuPont and Bayer AG.

ILSI has valuable 'insider' status[321] at WHO governing body meetings and the chairmanship of Professors Boobis and Moretto indicates close industry relationships.

Annual meetings, or 'sessions' of the Codex Committee on Pesticide Residues are well stocked with industry employees and lobby groups. Issues regarding pesticide toxicity and residue data are discussed. There appears to be little representation from the public health sector.[322]

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[317] Myers JP, Vom Saal FS, et al 2009. Good Laboratory Practice: The case of bisphenol A.
[318] UN/WHO panel in conflict of interest row over glyphosate cancer risk. A.Neslen. *The Guardian.* 17 May 2017 https://www.theguardian.com/environment/2016/may/17/unwho-panel-in-conflict-of-interest-row-over-glyphosates-cancer-risk
[319] JOINT FAO/WHO MEETING ON PESTICIDES RESIDUES (JMPR) - 9-13 MAY 2016 List of experts http://www.who.int/foodsafety/areas_work/chemical-risks/JMPR_2016_ListOfExperts.pdf?ua=1
[320] www.sourcewatch.org International Life Sciences Institute (ILSI). Accessed 4 May 2017 http://www.sourcewatch.org/index.php/International_Life_Sciences_Institute#World_Health_Organisation
[321] Tim Lougheed Policy: WHO/ILSI Affiliation Sustained. *Environ Health Perspect*. 2006 Sep; 114(9): A521.
[322] JOINT FAO/WHO FOOD STANDARDS PROGRAMME CODEX ALIMENTARIUS COMMISSION 39th Session Rome, Italy, 27 June – 1 July 2016 REPORT OF THE 48th SESSION OF THE CODEX

In May 2016, the JMPR 2016 evaluation concluded:

> The long-term dietary exposure to residues of glyphosate from uses that have been considered by JMPR is unlikely to present a public health concern.

The JMPR on page 257:

> Reaffirmed the group ADI for the sum of glyphosate, AMPA, N-acetyl-glyphosate and N-acetyl-AMPA of 0–1 mg/kg bw on the basis of the NOAEL of 100 mg/kg bw per day for effects on the salivary gland in a long-term study of toxicity and carcinogenicity in rats and application of a safety factor of 100.

The ADI daily exposure level, which New Zealand defers to, has retained the 24-year-old privately held study that has never been peer reviewed (Page 165 Atkinson et al. 1993b) to maintain the acceptable daily intake (ADI) exposure level for the public sector.

Many of the studies present in JMPR 2016 are unpublished. Existing published literature demonstrating harm at much lower levels may not fulfil requirements of guidelines and protocols and so may be excluded.

4.5.2 European Commission – European Food Safety Authority

Regulation 1107/2009[323] requires EFSA to take into account all scientific literature when undertaking an evaluation. However, a significant quantity of data appears to be excluded by use of the industry (BASF) developed and controversial[324] 'Klimisch'[325] ranking. This guideline, recognised as insensitive, has the effect of only including studies for review if they fit narrow OECD standards, and dismissing, without analysis, research that may provide greater understanding of the chemical studied and reveal harm at delicate levels.[326]

Annex II, 2.1 of Regulation 1107/2009, (General decision-making criteria) includes the requirement that safeners and synergists must not be harmful,

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COMMITTEE ON PESTICIDE RESIDUES Chongqing, China, 25 - 30 April 2016. http://codexindonesia.bsn.go.id/uploads/download/REP16_PRe.pdf

[323] Regulation 1107/2009, Art.8.5: “Dossiers, The summary dossier shall include the following: Scientific peer-reviewed open literature, as determined by the Authority, on the active substance and its relevant metabolites dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of the dossier shall be added by the applicant to the dossier.”

[324] European Commission Working Group Ref. Ares(2015)2071689 - 18/05/2015 http://ec.europa.eu/dgs/health_food-safety/dgs_consultations/docs/dgs-consultations_working-groups_20150424_summary_en.pdf

[325] H.-J. Klimisch, M. Andreae, U. Tillmann, A Systematic Approach For Evaluating the Quality of Experimental Toxicological & Ecotoxicological Data, Regulat Toxicol & Pharmacol 25, 1–5 (1997).

[326] Missed and Dismissed: pesticide regulators ignore the legal obligation to use independent science for deriving safe exposure levels. 2014 *Pesticide Action Network Europe and Generation Futures* Tony Tweedale, Angeliki Lysimachou and Hans Muilerman

and that a Member State should consider the toxicity of co-formulants (e.g. including safeners and synergists):

> Authorisation in at least one Member State is expected to be possible for at least one plant protection product containing that active substance for at least one of the representative uses. [327]

There does not appear to be serious consideration of toxicity of 'plant protection product representative uses' (commercial and retail products) as per Annex II in the European regulatory process for glyphosate.

Despite good legislation in place, it is industry who then undertakes the bulk of the review, providing the reference data, related scientific conclusions and recommendations, and then member states approve the outcome. This has the effect of limiting data and industry controlling data submitted for consideration.

In the case of glyphosate, rapporteur Member State (RMS) BfR provided its initial evaluation of the dossier on glyphosate in the Renewal Assessment Report (RAR), which was received by EFSA on 20 December 2013. The European peer review was initiated on 22 January 2014 by dispatching the RAR for consultation of the Member States and the applicants of the European Glyphosate Task Force, represented by Monsanto Europe S.A.[328]

Accusations of industry aligned staffing, and conflicts of interest within the European Food Safety Authority (EFSA) have plagued the agency since its founding in 2002.[329]

In May 2015, Patrick van Zwanenberg wrote in The Guardian that European regulators:

> …based their evaluation on descriptions provided by the agrochemical industry (Glyphosate Task Force) …But those descriptions also contained the industry's assessment of the reliability and interpretation of each study. [330]

The IARC Working Group finding of 2a probable carcinogen is politically controversial, as European policy based on that finding would require a ban of glyphosate based herbicides.

The European Food Safety Authority (EFSA) Renewal Assessment Report (RAR) varies from the IARC Monograph. It excluded much of the published and peer reviewed literature available to the IARC Working Group, instead

[327] Regulation 1107/2009, Annex II, 2.1 General Decision Making Criteria. http://exporthelp.europa.eu/update/requirements/ehir_eu12_02v002/eu/auxi/eu_chemkt_ppp_annex2.pdf

[328] EFSA (European Food Safety Authority), 2015. Peer review of glyphosate. doi:10.2903/j.efsa.2015.4302.

[329] Robinson C, Holland N, Leloup D, et al.2013. Conflicts of interest at EFSA erode public confidence.

[330] Chemical reactions: glyphosate and the politics of chemical safety. *The Guardian* May 2015, P. van Zwanenberg. https://www.theguardian.com/science/political-science/2015/may/13/chemical-reactions-glyphosate-and-the-politics-of-chemical-safety

using studies selected and supplied by industry, the Glyphosate Task Force.

The Van Zwanenberg article also brought to public notice that the European RAR:

> …was not actually written by scientists working for the German Federal Institute for Risk Assessment (BfR), but rather by the European Glyphosate Task Force, a consortium of agrochemical firms.
>
> BfR officials explained that due to the quantity of evidence they did not have the time to report the original studies in detail, but instead based their evaluation on descriptions provided by the agrochemical industry. [331]

This is a common problem, there is an inordinate amount of complex data to comprehend, and Regulators have limited funding. The NZ EPA is similar, with a restricted group of scientists available to scrutinise complex papers. This leads to a reliance on the always helpful but naturally, conflicted agrichemical industry.

A reasonable person might consider, considering these circumstances, that cash strapped regulators would, as a result, defer to the authority of the IARC.

Lack of transparency and academic integrity within the European Food Safety Authority (EFSA) Renewal Assessment Report is best described by Portier et al.

> An 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 elements of transparency do not exist for the RAR. For example, citations for almost all references, even those from the open scientific literature, have been redacted.
>
> The ability to objectively evaluate the findings of a scientific report requires a complete list of 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 where financial support, conflicts of interest and affiliations of authors are fully disclosed. 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. [332]

A later May 2016 Guardian investigative report threw light on the conflicts of interest integrated into European risk assessment. The Guardian reported:

> The debate over the scientific bona fides of the ILSI also has a fractious back story. In 2012, the European parliament suspended funding to the

[331] Ibid
[332] Portier CJ et al 2016 Commentary. doi:10.1136/jech-2015-207005

> European food safety authority (Efsa) for six months over a string of conflicts of interest allegations involving ILSI members on the board of Efsa and on its committees.
>
> The dispute saw the resignation of the chair of the Efsa management board, as well as Moretto standing down as a member of the Efsa pesticides panel, for failing to declare links with the industry and ILSI. An advisory position held by Boobis at Efsa was discontinued in 2012. At that time, ILSI described itself as a "key partner for European industry", but it now says that it is a non-profit guided by scientific and environmental concerns and that it does not lobby or make policy recommendations.[333]

After failure to arrive at a consensus, amid controversy and indecision due to the impact of the independent IARC Monograph, the Europeans extended the authorisation of glyphosate for 18 months until the Helsinki based European Chemicals Agency (EChA) concluded a review.

Public and NGO pressure on the European Commission may have helped contribute to the passing of resolutions that cautiously acknowledge exposures of GBHs should be minimised.

A European Parliament news[334] press release advised of resolutions passed in March 2016 by the Environment Committee which included:

- The EU Commission should renew its marketing approval for just 7 years, instead of 15
- Glyphosate based herbicides are utilised professional uses only
- MEPs call for an independent review and the publication of all the scientific evidence that the European Food Safety Authority (EFSA) used to assess glyphosate.
- Advice that it should reassess its approval of glyphosate in the light of its pending classification by the European Chemicals Agency (EChA), under separate legislation.
- Requirement that the Commission table a new draft in order to better address the sustainable use of herbicides containing glyphosate and also to launch an independent review of the overall toxicity and classification of glyphosate, based not only on data relating to carcinogenicity but also on possible endocrine-disruptive properties.
- A demand for more transparency in the science used to prove safety of glyphosate. MEPs urge the 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".

[333] UN/WHO panel in conflict of interest row over glyphosate cancer risk. A.Neslen. *The Guardian.* 17 May 2017

[334] Glyphosate herbicide: don't renew its authorisation, urge MEPs. European Parliament News Press Release. March 22, 2016. http://www.europarl.europa.eu/news/en/press-room/20160321IPR20296/glyphosate-herbicide-don-t-renew-its-authorisation-urge-meps

- MEPs also condemn as ‘unacceptable’ the use of glyphosate in a farming practice known as ‘green burndown’, (pre-harvest treatment, desiccation), ie the killing of the actual crop plant before harvest in order to accelerate ripening and facilitate harvesting. This practice leads to, amongst other things, increased human exposure.
- Glyphosate should not be approved for use in or close to public parks, public playgrounds and public gardens.

In June 2016, a European Commission Fact Sheet[335] on glyphosate noted resolutions which have been presented to Member States (who would have responsibility for enforcing these measures):

> **1)** ban a co-formulant called POE-tallowamine from glyphosate based products;
>
> **2)** minimise the use of the substance in public parks, public playgrounds and gardens;
>
> **3)** minimise the pre-harvest use of glyphosate.

The EChA CLH report, released March 15, 2016, concluded glyphosate did not did not meet the criteria in the CLP Regulation to classify glyphosate for specific target organ toxicity, or as a carcinogen, as a mutagen or for reproductive toxicity.[336] [337] EChA's Committee for Risk Assessment’s (RAC) opinion regarding the harmonised classification of glyphosate was presented to the European Commission in 2017.[338] [339]

The committee concluded that the scientific evidence available warranted the following classifications for glyphosate according to the CLP Regulation CLP Regulation (EC) No. 1272 / 2008 [340]:

- Eye Damage 1; H318 (Causes serious eye damage)
- Aquatic Chronic 2; H411 (Toxic to aquatic life with long lasting effects)

The dossier submitter, German Federal Institute for Occupational Safety and Health (BAuA) recommended H373: May cause damage to organs through prolonged or repeated exposure. However, this recommendation was not accepted by EChA's RAC.

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[335] European Commission - Fact Sheet. FAQs: Glyphosate Brussels, 29 June 2016. Frequently Asked Questions on Glyphosate. http://europa.eu/rapid/press-release_MEMO-16-2012_en.htm

[336] CLH report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 . https://echa.europa.eu/documents/10162/13626/clh_report_glyphosate_en.pdf

[337] Glyphosate not classified as a carcinogen by ECHA ECHA/PR/17/06 https://echa.europa.eu/-/glyphosate-not-classified-as-a-carcinogen-by-echa

[338] ECHA’s opinion on classification of glyphosate published. ECHA/NI/17/20 Helsinki, 15 June 2017 https://echa.europa.eu/-/echa-s-opinion-on-classification-of-glyphosate-published

[339] CLH report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 Substance Name: N-(phosphonomethyl)glycine; Glyphosate (ISO) https://echa.europa.eu/documents/10162/2d3a87cc-5ca1-31d6-8967-9f124f1ab7ae

[340] CLP Regulation (EC) No. 1272 / 2008 on the classification, labelling and packaging of substances and mixtures. http://www.hsa.ie/eng/Publications_and_Forms/Publications/Chemical_and_Hazardous_Substances/CLP_Poster_1_A1_size_.pdf

The decision-making by EChA is not without controversy. In March 2017, a large group of European NGOs including Greenpeace expressed concern that members of the EChA review had conflicts of interest according to EChA's own criteria. [341]

Members of the European Parliament (MEPs) questioned the impartiality of the EChA study.[342]

In May of 2017 Dr Christopher Portier (Former Director US National Center for Environmental Health and Former Director US Agency for Toxic Substances and Disease Registry) wrote an open letter to the European Commission president outlining concerns that there were serious omissions in both EFSA and EChA assessments and both had failed to identify tumour incidences.[343]

The European Commission is expected to issue a proposal on the future of glyphosate late 2017, which members will vote on, to enable a decision to be made before the December cut-off date for the extended glyphosate licence. [344]

4.5.3 U.S. Environmental Protection Agency Office of Pesticide Programs September 2016 Issue Paper

There is controversy concerning whether key documents used by EChA and other regulators including the US EPA were ghost written by Monsanto.[345] The released court documents also create uncertainty in the US as the scientific paper believed to be in question, Williams et al 2000[346], has been used in US evaluations including the most recent.

The US EPA Office of Pesticide Programs (OPP) released September 12, 2016, a proposed position paper, 'Glyphosate Issue Paper: Evaluation of Carcinogenic Potential,'[347] a month after the NZ EPA carcinogenicity review was released.

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[341] Open letter on the independence and transparency of ECHA's Risk Assessment Committee 6 March 2017 http://www.greenpeace.org/eu-unit/Global/eu-unit/reports-briefings/2017/20170306_Open_Letter_ECHA_CoI_Concerns.pdf

[342] MEPs slam ECHA's ruling on glyphosate and call on Commission President for a ban. A.Kay 5 April 2017. *FG Insight* https://www.fginsight.com/news/meps-slam-echas-ruling-on-glyphosate-and-call-on-commission-president-for-a-ban--19978

[343] https://corporateeurope.org/sites/default/files/attachments/letterjuncker28may2017.pdf See Section 4.3

[344] The EU glyphosate timeline. 8 February 2017. *Greenpeace.* http://www.greenpeace.org/eu-unit/Global/eu-unit/banners/2017/20170208%20BR%20glyphosate%20timeline%20ECI%20launch.pdf

[345] Patients: Roundup gave us cancer as EPA official helped the company. H.Yan May 15 2017. *CNN* http://edition.cnn.com/2017/05/15/health/roundup-herbicide-cancer-allegations/index.html

[346] Williams et al 2000. Safety Evaluation and Risk Assessment of the Herbicide Roundup and its active ingredient, glyphosate

[347] Glyphosate Issue Paper: Evaluation of Carcinogenic Potential *Office of Pesticide Programs* Sept.12, 2016 https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf

The paper is not definitive, releasing a ‘proposed conclusion’ of 'not likely to be carcinogenic to humans' at doses relevant to human health risk assessment.

The mission of the US Environmental Protection Agency (US EPA) is to *‘protect human health and the environment'.* The *‘*Glyphosate Issue Paper: Evaluation of Carcinogenic Potential’ issue paper appears to repeat much of the rationale of other agencies from which to draw its narrow ‘weight of evidence.' As with other recent assessments, it excludes studies considered by the IARC Working Group, ignores full formulation toxicity, and therefore should be considered outdated and irrelevant.

4.5.3.1 US EPA OPP 2016 Issue Paper: Ignoring full exposures to the public

The OPP elects ignores full formulation exposures however, epidemiological studies are concerned with exposure to full formulation marketed product.

The OPP Issue Paper ‘hypothesized that glyphosate formulations may be more toxic than glyphosate alone’.

It is absurd and scientifically implausible to remove discussion concerning GBHs, ignore the wide body of scientific evidence regarding greater toxicity of full formulation exposures, and then, in the paper’s proposed conclusion, recommend more research to investigate toxicity of the full formulation of GBHS.

There are doubts – the OPP acknowledges ‘there are data suggesting glyphosate may be genotoxic or cause oxidative stress.’ Yet the OPP appears to place little consideration on the related risk of carcinogenesis and how a combination of ingredients (e.g. the GBH formulation) may contribute to cancer hallmarks, or ‘capabilities that allow cancer cells to survive, proliferate, and disseminate’.

Nor does the OPP appear to consider lifetime exposure and vulnerability of children which may lead to morally unacceptable harm.

The US has traditionally taken a more precautionary stance (where evidence is scientifically plausible but uncertain) than the WHO – FAO.[348]

[348] Harvard Centre for Risk Analysis: The precautionary principle in practice: Comparing US EPA and WHO pesticide risk assessments. *Risk in Perspective.* Vol 12 https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1273/2013/06/RISK_IN_PERSP_JANUARY2004.pdf

4.5.3.2 US EPA OPP 2016 Issue Paper: Industry focus

The OPP Issue Paper claims to have conducted an open literature review, then resorts to established guidelines to exclude much of the non-industry data and formulate the 'scientific evidence' from which it draws its 'weight of evidence' conclusion.

Yet much literature was industry provided. Studies submitted to the Agency were 'cross-referenced with review articles from the open literature [Chang and Delzell (2016), Greim et al. (2015), Kier and Kirkland (2013), Kier (2015), Mink et al. (2012), Schinasi and Leon (2014), and Williams et al. (2000).]'

The OPP Issue Paper then advises in footnotes, 'All review articles, except Schinasi and Leon (2014), were funded and/or linked to Monsanto Co. or other registrants.'[349]

This rationale may arguably result in a weight-of-evidence finding from cross-referencing with industry data that is vulnerable to accusation of bias.

There is little transparency. Where studies from registrants (industry) have been supplied, in contrast to earlier EPA re-registrations, registrant details do not appear to have been supplied for public information.

4.5.3.3 US EPA OPP 2016 Issue Paper: Outdated science and outdated guidelines

The OPP, in synchronicity with other regulators, continues to place emphasis on dose-response relationships (excluding non-linear relationships and their relationship to endocrine effects); GLP-compliant data and OECD guideline requirement; reliance on industry produced claims that tumours were 'not considered treatment-related'; and retention of the existing paradigm that excludes consideration of full formulation effects in favour of arguably irrelevant technical grade active ingredient. This enables the OPP to build their case for a weight of evidence approach that results in an assessment of "not likely to be carcinogenic to humans" at the doses relevant to human health risk assessment for glyphosate.

The OPP acknowledges there are 'data gaps' regarding formulation toxicity. Yet there appears no capacity to judge risk from a public law standpoint. Risk is greater in a population that is exposed to glyphosate daily. The paper acknowledges that young children may be exposed to up to 3 times the dietary glyphosate of adults as a proportion to body weight, (possibly

[349] Glyphosate Issue Paper: Evaluation of Carcinogenic Potential *Office of Pesticide Programs* Sept.12, 2016 P.22 https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf

exposed to .47mg/kg glyphosate in bodyweight per day), yet does not appear to consider the greater vulnerability of children, and the critical stages of development where 'the timing, duration and pattern of exposure are at least just as important as the dose' [350] and act with caution.

The OPP refers in page 136 to 'the extensive size of the glyphosate database, which includes a multitude of well-designed and well-conducted studies.'

The OPP fails to acknowledge the exclusion of non-industry data, the paucity of unbiased studies separately produced from industry. This includes information relating to childhood exposures, endocrine disruption and carcinogenesis, neurotoxicity, or chronic exposures at environmentally relevant levels.

Current cancer research is unravelling the 'multistep process of human tumour pathogenesis.' Referring again to the 2011 Hallmarks of Cancer paper, the:

> …biology of tumors can no longer be understood simply by enumerating the traits of the cancer cells but instead must encompass the contributions of the "tumor microenvironment" to tumorigenesis. [351]

A new strategic agenda is apparent with Agency insistence that primary DNA damage and toxicity should infer higher priority if effects demonstrably lead to heritability or mutagenicity. This priority appears to neglect scientific knowledge of the potential for harm from multiple pathways and the potential for chemicals to act as a mechanism for cancer development, and the obligation of risk assessment to progress in line with science.

This appears to reconfigure the conversation in favour of industry – creating new hoops for independent scientists to jump through. As discussed earlier, DNA is very stable and mutagens are rare.

This US EPA carcinogenicity issue paper is arguably deficient in failing to consider complexity of cancer development, full formulation effects at population levels, and appears at risk of bias in placing a weight of evidence priority on industry developed evidence. It appears dependent on industry selection of favourable studies, but does not require industry to disclose unfavourable studies.

These relevant considerations, ignored in the Issue paper, should be integral for any public health risk assessor considering possibility of harm which may result in increased risk of cancer on a population basis. It results in an arguably irrelevant paper that appears to assure protection of trade

[350] Gray et al 2009. State of the Evidence - The Connection Between Breast Cancer and the Environment. *Int J Occup Environ Health* 2009;15:43–78
[351] Hanahan D., et al. (2011) Hallmarks of cancer: the next generation. *Cell*, 144, 646–674.

based interests, rather than act with caution as required by its legislation to 'protect public health and the environment.'

A response paper[352] submitted to the US EPA by the Centre for Food Safety (Docket EPA-HQ-OPP-2016-0385) provides a detailed analysis that address significant concerns raised by the US EPA OPP Issue paper.

In March 2017, a FIFRA[353] scientific advisory panel were 'split' and unable to reach consensus regarding the findings of the Issue Paper.[354] The panel recommended that the Issue Paper consider rodent cancer bioassays of glyphosate-based formulations. The panel noted the uncertainties surrounding the Issue Papers decision to exclude studies (with the exception of epidemiological studies) concerning full formulation. The panel also suggested that:

> …workers in companies that manufacture, formulate, or handle and sell glyphosate on a wholesale basis comprise a promising resource that should be investigated. *[355]*

California is moving separately to regulate glyphosate. The 'Californian Office of Environmental Health Hazard Assessment (OEHHA) determined that glyphosate (CAS No. 1071-83-6) will be added to the list of chemicals known to the state to cause cancer for purposes of Proposition 65.'*[356]*

In April, the OEHHA proposed a No Significant Risk Level (NSRL) for the chemical glyphosate of 1100 micrograms (1.1milligrams) per day for glyphosate.[357] This is over one hundred times lower than the US EPA limit. Dr Olga Naidenko Senior Science Advisor for Children's Environmental Health at Environmental Working Group (EWG) released a report stating that the new level does not protect children.

> Applying the tenfold children's health factor and a one-in-a-million cancer risk standard, EWG believes that the No Significant Risk Level for glyphosate should be no more than 0.01 milligram, or 10 micrograms, per day. This maximum intake limit should apply to all exposures.*[358]*

If the US 10x safety margin for children was applied to water guidelines this would result in a limit of 5 ppb, or 5 ug/L for glyphosate.

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[352] Centre for Food Safety. OPP Docket- US EPA. Docket EPA-HQ-OPP-2016-0385. October 12, 2016.
[353] Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
[354] FIFRA Scientific Advisory Panel Meeting Minutes and Final Report No. 2017-01 A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: EPA's Evaluation of the Carcinogenic Potential of Glyphosate https://www.epa.gov/sites/production/files/2017-03/documents/december_13-16_2016_final_report_03162017.pdf
[355] Ibid P.17
[356] OEHHA Press Release March 28 2017. https://oehha.ca.gov/proposition-65/crnr/glyphosate-be-listed-under-proposition-65-known-state-cause-cancer
[357] To be adopted into regulation in Title 27, California Code of Regulations, section 25705. Notice of Proposed Rulemaking: Amendment to Section 25705, Specific Regulatory Levels Posing No Significant Risk: Glyphosate https://oehha.ca.gov/proposition-65/crnr/notice-proposed-rulemaking-amendment-section-25705-specific-regulatory-levels#_ftn2
[358] http://www.ewg.org/research/california-proposes-safe-level-roundup-more-100-times-lower-epa-limit/californias-proposed

The European Commission Council Directive for pesticides 98/83/EC states a maximum limit in drinking water for pesticides of 0.10 µg/l (.01 ppb or 0.0001 mg/L)[359] This is one of the lowest levels, and aims to protect children. At time of authorisation it was thought to be the lowest level detectable. The sum of all pesticides in European drinking water must be below 0.5 µg/l.[360]

As New Zealand doesn't consider glyphosate a chemical of concern, there is no established level for glyphosate. (See section 6.2.2 Local Authorities – Water Monitoring)

5.0 New Zealand legislation, regulations and/or policies that may come into force if a chemical or its formulations were declared a 'probable carcinogen.'

NB: Further information to Section 5 is contained in the Appendix V.

A Workshop held at the European Parliament stated that:

> The criteria used by the IARC for Group 2A are comparable to those for Category 1B in Regulation (EC) No 1272/2008.[361]

The European Parliament has legislation that requires that if plant protection products receive a classification of European category 1A or 1B, they cannot be approved for sale for use where residues exceed 0.01mg/kg.[362] (see Appendix VI –Section 7(1) Best Practice European Union)

This would result in an effective ban on glyphosate use, on and near, food and feed crops.

Legislation such as this would likely prohibit pre-harvest desiccation of glyphosate based herbicides on European food and feed crops.

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[359] Council Directive 98/83/EC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF

[360] P. Grandjean. Only One Chance: How environmental pollution impairs brain development – and how to protect the brains of the next generation. Oxford University Press. 2013. ISBN 978-0-19-023973-2 P.154

[361] European Parliament resolution of 13 April 2016 on the draft Commission implementing regulation renewing the approval of the active substance glyphosate in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Implementing Regulation (EU) No 540/2011 (D044281/01 – 2016/2624(RSP)) http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P8-TA-2016-0119+0+DOC+XML+V0//EN

[362] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

How would this classification affect New Zealand?

The IARC determination of 'probable carcinogen' 2A appears equivalent with the New Zealand Category 'substances that are known or presumed human carcinogens,' 6.7A. If the IARC were to be accepted as the world authority on carcinogenicity by the New Zealand government, such substances would be declared 'toxic' (a class 6 substance) under the Hazardous Substances and New Organisms Act 1996 (HSNO Act) and its regulations.

Three interconnected Acts form the significant framework of chemicals regulation in New Zealand should a chemical or substance be considered a 'probable' or 'presumed' carcinogen.

The New Zealand Environmental Protection Authority (NZ EPA) is New Zealand's single national-level environmental regulator. In addition to other administrative duties, the NZ EPA holds the responsibilities, functions, duties and powers under the HSNO Act.

In addition to other administrative duties, the Ministry for Primary Industries (MPI) has responsibilities, functions, duties and powers under the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM)[363] to ensure agricultural compounds (which may be hazardous and fall under the HSNO Act) sold and used in New Zealand are managed safely. MPI also administers the Food Act 2014.

The Food Act confers responsibility for setting of maximum residue levels (MRLs) and Food Regulations 2015 advise the authorities and information that New Zealand defers to when setting MRLs on food.

If glyphosate were declared 'toxic' under the HSNO Act, it would be subject to controls under HSNO regulations.

- Written records must be made of all applications where members of the public may be present.
- Protective clothing and equipment must ensure operator does not come into contact with the substance and the handler must have information showing this is fit for purpose and clothing is properly maintained.
- Quantities of 10 litres or greater must be under the control of an approved handler and locked away.
- Acceptable daily and workplace exposure values would need to be set.
- Tolerable exposure limits would need to be set (to help assess workplace exposures).

[363] Agricultural Compounds and Veterinary Medicines Act 1997 http://www.legislation.govt.nz/act/public/1997/0087/latest/whole.html#DLM414583

•Workplace standards should take into account toxicity data concerning full formulation

(Many of the HSNO control regulations require urgent external review as they are severely outdated and hampered by outmoded scientific assumptions. They are at risk of failing to establish safe daily limits. Problems include a regulated minimum exposure level, failure to account for risk of comorbidity, failure to account for sensitive populations, and outdated dose-response mechanism assumptions.)

The purposes of all three Acts should assure that public servants and agencies operating under these acts place a priority on the protection of public health:

1. HSNO Act: protect the environment, and the health and safety of people and communities

2. ACVM Act: prevent or manage risks associated with the use of agricultural compounds, including to public health and animal welfare

3. Food Act: provide for risk-based measures that minimise and manage risks to public health and protect and promote public health.

Legitimate expectations derive from the purpose and intent of the Acts under which these agencies operate. The public exercise a great deal of trust in the public servants and agencies who have the responsibility for exercising what appear to be a great deal of discretionary powers, captured within the regulations contained above.

Despite the significant quantity of legislation, regulation and policy, it is apparent that all three Acts appear to make discretion by government agencies and Ministers the principal mechanism for restrictions on human exposure to probable/presumed carcinogens.

1. HSNO Act provides that any person or the chief executive may request the NZ EPA to decide whether there are grounds for assessing a substance where 'significant new information has become available.' This is referred to as a Chief Executive Initiated Reassessment (CEIR)

The author asked the NZ EPA to clarify processes involved in the CEIR glyphosate monitoring process that is undertaken by the NZ EPA, and whether it will take into account studies of the full formulation published in the scientific literature.' (August 25, 2016) A NZ EPA strategy and risk advisor responded that:

> There are a number of other pesticide active ingredients on the EPA's Chief Executive Initiated Reassessment list that we consider to be of greater potential concern for human health and the environment than glyphosate. (September 6, 2016)

2. There appears to be no regulatory instrument in the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act) or its regulations that requires an immediate regulatory response should an agricultural compound, which is a hazardous substance, be declared toxic and a probable or presumed carcinogen under the HSNO Act. However, the Director General may call for reassessment if 'significant new information concerning the product is made available.'

3. The Food Act and its regulations do not appear to require reduced chemical residues on food should that chemical be considered a probable carcinogen. The main mechanism within the Food Act to alter MRLs appears to be that the Governor-General may amend food residues following a recommendation of the Minister for Primary Industries

Outcomes from discretionary decision-making relating to these decisions may expose inherent weaknesses in the operating authorities. Decision outcomes depend heavily on the culture and convention contained in the agencies above.

The reliance of Ministry of Health (MoH) on the NZ EPA and MPI for advice following the IARC finding of glyphosate to be a probable carcinogen was expressed to Green MP Steffan Browning by the Director-General of Health during the 2014/2015 Annual Review deliberations. This reliance by MoH is concerning when the advice received appears contradictory, challenging the authority of IARC. NZ EPA and MPI appear in this instance, to be intentionally finding against IARC.

If traditionally, these agencies depend heavily on industry science to make decisions, and these agencies are reluctant to consider full formulation toxicities, and their regulations and policies are slow to adapt and are inconsistent with twenty first century science which recognises greater vulnerability of the infant and child to toxic substances at delicate environmental levels, and high level decision-makers are more comfortable placing economic considerations before health considerations, then the implicit trust required by the public may further erode.

It is increasingly evident that trust in government regulators the chemical industry has eroded and it is timely to develop the political will to use principled and science-based action to rebuild public trust in regulators.

6.0 Discussion: politicisation of glyphosate-based herbicides - safety issues

The pervasiveness of glyphosate-based herbicide formulations across food and environment and their still fast-expanding growth-of-use is unprecedented and well-documented. Pre-harvest applications which are

applied to desiccate, or dry-down common human food and animal feed crops close to harvest has increased exposure rates to non-agricultural populations.

Lifetime exposures – and increased risk of adverse effects – seems to be under-pinning new studies that suggest that glyphosate-based herbicides (GBH) should be regarded more cautiously than has been the case previously:

> Regulators have dramatically increased official tolerance levels in maize, oilseed (soybeans and canola), and alfalfa crops and related livestock feeds. Animal and epidemiology studies published in the last decade, however, point to the need for a fresh look at glyphosate toxicity.[364]

Babies conceived now commence immediate exposure to glyphosate-based herbicides as an unborn foetus; studies have found the product in breast milk and infant formula[365]; the US Food and Drug Administration has detected glyphosate in cereals[366] and honey[367]; and young children using playgrounds are at risk of exposure.[368] Children consuming intensively-grown foods and are vulnerable to exposure from ground and surface waters[369] for the rest of their adult lives.

Children have higher levels of pesticides in their urine than adults, possibly because they consume more food relative to bodyweight.[370]

(Despite the controversy surrounding this chemical, it is yet to be included in the New Zealand National Survey of Pesticides in Groundwater[371] for testing.)

Unlike their grandparents, the public today has a lifetime of glyphosate-based herbicides exposure at low levels that can affect their hormone system and that could lead to the growing epidemic of cancer.

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[364] Myers J P et al (2016). Glyphosate Consensus Statement. DOI 10.1186/s12940-016-0117-0.
[365] Fears over Roundup herbicide residues prompt private testing. C.Gillam. April 10 2015. *Reuters.* http://www.reuters.com/article/us-food-agriculture-glyphosate-idUSKBN0N029H20150410
[366] FDA Tests Confirm Oatmeal, Baby Foods Contain Residues of Monsanto Weed Killer C.Gillam. Sept 30 2016.
The Huffington Post. http://www.huffingtonpost.com/carey-gillam/fda-tests-confirm-oatmeal_b_12252824.html
[367] FDA Finds Monsanto's Weed Killer In U.S. Honey. C.Gillam. 15/9/2016 *The Huffington Post.* http://www.huffingtonpost.com/carey-gillam/fda-finds-monsantos-weed_b_12008680.html
[368] Children dance on weed-killer; Auckland Council says it's perfectly safe. S.Smith. March 4 2017. *Stuff.* http://www.stuff.co.nz/environment/89907959/Children-dance-on-weed-killer-Auckland-Council-says-its-perfectly-safe
[369] SURVEY OF GLYPHOSATE AND AMPA IN GROUNDWATERS AND SURFACE WATERS IN EUROPE - UPDATE 2012. Helene Horth (Independent Adviser, Water Quality and European Policy & Legislation). http://www.glyphosate.eu/system/files/mc-files/iia_7.12_07_horth_2012.pdf
[370] European Parliament. Human health implications of organic food and organic agriculture. 2016. PE581.922
http://www.europarl.europa.eu/RegData/etudes/STUD/2016/581922/EPRS_STU(2016)581922_EN.pdf
[371] National Survey of Pesticides in Groundwater 2014 ESR. B.Humphries and M.Close. https://www.marlborough.govt.nz/repository/libraries/id:1w1mps0ir17q9sgxanf9/hierarchy/Documents/Environment/Groundwater/Groundwater%20Reports%202015%20List/National_Survey_of_Pesticides_in_Groundwater_Report_final.pdf

Exposure that leads to greater risk of multiple conditions (comorbidity, the presence of other disorders or diseases in addition to the primary disease or disorder)[372] and the associated economic burden is yet to be addressed in risk assessment.

Health based experts interested in the environmental origins of disease may be interested in understanding that concern is not limited to glyphosate. This chemical is simply the most ubiquitous, with a large amount of published literature that questions its current and controversial safety status.

In the U.K. in 2014 the average number of pesticide applications on all arable crops consisted of six spray rounds, 12 products and 17 active substances.[373] [374] This excludes seed treatments (neonicotinoid insecticides and fungicides) which are commonly applied to most of these crops.

> Fungicides accounted for 40% of the total pesticide-treated area of arable farm crops grown in the United Kingdom in 2014, herbicides 31%, growth regulators 11%, seed treatments 9%, insecticides & nematicides 8%, molluscicides 2% and sulphur less than 1%.
>
> By weight, herbicides accounted for 44% of the pesticide active substances applied, fungicides 34%, growth regulators 17%, insecticides & nematicides, molluscicides & seed treatments 1% each, and sulphur less than 1%.
>
> Glyphosate was the herbicide used most extensively by weight applied, accounting for almost 1,800 tonnes of active substance. [375]

Multiple crop treatments reflect widespread practice and are not limited to the UK.[376]

The NZ EPA and the government agencies responsible for assessing risk and toxicity are fully aware that there is unprecedented cumulative exposure to multiple chemicals following multiple pesticide treatments. There appears no intention to assess the potential for harm from cumulative multi-formulation exposures.

[372] For example, Sogaard M, Thomsen RW, Bossen KS, Sorensen HT, Norgaard M. The impact of comorbidity on cancer survival: a review. *Clin Epidemiol* 2013; 5: 3–29. doi: 10.2147/CLEP.S47150 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820483/
[373] UK Food and Environment Research Agency (Fera) Pesticide usage on oilseed rape. Feb 2016 Vol 98 No2
[374] Pesticide Usage Survey Report 263 Arable Crops in the United Kingdom. 2014. *FERA*. Figure 9 - Average number of applications made to arable crops in the United Kingdom – 2014. P.6.
[375] Ibid.
[376] World record oilseed crop landed NZ Rural News Group Sunday, 08 February 2015. http://www.ruralnewsgroup.co.nz/rural-news/rural-general-news/world-record-oilseed-crop-landed

6.1 Farmers

Farmers and pesticides contractors traditionally worry about the acute risks of pesticides, e.g. from exposure from spills when putting together a tank mix. Farming media rarely discusses the long term, chronic exposures, which may over years, create more health issues than an occasional glyphosate spill.

Rates of depression, Parkinson's disease, rheumatoid arthritis and lymphatic cancers – among other illnesses – and associated comorbidity should be assessed with full consideration of lifetime pesticide exposures.

Media publications which criticise the IARC Monograph (and the published and peer reviewed literature considered by IARC Working Group) may be considered disingenuous and hypocritical, when the core studies the New Zealand EPA use to approve glyphosate and establish levels of exposure, remain neither published nor subject to peer review.

Careful and cautious risk assessment of the full formulation has never been undertaken by the major risk assessment agencies.

The HSNO Act requires that regulators 'protect the health and safety of people and communities'[377]; and the Agricultural Compounds and Veterinary Medicines Act 1997, requires that government employees 'prevent or manage risks associated with the use of agricultural compounds, being: a) risks to public health'.[378]

The farming media rarely discusses emerging scientific understanding outlining the toxicity of glyphosate and its formulations, despite studies which indicate glyphosate treated pasture and feed may impair reproduction rates,[379] [380] reduce nutrient availability and contribute to immune-related deficiencies in farm animals.

Farming media is constrained by advertiser interests. However, this has left farmers on the back foot when it comes to realising that a strong body of evidence about glyphosate and its formulations, (considered benign for so long by so many) could be seriously harmful.

[377] Hazardous Substances and New Organisms Act 1996. http://www.legislation.govt.nz/act/public/1996/0030/latest/whole.html
[378] *Agricultural Compounds and Veterinary Medicines Act 1997*. Section 4. Reprint 2016
[379] Chiu, Y.H., et al., Intake of Fruits and Vegetables with Low-to-Moderate Pesticide Residues Is Positively Associated with Semen-Quality Parameters among Young Healthy Men. J Nutr, 2016. http://jn.nutrition.org/content/early/2016/04/13/jn.115.226563.abstract
[380] Clair E, Mesnage R, Travert C and Séralini G-E. A glyphosate-based herbicide induces necrosis and apoptosis in testicular cells in vitro, and testosterone decrease at lower levels. Toxicology in Vitro 2012, 26, 269-279. http://www.gmoseralini.org/wp-content/uploads/2013/01/Clairal_ToxInVitro_2012-1.pdf

Organisations concerned with glyphosate resistance recommend mixing other pesticides with GBHs – rather than ceasing use. Toxicity of replacement products are not considered.[381]

Farmers depend on governments to apply best practice in policy and regulation to ensure export products are safe and in demand. Farmers may assume that best practice regulatory measures would synchronise with best scientific practice and commonly accepted scientific advancements regarding environmental exposures and human biological systems. This is not happening.

The current disconnect appears to place the interests of the agrichemical industry ahead of the health and safety of New Zealand farmers and their families. The same disconnect may result in downstream effects. For example, a lag in New Zealand farmer responsiveness to switching to high-value premium and health-focused markets that are wary of unwanted chemicals in food, despite the safety claims of regulators and risk assessment agencies.

6.2 Territorial Local Authorities

Local authorities are major users of GBH products: universally, they are on record as claiming that GBH use is far more 'cost-effective' than mowing and other means of control of unwanted growth of weed and vegetation species. Council chambers face increasing representations from health advocacy organisations and the public that challenge risk assessment based on industry paid studies, and instead request that local authorities consider scientific literature that indicates that adverse health events may be directly traced to exposure resulting from local agrichemical use.

Most LTAs contacted by the authors point to the NZ EPA as their authority as to the safety and regulatory acceptance of GBH. Legislation does allow for LTAs to limit and regulate GBH use in their localities, should they decide that the risks are too great or community concern demands it. Christchurch City Council is an example of an LTA that has responded to its community and is phasing out GBH in areas open to the public.

6.2.1 Auckland Council

Auckland Council was an early adopter of non-chemical weed and vegetation control. Auckland City and North Shore City had established comprehensive nonchemical policies with no chemicals on the roads and

[381] Managing glyphosate resistance. New Zealand Plant Protection Society K.C. Harrington, T.K. James and M.D. Parker http://resistance.nzpps.org/index.php?p=herbicides/glyphosate

progressive minimisation in the parks. These were in place for over 15 years.

The establishment of the Auckland Council Supercity in 2010 resulted in transfer of responsibility for road maintenance, including weed and vegetation control to Auckland Transport. This change resulted in Auckland Transport operating at 'arm's length' as a Council Controlled Organisation (CCO). In response to this new council structure, the Weed Management Advisory (WMA), a citizen advocacy group, was formed to advocate for the retention of the nonchemical policies and their adoption across the new city.

The WMA proposed that the new Supercity adopt Auckland City's sustainable nonchemical Weed Management Policy (WMP). This was rejected and a new WMP developed. The new WMP was adopted in 2013 after extensive public consultation and participation, establishing a framework that appeared to promise continuation of chemical free policies.

It appears that some council decision-makers do not consider that the authority of the WMP extends to operations under the CCO, Auckland Transport. As a result, separate operational recommendations appear to have been jointly developed by Auckland Council and Auckland Transport. WMA documentation demonstrates that new Auckland Transport contractors are integrating chemical road weed and vegetation control across the Supercity.

In contrast, the public, and some councillors consider that the WMP framework applies to the CCO. Citizens have expressed concern via petitions, protests and submissions, particularly regarding potential public exposure to GBHs. A Human Rights Impact Assessment (HRIA), commissioned to investigate Auckland Transport's use of chemicals revealed there were a significant number of international human rights norms of concern that were applicable to Auckland Transport's operations.[382]

Much of the public outcry is directly attributable to the widespread use within Auckland Council and Auckland Transport of GBHs. Auckland Transport's response to the HRIA, was to advise WMA that Auckland Transport is not aware:

> …of any evidence to suggest that the use of glyphosate poses any risk to human health' and that Auckland Transport will 'continue to use glyphosate because they take their advice from the Environmental Protection Agency and the EPA have not reassessed its classification.[383]

[382] Environment and Human Rights Advisory. A Human Rights Impact Assessment of Auckland Transport's Road Corridor Vegetation Control doc 141120/1 November 2014. http://www.environmentandhumanrights.org/wp-content/uploads/2013/05/NZ-AT-HRIA-1411201.pdf
[383] Weed Management Advisory June 2016. https://weedmanagementadvisory.wordpress.com/mayor-rejects-petition-plea-to-ban-toxic-chemical/

At an Auckland Council Regional Strategy and Policy Committee debate on the Weed Management Review in September 2016, Auckland Council CEO Dean Kimpton also noted that Auckland Council relies on the expertise of the EPA.

The position of Auckland Council clearly demonstrates the problems that arise when policymakers rely on incomplete regulatory decision-making. Risk is two-fold. Risk of harm is not fully considered, and Auckland Council and Auckland Transport potentially face greater risk of expensive litigation. Court action would not restrict scientific evidence to data selected for narrow regulatory assessment.

Regulatory delay in adopting the advice of the world authority in cancer, has downstream effects that potentially expose the public, and particularly children to risk. A business as usual approach by Auckland Council resulted in extensive chemical applications to a park the day before a family event, on February 25 2017.

Rod Sheridan, General Manager of Community Facilities responded to a letter to Auckland Council by WMA's Hana Blackmore requesting all parks participating in the summer series cease chemical applications because of risk to children attending. Mr Sheridan advised:

> Auckland Council and Auckland Transport are satisfied that their use of glyphosate fully complies with the requirements of NZS 8409:2004 Management of Agrichemicals. Both organisations are actively working with contractors to ensure that use reflects national standards and industry best practice at all times.
> We have investigated the issue raised by yourself and are confident that the contractor sprayed according to the guidelines for use and that there was no health and safety risk to park users.

By citing adherence with the requirements of the 2004 New Zealand agrichemical manual and guidelines for use, Mr Sheridan indicates that Auckland Council have fulfilled their obligation to the public.

The response relies on the authority of the 2004 New Zealand agrichemical manual and product guidelines, whose utility in the public interest is contingent upon effective and safe rendering of the HSNO and ACVM Acts to assess risk and protect the public from exposure to harmful substances.

It is implied that Mr Sheridan and Auckland Council place trust in the regulatory assessment of the complete substance (or product) the public is exposed to. It may be inferred, for example, that Auckland Council and Auckland District Health Board (ADHB) trust that the EPA and MPI would conduct risk assessment using the latest scientific knowledge, to ensure that the public, in this case children, would be safe when exposed to the full formulation, that the assessment would take into account new knowledge that residues may persist for longer than previously acknowledged, and therefore that children would be safe at the levels of exposure that persist in the environment one day after an application.

The ADHB would assume that evaluation of the formulation by the EPA and MPI would ensure there would be no risk to the endocrine system, nor risk that GBH would impact the biological pathways (hallmarks of cancer) that could lead to development of cancer tumours. So, as Mr Sheridan noted, adherence to agrichemical manual and approved guidelines for use result in no risk to children.

It is unfortunate that current risk assessment does not consider the above issues. Therefore, citing the agrichemical manual and guidelines does not prove public safety and in contrast, may provide the Auckland Council with a false sense of security that the product they are using is safe to both the public and council workers.

Distinguished Professor Bruce Baguley presented to a public forum at Ōrākei Local Board, December 8, 2017. He advised:

> My opinion is that because childhood cancers take a long time (typically twenty years) to develop, exposure of populations to a low dose of glyphosate over a long time represents a more significant risk than exposure to a high dose for a short time. The lack of data as to whether children are more susceptible to this risk than adults is also concerning.... Councils who ignore the published evidence from the World Health Organisation on the potential carcinogenicity of glyphosate may face liability issues in the future. My understanding is that some regions have adopted chemical-free weed control in urban areas, and I urge this council to adopt the same policy. [384]

Local authorities including Christchurch[385] and Tauranga[386] are turning away from the NZ EPA as a recognised authority and instead deferring to international findings and limiting use of glyphosate-based herbicides.

Local authorities including Tauranga[387] and Christchurch[388] are cautiously restricting glyphosate, despite NZ EPA assurances of the safety glyphosate. Many countries have acted to regulate glyphosate, and internationally, local authorities are acting to voluntarily restrict glyphosate based herbicides as they consider the product presents too great of a risk to residents.[389]

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[384] Public Forum - Use of Weed Sprays containing Glyphosate - Bruce Baguley A. Bruce Baguley supporting document .http://infocouncil.aucklandcouncil.govt.nz/Open/2016/12/OR_20161208_MAT_7001.PDF

[385] Christchurch City Council signals reducing use of dangerous weedkiller TINA LAW. March 10 2016. http://www.stuff.co.nz/the-press/news/77651604/Christchurch-City-Council-signals-reducing-use-of-dangerous-weedkiller

[386] Tauranga City Council Strategy and Policy. August 8 2016. http://econtent.tauranga.govt.nz/data/bigfiles/committee_meetings/2016/september/agen_council_20sept2016_minsstratpol8th.pdf

[387] Tauranga City Council Strategy and Policy. August 8 2016. http://econtent.tauranga.govt.nz/data/bigfiles/committee_meetings/2016/september/agen_council_20sept2016_minsstratpol8th.pdf

[388] Christchurch City Council signals reducing use of dangerous weedkiller TINA LAW. March 10 2016. http://www.stuff.co.nz/the-press/news/77651604/Christchurch-City-Council-signals-reducing-use-of-dangerous-weedkiller

[389] Bans and restrictions. http://www.pan-uk.org/glyphosate/ (see lower in document)

6.2.2 Local Authorities – Water Monitoring

To demonstrate chemical compliance with the Drinking-Water Standards for New Zealand (DWSNZ), water suppliers are required to undertake occasional monitoring to identify whether there are new contaminants (referred to as Priority 2 determinands, which include pesticides) present in their supplies. If these determinands are present at concentrations exceeding 50% of their DWSNZ maximum acceptable value (MAV) they may become a Priority 2 (P2) determinand. Once a determinand becomes P2, it is monitored frequently (for example monthly or weekly).

No pesticides appear to be considered sufficiently a threat thereby requiring monthly or weekly testing.)[390] However, pesticides with an established MAV are screened for. Frequency alters with different water suppliers.

> The Drinking water standards for New Zealand (DWSNZ)[391] specify (maximum acceptable values) MAVs for the microbial, chemical and radiological determinands[392] of public health significance in drinking-water and provide compliance criteria and procedures for verifying the water supply is not exceeding these values.

DWSNZ MAVs are drawn from the WHO Guidelines for Drinking Water Quality.[393] In cases where there is no WHO guideline value, the Ministry of Health may establish a Provisional MAV (PMAV). PMAVs have the same compliance requirement as a MAV.

As of 2017 there is no MAV established for glyphosate. WHO Guidelines released in 2017 do not provide a MAV for glyphosate. WHO Guidelines defer to JMPR decision-making and consider glyphosate of 'low toxicity.' They note the last assessment date as 2003.

As a result of no MAV listing, there is no testing in New Zealand drinking water to identify whether glyphosate, the most common herbicide in New Zealand, is present. Ministry of Health is dependent on the NZ EPA which defers to WHO Guidelines (which base their decisions on JMPR evaluations), which prioritise industry selected studies to provide evidence of safety.

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[390] Water Information New Zealand (WINZ) Database. Currently Assigned Official Priority 2 Determinands
http://www.drinkingwater.esr.cri.nz/supplies/priority2determinands.asp
[391] Drinking-water Standards for New Zealand 2005 (Revised 2008)
http://www.health.govt.nz/publication/drinking-water-standards-new-zealand-2005-revised-2008
[392] A determinand is a constituent or property of the water that is determined, or estimated, in a sample. It may be chemical, microbial, or radiological.
[393] Guidelines for drinking-water quality: fourth edition incorporating the first addendum ISBN 978-92-4-154995-0 http://apps.who.int/iris/bitstream/10665/254637/1/9789241549950-eng.pdf?ua=1

The reason given by the WHO for not establishing a guideline value was that the glyphosate and its metabolite AMPA 'Occur in drinking-water at concentrations well below those of health concern.'[394]

Observers may note that if there is no WHO guideline value, countries are unlikely to establish a MAV. Suppliers are then not impelled to test for the chemical, and by default countries have no knowledge of concentrations the chemical may, or may not, occur in drinking water.

The Ministry of Health, the responsible agency for drinking water safety, appears slow to address the complex challenges of environmental chemical contamination relating to drinking water exposures. The Draft Users' Guide: National Environmental Standard for Sources of Human Drinking Water[395] advises 'The DWSNZ are revised every two years and updated every five years.' The most recent revision was in 2008.

New Zealand authorities may be underestimating chemical contamination in drinking water as there is no requirement to monitor metabolites (chemical breakdown products) in drinking water monitoring programs. This is a serious omission.

The 2016 Ministry of Health Guidelines for Drinking Water admitted:

> Another uncertainty is that most water monitoring programmes do not include pesticide degradation products, some of which are equally toxic or even more toxic and also more polar, thus more mobile than the corresponding parent compounds. However, there are generally no established standards for metabolites, even though metabolites may have similar effects to their parent compounds.[396]

The IARC was unequivocal in stating that it considered that it was not just glyphosate, but the formulations and glyphosate's metabolite AMPA, that could cause oxidative stress.[397] The IARC Monograph considered data (page 9) revealing AMPA, which is more persistent than glyphosate, has been detected more frequently than glyphosate in water. If authorities aren't screening for the toxic breakdown product, it will not be detected.

Water suppliers variously test for pesticide MAVs using a multi-residue screen. Glyphosate is difficult to detect and is not included in the common multi-residue screen used by water suppliers. It is noteworthy that a separate (and expensive) residue test is required to evaluate presence of glyphosate and its similarly toxic breakdown, or degradation product (metabolite) aminomethylphosphonic acid (AMPA).

[394] Ibid P.182
[395] Ministry for the Environment. 2009. Draft Users' Guide: National Environmental Standard for Sources of Human Drinking Water. Wellington: Ministry for the Environment.
[396] Guidelines for Drinking-water Quality Management for New Zealand 2016 Chapter 10: Chemical Compliance – March 2016. P.396
[397] IARC Monograph Page 7.

In order to correctly gauge exposures, it is critical that water suppliers consider the combined toxicity of the active ingredient in combination with its metabolite. This substantial gap in regulatory oversight warrants consideration and raises further questions.

As such, in addition to assessing the active chemical and its metabolite, it is not evident that Ministry of Health (MoH) has developed transparent protocols to assess combined toxicities of pesticides (e.g. azole or organophosphate groups) that may similarly affect, for example, biological pathways.

Nor is it evident whether the narrow range of laboratories used by drinking water suppliers to carry out multi-residue pesticide testing has the best practice instrumentation and transparently published methodologies, which would stand up to rigorous public scrutiny outside of Australia and New Zealand, and that can detect at the lowest limits possible in the public interest.

Another challenge that remains to be publicly addressed is the methodology by which individual water suppliers located in horticultural and cropping regions with intensive agrichemical use, are tracking and assessing risk from agrichemicals specific to that region, that may or may not be on the existing screening programs used to detect pesticides in water. It is unclear if the WHO or New Zealand has guideline values for many of these region-specific agrichemicals.

Individual responsibility for drinking water health lies with individual water suppliers, yet chemical pollution is borderless.

Before 2004 there was a nationally managed 'Priority 2 Chemical Determinands Identification Programme' (P2) managed by ESR. After this date, the responsibility to identify chemicals that present a risk to public health was transferred to individual water suppliers, typically LTAs.

There appears to be declining national commitment to resourcing for protection of New Zealand drinking water quality. ESR now provides a support role, and any analysis is charged to the water supplier, a disincentive for any in-depth investigation. ESR did produce a 'Priority 2 Determinand Identification Guide' for Ministry of Health in 2012. Like the DWSNZ, this is also out of date.

It may be overly optimistic to consider that each water supplier in New Zealand has the resources to analyse the emerging scientific evidence indicating that GBH might be a probable carcinogen, or to identify threats relevant to their regions. It is natural that these organisations should trust the Ministry of Health to provide the most up-to-date knowledge, assess emerging issues and act proactively to address new environmental challenges. In regards to pesticides, this does not appear to be the case.

6.2.3 Auckland Drinking Water Catchment Contamination – three occasions in three years

Drinking water suppliers are acutely dependent on the health of the surrounding environment. Effective management of drinking water requires that risk from contamination is minimised. However, without indication from regulators that a chemical is considered harmful, environmental (downstream) use of glyphosate will not be restricted by regional industries and councils that immediately benefit economically from its use. Industry does not bear the cost of environmental contamination.

Auckland based Watercare struggled with contamination of glyphosate for the years 2014, 2015 and 2016, as the logging industry surrounding the catchment applied GBH via aerial spraying in close proximity to Auckland drinking water sources. There is no MAV for glyphosate, it is fortunate that Watercare is testing. The testing appears part of the Baseline Hunua Reservoirs Water Quality Monitoring Program.

- May 2014 – Cosseys and Wairoa lakes removed from service. Aerial spraying by forestry operations with glyphosate and metsulfuron. Positive tests recorded from May 15 until July 21. No contaminated water entered the supply network and both lakes were returned to service in September. Watercare met with Auckland Council, who leases the land to the forestry operator, to try and ensure it does not happen again.[398]
- July 2015 – Cosseys Dam Isolated. Samples taken in Cosseys 2 sample location result was 0.0016mg/L (the method detection limit for the test is 0.0010mg/L). [399]
- June 2016 – Wairoa Dam proactively removed from service after advice of aerial forestry herbicide application in the catchment area. 41 days after the east aerial spraying a tributary was detected to contain glyphosate and the dam remained out of service.[400]

Water catchments for New Zealand's largest resident population were contaminated three times in three years yet New Zealand's regulator considers there is no risk from GBH toxicity.

> Watercare has and continues to oppose the use of any herbicide within Auckland's water supply catchments. Watercare has reiterated its opposition to Waytemore Forest's application of herbicides within water supply catchments, to Auckland Council.*[401]*

[398] Watercare Board agenda papers of 22 October 2014.
[399] Watercare Memorandum from A Holliday and M Hubrick 25 September 2015. Cosseys Dam – Glyphosate contamination event investigation and risk assessment.
[400] OIA To Watercare: Cosseys Dam and the Ardmore Water Treatment Plant. December 8 2016.Minutes of the Board.
[401] Wairoa Dam remains out of service. *14 June 2016* https://www.watercare.co.nz/about-watercare/news/Pages/Wairoa-Dam-out-of-service-temporarily.aspx

An internal board Memorandum to Mayor Phil Goff advised Watercare was taking over the long-term lease of Waytemore Forests Ltd 'so that they can ensure no future spraying is done in the water catchment there.'[402] The public has not been advised that spraying is the reason for purchase.[403] Board meeting minutes advise the reason for purchase was 'improving forestry management and effects on the Hunua Dam catchments.'[404]

On 23 January 2017 Watercare acquired the shares in Waytemore Forests Limited (now called Hunua Forests Limited) which is the Grantee of the Forestry Right in the Hunua Ranges. The acquisition price of the shares is subject to a confidentiality clause.

One positive result of this is that the affiliated Watercare Laboratory Services now list New Zealand's lowest level of detection test for glyphosate and its metabolite AMPA. Their Glyphosate & AMPA by Liquid Chromatography-Mass Spectrometry screening detects at a very low method detection limit (MDL) of 0.04 µg/L (0.00004 mg/kg). Their nearest public competitor lists a default detection limit of 1 µg/L (0.001 mg/kg).

6.2.4 Regional Councils – more resourcing to address chemical pollution

LTAs including Regional Councils dependent on the National Survey of Pesticides in Groundwater[405] will find that it does not test glyphosate. As of writing there is indication it may be including in the 2018 survey, but this is yet to be confirmed.

Regional councils are responsible for water quality via an environmental mandate to protect regional ecology and river systems. Failure of the NZ EPA to conduct broad-ranging literature reviews and evaluate emerging science concerning GBH, weakens regional regulation of possible environmental impacts from glyphosate (and other pesticides) near and on surface waters.

Regional researchers may neglect to consider risk to water ecosystems and the potential of the GBH substance to act as an antimicrobial agent

[402] Auckland Council Memorandum from Barry Potter (Director Infrastructure and Environmental Services) to Mayor Phil Goff. November 21, 2016. Subject: Weed management issues from Barry Potter, Director Infrastructure and Environmental Services. Page 4. No.36.
[403] Watercare to regenerate pine forest in Hunua Ranges May 1, 2017. http://www.stuff.co.nz/auckland/local-news/papakura-courier/91858455/watercare-to-regenerate-pine-forest-in-hunua-ranges
[404] Watercare Services Limited Subject: Chief Executive Report – April 2017 Date: 23 May 2017. Page 48 & 60. http://www.watercare.co.nz/SiteCollectionDocuments/AllPDFs/Board_Agenda_30_May_and_minutes_20_April_2017.pdf
[405] National Survey of Pesticides in Groundwater 2014 ESR. B.Humphries and M.Close. https://www.marlborough.govt.nz/repository/libraries/id:1w1mps0ir17q9sgxanf9/hierarchy/Documents/Environment/Groundwater/Groundwater%20Reports%202015%20List/National_Survey_of_Pesticides_in_Groundwater_Report_final.pdf

and inhibit and disrupt aquatic flora and fauna. Data-gaps may lead to lags in risk evaluation of potential causes of ecosystem dysbiosis. Environmental chemicals may accelerate degradation while fostering growth of invasive organisms including blue-green algae. Further downstream effects include contamination of groundwaters and aquifers sourced for drinking water.

The 'National Policy Statement for Freshwater Management 2014'[406] does not provide national guidelines for identification or management of chemical and industrial pollution in New Zealand freshwater that address greater challenges of agricultural and industrial chemical contamination.

Ministry for the Environment document 'Our Fresh Water 2017'[407] which outlines New Zealand fresh water monitoring to 2016 pays little attention to chemical contamination.

6.2.5 Safeguarding environment: Complex systems management to address toxic synergies

There are many challenges requiring significant resourcing increases if scientists are to comprehensively address the interactions of chemicals in the environment specific to New Zealand.

Chemical mixtures (including agricultural, medical, industrial) and their relationships with and in the aquatic environment is complex, rather than complicated. Chemical mixture interactions with human biological systems and aquatic systems and the implications for human and environmental health are also non-linear and difficult to predict.

A machine is complicated and has a predictive outcome based on a series of events. Addressing the future of New Zealand human and environmental health may require a significant and dedicated commitment that incorporates key aspects of complexity science to help anticipate future risk.

NZ EPA and other government agencies have shown little tendency to address this pressing issue, despite emerging science that acknowledges the role of environmental chemicals in human disease. New understanding requires a culture change to urgently shift away from an outdated mechanistic system, (one active ingredient only) viewpoint, to place greater

[406] NATIONAL POLICY STATEMENT for Freshwater Management 2014 issued by notice in gazette on 4 July 2014 http://www.mfe.govt.nz/publications/fresh-water/national-policy-statement-freshwater-management-2014%20

[407] Ministry for the Environment & Stats NZ (2017). New Zealand's Environmental Reporting Series: Our fresh water 2017. http://www.mfe.govt.nz/sites/default/files/media/Environmental%20reporting/our-fresh-water-2017_1.pdf

accord on the complex interrelationships of chemical mixture interactions in our aquatic systems.

The nature of complexity means that a small event could result in a very big change. An adverse event, or systemic shock, could happen very quickly. New Zealand requires dedicated scientists equipped with state of the art computer modelling technology and budgets to screen widely for unanticipated contaminants; understand variability and model synergistic toxicity.

Future costs to extract chemical contaminants from water must also be addressed. For example, it may be very difficult to extract glyphosate from a water source. Without freedom to research and address these complex questions, 'risk' cannot be addressed.

Requirements to meet 'international obligations' requires scrutiny if treaties, protocols and agreements with foreign jurisdictions impair the public sector's power to address these twenty-first century challenges and protect New Zealand environmental and human health.

It is important that international treaties do not quietly side-line consideration of risk:

> *'The public health community should not regard the settlement of trade-health issues as belonging to trade realm, neither should trade-health conflicts be considered as issues for only trade experts.'* [408]

Traditional economic modelling labelled low level pollution an 'externality' and ignored it as a cost of business. Pollution is borderless, can rapidly degrade aquatic systems and threaten groundwater. Scientific understanding recognises low level chemical effects can be neurotoxic to children, contribute to obesity and damage pathways recognised as hallmarks of cancer. These quietly ignored, sub-lethal, chronic 'externalities' are part of a non-linear, complex and interwoven system of chemical contamination that is increasingly depicted in the scientific literature as a profound threat to health and environment.

> ''*Externalities' in twentieth-century theory have turned into defining social and ecological crises in the twenty-first century.*'[409]

Arguably good government requires that the safety of people and the wider environment cannot be allowed to become a victim of a permissive industry-centric doctrine that fails to safeguard their future quality of life from emerging environmental pollutants; are obstructed by treaty provisions and threats from global interests; or frustrated by inadequate financial provision for effective government controls; or suffer because of restricted

[408] Mamudu et al 2011. International trade versus public health during the FCTC negotiations, 1999-2003. *BMJ Tob.Control* doi: 10.1136/tc.2009.035352
[409] Doughnut Economics. Kate Raworth. Random House. 2017 ISBN 9781847941374

political direction of associated resources required to operate effective controls in the public interest.

6.3 'Using the most relevant knowledge available' in risk assessment

A report to the European Parliament comparing the scientific evidence regarding the effects of an organic or conventional diet on human health, remarked on the deficits in current assessment processes:

> *'Nonetheless, there are concerns that this risk assessment is inadequate at addressing mixed exposures, specifically for carcinogenic effects as well as endocrine-disrupting effects and neurotoxicity. Furthermore, there are concerns that test protocols lag behind independent science, studies from independent science are not fully considered and data gaps are accepted too readily.'*[410]

New Zealand observers may note NZ EPA pesticides approvals for new chemicals to market are apparently efficiently processed, normally within 6 months. Even should these new chemicals be rigorously assessed, our NZ EPA lacks resources to thoroughly assess highly profitable off patent and old chemicals. These are rarely addressed, and the wait time for assessment can take years. During this time, the chemical accumulates in the environment and in groundwater. Decisions withdrawing chemicals from commercial use tend to lag behind more progressive agencies, e.g. Europe.

New Zealand is lax in updating legislation and corresponding regulations, resulting in out of date parameters that fail to take into account new scientific knowledge and result in 'evidence based' decisions that rely on an antiquated, linear single chemical approach.

Professor Peter Gluckman acknowledged the increasing complexity of science in the 2011 paper 'Towards better use of evidence in policy formation: a discussion paper':

> Science in its classic linear model can offer direct guidance on many matters, but increasingly the nature of science itself is changing and it has to address issues of growing complexity and uncertainty in an environment where there is a plurality of legitimate social perspectives.
>
> In such situations, the interface between science and policy formation becomes more complex. Further, many decisions must be made in the absence of quality information, and research findings on matters of

[410] European Parliament. Human health implications of organic food and organic agriculture. 2016. PE581.922 http://www.europarl.europa.eu/RegData/etudes/STUD/2016/581922/EPRS_STU(2016)581922_EN.pdf P.29

> complexity can still leave large areas of uncertainty. In spite of this uncertainty, governments still must act.
>
> Many policy decisions can have uncertain downstream effects and on-going evaluation is needed to gauge whether such policies and initiatives should be sustained or revised. But, irrespective of these limitations, policy formed without consideration of the most relevant knowledge available is far less likely to serve the nation well. [411]

Many of the published reviews and papers cited in this response paper express repeatedly, the need for radically improved transparency, accountability and independence in risk assessment policy and practice. A reasonable person may well ask 'has something gone wrong?'

These recently published papers present non-linear models and recommendations to progress chemical risk assessment. The papers reflect established scientific understanding that acknowledges chemical and biological complexity; requires that toxicity assessment should that take into account full formulation; low dose, environmentally relevant levels.

These papers demonstrate that there is a knowledgeable scientific community on hand to aid regulatory adoption of public-interest health-based policies and guidelines. Other papers present considerable evidence that associated 'externalised costs' associated with pesticide use, have potential to result in more harm than benefit. Endocrine disruption and epigenetic alterations, discussed earlier, are merely two spokes in an extremely complex wheel.

Externalised costs may include regulatory costs, human health costs, environmental costs, and defensive measures (expenses by farmers and society to prevent pesticide exposure, such as the purchase of organic food or bottled water consumption). [412]

Wider conversation and input is required from the greater New Zealand public health community. This is essential to encourage and facilitate whether New Zealand legislation has been interpreted properly and fairly by both Ministers of Government and public servants, or has narrow interpretation of (outdated) subordinate legislation prevented decision-makers from acting in the best interest of the public? Or are these circumstances that expose the EPA to judicial review?

Without pressure to evaluate multiple exposures of multiple pesticide-formulation applications and consider lifetime exposures and the biological chain reaction at a molecular level – using the 'most relevant knowledge available' – risk assessment will remain primitive and narrowly defined.

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[411] Prof. Gluckman. Towards better use of evidence in policy formation: a discussion paper. 2011. *PMSCA.* http://www.pmcsa.org.nz/wp-content/uploads/Towards-better-use-of-evidence-in-policy-formation.pdf

[412] D. Bourguet, T. Guillemaud. The hidden and external costs of pesticide use. *Sustainable Agriculture Reviews*, 18, Springer International Publishing, 399 p., 2016, 978-3-319-26776-0. DOI 10.1007/978-3-319-26777-7_2>

It is entirely possible for the NZ EPA to absorb these recommendations and transparently respond to the evolving challenges within risk assessment in a responsive and dynamic public health oriented environment. This would involve a significant culture change, increased budgets and would demand impartiality of science, free from conflicts of interest.

6.4 Where should New Zealand look for best guidance?

Complex, dynamic regulatory environments require considerable resources and as a result, are vulnerable to regulatory capture by outside influences. Vested interest groups (industry) work closely with public servants, commissioned agents and working groups to help smooth the regulatory process for hazardous substances. With this in mind, our risk environment is vulnerable to 'cognitive capture' where the regulator thinks like the regulated industry. Bernstein noted:

> *'The most familiar charge against independent commissions is that they develop an orientation toward the views and interests of their clientele and become ripe for capture."*[413]

A captured agency may be more harmful than no agency at all, as it will carry the authority of government. New Zealand is in a fragile position as its government agencies do not have the resources to address the complexity of human and environmental chemical risk in the twenty-first century, yet the potential for long-term downstream environmental and human harm is significant.

The controversy of glyphosate risk assessment clearly demonstrates that the large regulatory agencies are also vulnerable and perceptions and priorities can become distorted. The environment is dynamic and can be influenced by, among other factors, industry resources and relationships, degree of transparency, resources (or lack thereof) of advocacy groups and changing political, media and societal culture. Caution is paramount, as any risk assessment agency that New Zealand would select as an authority may act within a profoundly different framework a decade from now.

It appears that we must pay constant attention to developing *'all the checks and balances that human ingenuity can devise."*[414] Integral to this is

[413] Independent regulatory agencies: a perspective on their reform M. H. Bernstein. The Government as Regulator. American Academy of Political and Social Science. - 1972, p. 23
[414] James Madison, "The Federalist No. 51: The Structure of the Government Must Furnish the Proper Checks and Balances Between the Different Departments," Independent Journal, Wednesday, February 6, 1788. P.427

transparency; external, meaningfully independent review, and 'adequate regulatory capacity.'[415]

With these challenges in mind, perhaps New Zealand should move to pragmatically adopt decisions made by other regulators (EFSA) and more progressive countries (eg. Swedish KEMI, Danish EPA) that integrate the precautionary principle in decision-making.

Despite the criticisms levelled on the European Commission and EFSA, which include industry capture of guidelines and protocols that weaken higher level legislation, decisions made by the European Commission regularly set the bar in hazard and risk assessment.

Europe moved more quickly to consider endocrine disruption (which is facing similarly industry challenges), set in place protections for local communities[416] and consider challenges posed by new technology eg. nanotechnology and nanotransparency;[417] and established more stringent national and regional policies to address sustained upward pollution trends.

> *'The challenge of food security is to assure that all people have access to enough food to lead productive lives, but a large part of food security is assuring the food is safe from a chemical, physical or biological aspect.'*[418]

Cautions surrounding chemical contamination contributes to consumer demand for organic food. This may be a reflection of many factors including weaker regulatory environments, food scares (eg. Melamine), desire to restrict environmental pollution and perceived nutritional benefit.

Strategically, adoption of transparent, best practice risk assessment for hazardous substances, may help drive premium demand for 'safe' New Zealand product in a food insecure world.

A higher safety bar may also restrict harmful substances in the environment. It may act as a compelling mechanism within the policy toolkit that is required in order to reshape and address the profound degradation, recently reported in the OECD's third Environmental Performance Review of New Zealand.[419]

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[415] Understanding Regulatory Capture: An Academic Perspective from the United States. The Making of Good Financial Regulation. L.G. Baxter *ICRF*. P.35.
'Important factors for ensuring adequate regulatory capacity are that: (i) the missions of the agencies be clearly defined and coordinated; (ii) the regulatory agencies be adequately funded; (iii) regulators be properly incentivized through public funds, not promises of ultimate private reward from those they regulate; (iv) regulators possess or can obtain expertise that understands the businesses they regulate; and (v) regulators be rotated, just like executives in good companies, so that they do not develop too narrow a focus of their responsibilities or too close an affinity with those they regulate.
http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=5262&context=faculty_scholarship

[416] European Food Safety Authority. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA J 2014; 12: 3874–3874.

[417] European Commission Key Enabling technologies.
http://ec.europa.eu/research/industrial_technologies/policy_en.html

[418] Hanning, I. B., O'Bryan, C. A., Crandall, P. G. & Ricke, S. C. (2012) Food Safety and Food Security. *Nature Education Knowledge* 3(10):9

[419] OECD (2017), *OECD Environmental Performance Reviews: New Zealand 2017*, OECD Publishing, Paris. http://dx.doi.org/10.1787/9789264268203-en

7.0 ‘Has something gone wrong?’

Relevant principles of administrative law that are supposed to guide regulatory decision-making.

The evidence suggests that the NZ EPA Review does not give effect to the purpose of the HSNO Act, which is:

> *‘..to protect the environment, and the health and safety of people and communities, by preventing or managing the adverse effects of hazardous substances and new organisms.’* [420]

The NZ EPA Review may have little lawful utility for New Zealand policy formulation, or public guidance.

> *‘Decision makers abuse their powers when they exercise their power in a way that ‘which cannot rationally be regarded as coming within the statutory purpose.’* [421]

The issues raised in this document highlight deficiencies which appear to obstruct or compromise Parliament's legislative purpose. The considerations presented may extend beyond mere error, i.e. having *‘minor or technical effect’* – rather – the problems identified within the NZ EPA Review and resultant risk assessment suggests a significant error in which *‘the decision-making has gone wrong.’* [422]

Has New Zealand legislation been interpreted properly and fairly by both Ministers of the Crown and public servants, in this case the NZ EPA? If this is not the case, the EPA may find itself exposed to judicial review.

> *'Judicial review ensures that public authorities act within the law by defining the principles of law that govern administration, and by safeguarding individual interests against illegal or unreasonable administrative action, or administrative action taken without following proper procedures.'* [423]

Grounds of challenge can be divided into (a) illegality; (b) unfairness and (b) unreasonableness. There are subcategories within these grounds. Decisions may be challenged on a number of grounds, and grounds may overlap.

Special acknowledgement: the principles highlighted draw almost exclusively for their foundation and authority upon a text (especially its chapter entitled 'Illegality') contained within a book authored by Philip A

[420] Hazardous Substances and New Organisms Act 1996. http://www.legislation.govt.nz/act/public/1996/0030/latest/whole.html
[421] *Constitutional and Administrative Law in New Zealand, 4th Ed., P.A Joseph* 23.1 P.939
[422] Ibid P.869
[423] March 2005. The Judge over your shoulder. A guide to judicial review of administrative decisions. Crown Law Office. ISBN 0-478-04451-8.

Joseph, “Constitutional and Administrative Law in New Zealand, 3rd and 4th Editions, Brookers Thomson.

7.1 Statutory discretionary powers

7.1.1 *‘Statutory powers are never ‘at large’ but are circumscribed by the statutory purpose(s).’*[424]

7.1.2 Other facets of compliance with administrative law principles may also apply: for example the exercise of an administrator's statutory discretion must always be 'reasonable' and must take into account all relevant considerations.

7.1.3 Policy-making is a form of regulation: however, a policy may be judged illegal and of no effect if it directs statutory discretion in a manner that constrains the scope of decision-making regardless of (for example) 'particular circumstances'; regardless of reasonableness; regardless of all relevant considerations; regardless of the public interest; or counter to Parliament's purpose.

7.1.4 A deficient approach to policy formulation may leave the agency exposed to regulatory or judicial review on the grounds of illegality. Illegality encompasses three situations:-

> *(1) Abusing a discretionary power under the Wednesbury principle (for example, exercising a power for an improper purpose)*
>
> *(2) Abdicating a discretionary power (for example, adopting a rigid rule or policy); and*
>
> *(3) Committing a reviewable error in making findings of law or fact.’* [425]

7.2 Policy rules and guidelines – a form of discretionary power

7.2.1 Policy is a form of regulation and requires all of the rigour that is required to apply to proposed exercise of regulatory powers.[426]

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[424] *Constitutional and Administrative Law in New Zealand, 4th* Ed., P.A Joseph, 23.2.2P.942
[425] Ibid, 23.1 P.939
[426] *Constitutional and Administrative Law in New Zealand,* 3rd Ed., Philip A Joseph, Thomson Brookers, 2007

Policy rules can be successfully challenged if they contravene the statutory purpose of the act under which they operate.

7.2.2 Policy rules which may include protocols or guidelines, may be invalid if, in their making:

> *'the decision-maker fails to take into account relevant considerations, or is influenced by conditions that are legally irrelevant. It is only when a decision maker fails to have regard to a mandatory consideration that the decision-maker makes a reviewable error of law.'*[427]

7.2.3 The public may question as to whether a regulator insisting on external protocols and guidelines for risk assessment may represent an unlawful abdication of discretionary power.

> *'An authority may unlawfully abdicate its statutory function by refusing or failing to act. A public body must not renounce its decision-making responsibility, nor preclude itself from inquiring into matters relevant to its inquiry.'* [428]
>
> *'An authority must not (1) adopt a fixed rule of policy;'*[429]
>
> *'Abdication of discretion under fixed rules of policy is a common ground of administrative law challenge….. Every case should be decided on its merits, even where decision-makers have adopted guidelines or policies to facilitate decision-making… If a policy is so phrased to admit of no exceptions, it is unlawful.'* [430]

7.2.4 Where regulators sit on their hands and refuse to act, courts may consider that there is unlawful abdication of power whether or not the authority's inaction was deliberate.

7.2.5 Policy rules that are inconsistent with a greater statutory purpose may leave decision makers open to a challenge of abuse of discretionary power on any of three grounds: pursuing improper statutory purpose, breach of legitimate expectation, and unlawfully fettering the exercise of discretion.

> *'Policy rules must not impede the exercise of a decision-maker's statutory functions: "Statements of policy could not… be elevated to the character of conditions which restricted the decision makers' statutory duty. A policy rule that fails to promote the statutory purposes will invite challenge in the courts. A rule which fails those*

[427] *Constitutional and Administrative Law in New Zealand, 4th* Ed., P.A Joseph, 23.2.3 P.948
[428] Ibid P.972
[429] Ibid P.964
[430] Ibid P.965-5

purposes or which impedes the exercise of the decision-maker's statutory functions, will not give rise to a legitimate expectation.' [431]

'Decision makers must 'genuinely weigh matters that ought to be taken into account.' [432]

Professor Joseph notes that: *'the listed criteria need not be exhaustive.'* [433]

'The more comprehensive and detailed the criteria, the more likely they will be construed as exhaustive. If listed criteria are open-ended a court may hold that the criteria are not exhaustive and concede the decision-maker greater latitude." [434]

Comprehensive, detailed, linear and inflexible policy rules may restrict informed best practice evaluation of risk of carcinogenesis and limit 'evidence' (consideration) of the complexity of human biological systems.

Agencies may attract scrutiny by the courts. In light of current scientific knowledge, failure to address new complexities (cancer hallmarks, full formulation toxicity) may impair public trust in government regulatory agencies' ability to *protect the health and safety of people and communities*.

7.3 Relevant considerations

'The criterion 'the public interest' is a yardstick of indeterminate length." [435]

Public authorities have a duty to take into account relevant considerations.

That principle is of particular importance when an administrator is formulating public policy.

Established legislation and policy affecting probable issues of public and environmental safety – entrenched rules for risk assessment for a chemical or formulation to ensure best protection of public health under the HSNO Act - is vulnerable to examination by the courts:

'the exercise of a discretionary power, even for a proper purpose, may be invalid if the decision-maker fails to take into account relevant considerations, or is influenced by considerations that are legally irrelevant.' [436]

[431] Ibid 23.2.5 P.959
[432] Ibid. 23.2.3 (1) and (4) P.949 Mandatory relevant consideration
[433] Ibid 23.2.3(2) P.950
[434] Ibid. 23.2.3(2) P.950
[435] Ibid. 23.2.3 (4) P.950
[436] Ibid 23.2.3(1) P.948

7.3.1 The following illustrative points may be considered by decision-makers to be mandatory relevant considerations in relation to glyphosate-based herbicides and carcinogenicity:-

7.3.2 Obligation to consider full formulation of toxicity in relation to public health.

7.3.3 Effects of environmentally relevant (low dose) and chronic (long term) exposure.

7.3.4 Established science recognising the role of the endocrine system in cancer development and complexity of dose-response and non-linear endocrine effects.

7.3.5 Harmful effects of chronic, long-term neonatal and childhood exposures.

7.3.6 A requirement to adopt the precautionary principle where there may be a reasonable probability of reasonable doubt about public and environmental safety outcomes.

7.3.7 Environmental and health risk from residue build-up in ground and drinking water.

7.3.8 Obligation to consider comorbidity (accompanying disease or disorders).

7.4 Science 'certainty'; scientific 'probability' plus 'relevant considerations' and 'reasonableness'

7.4.1 Scientific proof is usually considered conclusive when the probability that x = y is equal to or better than 95 per cent – especially when interdependent repetition confirms results.

7.4.2 However, public policy formulation requires that where science findings indicate that there is a 'reasonable probability' (i.e. a chance equal to or greater than 50 per cent probability that x = y) then matters where such a probability targets potentially material adverse outcomes for public and environmental safety (for example), reasonableness may require public policy statutory decision-makers to invoke the precautionary principle in order to protect the public interest and to retain the public's confidence in government.

7.4.3 However, 'science' is increasingly not nearly as clear-cut as that. There are many 'unknowns' and other complexities that confound simple x = y findings.

7.4.4 For example, this paper points out a potential for a chemical formulation to produce adverse outcomes for people and the environment

by perhaps first-order or second-order steps (e.g. a chronic exposure to a chemical formulation producing chronic inflammation that is a known precursor for the development of cancers.

7.5 Precautionary Principle

New Zealand HSNO legislation recognises the precautionary principle (Section 7). Given the authority of IARC, and that IARC considers glyphosate and glyphosate based herbicides to be a probable carcinogen,that should result in an automatic application of HSNO from a public health perspective.

NZ EPA in regulation of hazardous substances, appears to place more weight on JMPR risk assessment than on European Commission decisions. Europe interprets the precautionary principle more strictly. JMPR risk assessments have no obligation to consider the precautionary principle. Many hazardous substances unauthorised for use in Europe are in use in New Zealand.[437]

7.5.1 UNESCO defines the precautionary principle as follows:

'When human activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish that harm. Morally unacceptable harm refers to harm to humans or the environment that is

- *threatening to human life or health, or*
- *serious and effectively irreversible, or*
- *inequitable to present or future generations, or*
- *imposed without adequate consideration of the human rights of those affected.*

The judgement of plausibility should be grounded in scientific analysis. Analysis should be ongoing so that chosen actions are subject to review. Uncertainty may apply to, but need not be limited to, causality or the bounds of the possible harm. Actions are interventions that are undertaken before harm occurs that seek to avoid or diminish the harm. Actions should be chosen that are proportional to the seriousness of the potential harm, with consideration of their positive and negative consequences, and with an assessment of the moral implications of both action and inaction. The choice of action should be the result of a participatory process.

[437] For example chloropicrin and 1,3 dichloropropene are unauthorised for use in Europe but used as fumigants in New Zealand.

7.5.2 Section seven of the HSNO Act stipulates a precautionary approach:

> *'All persons exercising functions, powers, and duties under this Act … shall take into account the need for caution in managing adverse effects where there is scientific and technical uncertainty about those effects.'* [438]

7.5.3 NZ Treasury considers that while there is no direct 'preference to precaution' in the Resource Management Act 1991, it is implicit in the way the Act is implemented.[439]

> *'Risk assessment tries to determine how much harm we will tolerate. Precaution asks how much harm we can avoid.'* [440]

7.5.4 The public policy formulation level of probability that invokes the precautionary principle for policy-making is based on 'reasonable probability' of harm – i.e. greater than 50%.

7.5.5 European regulators and to a lesser extent, US regulators reflect the precautionary principle in decision-making, particularly when it comes to food safety.[441]

7.5.6 There is no consideration of the precautionary principle relating to risk assessment of chemicals in food in WHO-FAO JMPR toxicological assessment.[442] However New Zealand tends to predominantly follow WHO-FAO JMPR decisions in pesticide risk assessment.

7.6 Bias or predetermination

> *'The test for apparent bias reflects the standards of the fair-minded lay observer: would the lay observer, having been fully informed of the facts, reasonably suspect that the decision maker may have been biased?'* [443]

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[438] Hazardous Substances and New Organisms Act 1996
http://www.legislation.govt.nz/act/public/1996/0030/latest/whole.html#whole

[439] Environmental Risk Management in New Zealand – Is There Scope to Apply A More Generic Framework?
Linda Cameron. New Zealand Treasury Policy Perspectives Paper 06/06. July 2006.
http://www.treasury.govt.nz/publications/research-policy/ppp/2006/06-06/tpp06-06.pdf

[440] Pesticide Action Handbook: A Guide for Central and Eastern European NGOs ...and others. 2003. Pesticide Action Network Germany. http://www.pan-germany.org/download/pan_action_handbook.pdf

[441] The Legacy of the Precautionary Principle in US Law: The Rise of Cost-Benefit Analysis and Risk Assessment as Undermining Factors in Health, Safety and Environmental Protection Nicholas A. Ashford. 2006. http://ashford.mit.edu/sites/default/files/documents/C28.%20LegacyOfPrecaution_19.pdf

[442] World Health Organisation. Food Safety. Project to update the principles and methods for the assessment of chemicals in food. EHC 240. ISBN 978 92 4 157240 8 (WHO, 2009).
http://www.inchem.org/documents/ehc/ehc/ehc240_front.pdf

[443] *Constitutional and Administrative Law in New Zealand,* P.A. Joseph 4th Ed. 2014 25.5.1 P.1076

7.6.1 *'No one may judge his or her own cause.'* Persons administering statutory obligations do so in circumstances in which the public is obliged to trust the administrator: *'impartiality is demanded in decision-making for doing justice between parties and maintaining public confidence in the administration of justice.'* [444]

7.6.2 Evidence based science relating to public policy and health requires that reasoning has an obligation to take into account conflicts of interest and potential for bias.[445]

7.6.3 Impartiality, ensures the best information is based on relevant information and not prejudiced, nor exercising preference towards one of the parties.

7.6.4 The *possibility* (not probability) of bias must be real rather than remote.

7.6.5 Predetermination is concerned with 'closed mind' decision-making, while bias is concerned with public perception as to impartial decision-making.[446]

7.6.6 Predisposition must be founded on general policy, not an individual case.[447]

Professor Joseph notes

> *'The courts are most inclined to intervene where challenges are to determinations of essentially 'legal' questions. Decisions will also be set aside as unreasonable when misinformation or misrepresentation leads to a gap in the chain of reasoning.'* [448]

8.0 Conclusion and recommendations

The NZ EPA Review is arguably and inappropriately narrowly-focussed, deficient and irrelevant.

It addresses singular glyphosate chemistry and not glyphosate-based formulations that are used in 'the real world' and that are obviously of the essence.

[444] Ibid. 25.5.1 P.1076
[445] Prof. Gluckman. Towards better use of evidence in policy formation: a discussion paper. 2011
[446] *Constitutional and Administrative Law in New Zealand, 4th* Ed., P.A Joseph. 25.5.5 P.1089
[447] Ibid. 25.5.5 P.1089
[448] Ibid.

The NZ EPA Review unreasonably makes every effort to discredit a finding by the NZ EPA's own authority on cancer, the IARC. The IARC Working Group reviewed studies - including glyphosate-based formulations that are used in the 'real world' – and therefore are arguably of the essence. An ordinary and reasonable person may be concerned the NZ EPA took that course of action.

Furthermore, the NZ EPA Review appears to give exclusive consideration and weight to industry-paid and industry-supported studies and reviews as well as arguably out-dated and industry-developed guidelines. Such a focus appears to be industry-centric to the exclusion of 'probable' and material public and environmental public safety threats.

Rather than taking the opportunity to consider the wealth of studies and cumulative cancer findings, and of deciding cautiously in the publics' interest, the NZ EPA Review appears to have elected to regard studies narrowly and separately – frequently basing resultant findings on industry data.

Where there are weaknesses in studies or lack of definite findings, or where they do not conform to (problematic) guidelines, they are frequently discarded by the NZ EPA Review.

Strangely, the NZ EPA's own manual 'Thresholds and Classifications under the HSNO Act 1996' lists the IARC as one of the two respected sources for information on carcinogenicity.

The NZ EPA Review fails to address twenty-first century scientific understanding of the factors that pre-dispose to risks of cancer development – ignoring new data from toxicology and cancer biology.

> The epidemiological, molecular biology, and toxicological evidence emerging from recent literature assessing the link between specific pesticides and several cancers including prostate cancer, non-Hodgkin lymphoma, leukemia, multiple myeloma, and breast cancer are integrated. …. the literature does strongly suggest that the public health problem is real.[449]

The IARC Working Group consisted of 17 international expert scientists. By contrast, the NZ EPA Review was produced by one retired scientist, with the help of a former colleague, and was apparently peer-reviewed by unidentified toxicologists within the MPI and EPA.

The title of the recent NZ EPA published review *'Review of the Evidence Relating to Glyphosate and Carcinogenicity'*, appears to infer that it is a carcinogenicity review, and in its introduction - perhaps misleadingly - claims that the report will discuss 'relevant data' on glyphosate, 'especially

[449] Alavanja, M. C. R., Ross, M. K. and Bonner, M. R. (2013), Increased cancer burden among pesticide applicators and others due to pesticide exposure. CA: A Cancer Journal for Clinicians, 63: 120–142. doi:10.3322/caac.21170

the more recent studies'. (Note that the paper does not claim to address glyphosate-based formulations.)

The NZ EPA Review was released 15 months after the IARC Monograph. So it seems reasonable to expect that the compass of the NZ EPA Review would have included studies published since the IARC review that focussed on more recent findings concerning relevant toxicity of glyphosate-based herbicides; but the NZ EPA Review does not include assessments of such studies. Rather, the NZ EPA may be at risk of cherry picking studies to suit an apparent predetermination.

The NZ EPA Review does not reflect the transparent nature and integrity of the IARC Monograph that covered -

> *'…*reports that have been published or accepted for publication in the openly available scientific literature' and 'data from governmental reports that are publicly available' to reach its conclusion of 'probable carcinogen.*'*

The NZ EPA Review appears to place priority on older papers that are unavailable for peer review (and replication), on industry produced papers and reviews that contained unpublished data that again, are exempt from peer review (for example the recent EFSA review) and then purports to arrive at a 'weight of evidence' conclusion that is arguably arrived at through inappropriate exclusion of other relevant study findings.

The ability of the chemical industry to select studies for review by regulators, rather than compulsorily require disclosure of all studies, further impairs the integrity of risk assessment.

The narrow (and therefore arguably irrelevant) scope of the August 2016 NZ EPA commissioned review cannot reasonably be given any weight in NZ government policy-making and policy review, for the sum of the reasons set out in this assessment within this paper.

> Decision-makers must not disable themselves from considering information relevant to their statutory function…they must weigh mandatory considerations on a 'fine grained basis', 'openly and transparently', or risk a finding of 'no weight*...*[450]

An investigation must ask why the EPA ignored its own recognised authority on cancer (the IARC) and instead revert to a paper produced with such limited resources?

If regulators are going to responsibly permit chemicals into food at the meteoric rate applications and approvals are currently sanctioned – the long-term effects and synergies of the chemical exposures must be addressed using transparent 21st century science.

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[450] *Constitutional and Administrative Law in New Zealand, 4th* Ed., P.A Joseph. 23.2.3 P.954

Risk assessment fails if scientists do not have the freedom to consider emergent properties of risk in a modern context. As stated in the summary, the authoritative text on public law in New Zealand, 'Constitutional and Administrative Law advises:

> The exercise of a discretionary power, even for a proper purpose, may be invalid if the decision-maker fails to take into account relevant considerations, or is influenced by considerations that are legally irrelevant. [451]

However, it is also common sense and plain, good science. New Zealand Prime Minister's Chief Science Adviser, Professor Sir Peter Gluckman maintains that policy development (which also includes development of rules and guidelines, or standards) should reflect 'the most relevant knowledge available':

> Many policy decisions can have uncertain downstream effects and on-going evaluation is needed to gauge whether such policies and initiatives should be sustained or revised. But, irrespective of these limitations, policy formed without consideration of the most relevant knowledge available is far less likely to serve the nation well. [452]

Yet our regulatory authorities ignore their own authority on cancer, the IARC; they place significant weight on industry produced unpublished studies, raising questions of transparency and bias; they are fully aware of the greater toxicity (efficacy) of full formulations yet do not assess them for toxicity; and (frequently toxic) adjuvants are specifically excluded from registration in New Zealand legislation.[453]

The NZ EPA Review may appear to have based their decision-making on outdated guidelines and protocols. This narrowly defined, by all appearances, dogmatic attitude to policy raises questions of illegality and breach of public trust.

A reasonable person may query, 'have EPA operations acted consistently with the purpose and intent of the principal HSNO Act?'

Has New Zealand legislation been interpreted properly and fairly by both Ministers of Government and public servants, or has a reductively narrow interpretation of (outdated) subordinate legislation prevented decision-makers from acting in the best interest of the public? Are these circumstances that might expose the EPA to judicial review?

These issues indicate a protectionist regulatory culture that may be argued, is unable to place complex public health needs first when it produces a critique of its own cancer authority, and then privately peer reviews its own

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[451] Ibid. P.948
[452] Prof. Gluckman. Towards better use of evidence in policy formation: a discussion paper. 2011
[453] Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. Schedule 2. Part C. Exemptions for agricultural compounds used to manage plants or plant production (28)
http://www.legislation.govt.nz/regulation/public/2011/0327/latest/DLM3982848.html

paper, rather than exposing the review to the scrutiny of external specialists in carcinogenicity.

After all, *'No one may judge his or her own cause.'*[454]

8.1 Downstream considerations – no monitoring, unknown exposure, unintended consequences

In New Zealand, GBHs are sprayed on food, in drains and in public areas. Glyphosate has been detected in groundwater in Europe, Canada and the USA. New Zealand does not test for glyphosate in groundwater. Glyphosate can accumulate and contaminate drinking water via rainwater, surface runoff and leaching into groundwater. As discussed, glyphosate has contaminated major water sources for Auckland, three years running.

Reason suggests that the potential for both direct and indirect exposures to people; microflora; and components of food-chains is significant.

Scrutiny of downstream effects which may magnify the threat to population health should form a component of risk assessment and may be outsourced from other agencies or jurisdictions independent of the regulator. The following permissible relevant considerations may include but are not limited to:

- Increased glyphosate exposures permitted in food and environment for the New Zealand public may contribute to increasing cancer and illness rates via multiple (perhaps including second and third-order inflammatory) pathways.
- New Zealand monitoring of glyphosate and the metabolite AMPA residues in food; animal feed and groundwater is negligible - i.e. there are no effective controls on the application of glyphosate-based formulations that provide any assurance about levels of threat to people and the environment.
- Failure to consider synergistic and cumulative effects of other ingredients in pesticides formulations – in combination with other treatments applied to the same crop. Many crops have several different pesticide formulation treatments.
- Failure to assess risk of contribution of agrichemical treatments (on food, feed, drinking water) to rise of antimicrobial resistance (AMR) in human and animal populations.
- Failure to consider the unique sensitivities of the pregnant female, and prenatal, childhood and adolescent risk during vulnerable developmental windows, and to assess the implications of early exposures as a developmental basis of adult onset disease.

[454] *Constitutional and Administrative Law in New Zealand,* P.A. Joseph 4th Ed. 2014 25.5.1 P.1076

- Obligation to assess full formulation exposure and incorporate new knowledge of risk of harm to intergenerational population health caused by endocrine disruption and other pathways which may negatively impact transgenerational epigenetic inheritance.

8.2 Recommendations

In the interests of public health this paper recommends that the New Zealand government respect the IARC conclusion as a leading authority and adopt the IARC determination that the:

a) Active ingredient glyphosate is '*probably carcinogenic to humans*' (Group 2A); and that

b) *'There is strong evidence that exposure to glyphosate or glyphosate-based formulations is genotoxic,'* and *'There is strong evidence that glyphosate, glyphosate-based formulations, and aminomethylphosphonic acid can act to induce oxidative stress.'*

Suggested new HSNO, ACVM, Regional and Local Council Restrictions (Controls) for GBH:

(1) No applications on human food crops;

(2) No applications on animal feed or pasture destined for consumption by animals;

(3) No applications near or on surface waters (standard EPA distance for safety);

(4) No applications on or near drains (including roadside drainage applications);

(5) Withdrawn from commercial sales - unavailable retail sales (this is one of the first steps taken when agrochemicals are recognised as an unacceptable risk to the public);

(6) Application only by trained and certified commercial operators;

(7) Agricultural use limited to only one application per year (may address resistance);

(8) No applications in areas accessed by the public (including parks, playgrounds, roadsides, golf courses, frequented areas under DOC).

(9) No agricultural use within 400m distance of sensitive areas (including roadsides, schools, playcentres, residential houses).

(10) Establish a MAV (maximum acceptable value) for glyphosate in drinking water of 0.10 µg/l (.01 ppb or 0.0001 mg/L)– as per European Commission Council Directive for pesticides 98/83/EC [455]

(11) Transition to GBH free food products within two years.

Further Recommendations:

It is recommended that the NZ EPA Review dated August 16, 2016 is unfit to play any part in New Zealand government policy review or policy formulation on matters affecting public and environmental safety.

It is recommended that the IARC retains status as the authority on cancer. It is recommended that future New Zealand risk assessment evaluations prioritise published and peer reviewed (transparently available) data and base risk assessment on toxicity of pesticide formulations.

It is recommended that, as a condition of assessment, applicants requesting registration of new products or reassessment of existing products marketed in New Zealand, must supply published toxicological studies that research the toxicity of the full pesticide formulation.

It is recommended that regulators, (not industry), conduct the literature review.

It is recommended that, in the public interest, risk assessment of Hazardous Substance in New Zealand refocuses and aligns with best practice overseas jurisdictions which incorporate the precautionary principle in decision-making. EFSA has extremely good legislation in place, but this can be obfuscated by politically influenced policies and guidelines, as discussed.

Some European countries (e.g. Swedish KEMI, Danish EPA, Austria) may also be considered as best practice regarding chemical and food safety. It is not recommended that we retain reliance on WHO-FAO JMPR decisions which have no obligation to reflect the precautionary principle.

It is recommended that the present exemption from registration of adjuvants is withdrawn from New Zealand legislation.

It is recommended that MPI includes glyphosate as an Agricultural Compound listed for residues screening of food samples in the Total Diet Study (NZTDS).

It is recommended that New Zealand screens for glyphosate and its metabolite AMPA in the National Groundwater Survey; and that it is mandatory for drinking water suppliers when conducting multi-residue

[455] Council Directive 98/83/EC http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF

pesticide screening to also test for pesticide breakdown products (metabolites).

The MoH, operating under the Health Act 1956 has an obligation to *'protect the health and safety of people and communities by promoting adequate supplies of safe and wholesome drinking water from all drinking-water supplies.'*

In light of omissions considered earlier in this document[456] (including failure to include metabolites for compulsory screening and outdated drinking water standards) and the challenges posed by agrichemical runoff as a diffuse pollution source; serious scrutiny of MoH capacity to provide national leadership and resourcing to address complex future challenges relating to chemical contamination and water security may be warranted.

In order to pursue effective compliance with relevant statutory duties and related safety of pesticides in New Zealand, an inquiry, independent and external to the agencies involved, is recommended.

The inquiry initially by the Ombudsman would include consideration of the relationships between industry, MPI and the EPA, and either investigate the ability for the agencies to meet the purposes of HSNO, or recommend how a full and independent inquiry might investigate the functioning of the EPA and MPI, and those agencies' ability to function independently and protect the health of the community.

Such an investigation could have terms of reference incorporating risk assessment of the full formulations of chemicals the population and environment is exposed to and ensure a broader interdisciplinary 'complex systems' approach that must encompass long term (chronic) environmentally relevant exposure to the multiple chemicals permitted in food and environment – and address risk arising from synergies between the chemicals and their metabolites.

The inquiry would critically *assess* New Zealand regulatory authorities demonstrated unwillingness to undertake integrated, precautionary 'big picture' risk assessment that takes into consideration the consistency or patterns of harm evident in cancer studies, (also, but not limited to, neurotoxicity, reproductive and hormonal health, acute and chronic studies), and where patterns supportive of potential risk emerge in epidemiological and mechanistic data (including low level endocrinologic and epigenetic mechanisms that may influence cancer and chronic disease development).

There will be relevant instances where study design may not be perfect (though published, transparent and subject to peer review) but will demonstrate evidence of risk of adverse harm consistent with other data.

[456] 6.2.2 Local Authorities – Water Monitoring

The 2008-2009 President's Cancer Panel recommended:

> A precautionary prevention-oriented approach should replace current reactionary approaches to environmental contaminants in which human harm must be proven before action is taken to reduce or eliminate exposure.[457]

It is recommended that this review include cross-disciplinary independent expertise briefed to understand the rigor and transparency required for public policy formulation concerning issues of environmental and public safety and considers hidden externalities – downstream consequences that present costs to both the taxpayer and the environment, yet to be addressed in New Zealand. This may include comorbidity, the costs of endocrine disruption, and impact on future water quality.

The Endocrine Society recommended a research approach that could well serve to review current approaches to risk assessment:

> *'The team science approach, including teams of basic, translational, and clinical scientists, epidemiologists, health care providers, and public health professionals, needs to be a priority for future research and funding.'*[458]

It is recommended that experts external to the MPI and EPA address the cultural and institutional change which may be necessary to disengage a pro-chemical industry regulatory environment that, it may be argued, demonstrably fails to address the purposes of the APVM and HSNO Acts, and place complex public health needs first.

There is an inherent obligation that responsible government dedicate significant resourcing to evaluate human and environmental risk in terms of chronic systemic chemical contamination from multiple diffuse sources, and the future likelihood that these risks may present as non-linear and complex systemic future shocks – profoundly impacting the quality of life of the New Zealand public and environment.

Public interest health-based concerns should not be outweighed by trade-based considerations, nor mired in outdated convention.

To quote Rear Admiral Grace Hopper:

> *"The most dangerous phrase in the language is – we've always done it this way."*

[457] Presidents Cancer Panel: Reducing Environmental Cancer Risk: What we can do now. 2008-2009 https://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP_Report_08-09_508.pdf
[458] Gore AC et al 2015. Endocrine Society's Second Scientific Statement. DOI:10.1210/er.2015-1093

9.0 NZ EPA References Commercially Influenced Studies

References listed throughout the NZ EPA Review do not declare who paid for and produced the studies used to arrive at a weight of evidence finding. Regulatory agency (US EPA, EFSA, BfR, WHO-FAO JMPR, NZ EPA) studies rely predominantly on industry selected information, particularly to arrive at critical end-points. These are used to derive the acceptable daily intake (ADI) for New Zealanders, for glyphosate, and directly relate to permitted use and application rates on agricultural crops. Regulators may leave themselves exposed to accusations of conflict of interest.

NB. The studies below in bold are either authored by pesticide industry paid consultants or employees, or have based their findings on unpublished studies supplied and selected by the pesticides industry. As discussed in this paper, the weight of evidence finding by the NZ EPA relied predominantly on determinations by other regulatory agencies, or reviews by industry (eg. Greim) that dismiss or minimise occurrence of cancer.

- Alavanja MC, Samanic C, Dosemeci M, et al. Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. American Journal of Epidemiology 157: 800–814.

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five Columbian regions: association to occupational exposure to glyphosate. *J Toxicol Environ Health* A, 72(15–16):986–97.

- Brown LM, Blair A, Gibson R, et al (1990). Pesticide exposures and other agricultural risk factors for leukemia among men in Iowa and Minnesota. *Cancer Res* 50: 6585–91.

- Brown LM, Burmeister LF, Everett G, et al (1993). Pesticide exposures and multiple myeloma in Iowa men. Cancer Causes Control 4: 153–6.

- Cantor KP, Blair A, Everett G, et al (1992). Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Iowa and Minnesota. *Cancer Res* 52: 2447–55. University of Nebraska-Lincoln

- Dennis LK, Lynch CF, Sandler DP, et al (2010). Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural health study. *Environ Health Perspect* 118: 812–7.

- De Roos AJ, Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, Burmeister LF et al, (2003). Integrative assessment of multiple pesticides as risk factors for non-Hodgkins lymphoma among men. *Occup Environ Med,* 60(9):E11.

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- Pesticide use and breast cancer risk among farmers' wives in the agricultural health study. Am J Epidemiol 161: 121–35.

- Erikkson M, Hardell L, Carlberg M, Akerman M (2008). Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. Int J Cancer, 123(7):1657–63.

- **European Food Safety Authority. EFSA explains the carcinogenicity assessment of glyphosate. 12 November 2015. www.efsa.europa.eu. 18 EFSA (European Food Safety Authority), 2015. Peer review of the pesticide risk assessment of the active substance glyphosate. EFSA Journal 2015;13(11):4302, 107 pp. doi:10.2903/j.efsa.2015.4302.**

- Flower KB, Hoppin JA, Lynch CF, et al. Cancer risk and parental pesticide application in children of Agricultural Health Study participants. Environ Health Perspect 2004; 112: 631–5.

- **Greim H, Saltmiras D, Mostert V, Strupp C (2015). Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/carcinogenicity rodent studies. Crit Rev Toxicol, 45(3):185–208. Hoar SK, Blair A, Holmes FF, et al. Agricultural herbicide use and risk of lymphoma and soft tissue sarcoma. JAMA 1986; 256: 1141–7. Glyphosate Task Force**

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- McDuffie, HH, Pahwa, P, McLaughlin, JR, Spinelli, JJ, Fincham, S, Dosman, JA, Robson, D, Skinnider, LF & Choi, NW (2001) Non-Hodgkin's lymphoma and specific pesticide exposure in men: Cross-Canada study of pesticides and health. Cancer Epidemiol. Biomark. Prev., 10, 1155–1163.

- **Mink PJ, Mandel JS, Sceurman BK, Lundin JI. (2012). Epidemiologic studies of glyphosate and cancer: a review. Regul Toxicol Pharmacol, 63,440–52. Morgan GJ, Davies FE, Linet M. Myeloma aetiology and epidemiology. Biomedicine and Pharmacotherapy 2002; 56(5): 223–34. Supported by the Monsanto Company, St. Louis, Missouri**

- L Niemann, C Sieke, R Pfeil and R Solecki (2015). A critical review of glyphosate findings in human urine samples and comparison with

the exposure of operators and consumers. Verbr. Lebensm. (2015) 10: 3. doi:10.1007/s00003-014-0927-3

- Schinasi L, Leon ME. 2014. Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and metaanalysis. Int J Environ Res Public Health 2014 Apr 23;11(4):4449-527. doi: 10.3390/ijerph110404449.

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- **Williams GM, Kroes R, Munro IC (2000). Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Reg Toxicol Pharmacol 31: 117–65.**

- Zahm SH, Weisenburger DD, Babbitt PA, et al. A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. Epidemiology 1990; 1: 349–56.

10.0 APPENDICES

APPENDIX I(a) Published literature demonstrating greater toxicity of full formulation

Evidence is accumulating in published literature of the increased toxicities exerted by full formulations of pesticides, and the role adjuvants play, in comparison to the active ingredient, that is traditionally the only ingredient assessed in a pesticide formulation.

The following studies represent a sample of available research regarding toxicity of full formulation glyphosate based herbicides. For example, Mesnage et al 2014 noted the following in this study:

Mesnage R., Defarge N., Vendomois, J. S., Seralini G-E. (2014) Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. BioMed Research International. Vol 2014, Article ID 179691.

> *"We tested the toxicity of 9 pesticides, comparing active principles and their formulations, on three human cell lines (HepG2, HEK293, and JEG3). Glyphosate, isoproturon, fluroxypyr, pirimicarb, imidacloprid, acetamiprid, tebuconazole, epoxiconazole, and prochloraz constitute, respectively, the active principles of 3 major herbicides, 3 insecticides, and 3 fungicides..... Despite its relatively benign reputation, Roundup was among the most toxic herbicides and insecticides tested. Most importantly, 8 formulations out of 9 were up to one thousand times more toxic than their active principles. Our results challenge the relevance of the acceptable daily intake for pesticides because this norm is calculated from the toxicity of the active principle alone. Chronic tests on pesticides may not reflect relevant environmental exposures if only one ingredient of these mixtures is tested alone*."

C.Cox & M.Surgan. 2006. Unidentified Inert Ingredients in Pesticides: Implications for Human and Environmental Health. Environ Health Perspect 114:1803–1806 (2006). doi:10.1289/ehp.9374 available via http://dx.doi.org/

Defarge N., Takacs E., Lozano VL., Mesnage R., Spinoux de Vendomois J., Seralini, GE., Szekacs, A. (2016) Co-Formulants in Glyphosate-Based Herbicides Disrupt Aromatase Activity in Human

Cells below Toxic Levels. Int J Environ Res Public Health. 2016, 13, 264; doi:10.3390/ijerph13030264

Mesnage R., Bernay B., Séralini G-E. 2013. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology 313(2-3):122-8.

Richard, S., Moslemi, S., Sipahutar, H., Benachour, N., Séralini, G-E. 2005. Differential effects of glyphosate and Roundup on human placental cells and aromatase. Environmental Health Perspectives 113: 716–20.

Benachour, N., Sipahutar, H., Moslemi, S., Gasnier, C., Travert, C., Séralini, G-E. 2007. Time- and dose-dependent effects of roundup on human embryonic and placental cells. Archives of Environmental Contamination and Toxicology 53, 126–33.

APPENDIX I(b) POEA

Documents relating to Official Information Act material.

(i) NZ EPA will not release retail names of GBHs containing POEA for commercial confidentiality reasons.

From: Tim Onnes
Sent: Wednesday, 14 June 2017 2:41 p.m.
To: Steffan Browning <Steffan.Browning@parliament.govt.nz>
Subject: FW: 10154 (2016) Published - Environment - Corrected Reply

From: qwawf
Sent: Wednesday, 10 August 2016 10:54 a.m.
To: Tim Onnes
Cc: Steffan Browning; Steffan Browning
Subject: 10154 (2016) Published - Environment - Corrected Reply

Question: Which Glyphosate Based Herbicides (GBH) products if any contain Polyoxyethylene tallow amine (POEA) ?

Portfolio: Environment

Minister: Hon Dr Nick Smith

Date Lodged:28/07/2016

Answer Text: I am advised that the EPA is not prepared to release the names of the 69 glyphosate-based herbicides containing POEA, because the composition of the formulations is commercial-in-confidence information.

Attachment: None

Date Received:10/08/2016

(ii) 69 out of 91 – 75% of GBH formulations contain POEA

---------- Forwarded message ----------
From: <qwawf@parliament.govt.nz>
To: <Timothy.Onnes@parliament.govt.nz>
Cc: <Steffan.Browning@parliament.govt.nz>
Bcc:
Date: Wed, 10 Aug 2016 10:53:55 +1200
Subject: 10151 (2016) Published - Environment - Corrected Reply
Question: How many Glyphosate Based Herbicide (GBH) products if any are approved for use in New Zealand?

Portfolio: Environment

Minister: Hon Dr Nick Smith

Date Lodged:28/07/2016

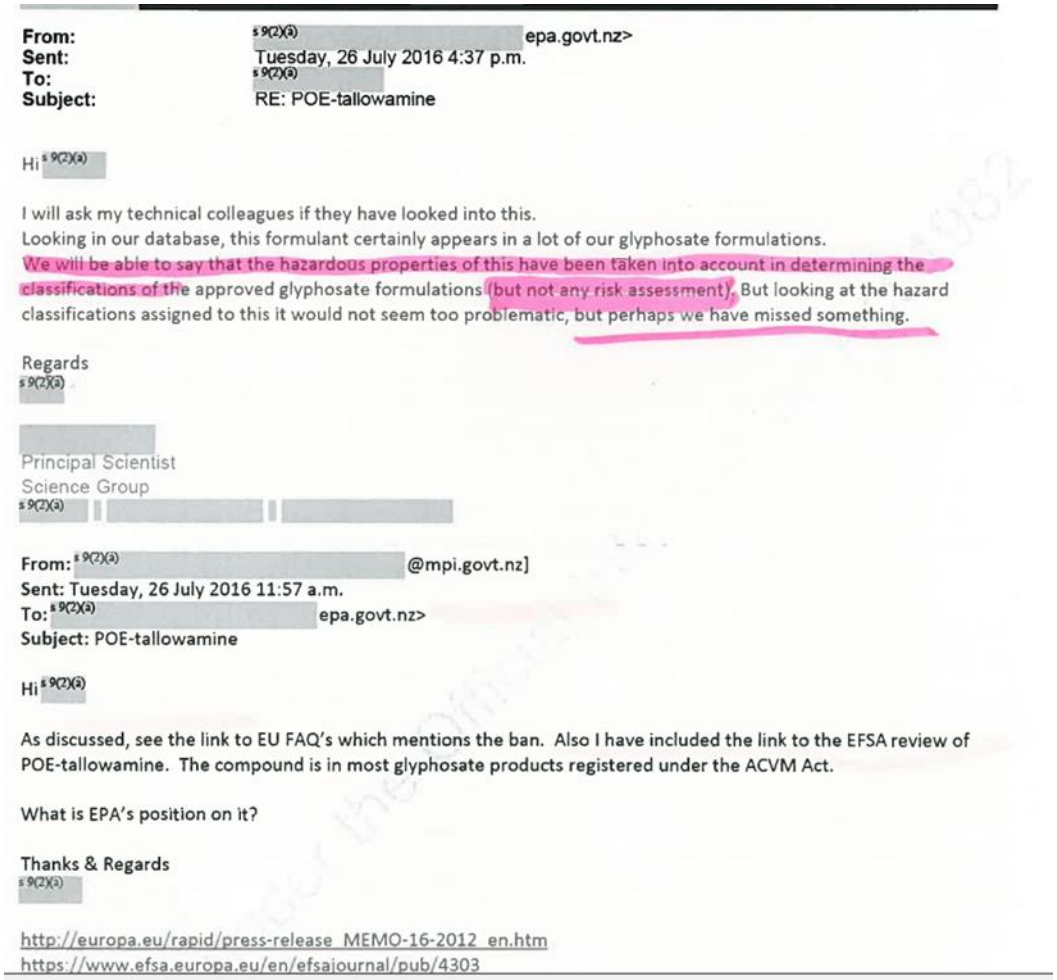
Answer Text: The EPA has advised that glyphosate-based herbicides are approved by two processes in New Zealand. 91 products are registered by the Ministry for Primary Industries under the Agricultural Chemicals and Veterinary Medicines Act 1997 (as at 1 August 2016). Approximately 60 approvals for glyphosate-based herbicides have been issued under the Hazardous Substances and New Organisms Act 1996. The reason for the difference in number of approvals between the two regulation regimes results from three differences. • Firstly, more than one MPI registration can match the same HSNO approval. • Secondly, some glyphosate-based formulations may not require an a MPI registration as they are limited to non-agricultural (home/industrial use) settings. • Thirdly, it is possible some HSNO approvals are for products which have been deregistered by MPI.

Attachment: None

Date Received:10/08/2016

---------- Forwarded message ----------
From: <qwawf@parliament.govt.nz>
To: <Timothy.Onnes@parliament.govt.nz>
Cc: <Steffan.Browning@parliament.govt.nz>
Bcc:
Date: Wed, 10 Aug 2016 10:53:55 +1200
Subject: 10152 (2016) Published - Environment - Corrected Reply
Question: What are the names of the approved Glyphosate Based Herbicide (GBH) products if any?

(iii) No risk assessment completed for the adjuvant POEA



From: [redacted] epa.govt.nz>
Sent: Tuesday, 26 July 2016 4:37 p.m.
To: [redacted]
Subject: RE: POE-tallowamine

Hi [redacted]

I will ask my technical colleagues if they have looked into this.
Looking in our database, this formulant certainly appears in a lot of our glyphosate formulations.
We will be able to say that the hazardous properties of this have been taken into account in determining the classifications of the approved glyphosate formulations (but not any risk assessment). But looking at the hazard classifications assigned to this it would not seem too problematic, but perhaps we have missed something.

Regards
[redacted]

[redacted]
Principal Scientist
Science Group
[redacted]

From: [redacted] @mpi.govt.nz]
Sent: Tuesday, 26 July 2016 11:57 a.m.
To: [redacted] epa.govt.nz>
Subject: POE-tallowamine

Hi [redacted]

As discussed, see the link to EU FAQ's which mentions the ban. Also I have included the link to the EFSA review of POE-tallowamine. The compound is in most glyphosate products registered under the ACVM Act.

What is EPA's position on it?

Thanks & Regards
[redacted]

http://europa.eu/rapid/press-release_MEMO-16-2012_en.htm
https://www.efsa.europa.eu/en/efsajournal/pub/4303

(iv) Email to Wayne Temple August 2 2016 - titled 'additional wording proposal re. Glyphosate report' requesting that 'minority of products' is deleted.

From: Section 9(2)(a)
Sent: Tuesday, 2 August 2016 11:15 a.m.
To: Wayne Temple
Cc: Section 9(2)(a)
Subject: Additional wording proposal re glyphosate report

Hi Wayne

We have another question about the wording of your report.
As a result of a recent enquiry we have discovered that we estimate 69 glyphosate-based herbicides in New Zealand are believed to contain POEA, which is more than half of the 91 ACVM-registered formulations.

Therefore we consider that the current wording of the report on p11 should modified. The report currently includes the following paragraph:

"As regards glyphosate-based commercial formulations, a number of formulations with unknown composition have given positive results when tested *in vitro* and *in vivo*. However some of the test systems are not validated and/or interpretation is difficult due to possible confounding, such as cytotoxicity, specific organ toxicity or unclear relevance to humans (such as tests in fish, amphibians, or invertebrates). **Some of the co-formulants (such as polyethoxylated tallowamine (often abbreviated to POEA), used in a minority of products) may be more systemically toxic than glyphosate.** However EFSA concluded that the genotoxic potential of such complete formulations should be further assessed."
Based on the information we have gathered we no longer consider it accurate to refer to POEA being in a minority of products, so we suggest the highlighted sentence is amended by deleting **", used in a minority of products"** so that it reads:

"Some of the co-formulants (such as polyethoxylated tallowamine (POEA)) may be more systemically toxic than glyphosate."

Please advise whether you are happy to accept this change.

APPENDIX I (c) 20% GBH products exempt from registration under ACVM Act

Out of Scope

From: s 9(2)(a)
Sent: Tuesday, 2 August 2016 8:06 a.m.
To: s 9(2)(a) ; Info
Cc: s 9(2)(a)
Subject: RE: URGENT: Glyphosate product list

Hi s 9(2)

As noted in my email there will be some glyphosate products not within the scope of the ACVM Act. This is because they are used in a manner not in line with the definition of an ag compound under the ACVM Act. Examples would include both commercial and home garden products solely with a claim to control weeds around footpaths, roads and industrial sites.

However, that does remind me that there will be also be some glyphosate products that are within the scope of the ACVM Act, but are exempt from registration. Again we would not have any information on what products are being sold under this scenario.

So in answer to your questions:

1 Based on the above advice, not all glyphosate products would have a ACVM registration.
2 There would be some home garden products falling into both the exempt from registration and out of scope categories. Also, without checking all the labels and pack sizes of the registered based glyphosate products, I am pretty sure some would be sold in a home garden situation.

At a ballpark guess, I imagine the number of glyphosate products registered under the ACVM Act would be probably at least 80% of the total number of such products out in the market place.

Finally, can I suggest MfE may wish to answer the question by saying EPA does not hold this information, although I appreciate this may not be the approach they wish to take.

Regards
s 9(2)(a)

Systems Audit, Assurance, & Monitoring Directorate | Regulation & Assurance Branch
Ministry for Primary Industries | Pastoral House, 25 The Terrace | PO Box 2526 | Wellington | New Zealand
s 9(2)(a) | Web: www.mpi.govt.nz

APPENDIX II Case Study: Problems with historical incidence

Lankas, G.R.; Hogan, G.K. (1981): A Lifetime Feeding Study of Glyphosate (Roundup Technical) in Rats: Project No. 772062. Unpublished study received Jan 20, 1982 under 524-308; prepared by Bio/dynamics, Inc., submitted by Monsanto Co., Washington, D.C.; CDL:246617-A; 246618; 246619; 246620; 246621. MRID 00093879.

Many private, unpublished studies declare that results fall within the range of 'normal' aligned with historical control data, yet the data used to declare this, is unavailable to the public or for peer review. For example, the US EPA 1993 reregistration stated, in regards to Lankas and Hogan 1981, the Monsanto paid private study 'the incidence of thyroid carcinomas was not statistically significant and the incidence of testicular tumors was within the historical incidence.'

Lankas and Hogan is an unpublished study that has never been peer reviewed, was produced in a mysterious laboratory, yet has provided the considered safe level used by regulators to establish the acceptable daily intake (ADI) for the European Union and previously, in 1986, for the World Health Organisation. At the same level declared safe, the level providing the endpoints to establish the ADI – there are tumours in 15% of the rodents.

However as historical data used for the Lankas and Hogan study is unavailable, public domain (independent) scientists cannot evaluate the merits of the statement. They cannot confirm whether this trial is replicable and as such, is good science. The extent of this study available to the public can be found on INCHEM at http://www.inchem.org/documents/jmpr/jmpmono/v86pr08.htm

It becomes more critical to understand the decision-making process within studies such as these, as this study was also incorporated in the JMPR 2006 assessment. It is extremely influential and widely cited by the major regulators. The JMPR states in INCHEM, (Chemical Safety Information from Intergovernmental Organizations):

> There were no increases in tumours that were treatment related. The incidence of interstitial cell tumours of the testes was slightly high in the high-dose group (control, 0/15; low-dose, 2/26; mid-dose, 1/16; high-dose, 4/26). However, this tumour is common in aged rats and the incidence was not above historical control levels. The no-observed-effect level exceeded 31 mg/kg b.w./day in the diet (Lankas, 1981)[459]

Many scientists are curious also, when, a private unpublished study declares tumours to be 'not treatment related.' How is this fact established?

[459] INCHEM http://www.inchem.org/documents/jmpr/jmpmono/v86pr08.htm

Information is hidden behind commercial confidentiality clauses, agreements between regulator and, in this case, Monsanto.

This study does not appear to have been incorporated in the IARC carcinogenicity review, as the IARC working group paper selected “reports that have been published or accepted for publication in the openly available scientific literature” and “data from governmental reports that are publicly available.”

This example of the power of a private study, that indicated tumour development, but discounted signs of carcinogenicity (‘no treatment-related effects’) using unknown parameters, has provided such an important part of regulatory review and enabled high permissible daily exposure levels within the European Union, World Health Organisation and US EPA that it is no wonder independent scientists are critical. There are very few carcinogenicity studies held within these agencies for the reviews mentioned in the NZ EPA Review, but at this point in time they are unpublished and industry selected and supplied. It is studies such as Lankas and Hogan that the NZ EPA review appears to prioritise over the IARC paper.

APPENDIX III Knezevich and Hogan

Three apparently separate papers are drawn from the one study. The original study was contentious. It required further analysis by the US EPA and a pathology report was produced by a Monsanto paid consultant pathologist from this study in 1985. Another histopathological report was prepared in 1986. Thus the one study may have references that include 1983, 1985, and 1986.:

IARC Monograph: EPA (1983). Review of Knezevich A, Hogan G (1983). A chronic feeding study of glyphosate (Roundup Technical) in mice: Project No. 77–2061: Bdn-77- 420. Final Report. **MRID 00130406.**

Discussed in the 1993 US EPA Reregistration Eligibility Decision (RED) Document Case 0178:

Knezevich, A.; Hogan, G. A chronic feeding study of glyphosate (Roundup technical) in mice. Unpublished Report no. BDN-77420, project no. 77-2061, 1983, submitted to U.S. Environmental Protection Agency by Monsanto Company, prepared by BioDynamics, Inc. Reregistration Eligibility Decision (RED) Glyphosate; EPA-738-F-93-011; U. S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1993. **MRID 00130406**

Extract from the US EPA 1993 P.14 : This is the study that decided the classification of Group C Carcinogen –

> *A carcinogenicity study in mice was conducted with CD-1mice fed diets containing 0, 150, 750 or 4500 mg/kg/day of glyphosate for 18 months. No effects were observed in the low-dose and mid-dose groups. The following findings were observed in the high-dose group: (1) decreased body weight gain in males and females; (2) increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis in males; (3) increased incidence of proximal tubule epithelial basophilia and hypertrophy in females; and (4) slightly increased incidence of renal tubular adenomas, a rare tumor, in males. Based on these effects, the systemic NOEL and LOEL were 750 mg/kg/day and 4500mg/kg/day, respectively. The Agency concluded that the occurrence of these adenomas was spontaneous rather than compound-induced because the incidence of renal tubular adenomas in males was not statistically significant when compared with the concurrent controls. An independent group of pathologists and biometricians also conducted extensive evaluations of these adenomas and reached the same conclusion. Therefore, glyphosate was not considered to be carcinogenic in this study. (MRIDs 00130406, and 00150564)* End extract.

A pathology report was produced two years later by the registrant (Monsanto):

McConnel, R. A chronic feeding study of glyphosate (Roundup technical) in mice: pathology report on additional kidney sections. Unpublished project no. 77-2061A, 1985, submitted to U.S. Environmental Protection Agency prepared by BioDynamics, Inc. Reregistration Eligibility Decision (RED) Glyphosate; EPA-738-F-93-011; U. S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1993.Study: MRID 00150564

This may be EPA (1985b). EPA Reg.#: 524–308; Roundup; glyphosate; pathology report on additional kidney sections. Document No. 004855. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency. Available from: http://www.epa.gov/pesticides/chemicalsearch/ chemical/foia/cleared-reviews/reviews/103601/103601206.pdf, accessed 10 March 2015.

> Knezevich A, Hogan G (1983) *'1985, the Registrant directed a re-evaluation of the original renal section by a consulting pathologist (Dr. Marvin Kuschner). This evaluation identified a small renal tubule adenoma in one control male mouse (animal number 1028) which was not diagnosed as such in the original pathology report (TXR No. 0004855)'*.

US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee Page 51
http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/EPA-HQ-OPP-2009-0361-0057.pdf Accessed 10/5/2017

The IARC refers to the following as EPA (1986). Glyphosate; EPA Registration No. 524–308; Roundup; additional histopathological evaluations of kidneys in the chronic feeding study of glyphosate in mice. Document No. 005590. Washington (DC): Office of Pesticides and Toxic Substances, United States Environmental Protection Agency.

> Knezevich A, Hogan G (1983) *'In 1986, at the request of the agency, additional renal sections (3 sections/kidney/mouse spaced at 150 micron intervals) were evaluated in all control and all glyphosate-treated male mice in order to determine if additional tumors were present. The additional pathological and statistical evaluations concluded that the renal tumors in male mice were not compound-related (TXR No. 0005590).'*

US EPA October 1 2015 Memorandum. Report of the Cancer Assessment Review Committee. Page 51
http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/EPA-HQ-OPP-2009-0361-0057.pdf Accessed 10/5/2017

APPENDIX IV IARC Working Group List of Participants

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans [460]

VOLUME 112: SOME ORGANOPHOSPHATE INSECTICIDES AND HERBICIDES: DIAZINON, GLYPHOSATE, MALATHION, PARATHION, AND TETRACHLORVINPHOS Lyon, France: 3-10 March 2015 LIST OF PARTICIPANTS

Working Group Members and Invited Specialists served in their individual capacities as scientists and not as representatives of their government or any organization with which they are affiliated. Affiliations are provided for identification purposes only.

Members

Isabelle Baldi, University of Bordeaux,
France Aaron Blair, National Cancer Institute, USA [retired] (Overall Chair)
Gloria M. Calaf, Tarapaca University, Chile

[460] IARC Working Group List of Participants. http://monographs.iarc.fr/ENG/Meetings/vol112-participants.pdf. Posted on 26 January 2015, updated 19 October 2016

Peter P. Egeghy, U.S. Environmental Protection Agency, USA1 (Unable to attend)
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Yann Grosse, Section of IARC Monographs

Neela Guha, Section of IARC Monographs

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Kurt Straif, Section of IARC Monographs (Section Head)

Jiri Zavadil, Section of Mechanisms of Carcinogenesis

NOTE REGARDING CONFLICTS OF INTERESTS: Each participant submitted WHO's Declaration of Interests, which covers employment and consulting activities, individual and institutional research support, and other financial interests. Participants identified as Invited Specialists did not serve as meeting chair or subgroup chair, draft text that pertains to the description or interpretation of cancer data, or participate in the evaluations. The Declarations were updated and reviewed again at the opening of the meeting.

NOTE REGARDING OBSERVERS: Each Observer agreed to respect the Guidelines for Observers at IARC Monographs meetings. Observers did not serve as meeting chair or subgroup chair, draft any part of a Monograph, or participate in the evaluations. They also agreed not to contact participants before the meeting, not to lobby them at any time, not to send them written materials, and not to offer them meals or other favours. IARC asked and reminded Working Group Members to report any contact or attempt to influence that they may have encountered, either before or during the meeting.

APPENDIX V An analysis of New Zealand legislation relating to pesticide classification.

Digging down into New Zealand regulations (as best possible).

1.0 Current (2017) New Zealand classification of glyphosate.

As at February 2017 the NZ EPA Chemical Classification and Information Database (CCID)[461] classifies glyphosate (CAS no. 1071-83-6) under the following classification codes:

Health Hazard:

> 6.1E (oral exposure route) Substances that are acutely toxic –May be harmful, Aspiration hazard;
>
> 6.4A Substances that are irritating to the eye

Environmental hazards:

> 9.1B (All) Substances that are ecotoxic in the aquatic environment
>
> 9.1D (fish) Substances that are slightly harmful to the aquatic environment or are otherwise designed for biocidal action

2.0 How does NZ Classification for carcinogenicity sit with the IARC classification?

The IARC determination of 'probable carcinogen' 2A appears equivalent with the New Zealand Category 'substances that are known or presumed human carcinogens,' 6.7A.[462]

2.1 Globally Harmonised System (GHS)

The Globally Harmonised System[463] (GHS) for Classification and Labelling of Chemicals, carcinogenicity classification lists carcinogen Category 1B

[461] NZ EPA Chemical Classification and Information Database (CCID) http://www.epa.govt.nz/search-databases/Pages/ccid-details.aspx?SubstanceID=3208

[462] Washington State Department of Ecology. Quick Chemical Assessment Tool (QCAT) Version 2.0. Appendix 8 Chemical Ranking Criteria. http://www.ecy.wa.gov/GreenChemistry/documents/Appendix08-ChemicalRankingCriteria.pdf

[463] Globally Harmonised System (GHS) for Classification and Labelling of Chemicals Fourth revised edition. United Nations 2011.

‘Presumed to have carcinogenic potential for humans, the placing of a substance is largely based on animal evidence.

A 2012 NZ EPA Information Sheet [464] confirms the GHS Category 1B is equivalent to New Zealand classification for carcinogenicity of 6.7A.

Europe has implemented the GHS classification system. The European Parliament considers that the IARC 2A classification corresponds roughly to Category 1B within the Globally Harmonised System (GHS) for Classification and Labelling of Chemicals, carcinogenicity classification. A Workshop[465] held at the European Parliament in Brussels in May 2016 stated that:

> *‘The criteria used by the IARC for Group 2A are comparable to those for Category 1B in Regulation (EC) No 1272/2008.’*

3.0 New Zealand: What restrictions on food are required after a pesticide classification of ‘probable (or presumed) carcinogen’?

There are three interconnected Acts that form the backbone regulation of chemicals and directly relate to exposures of pesticides in New Zealand. All three Acts appear to make discretion by government agencies and Ministers the principal mechanism for restrictions on human exposure to probable/presumed carcinogens.

The NZ Environmental Protection Agency (EPA) administers HSNO. The Ministry for Primary Industries administers the ACVM and Food Acts, and related regulations.

The Hazardous Substances and New Organisms Act 1996 (HSNO) relate to assessing and approving hazardous substances for importation or manufacture, in addition to classifying and placing controls on use of hazardous substances to ensure protection of people and environment. Trade name products will be registered under the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM). The ACVM Act regulates the use of an agricultural compound, which may or may not be considered a hazardous substance, including assessing and controlling compounds to ensure maximum residue limits[466] are not breached.

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https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf

[464] Correlation between GHS and New Zealand HSNO Hazard Classes and Categories. Information Sheet. January 2012 EPA0125 http://www.epa.govt.nz/Publications/hsnogen-ghs-nz-hazard.pdf Page 4.

[465] Directorate General for Internal Policies. Policy Department A: Economic and Scientific Policy. EU’s Pesticide Risk Assessment System: The Case of Glyphosate. Brussels, 24 May 2016. P.7

[466] Agricultural Compounds and Veterinary Medicines Act 1997 Section 4A (5) (a) http://www.legislation.govt.nz/act/public/1997/0087/latest/whole.html#DLM414583

The Food Act is directly concerned with food available for sale in New Zealand. Chemical residue levels on food (but not animal feed) are set by establishing maximum residue limits (MRLs) for agricultural compounds (including pesticides) in separate food items (from milk to fruit, vegetable or cereal crops etc.) under the Food Act via the Food Regulations 2015

3.1 Would the finding of 'probable carcinogen' protect the public from adverse exposures on food according to New Zealand legislation?

There appears to be no existing legislative or policy instrument in New Zealand that would automatically require a chemical to be reduced or withdrawn as a chemical residue on food, should a chemical ingredient (eg. glyphosate) be classified as a probable or presumed carcinogen, and therefore considered 'toxic' (a class 6 substance) under the HSNO Act.

3.1.1 Establishing exposures on food

A 2015 reassessment for the organophosphate insecticide dichlorvos[467] [468] provides a recent example of the interlinking nature of the HSNO and ACVM Acts regarding exposures of agricultural compounds (including pesticides):

> *'The EPA has the legislative mandate under the Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001 to set exposure standards for hazardous substances. This includes setting values for the ACVM Group to use in assessing the human health significance of food residues for pesticide and veterinary medicine active ingredients.'*
>
> *'After setting the values, the EPA advises the ACVM Group of the ADE and PDEs, with particular attention to the PDE food as this value is used by ACVM as the ADI.'*

Authority to establish maximum residue levels in food is contained in Section 406 (u) of the Food Act, *'Notices relating to specifications or*

[467] NZ EPA Decision. Application for the Reassessment of a Group of Hazardous Substances under Section 63 of the Hazardous Substances and New Organisms Act 1996 15 September 2015. APP202097: Dichlorvos and its formulations

[468] (The dichlorvos reassessment is a relevant example as it concerned a Class 6 toxic substance. The ADI of .0001 mg/kg may appear conservative in contrast to glyphosate. Yet it is concerning as it applies a narrow 10-fold safety factor which is insufficient for the protection of children. The ADI was derived from a single 1967 study.)

requirements for specific matters', which includes the power to issue notices relating to maximum residue levels.[469]

If an agricultural compound or food combination is not specifically listed on the Ministry for Primary Industries Food Notice: Maximum Residue Levels for Agricultural Compounds the product will default to a permitted maximum residue level (MRL) of 0.1mg/kg.[470]

Other than for fruit (0.01mg/kg), glyphosate is not mentioned. This should result in a MRL of 0.1mg/kg.

Several published papers consider that agrichemicals in conventional foods constitute the primary source of exposure for the general population.[471] [472] [473]

The Food Regulations 2015 advise that criteria for establishing MRLs must follow international best practice, and synchronise with the Codex standard.[474] Codex standards are derived from Reports of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues (JMPR) in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues.

However, 'best practice' in relation to establishing maximum residue levels on food, might be interpreted as most accurately testing for MRLs via crop trials, and then adopting the highest residues as a MRL.

To illustrate, the 2005 FAO Plant Production and Protection Paper 183[475] trialled glyphosate on various crops. Following recommendation made within this 2005 paper by the JMPR, in the year following, 2006, Codex Alimentarius increased permitted residue levels.[476] Soon after the US increased glyphosate tolerances for residues.[477]

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[469] Food Act 2014 Sn 406 (u) http://legislation.govt.nz/act/public/2014/0032/latest/whole.html#DLM5431612

[470] Ministry of Primary Industries Food Notice Maximum Residue Levels for Agricultural Compounds. 20 October 2016 (PDF) mpi.govt.nz/document-vault/11329

[471] European Parliament. Human health implications of organic food and organic agriculture. 2016. PE581.922 http://www.europarl.europa.eu/RegData/etudes/STUD/2016/581922/EPRS_STU(2016)581922_EN.pdf

[472] Determination of Glyphosate residues in human urine samples from 18 European countries Test Compound Glyphosate and AMPA. Medical Laboratory Bremen. http://www.gmoevidence.com/wp-content/uploads/2013/06/glyphosate_studyresults_june12.pdf

[473] Brändli D, Reinacher S; Herbicides found in Human Urine. Ithaka Journal 1/2012: 270–272 (2012) www.ithaka-journal.net Editor: Delinat-Institute for Ecology and Climatefarming, CH-1974 Arbazwww.delinat-institut.org, ISSN 1663-0521 http://www.ithaka-journal.net/druckversionen/e052012-herbicides-urine.pdf

[474] Food Regulations 2015. Part 6 Food standards in relation to agricultural compounds Sn. 140-143 http://legislation.govt.nz/regulation/public/2015/0310/latest/whole.html#whole

[475] 2005 FAO Plant Production and Protection Paper 183. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 20–29 September 2005. http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/JMPR05report.pdf

[476] Pesticide Residues in Food and Feed Pesticides Database Search: 158 – glyphosate http://www.fao.org/fao-who-codexalimentarius/standards/pestres/pesticide-detail/en/?p_id=158

[477] US EPA Electronic code of federal regulations: Title 40: Protection of the environment. PART 180—TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD. Subpart C specific tolerances: Glyphosate tolerances for residues: S 180.364.

The exemptions relating to agricultural compounds, which includes pesticides, within the new Food Act's regulations warrant careful consideration by health specialists and toxicologists. For example, exemptions are applied to animal products that may contain toxic ingredients which are given to animals during the process of 'management.'

Exemptions are also applied to food that is dried or concentrated. This may include products containing milk powder, for example.[478]

3.1.2 Changing exposures on food to reflect new risk

The NZ EPA under HSNO may elect to reduce daily population exposures via control regulations. MPI may lower the chemical residues on food under the Food Act to ensure the ACVM Act purpose (4b) is adhered to*: 'ensure that the use of agricultural compounds does not result in breaches of domestic food residue standard*.'

However, if ADI exposures are adjusted under the HSNO Act there does not appear to be specific legislation requiring the Food Act or ACVM regulations to adjust maximum residue levels of agricultural compounds (eg. pesticides) in food in response.

The main mechanism within the Food Act to alter MRLs may be under Section 383. The Governor-General may amend food residues following a recommendation of the Minister for Primary Industries:

> *383 (3) The Governor-General may, by Order in Council made on the recommendation of the Minister, make regulations setting standards in relation to food that specify the criteria that all or any of the following must meet to ensure that food is safe and suitable:*
>
> *(4) Regulations referred to in subsection (3)(k) may (without limitation)—*
>
> *(a) specify how residue levels are to be determined for specified foods:*
>
> *(b) prohibit the sale of any food containing residues of a substance that exceed limits specified by a notice under section 406(1)(u):*
>
> *(c) provide for exemptions from specified requirements of the regulations where the residues present in the food concerned are within allowable limits specified in a notice under section 406(1)(u) and the food complies with any other requirements specified in the notice.*

[478] Food Regulations 2015. Part 6 Food standards in relation to agricultural compounds Sn 141 (2) and 142

The EPA may also reassess a hazardous substance and revoke an approval. (See next section).

(Alternative 'best practice' policy instruments can be drawn from European legislation, where should adverse harm or risk be identified, there is an obligation to remove residues from food. See 7(i))

3.2 Reassessment – 'significant new information'

Section 62 of the HSNO Act provides that any person or the chief executive may request the EPA to decide whether there are grounds for assessing a substance (although 62(1) neglects to use the world 'substance') where significant new information has become available.

As of writing, following the NZ EPA review, glyphosate is listed on the Chief Executive-initiated Reassessment Programme and is being 'monitored' by the NZ EPA.

> *'This means we continue to keep a watching brief on its status, and monitor international scientific findings or developments. If any new information comes to hand that makes us think further action is necessary, we can consider a formal review of its use.'*[479]

Approvals are valid until declined via reassessment.

The Director-General of MPI may also call for reassessment under Section 29 of the ACVM Act if significant new information on a matter related to the use of the registered trade name product or group of trade name products has become available.

There appears to be no example of the EPA adopting an IARC classification recommendation without undertaking a reassessment. However, should the EPA accept the IARC classification without reassessment, we consider the following HSNO controls would apply.

Alternatively, the EPA could make a technical amendment under Section 67A of the HSNO Act:

> ***Minor or technical amendments to approvals -*** *The Authority may, of its own motion, amend any approval given by it under this Part if it considers that the alteration is minor in effect or corrects a minor or technical error.*[480]

[479] EPA report concludes glyphosate an unlikely carcinogen. 11 August 2016. http://www.epa.govt.nz/news/epa-media-releases/Pages/EPA-glyphosate-report-released.aspx Accessed 4/5/2017

[480] **Hazardous Substances and New Organisms Act 1996. Sn 67A**
http://www.legislation.govt.nz/act/public/1996/0030/latest/whole.html#whole

However, a minor technical adjustment may not go to the lengths required to appropriately protect the public.

4.0 How does HSNO work? Establishing a substance as a 'probable carcinogen.'

It can be challenging to understand how the myriad of regulations and classifications that come under an Act of Parliament, such as HSNO, work to effectively protect the public.

This section concerns the regulations under the HSNO Act that provide decision-makers with the parameters to define and categorise toxic substances.

It is essential that the evidence used to declare a chemical toxic (a class 6 substance) or not, is unbiased and represents toxicity accurately, in order that the relevant legislation can act to protect the public.

Once classified as a highly toxic Class 6 substance and biological hazard, tighter controls (regulations concerning its availability and use) to protect public and environmental health are put in place. (Detailed in section 5).

The Forward to HSNO Control Regulations explains how HSNO regulations work together:

> *'The HSNO Act provides for a series of regulations to manage the risks associated with hazardous substances. One set of regulations deals with defining a hazardous substance ('Minimum Degrees of Hazard ("Threshold") Regulations') while another provides for the levels of the various types of hazards to be classified ('Classification' Regulations). Detailed explanation and interpretation of these can be found in the EPA User Guide to the HSNO Thresholds and Classifications. A third set of regulations provides for a range of controls to manage hazardous substances in order to minimise adverse effects. This group of regulations covers both controls on the hazardous properties of substances and controls on the lifecycle and infrastructure surrounding the substances. These 'Controls' Regulations are the subject of this User Guide.'*[481]

Toxic means capable of causing ill health in, or injury to, human beings.

The HSNO Control Regulations User Guide[482] notes 'highly toxic substances are those that are acutely toxic with classifications of 6.1A,

[481] EPA0148 User Guide to the HSNO Control Regulations February 2012 (as originally written 2001). P.3 http://www.epa.govt.nz/publications/er-ug-05.pdf
[482] Ibid. P.110

6.1B or 6.1C; mutagens of classification 6.6A; carcinogens of classification 6.7A; or substances that exhibit high reproductive or developmental toxicity (6.8A), or are highly toxic to target organs (6.9A)'.

'Biological property controls', are aimed at limiting the exposure and the adverse effects of exposure, of hazardous substances to people and the environment.[483] Controls are the restrictions and/or requirements – the regulations that apply when a hazard is established.

It is useful to understand how these regulations interact to protect people and the environment from a pesticide considered a probable carcinogen.

The first step is to establish thresholds of toxicity for a substance.

4.1 Evidence required – thresholds – for toxicity.

Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001[484]

Section 2 within Schedule 4 of the Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001 contains the criteria that defines minimum degrees of hazard – thresholds - for substances with toxic properties, contains relevant definitions, hazard endpoints following toxicological studies of the substance.

What evidence is required to consider a substance 'probably carcinogenic'?

Minimum degrees of hazard concerning mutagenicity, genotoxicity and carcinogenicity are listed in Section 2 of Schedule 4, regulations (n) to (p):

> *(n) data for the substance indicates evidence of—*
>
> > *(i) genotoxic effects as a result of mammalian in vivo exposure to the substance; and*
> >
> > *(ii) mutagenic effects as a result of in vitro exposure to the substance; or*
>
> *(o) data for the substance indicates evidence of mutagenic effects as a result of in vitro exposure of mammalian cells to the substance and the substance has a structure–activity relationship to known germ cell mutagens, where—*
>
> *(i) structure–activity relationship means a significant correlative relationship between the chemical structure of the substance and the chemical structure of a known germ cell mutagen; and*

[483] Ibid. P.114
[484] Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001 http://www.legislation.govt.nz/regulation/public/2001/0112/latest/whole.html#DLM33367

(ii) the relationship relates to that germ cell mutagen activity; or

(p) reliable information for the substance indicates to an expert that exposure to the substance causes the development of cancer or an increase in the incidence of benign or malignant tumours in an organ or an organism.

A toxic substance must first meet the minimum degree of hazard prescribed by Schedule 4 of the Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001 for a substance with toxic properties. Then it is classified as follows.

4.2 Classifying toxicity into various levels, or classes of hazard.

The Hazardous Substances (Classification) Regulations 2001[485] specify data requirements to define a hazard classification of 6.7A. The classification regulations set out the criteria and classes (and subclasses) of hazardous substances to help the public and private sector identify clearly, in what way a product is toxic, flammable, or ecotoxic.

The criteria required for a substance to achieve a hazard classification of 6.7A are listed in Schedule 4 Classification criteria for toxic substances, Section 2, Table of hazard classifications:

(a) a substance for which data indicate sufficient evidence in humans of a causal relationship between exposure to the substance and the development of cancer in humans; or

(b) a substance for which data indicate sufficient evidence in animals of a causal relationship between exposure to the substance and an increased incidence of tumours; or

(c) a substance for which data indicate—

(i)limited evidence in humans of a positive correlation between exposure to the substance and the development of human cancer; and

(ii)limited evidence in animals that exposure to the substance may lead to an increased incidence of tumours.

[485] Hazardous Substances (Classification) Regulations 2001. Schedule 4 Classification criteria for toxic substances. Table of Hazard Classifications. Hazard Classification: 6.7A http://www.legislation.govt.nz/regulation/public/2001/0113/latest/DLM33833.html

For purposes of comparison, the IARC Working Group advised [486]:

> '6.1 Cancer in humans: There is *limited evidence* in humans for the carcinogenicity of glyphosate. A positive association has been observed for non-Hodgkin lymphoma.'
>
> '6.2 Cancer in experimental animals: There is *sufficient evidence* in experimental animals for the carcinogenicity of glyphosate.'

4.3 Once a hazardous substance is classified, what are the rules or 'controls' under HSNO to keep people safe?

Consultation of the NZ EPA User Guide Control Regulations publication may enable the reader to understand how control regulations are presented to the public within NZ EPA manuals.

Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001[487]

Toxic Property Controls Chart lists the regulatory framework, the range of controls (for example requirements to protect the pesticide applicator) used to minimise adverse effects. This chart is reproduced from the User Guide to the HSNO Control Regulations February 2012.[488] The information in the chart is drawn from the Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001:

4.3.1 Toxic Property Controls

The controls applicable to the IARC Working Group 2A classification appear to correspond with HSNO *Carcinogen 6.7 - Degree of Hazard B* (within the Hazardous Substances (Classification) Regulations 2001[489]) - *a substance for which data indicate sufficient evidence in animals of a causal relationship between exposure to the substance and an increased incidence of tumours.*

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[486] IARC Working Group. Glyphosate. In: Some organophosphate insecticides and herbicides:diazinon, glyphosate, malathion, parathion, and tetrachlorvinphos. Vol 112. IARC Monogr Prog, 2015:1–92. http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf

[487] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#whole

[488] EPA0148 User Guide to the HSNO Control Regulations February 2012 (as originally written 2001) Page 42 and 43 http://www.epa.govt.nz/publications/er-ug-05.pdf

[489] Hazardous Substances (Classification) Regulations 2001. Schedule 4 Classification criteria for toxic substances. Table of Hazard Classifications. http://www.legislation.govt.nz/regulation/public/2001/0113/latest/DLM33833.html

It would be expected that acceptance by the NZ EPA of the IARC 2A glyphosate classification would result in adoption of the New Zealand standard controls for a Hazard B substance.

Hazard [B] controls are included in the below chart, contained within the User Guide to HSNO Control Regulations: T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8,EM11,EM12 [490]

- T class: Toxic substances (incl biological corrosives). Relates to exposure and the public.
- I = identification
- P = packaging
- D = disposal
- EM = emergency management

Toxic Property Controls

Degree of Hazard	Nature of Toxic Hazard							
	Acute Toxicity 6.1	**Skin Irritant 6.3**	**Eye Irritant 6.4**	**Sensitiser (respiratory & contact) 6.5**	**Mutagen 6.6**	**Carcinogen 6.7**	**Reproductive/ Developmental 6.8**	**Target Organ Systemic 6.9**
A	T1,T2,T3,T4,T5,T6,T7,T8, I1,I8,I9, I16,I17,I18,I19, I20,I21,I28,I29,I30, P1,P13,PG1, D4,D6,D7,D8, EM1,EM6,EM8,EM11, EM12,EM13, TR1, AH1	T1,T2,T4,T7 I1,I9,I16,I19,I21,I28 P1,P3,P13* D4,D6,D7,D8 EM1,EM6,EM8, EM11,EM12	T1,T2,T4,T7 I1,I9,I16,I19,I21,I28 P1,P3,P13* D4,D6,D7,D8 EM1,EM6,EM8, EM11,EM12	T1,T2,T4,T5,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM1,EM6,EM8, EM11,EM12	T1,T2,T3,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG2 D4,D6,D7,D8 EM8,EM11,EM12	T1,T2,T3,T4,T5,T6,T7, I1,I9,I16, I17, I18,I19,I21,I28, P1,P3,P13,PG2, D4,D6,D7,D8, EM8,EM11,EM12, AH1	T1,T2,T3,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG2 D4,D6,D7,D8 EM8,EM11,EM12	T1,T2,T3,T4,T7 I1,I9,I16,I17,I18,I19,I21,I28 P1,P3,P13,PG2 D4,D6,D7,D8 EM8,EM11,EM12
B	T1,T2,T3,T4,T5,T6,T7,T8, I1,I8,I9,I16, I17,I18,I19, I20,I21, I28,I29,I30, P1,P3, P13,PG2, D4,D6,D7, D8, EM1, EM6,EM8, EM11, EM12,EM13, TR1, AH1	T1,T2,T4,T7 I1,I9,I16,I19,I21,I28 P1,P3,P13* D4,D6,D7,D8 EM1,EM6,EM8, EM11,EM12		T1,T2,T4,T5,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM1,EM6,EM8, EM11,EM12	T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8	T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8,EM11,EM12	T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8	T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8
C	T1,T2,T3,T4,T5,T6,T7,T8, I1,I8,I9, I16, I17, I18,I19, I20,I21, I28,I29,I30, P1,P3, P13,PG3, D4,D6, D7,D8, EM1,EM6, EM8,EM11,EM12,EM13, TR1, AH1						T1,T2,T4,T7 I1,I9,I16,I17,I18,I19,I 21,I28 P1,P3,P13,PG3 D4,D6,D7,D8 EM8	

The Hazard B Controls (above) can then be correlated with specific regulations on page 50 of the User Guide.

These regulations can be found in Part 1 and 2 of the Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001.[491]

T1 = Limiting exposure to toxic substances; setting values for acceptable daily exposure (ADE)/reference dose (RfD), potential daily exposure (PDE),

[490] The Key to Controls Codes information can be found on Page 47-54 of the EPA0148 User Guide. Chart on page 42. http://www.epa.govt.nz/Publications/ER-UG-05.pdf
[491] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688

tolerable exposure limit (TEL); prohibition on use of substances in excess of TEL. Regs 11-27

T2 = Controlling exposure in places of work and other ‘use’ situations; setting of workplace exposure standards (WES). Regs 29-30

T4 = Requirements for equipment used to handle substances. Reg 7

T7 = Restrictions on carriage of toxic substances on passenger service vehicles. Reg 10

Hazard B (in the spreadsheet) does not appear to include the following requirements:

- Regulation 8 requires that a person who handles a class 6.7A substance must use protective clothing or equipment.
- Regulation 9 requires that quantities of 10kg or more of class 6.7A substances must be under the control of an approved handler or secured.

This is surprising as it is desirable to minimise exposure to toxic substances, such as should occur with acceptance of the IARC 2A glyphosate classification.

If the controls for toxic substances are not considered appropriately safe, Section 75 of the HSNO Act allows for the Governor-General to create new controls:

Section 75 - Regulations prescribing hazard classification control:

> *(1) Subject to section 141, the Governor-General may, from time to time, by Order in Council make regulations prescribing controls for each hazard classification for the following purposes:*
>
> *(e) for substances with toxic properties:*
>
> *(i) to reduce the likelihood of any unintended exposure to any such substances:*
>
> *(ii) to control the adverse effects of any exposure to such substances:*

5.0 What restrictions under the HSNO Act apply if glyphosate based herbicides were categorised as a ‘probable carcinogen’?

A categorisation of ‘probable carcinogen’ would result in glyphosate based herbicides being listed as a class 6 toxic substance. The Hazardous

Substances (Classes 6, 8, and 9 Controls) Regulations 2001 would then apply, and the 'controls' contained in Part 1 (concerning keeping records, protective equipment and handling the chemical) and Part 2 (setting population daily exposures). The regulations that would apply to products containing glyphosate, outlined in the above section, are further explored here.

5.1 Part 1 – General Requirements (Keeping records, protective equipment, approved handlers)

A 6.7A classification would require, under the Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001[492] the following controls (regulations) to be put in place:

Reg.5 A written record must be made of each application where members of the public may be present or substance could enter air or water or 'leave the place.'

Reg.6 Records must include substance name, date and time, classification, amount used, location, wind speed and direction if discharged into the air and users name and address

Reg.7 Equipment used to handle substances. This should already apply as glyphosate has some class 6 classification attributed to it – Equipment must be fit for purpose and accompanied by documentation complying with HSNO regulations.

Reg.8 Persons must use protective clothing and equipment that ensures the person does not come into contact with the substance and is not exposed to a concentration greater than the workplace exposure standard. Chemical handler must have documentation containing information specifying circumstances (including equipment pressures) for use and maintenance of clothing.

Reg.9 Quantities of 10 kg or more, if solid; 10 L or more, if liquid (see Schedule 1) must be under the control of an approved handler; secured by key or another device. A person who is not an approved handler may handle the substance if an approved handler is present.

5. 2 Part 2 - Requirements for class 6 substances (setting exposure values)

[492] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. Part 1 General Requirements http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688

A classification of Class 6 would result in formalisation of the exposure values as per Part 2, contained within Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 11-28:

> '*acceptable daily exposure value or 1 or more RfD values must be set for a substance'*.[493]

Current legislation was written in 2001. It stipulates in Classes 6, 8, and 9 Controls Regulations regulation 12 (3) that exposures for Class 6 (toxic) substances must be less than 2 mg/kg bw/day.[494] This rather high level of 2 may be considered out of date as peer reviewed and published science illustrates that harm may occur at much lower levels of exposure.

The legislation detailing uncertainty factors (regulations 14-21) appears complex – appears an arbitrary number and may have the effect of being overly restrictive for no apparent purpose and outdated, eg. regulations 14-21 stipulate that an uncertainty value cannot be more than ten.

Reg.11. If glyphosate were established as a toxic Class 6 substance, and if glyphosate is present in one or more environmental media or in food, and exposure has an appreciable toxic effect, exposure limits (per kilogram bodyweight per day) must be established.

Reg.12. (1) An acceptable daily exposure value or 1 or more RfD values must be set for a substance—

> *(a) by adopting, as the acceptable daily exposure value or an RfD value, a value that has been set for the substance—*
>
> > *(i) by an international scientific or regulatory body recognised by New Zealand; or*
> >
> > *(ii) in a convention that New Zealand has signed or ratified; or*
> >
> > *(iii) under any other Act; or*
>
> *(b) by calculating an acceptable daily exposure value or 1 or more RfD values in accordance with regulations 13 to 21.*

Reg.13. Advises the formula for calculating acceptable daily exposure value or RfD value.

Regulations 14-21 concern uncertainty factors, which are then calculated in the Regulation 13 equation. A value of not less than 1 is set for uncertainties relating to sensitive subpopulations. This does not adequately protect, for example, a pregnant mother or young child.

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[493] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. Part 2. Sn. 12 http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688

[494] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. Part 2. Sn. 12 (3) http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688

Regulations 22 and 23 Require a potential daily exposure value (PDE) to be established.

Reg.24. Require the agency to establish a tolerable exposure limit (TEL) - as a concentration of the substance - for each environmental medium where a person exposed will receive a dose of the substance. TELs are used to assess workplace exposures.

Reg.25. Advises relevant matters for setting tolerable exposure limits

Reg.26. Advises that TELs can be higher or lower depending on a variety of factors including average bodyweight, whether the substance accumulates in tissue, duration of exposure.

Reg.27. Prohibits use of substance in an environmental medium that would exceed the TEL.

Reg.29. Workplace exposure standards concern risk of the substance in the air and aims to reduce harm via inhalation or dermal exposure. The value must be expressed as a concentration in air. As glyphosate can become airborne – a workplace exposure standard must be set.

Reg.30. The workplace value may be proposed by WorkSafe[495] New Zealand or may be set taking into consideration exposure routes, duration, extent of accumulation in the body, hazard classification and overall exposure. This regulation advises that if the substance is a mixture, the standard must be set for one or more components – and – workplace standards should consider toxicity data regarding the mixture (formulation).

5.3 Exposures - Current Situation

If glyphosate were to be classed as a toxic Class 6 substance, it appears that technically under HSNO, the current daily exposure rate (from food and environment) for glyphosate of 0 - 1.0mg/kg bw/day may be acceptable under regulation 12 (3).

The NZ EPA advises[496] that NZ EPA and Ministry for Primary Industries, currently defer to the JMPR 2006 acceptable daily intake (ADI) value of 0 - 1.0mg/kg bw/day[497] (which applies to the sum of glyphosate and its breakdown product Aminomethylphosphonic acid (AMPA).

[495] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. Part 2. Sn. 30 http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688
[496] Official Information Act request ENQ-28802-S9D1C3 September 14, 2015.
[497] JMPR Pesticide residues in food – 2004 Evaluations. Part II – toxicological ISBN 978 92 4 166520 9. WHO published 2006. P.161. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf

The JMPR 2006 level is lower than the maximum HSNO requirement for daily exposures of 2mg/kg bw/day.[498]

The EPA has not set an Acceptable Daily Exposure (ADE) or a reference dose (RfD) for the active ingredient glyphosate. In 2004 the NZ EPA's predecessor, ERMA, set a potential daily exposure for a formulation, G-Force Max of 0.27mg/kg.

This may have the effect of minor use changes but not result in significant changes to reduce avenues of exposure that would protect the New Zealand community.

5.4 Outdated and arguably illegal – control regulations urgently require external review

The points listed here do not constitute the limit of problems within the control regulations.

a. Lifetime, chronic exposures commencing in utero are not considered

b. Failure to account for comorbidity (risk from multiple pathways)

c. Regulations 14-21 dealing with uncertainty may be unfit for the purposes of modern risk assessment. When were these regulations last applied and how are these 'uncertainties' applied for practical purposes?

d. Public policy and 'burden of proof' is vastly different to establishing 'scientific certainty'.

Absolute, or close to 95% level of certainty before regulators act to prevent exposures has been demonstrated to have resulted in a level of pollution, and/or public harm, that exerts profound and costly consequences to the populations concerned, frequently for years following.[499]

e. Sensitive populations all but ignored – an extra x10 uncertainty factor should be a minimum requirement to reduce risk during prenatal, neonatal, childhood and adolescent periods. (The current ADI of 1 must be divided by 10 in order to provide a margin of safety for babies and children).

f. Dose response mechanism unfit to assess for risk of adverse harm to the endocrine system where endocrine related effects at low doses may produce non-monotonic dose responses.

[498] Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001. Part 2. Sn. 12 http://www.legislation.govt.nz/regulation/public/2001/0117/latest/whole.html#DLM39688 12 (3)
[499] P. Grandjean. Only One Chance: How environmental pollution impairs brain development – and how to protect the brains of the next generation. Oxford University Press. 2013. ISBN 978-0-19-023973-2

The Hazardous Substances (Classes 6, 8, and 9 Controls) Regulations 2001 is outdated and requires urgent revision in order that the New Zealand public and environment are protected from adverse harm and retains trust in their regulators.

Internationally, a baseline safety/uncertainty factor of 100X is used to protect the public. That value includes a factor of 10 (10X) where laboratory animal data is used, as humans may have greater sensitivity to the pesticide than for example, rodents, and an additional factor of 10X to account for potential variations in sensitivity within the human population. An additional uncertainty value of 10X is recommended to protect infants and children, but is rarely applied.

While the Regulations use the descriptor ‘substance’ NZ EPA does not assess or control full formulation pesticide toxicity. It is worth considering that the active ingredient may, for example, constitute only 34% or 54% of the full formulation by volume. Science has demonstrated that the full formulation is more toxic than the active ingredient.[500] However regulators fail to acknowledge that the full formulation increases toxicity via synergistic effects, posing a significantly greater risk than the weaker 'active' ingredient.

There appears to be a lack of capacity within the NZ EPA to effectively monitor and manage regulation and relevant controls in the public interest. Current deficiencies within risk assessment provide evidence that the EPA and MPI may not have the competencies required to undertake effective administration of the HSNO and ACVM Acts according to the purposes and intent of these Acts.

6.0 How does the Agricultural Compounds and Veterinary Medicines Act 1997 affect a classification of ‘probable (or presumed) carcinogen’?

There appears to be no regulatory instrument in the Agricultural Compounds and Veterinary Medicines Act 1997 **(**ACVM Act) or its regulations that requires an immediate regulatory response should an agricultural compound which is a hazardous substance, be declared toxic and a probable or presumed carcinogen under the HSNO Act.

As the legislation describes, the Director General may call for reassessment if significant new information concerning the product is made available.

[500] Eg. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Mesnage R, Bernay B, Séralini GE Toxicology. 2013 Nov 16; 313(2-3):122-8.

The ACVM Act assesses and controls compounds to ensure Food Act maximum residue levels are not breached.[501] Legitimate expectations by the public for safe risk management derive from the purpose and intent of the Act.

6.1 Delving deeper into the Agricultural Compounds and Veterinary Medicines Act 1997

A hazardous substance must first be approved by the NZ EPA under the Hazardous Substances and New Organisms Act 1996[502] before it can be imported or manufactured in New Zealand. After this process, approval may be registered as an agricultural compound (which may be a hazardous substance and come under the HSNO Act, or may not), to be used (including imported, manufactured, or sold) under the Agricultural Compounds and Veterinary Medicines Act 1997. It is only after approval that an agricultural compound, such as an herbicide, can be used in New Zealand.

Approval may be granted for one or more agricultural compounds under the HSNO Act, while the ACVM Act registration will only cover a single agricultural compound.

The purpose of the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act) is to prevent or manage risks associated with the use of agricultural compounds regarding public health, trade in primary produce, animal welfare and agricultural security. The Act also ensures that the use of agricultural compounds does not result in breaches of domestic food residue standards and is intended to ensure the provision of sufficient consumer information about agricultural compounds.

ACVM Act states in Section 4A (5) that:

> *(1) This Act aims to achieve its purpose by providing that no agricultural compound may be used (including imported, manufactured, or sold) in New Zealand unless that use is authorised by or under this Act.*
>
> *(3) Allows for the Director General to impose a range of conditions to manage the risks associated with agricultural compounds when products are registered.*

[501] Agricultural Compounds and Veterinary Medicines Act 1997 Section 4A (5) (b) http://www.legislation.govt.nz/act/public/1997/0087/latest/whole.html#DLM415060
[502] Hazardous Substances and New Organisms Act 1996 http://www.legislation.govt.nz/act/public/1996/0030/latest/whole.html#whole

(5) Generally, the outcomes for which this Act regulates are those set under the other related Acts. For example:

(a) maximum residue limits for food products are set under the Food Act 2014; while

(b) the ACVM Act assesses and controls agricultural compounds to ensure the Food Act residue limit is not breached

Sections 29 and 30 provides that the Director-General may decide to reassess a trade name product or a group of trade name products with the same active ingredient and similar formulations if, in the opinion of the Director-General, significant new information on the provisionally registered trade name product has become available.

Section 31 where a decision has been made in accordance with section 29 or section 30 to reassess a registered trade name product or group of trade name products, the Director-General may, if he or she thinks fit, prohibit or restrict the importation, manufacture, sale, or use of that trade name product or group of trade name products until a decision is made section 21 or section 27.

Section 19 requires that risk and benefit to public health must be considered when making a decision under Section 21.

6.2 Adjuvants excluded – fitness for purpose does not mention harm to humans

Adjuvants are listed as exempt within Schedule 2, Part C of the Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations.[503]

Section 7 of the Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011[504] concerns fitness for purpose for exempt agricultural compounds – this includes adjuvants. The Regulations specify that

'An exempt agricultural compound that is imported, manufactured, or sold must be such that, when used as recommended, it will not—

(h) otherwise create or be likely to create any of the risks specified in section 4(a) of the Act.

[503] Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. Schedule 2. Part C. Exemptions for agricultural compounds used to manage plants or plant production (28)
http://www.legislation.govt.nz/regulation/public/2011/0327/latest/DLM3982848.html
[504] Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. http://www.legislation.govt.nz/regulation/public/2011/0327/latest/DLM3982848.html

Section 7 discusses fitness for purpose concerning toxicity and distress for animals but does not mention potential to harm to human populations or environment.

These exclusions may be of interest to specialists as there is no effort to monitor the public health impact of adjuvants used in the full formulation, as they are exempt (including POEA).

Yet it is clear that adjuvants act to enhance toxicity and have been separately found to be toxic. Adjuvants are included in pesticide formulations applied to food crops and pesticides applied in public spaces.

This exemption appears inconsistent with the purpose of the ACVM Act.

7.0 What are other regulators doing – and who applies best practice?

7.1 Best Practice: European Union.

The European Parliament has legislation that requires that if plant protection products receive a classification of category 1A or 1B, they cannot be approved for sale for use where residues exceed 0.01mg/kg. Importantly and unfortunately food is rarely tested for glyphosate residues.

Regulation (EC) No 1272/2008[505] of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures came into force January 2009 and implemented the Globally Harmonized System for the classification and labelling of hazardous chemical substances.[506]

European Regulation 1107/2009 (which repealed earlier directives 79/117/EEC and 91/414/EEC) in force since June 2011[507] introduced for the first time into the EU, 'cut-off' criteria.

Section 3.6 Impact on Human Health, provides that regarding human health, cancer and genotoxicity and mutagenicity, an active substance, safener or synergist ***shall only be approved*** if:

> *'it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as **mutagen category 1A or 1B**. EN 24.11.2009 Official Journal of the European Union L 309/41.'*

[505] Legislation Regulation (EC) No 1272/2008 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF

[506] http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587309/IPOL_STU(2016)587309_EN.pdf

[507] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

*'it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as **carcinogen category 1A or 1B**, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.'*

Paragraph (8) on page 309/2 of Regulation (EC) No 1272/2008 is worth noting:

'The purpose of this Regulation is to ensure a high level of protection of both human and animal health and the environment and at the same time to safeguard the competitiveness of Community agriculture. Particular attention should be paid to the protection of vulnerable groups of the population, including pregnant women, infants and children. The precautionary principle should be applied and this Regulation should ensure that industry demonstrates that substances or products produced or placed on the market do not have any harmful effect on human or animal health or any unacceptable effects on the environment.'

NB: European Regulation 1107/2009 which contains cut-off criteria also contains 'wriggle room' to retain an approval for use if exposure is negligible:

'other approval criteria (carcinogens, toxic for reproduction and endocrine disruptors) have a strong hazard-component, but they can be authorised if under realistic conditions of use the exposure is negligible.'[508]

Annex II includes the requirement assessments thoroughly investigate the toxicity of safeners and synergists and understand toxicity relating to carcinogenicity, endocrine disruption etc, fate in water, and that the commercial product should be assessed for toxicity by at least one Member State.[509]

[508] XVIIIth CEUREG Forum 16-17 October 2014, Poznan, Poland Update on Regulation (EC) No 1107/2009 XVIIIth CEUREG Forum 16-17 October 2014, Poznan, Poland Wolfgang Reinert and Jeroen Meeussen European Commission DG SANCO (Health and Consumers Directorate-General) Unit Chemicals, contaminants, pesticides.
http://www.ceureg.com/18/docs/presentations/1_Wolfgang%20Reinert_EC.pdf

[509] Regulation 1107/2009, Annex II, 2.1 General Decision-Making Criteria.
http://exporthelp.europa.eu/update/requirements/ehir_eu12_02v002/eu/auxi/eu_chemkt_ppp_annex2.pdf

European legislation is light years ahead of New Zealand, and while not perfect, by allowing for uncertainty factors, focussing on the vulnerable groups and setting much lower levels in drinking water, it is demonstrating a progressive attitude to environmental health that neither the NZ EPA nor the JMPR has yet had the resources or inclination to consider.

7.2 World Health Organization and Food and Agriculture Organization Joint Meeting on Pesticides Residues Toxicological Evaluations. (JMPR)

If a pesticide is declared unsafe for human consumption the ADI may be withdrawn. This rarely happens and may not have occurred in the previous twenty years.[510]

The JMPR evaluations rely on data supplied by trade and industry and may appear to place priority on trade, rather than health based considerations. Where there are safety concerns, the JMPR may lower recommended maximum residue levels, but will rarely recommend a product is too dangerous for use.

The JMPR toxicological evaluations for DDT (2000) and Endosulfan (1998) are illustrative of an instance where chemicals were considered highly toxic by other regulators, while the JMPR maintained that continued use would be safe. JMPR reticence to effectively act in the public interest may reflect the fact that the JMPR are not required to use the precautionary principle in the face of uncertainty.

Toxicological evaluations undertaken by the JMPR may be considered highly conservative if not weak, and at risk of criticism of industry bias for public health purposes.

7.3 Subtleties in definition: Genotoxicity or Mutagenicity

The NZ EPA cites the UN 2007 definition of a carcinogen:

'A chemical substance or mixture of chemical substances that induce cancer or increase its incidence. Substances that have induced benign and malignant tumours in well-performed experimental studies on animals are considered to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.'

[510] Eg. Inventory of IPCS and other WHO pesticide evaluations and summary of toxicological evaluations performed by the Joint Meeting on Pesticide Residues (JMPR) through 2009. http://www.who.int/ipcs/publications/jmpr/pesticide_inventory_edition10.pdf

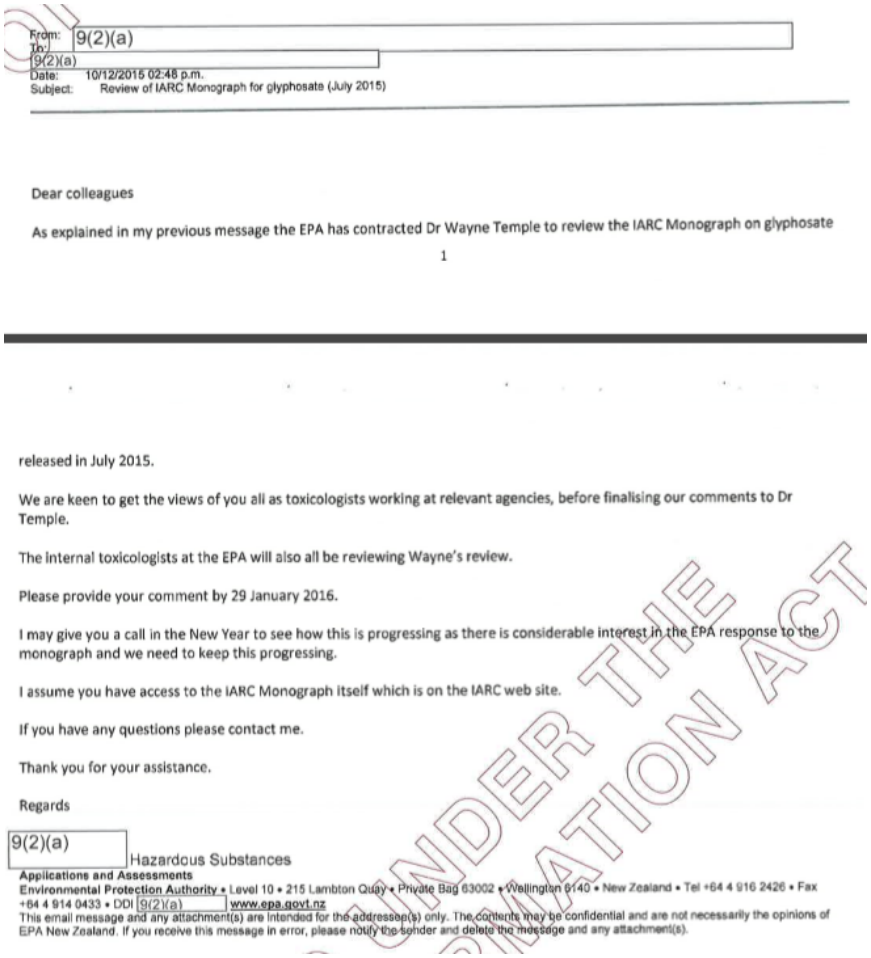
The IARC Monograph concerned evidence that glyphosate was probably carcinogenic, operating through two key characteristics of genotoxicity and oxidative stress. Genotoxicity is defined by the NZ EPA as *'Alterations to the structure, information content, or segregation of DNA.'*

NZ EPA appears to require assessment of carcinogenicity and mutagenicity. Mutagenicity is defined by the NZ EPA as *'A permanent change in the amount or structure of the genetic material in a cell.'*

Arriving at a declaration of 'mutagenicity' requires a higher bar of evidence, or 'proof'. Frequently toxicity at lower levels is harmful, but the harder-to-achieve 'mutagenicity' classification can result in harmful products staying on the market, while regulators taking into account 'uncertainty' might restrict a product at an earlier stage. Concerned citizens may consider the IARC focus on carcinogenicity and genotoxicity to represent a safer and more precautionary risk to the population.

APPENDIX VI Correspondence between NZ EPA and the Ministry of Health

Email from NZ EPA to the Ministry of Health, December 10, 2015, requesting views of 'toxicologists working at relevant agencies.'



From: 9(2)(a)
To: 9(2)(a)
Date: 10/12/2015 02:48 p.m.
Subject: Review of IARC Monograph for glyphosate (July 2015)

Dear colleagues

As explained in my previous message the EPA has contracted Dr Wayne Temple to review the IARC Monograph on glyphosate

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released in July 2015.

We are keen to get the views of you all as toxicologists working at relevant agencies, before finalising our comments to Dr Temple.

The internal toxicologists at the EPA will also all be reviewing Wayne's review.

Please provide your comment by 29 January 2016.

I may give you a call in the New Year to see how this is progressing as there is considerable interest in the EPA response to the monograph and we need to keep this progressing.

I assume you have access to the IARC Monograph itself which is on the IARC web site.

If you have any questions please contact me.

Thank you for your assistance.

Regards

9(2)(a) Hazardous Substances

Applications and Assessments
Environmental Protection Authority • Level 10 • 215 Lambton Quay • Private Bag 63002 • Wellington 6140 • New Zealand • Tel +64 4 916 2426 • Fax +64 4 914 0433 • DDI 9(2)(a) www.epa.govt.nz

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Response from the Ministry of Health to NZ EPA, January 12 2016, expressing caution at challenging an IARC decision.

9(2)(a)

From: 9(2)(a)
Sent: Tuesday, 12 January 2016 11:48 a.m.
To: 9(2)(a)
Cc:
Subject: Re: Review of IARC Monograph for glyphosate (July 2015)
Attachments: Glyphosate_Review_Temple_Draft_3.11.2015.doc

Hi 9(2)(a)

Thank you for sending Dr Wayne Temple's report and seeking the Ministry's view about the findings of his review. In order for us to meaningfully comment on his report we need to review the various articles that Wayne has considered in reaching his conclusions. Similarly, we may need to review as well the articles that IARC has reviewed in classifying glyphosate as a Group 2A carcinogen. This is a bigger commitment than originally anticipated when agreeing to review the report and we are unable to undertake the review due to our limited resources. I note that one of Wayne's criticisms is the IARC report "ignores an abundance of papers showing that glyphosate is not carcinogenic" - the preamble to the monograph which is generic to all IARC monographs clearly outlines how IARC selects studies that are pertinent to the evaluation of carcinogenicity.

Given the international standing of IARC and the expertise and methodology used to undertake these classifications, the Ministry of Health would be reluctant to criticise any classification based on the review of one individual. This would also be seen as a precedent for other classifications and other advice from WHO and its supporting organisations. If the EPA wishes to review or challenge the IARC classification, this would need to be carefully considered, with a detailed methodology and undertaken by an appropriate range of experts recognised in their relevant fields.

I note that EFSA considered the findings from the IARC regarding the potential carcinogenicity of glyphosate or glyphosate-containing plant protection products in the on-going peer review of the active substance and "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 according to Regulation (EC) No 1272/2008.".

I'm sorry I can't be of further assistance.

Kind regards

9(2)(a)
Environmental & Border Health
Public Health
Clinical Leadership
Protection & Regulation
Ministry of Health
DDI: 9(2)(a)
http://www.health.govt.nz
mailto: 9(2)(a)

APPENDIX VII Parliament's Local Government and Environment Select Committee 8 December 2016

NZ EPA CEO Dr Allan Freeth responses to questions during the Annual Review 2015/16 Environmental Protection Authority.

Browning	The reassessments—and you mentioned triclosan and glyphosate for example—and I've put in a petition of 6,000 people the other day on the neonics generally. I think you've done two reassessments in the last year, from memory, on the report, and I've been involved with several over the years and I realise they're big exercises. What's your budget for it, and why would you expect private individuals to be paying $50,000 to do a triclosan?
Freeth	So let's put some numbers in context out here, and I'll explain what they're doing about the reassessments. There are around 150,000 substances in New Zealand, made up of 28,000 chemicals that are on the registry. That's divided into 210 group standards based on hazard or on use.
Browning	You're talking about something that's in every home, probably?

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TRANSCRIPT: 2015/16 ANNUAL REVIEW ENVIRONMENTAL PROTECTION AGENCY

Transcript continues next page:

Freeth Of those 150,000, 300 have been identified as of substances of concern, that we're concerned about, and they are rated according to risk. We're just doing the review now on the basis of toxicity, use, volumes, and the geographic aspect of it. We had a budget, originally, of $300,000 per annum to do a number of reassessments. We're in the process of appointing, through cost-savings internally from baseline, one senior scientist and one analyst to begin to form a reassessment plan to begin a new program of reassessments. However, that will be limited.

The Minister has encouraged us to talk in the new NRS round for a Budget bid for further money for reassessments to take that through. The reassessment process, which people misunderstand—and I'll come to your question about funding. There are two stages to it: grounds for assessment, which is a very low threshold, easy to get through. So I have a number of chemicals that have grounds for reassessment that I can tell you we won't reassess probably in the next 5 years.

Browning You've got a list of how many in your—

Freeth We're changing that list as we speak because the list was based on pesticides, 30 very bad pesticides, that we're concerned about. So someone gets grounds, like triclosan, for reassessment. I then look at that and ask the scientists to give me a risk profile relative to everything else in the list. And that's why we say we're not going to get to it—relatively, it's of a very low risk for us, compared to all the others in front of us. One of the issues that we're talking to the Minister about is changing some amendments to the Act so we can rely on overseas jurisdictions, because it won't take 100 years to get through 300 substances.

Prendergast Can I just say, to correct you, Steffan, six reassessments in the year we're talking about, and the EPA—six and it's [*Inaudible* **10:44:47**] 22 since—

Browning I was probably looking at notified for reassessment—

Freeth All reassessments are notified.

Prendergast They're all notified, but you said there were only 2. There were 6.