Glyphosate: No Safe Level

2016 Report

Get glyphosate off the streets

Pathways of Toxicity – the published and peer reviewed literature that demonstrates there is no safe level of exposure to glyphosate or its formulations.

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Introduction

Increasing evidence of potential and realised harm from glyphosate based herbicides (GBH), the most well-known of which is Roundup, has been reported in recent years, and publication of new research reports or regulatory considerations appear monthly. This increasing weight of evidence and public awareness raises concern about the widespread use of glyphosate in our streets, parks and gardens, agricultural crops and, as a result, in our diets.

I have commissioned this report to bring together some of the peer-reviewed evidence available to support the call for glyphosate based herbicides to be removed from our immediate environment – reducing exposure in our communities, especially the vulnerable including our children. Removing GBH from streets and parks is an actionable and necessary first step.

The studies in this report have not been reviewed by the New Zealand Environmental Protection Authority (EPA). The last document containing studies examined by the EPA was a 2009 Decision Document, in which all studies were submitted by DowAgroscience. The NZ EPA has not consulted any published peer reviewed science submitted independently of the pesticides industry in regards to risk assessment for toxicity of glyphosate based herbicides.

In the twenty first century we have the technology to assess pesticides for toxicity to our endocrine and body systems at the low levels we are exposed to. We also have the technology to assess glyphosate-based herbicides in their full formulations, not just their separate ingredients, which are currently not evaluated. The international regulators who undertake international risk assessment do not assess low level, sub-lethal risk. The small selection of studies listed here helps demonstrate that glyphosate based herbicides pose far more risk to the human population than regulators such as the NZ EPA have effectively considered. Independent scientists now consider that there is no known safe exposure level of glyphosate and its commercial

formulations, and that there is a divergence of regulatory decisions from scientific evidence.

This report outlines evidence of just 12 major harm concerns relating to glyphosate based herbicides. It is compelling and concerning.

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New Zealand EPA: Seller sponsored studies exclusively used

The NZ EPA uses toxicological endpoints for assessing toxicity of new pesticides and approving them. These are based on a selection of toxicity studies that give a considered 'safe' NOEL/NOAEL (no observable effect level and no observable adverse effect level). These studies are critical in revealing what toxic levels affect the study subject, and how dangerous the pesticide is. These studies help define how much we can be exposed to, ie, what the application rate is, how much can be sprayed on our food per acre, and what our permitted residues.

In 2009, ERMA (the predecessor to EPA) approved the use of GF-1280, a herbicide containing glyphosate as its main ingredient, for importation and manufacture with controls by Dow AgroSciences. This decision has since been used by the EPA to inform subsequent applications for glyphosate rather than assessing each application and the uses for the herbicide in its own context. GF-1280 is now used as the 'decision document' proving reference points for toxicological safety of glyphosate in New Zealand.

The EPA note: 'This substance is used in similar ways to other glyphosate-containing herbicides and so the risks associated with these other substances are considered to be similar to the risks associated with the use of GF-1280. Decisions made on more recent glyphosate-containing substances have therefore been primarily based on the findings of the risk assessment performed for GF-1280'.[1]

All studies were submitted by DowAgroscience.[2] The NZ EPA has not consulted any published peer reviewed science submitted independently of

[1] Email from Stuart Creton, Snr Advisor, Hazardous Substances, Environmental Protection Agency to Jodie Bruning, Researcher
[2] Ibid

the pesticides industry in regards to risk assessment for toxicity of glyphosate based herbicides.

International Assessment – Outdated and predominantly seller-sponsored

a. World Health Organisation

The New Zealand Ministry for Primary Industries Food Safety glyphosate information page states that 'MPI agrees with the conclusion of the Joint Food and Agriculture Organization/World Health Organization Meeting on Pesticide Residues (JMPR) that glyphosate is of "very low toxicity".

The page advises that 'MPI will review its position on glyphosate in 2016 after a new JMPR report on the herbicide is released.'

The 2016 JMPR glyphosate report may face the most scrutiny of any pesticide toxicity assessment to date. Scientists and health based professionals will be keenly watching this process to ensure that the JMPR follow study criteria selection used by the 2015 WHO International Agency for Research on Cancer (IARC) review of glyphosate (discussed in section 1. Glyphosate probably causes cancer). The IARC criteria advised that only 'reports that have been published or accepted for publication in the openly available scientific literature' and 'data from governmental reports that are publicly available'.[3]

The Joint World Health Organization (WHO) /Food and Agriculture Organization (FAO) Meeting on Pesticide Residues (JMPR) 2004 Toxicological Evaluations used studies supplied by glyphosate producers and marketers to arrive at the No Observable Effect Level

[3] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Preamble.

(NOAEL), a level used to establish the acceptable daily intake (ADI), while published data was excluded.[4]

The new WHO glyphosate ADI resulting from the 2004 assessment was from an already decade old, unpublished corporate study: Atkinson et al 1993b. This 2-year study in rats (salivary gland effects) became the NOAEL that established the ADI of 1.0mg/kg bw (pp127-129). The private, unpublished ten-year-old study was submitted to WHO by Cheminova A/S, Lemvig, Denmark.

The 2011 JMPR glyphosate toxicological[5] evaluation consisted of a smaller Addendum - and small selection of unpublished, privately held studies were submitted to WHO by E.I. du Pont de Nemours and Company, Wilmington, DE, USA. Recently published papers held in the public domain were not included[6].

The 2004 risk assessment[7] dismisses tumours at the levels declared safe, due to the effects not being 'dose dependent'. Frequently animals were excluded from examination and effects are dismissed (by industry contracted laboratories), using terminology as follows: 'Studies at termination found no lesions attributable to treatment'; 'in the absence of a clear dose–response relationship, these were considered to have occurred by chance' and 'No adverse effects were seen at examination post mortem and no histopathological changes attributable to compound were found.'

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[4] Pesticide Residues in Food. Joint FAO WHO Meeting. 2004 Evaluations. http://apps.who.int/iris/bitstream/10665/43624/1/9241665203_eng.pdf

ADI is arrived at by dividing the NOAEL by a safety, or uncertainty factor of 100. P.160.

[5] WHO Toxicological Evaluations 2011 Glyphosate addendum

[6] Ibid

[7] http://www.inchem.org/documents/jmpr/jmpmono/v2004pr01.pdf

However these studies are held privately (unlike published research) and unavailable for public examination.[8]

b. US Environmental Protection Agency

The US EPA has been conducting a Reregistration Review of glyphosate. Commencing in 2009, this is a six year process with the final decision due in 2015. The decision may have been delayed as the US EPA take into account the IARC glyphosate decision.

The previous 1993 Reregistration used a limited range of industry selected and sponsored unpublished studies to arrive at toxicity endpoints. [9] There is significant national pressure to ensure that open scientific literature is incorporated in the review.

The current Review received a wide range of submissions/comments citing published scientific literature from concerned organisations. [10] Since submissions closed September 21, 2009, a significant proportion of new data has been published and should be consulted by the authorities, including sub-chronic, long term toxicity and endocrine disruption potential.

c. European Commission – European Food Safety Authority (EFSA)

As of November 2015 the European Food Safety Authority (EFSA) released its conclusion on glyphosate. EFSA concluded that glyphosate is unlikely

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[8] http://www.safesayswho.com/faowho-studies-on-reproductive-and-developmental-toxicity-of-glyphosate-how-we-get-to-the-codex-decisions-on-adi-and-residue-limits-in-food-and-animal-feed/

[9] September 1993 Glyphosate Reregistration Elegibility Decision (RED)

[10] Registration Review; Glyphosate Docket Opened for Review and Comment. Date Posted: Jul 22, 2009. Federal Register Number: E9-17404. This document is contained in EPA-HQ-OPP-2009-0361. 29 Comments (submissions).

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. EFSA also advised a permitted increase in ADI from .3mg/kg to .5mg/kg. [11] The background documents advise that a 19 year old unpublished study formed the NOAEL that EFSA. [12]

European organisations are deeply concerned that EFSA has ignored the published literature that indicates glyphosate may be toxic to human systems at very low levels of exposure. PAN Europe call it an 'un-scientific opinion' - and PAN Europe's Chemicals Officer Hans Muilerman noted *"in case of doubt they (EFSA) give the advantage of the doubt to industry instead of giving priority to the protection of human health and the environment".* [13]

Two papers have critiqued the fact that the report that contains the data for the European reassessment, the Renewal Assessment Report (RAR) by German Federal Institute for Risk Assessment (BfR), are missing relevant studies, and have failed to include recently published relevant studies. [14] The EFSA reassessment excluded much published, peer reviewed scientific literature, including studies for genotoxicity. Toxicologist Dr. Peter Clausing noted: *'Deficiencies include neglect and wrong description of important scientific publications, lack of applying up-to-date statistical analyses to the data provided by industry and false statements about historical control data'.*

The papers conclude that the RAR has failed to account for the more toxic effects of the full formulation of glyphosate based herbicides; and that

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[11] Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA Journal 2015;13(11):4302.
[12] Final addendum to the Renewal Assessment Report. October 2015
[13] EFSA's (un-)scientific opinion: glyphosate not a carcinogen. *Thursday, November 12, 2015*
[14] The Glyphosate Renewal Assessment Report: An Analysis of Gaps and Deficiencies. Dr. Peter Clausing
Testbiotech comment on the German Renewal Assessment Report (RAR) on the active ingredient glyphosate. Andreas Bauer-Panskus, Testbiotech October 2014

there is lack of enquiry into glyphosates potential to exert subchronic toxicity, long-term toxicity, genotoxicity, endocrine and ecotoxic effects.

The State of Science in 2015

In the twenty first century we have the technology to assess pesticides for toxicity to our endocrine and body systems at the low levels the human population is exposed to. We also have the technology to assess the wide ranging toxicological impact of the entire herbicide in its full formulation, for example Roundup as opposed to just testing glyphosate. The international regulators who undertake international risk assessment do not assess low level, sub-lethal risk. The small selection of studies listed here help demonstrate that glyphosate-based herbicides pose far more risk to the human population than regulators such as the NZ EPA consider. Currently available, published and peer-reviewed science clearly illustrates that the New Zealand governments stance, as per the WHO/FAO stance of 'very low toxicity' is based on an outdated and narrow mode of assessment.

Independent scientists now consider that there is no known safe exposure level of glyphosate and its commercial formulations and that there exists, in fact today, 'a divergence of regulatory decisions from scientific evidence.'[15]

Today, international and government regulators use OECD and industry set criteria that require Good Laboratory Practice (GLP) compliance. These requirements are frequently used by regulators to exclude peer reviewed and published academic studies. Unfortunately the unpublished and raw data presented to regulators are never made public, nor subject to peer scrutiny.

Independent scientists take into account the latest advances in basic science in study design, for example low dose endocrine disruptive effects[16], which regulators choose to ignore, 20 years after endocrine disruption was

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[15] Antoniou M, Habib MEM, Howard CV, Jennings RC, Leifert C, et al. (2012) Teratogenic Effects of Glyphosate-Based Herbicides: Divergence of Regulatory Decisions from Scientific Evidence. J Environ Anal Toxicol S4:006. doi: 10.4172/2161-0525.S4-006

[16] http://www.i-sis.org.uk/Banishing_Glyphosate.pdf

introduced as a health concern. Therefore independent studies can result in far more meaningful results in terms of toxic effects from chemicals at real world levels of exposure. It is the twenty first century, and regulatory dismissal of academic studies is not in accord with good and appropriate scientific practice.

The science presented here, not considered by the NZ EPA, covers twelve areas of interest. It is important to note that many sections cross over with each other, as our mammalian and environmental systems frequently interrelate in complex, unforeseen, and at times unknown ways.

1. Glyphosate probably causes cancer

2. Glyphosate is genotoxic at sub-lethal concentrations

3. Glyphosate is a hormone damaging endocrine disruptor at levels not studied in risk assessment

4. Glyphosate contributes to infertility, birth defects & other negative impacts on the reproductive system

5. Glyphosate contributes to digestive illness, gut disruption & nutrient deficiencies

6. Glyphosate-based herbicides can exert worrying effects on antibiotics

7. Glyphosate is neurotoxic at sub-lethal concentrations

8. How glyphosate affects organs: Damaged kidneys to arrhythmia.

9. Glyphosate's off-target adverse effects: From pollinators to skinks

10. Roundup is more toxic than glyphosate by itself.

11. Glyphosate's effect on groundwater

12. We don't know the safe level of glyphosate. Neither Glyphosate nor Roundup has ever been assessed by regulators at sub-lethal concentrations.

1. Glyphosate probably causes cancer

20 March 2015: The WHO International Agency for Research on Cancer (IARC) working group declared glyphosate a probable carcinogen in the paper 'Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate.'[17]

The IARC determined that glyphosate probably causes cancer (Category 2A) on the basis of 'limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals.' The IARC concluded that glyphosate operates in through two key characteristics of human carcinogens – there is strong evidence that:

1. Glyphosate and glyphosate formulations are genotoxic,
2. Glyphosate and its metabolite AMPA, and glyphosate formulations cause oxidative stress.

Criteria for data inclusion in the IARC required that only 'reports that have been published or accepted for publication in the openly available scientific literature' and 'data from governmental reports that are publicly available'. Today most science supplied to governments for regulatory and risk assessment purposes are unpublished and unavailable for review by the public.[18]

Further, a WHO taskforce established to evaluate the IARC findings concluded September 2015 that the IARC *referred to a significant amount of published peer reviewed scientific literature that had not been evaluated* by the most recent 2011 WHO JMPR evaluation (GLYPHOSATE (addendum) 375–388 JMPR 2011).

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[17] World Health Organisation International Agency for Research on Cancer (IARC) Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. 20 March 2015. Complete IARC Monograph Volume 112-02.

[18] http://www.theguardian.com/science/political-science/2015/may/13/chemical-reactions-glyphosate-and-the-politics-of-chemical-safety

The section above noted that the WHO 2011 evaluation comprised a limited range of studies supplied by DuPont.[19]

A selection of studies reviewed in the IARC Glyphosate Monograph Vol 112[20]:

DNA damage, or genotoxicity has been found in workers and children living near sprayed regions.

Paz-y-Miño C, Sánchez ME, Aréval M, Muñoz MJ, Witte T, De la Carrera GO and Leone PE. Evaluation of DNA damage in an Ecuadorian population exposed to glyphosate. Genet Mol Biol 2007, 30, 456-60.

Bolognesi C, Carrasquilla G, Volpi S, Solomon KR and Marshall EJ. Biomonitoring of genotoxic risk in agricultural workers from five Colombian regions: association to occupational exposure to glyphosate. J Toxicol Environ Health A 2009, 72, 986-97.

Bernari N, Gile N, Mañas F, Méndez Á, Gorla N snd Aiassa D. Assessment of the level of damage to the genetic material of children exposed to pesticides in the province of Córdoba. Arch Argen Pediatr 2015, 113, 126-32.

Human epidemiological studies confirm glyphosate is a cancer risk:

1. Exposure of pesticide applicators to glyphosate herbicide formulations was associated with higher incidence of multiple myeloma.

   De Roos AJ, Blair A, Rusiecki JA, et al. Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study. Env Health Perspect. 2005;113:49-54.

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[19] World Health Organisation International Agency for Research on Cancer (IARC) Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. 20 March 2015. Complete IARC Monograph Volume 112-02.

[20] World Health Organisation International Agency for Research on Cancer (IARC) Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. 20 March 2015. Complete IARC Monograph Volume 112-02.

2. Epidemiological studies conducted in Sweden found that exposure to glyphosate herbicide was linked with a higher incidence of non-Hodgkin lymphoma.

   Hardell L, Eriksson M. A case-control study of non-Hodgkin lymphoma and exposure to pesticides. Cancer. 1999;85:1353-1360. doi:10.1002/(SICI)1097-0142(19990315)85:6<1353::AID-CNCR19>3.0.CO;2-1.

   Hardell L, Eriksson M, Nordstrom M. Exposure to pesticides as risk factor for non-Hodgkin lymphoma and hairy cell leukemia: Pooled analysis of two Swedish case-control studies. Leuk Lymphoma. 2002;43:1043-1049.

   Eriksson M, Hardell L, Carlberg M, Akerman M. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. Int J Cancer. 2008;123:1657-1663. doi:10.1002/ijc.23589. *'Our study confirmed an association between exposure to phenoxyacetic acids and NHL and the association with glyphosate was considerably strengthened'.*

Studies have demonstrated that while a single dose may not cause chromosomal aberrations in the bone marrow of rats, mice dosed with a glyphosate based formulation revealed chromosomal aberrations in the bone marrow.

Li AP, Long TJ. An evaluation of the genotoxic potential of glyphosate. Fundam Appl Toxicol. 1988 Apr;10(3):537-46.

Prasad S, Srivastava S, Singh M, and Shukla Y, "Clastogenic Effects of Glyphosate in Bone Marrow Cells of Swiss Albino Mice," Journal of Toxicology, vol. 2009, Article ID 308985, 6 pages, 2009. doi:10.1155/2009/308985

A 2013 study confirmed the carcinogenic potential of Roundup herbicide using human skin cells (HaCaT) exposed to extremely low concentrations of Roundup.

George J, Shukla Y. Emptying of Intracellular Calcium Pool and Oxidative Stress Imbalance Are Associated with the Glyphosate-Induced Proliferation in Human Skin KeratinocytesHaCaT Cells. ISRN Dermatol. 2013 Aug 29;2013:825180. doi: 10.1155/2013/825180. eCollection 2013.

Glyphosate can induce DNA adducts in the liver of mice, while glyphosate formulations can cause a slight increase in the DNA adducts of the kidney. Glyphosate formulations can cause DNA strand breaks in the liver and kidney.

Bolognesi C, Bonatti S, Degan P, Gallerani E, Peluso M, Rabboni R, Roggieri P, and Abbondandolo A. Genotoxic Activity of Glyphosate and Its Technical Formulation Roundup. Centro Nazionale per lo Studio dei Tumori di Origine Ambientale, Istituto Nazionale per la Ricerca sul Cancro, Largo Rosanna Benzi 10, 16132 Genova, Italy J. Agric. Food Chem., 1997, 45 (5), pp 1957–1962 DOI: 10.1021/jf9606518

2. Glyphosate is genotoxic at sub-lethal concentrations

The IARC concluded that there is 'strong evidence for genotoxicity.'[21] Genotoxic chemicals damage our DNA and can cause mutations or cancer – at the low levels regulators never scrutinise. Professor Christopher Portier, one of the co-authors IARC report, said at a scientific briefing in London: "Glyphosate is definitely genotoxic. There is no doubt in my mind."

Roundup is cytotoxic and DNA-damaging to human epithelial cells following short exposure at environmentally relevant concentrations.

[21] IARC Monograph Glyphosate Vol112 Pp 77-78.

Roundup is more toxic than glyphosate.
Koller VJ, Fürhacker M, Nersesyan A, Mišík M, Eisenbauer M, Knasmueller S. Cytotoxic and DNA-damaging properties of glyphosate and Roundup in human-derived buccal epithelial cells. Arch Toxicol. 2012 May;86(5):805-13. doi: 10.1007/s00204-012-0804-8. Epub 2012 Feb 14.

Genotoxicity: Glyphosate & its formulations - Aquatic organisms & off-target effects.

Roundup poses a genetic hazard to fish and contributes to long lasting damage.
Moreno NC, Sofia SH, Martinez CB. Genotoxic effects of the herbicide Roundup Transorb and its active ingredient glyphosate on the fish Prochilodus lineatus. Environ Toxicol Pharmacol. 2014 Jan;37(1):448-54. doi: 10.1016/j.etap.2013.12.012. Epub 2013 Dec 31.

Agrochemicals (including GBH) inflict primary genotoxic damage at the DNA level at sublethal concentrations, regardless of the exposure time of the aquatic organisms under study
Vera-Candioti J, Soloneski S, Larramendy ML. Single-cell gel electrophoresis assay in the ten spotted live-bearer fish, Cnesterodon decemmaculatus (Jenyns, 1842), as bioassay for agrochemical-induced genotoxicity. Ecotoxicol Environ Saf. 2013 Dec;98:368-73. doi: 10.1016/j.ecoenv.2013.08.011. Epub 2013 Sep 5.

Results demonstrated that 48% glyphosate formulations (Panzer & Credit) - can be considered as glyphosate-based commercial formulations with genotoxic but not cytotoxic effect properties.
Vera-Candioti J 1 , Soloneski S, Larramendy ML. Evaluation of the genotoxic and cytotoxic effects of glyphosate-based herbicides in the ten spotted live-

bearer fish Cnesterodon decemmaculatus (Jenyns, 1842). Ecotoxicol Environ Saf. 2013 Mar;89:166-73. doi: 10.1016/j.ecoenv.2012.11.028. Epub 2012 Dec 25.

Sub-lethal concentrations induced DNA damage. Induction of oxidative was evidenced by increased lipid peroxidation level, while antioxidants namely superoxide dismutase, catalase and glutathione reductase responded in a concentration dependent manner.
Nwani CD, Nagpure NS, Kumar R, Kushwaha B, Lakra WS. DNA damage and oxidative stress modulatory effects of glyphosate based herbicide in freshwater fish, Channa punctatus. Environ Toxicol Pharmacol. 2013 Sep;36(2):539-47. doi: 10.1016/j.etap.2013.06.001. Epub 2013 Jun 7.

Newly hatched frogs were found to be more vulnerable to glyphosate formulations with clear evidence of cytotoxicity and DNA damage.
Meza-Joya FL, Ramírez-Pinilla MP, Fuentes-Lorenzo JL. Toxic, cytotoxic, and genotoxic effects of a glyphosate formulation (Roundup®SL-Cosmoflux®411F) in the direct-developing frog Eleutherodactylus johnstonei. Environ Mol Mutagen. 2013 Jun;54(5):362-73. doi: 10.1002/em.21775. Epub 2013 Apr 26

Roundup at environmentally relevant concentrations has lethal and genotoxic impact on E. cyanophlyctis; which may have long-term fitness consequence to the species.
Yadav SS, Giri S, Singha U, Boro F, Giri A. Toxic and genotoxic effects of Roundup on tadpoles of the Indian skittering frog (Euflictis cyanophlyctis) in the presence and absence of predator stress. Aquat Toxicol. 2013 May 15;132-133:1-8. doi: 10.1016/j.aquatox.2013.01.016. Epub 2013 Feb 8.

This study confirmed the genotoxic potential of this herbicide, oxidative damage was implicit as an important mechanism of genetic damage. The ability of DNA to repair was susceptible to inhibitory actions during the exposure period.
Marques A, Guilherme S, Gaivão I, Santos MA, Pacheco M. Progression of DNA damage induced by a glyphosate-based herbicide in fish (Anguilla anguilla) upon exposure and postexposure periods--insights into the mechanisms of genotoxicity and DNA repair. Comp Biochem Physiol C Toxicol Pharmacol. 2014 Nov;166:126-33. doi: 10.1016/j.cbpc.2014.07.009. Epub 2014 Aug 9.

Roundup induced oxidative DNA damage (pyrimidine bases oxidation) following short term exposure.
Guilherme S, Santos MA, Gaivão I, Pacheco M. Are DNA-damaging effects induced by herbicide formulations (Roundup® and Garlon®) in fish transient and reversible upon cessation of exposure? Aquat Toxicol. 2014 Oct;155:213-21. doi: 10.1016/j.aquatox.2014.06.007. Epub 2014 Jul 9.

It's not just glyphosate that is genotoxic, the adjuvants in the full formulation of Roundup can also be genotoxic. POEA can cause effects at various levels, such as hemolysis, DNA damage and lipid peroxidation, which are directly related to an imbalance in the redox state of the fish.
Navarro CD, Martinez CB. Effects of the surfactant polyoxyethylene amine (POEA) on genotoxic, biochemical and physiological parameters of the freshwater teleost Prochilodus lineatus. Comp Biochem Physiol C Toxicol Pharmacol. 2014 Sep;165:83-90. doi: 10.1016/j.cbpc.2014.06.003. Epub 2014 Jun 20.

Transorb herbicide is mutagenic and genotoxic to P. reticulate. This effect could be attributed to a combination of compounds contained in the

formulation with the active ingredient glyphosate.
De Souza Filho J, Sousa CC, Da Silva CC, De Sabóia-Morais SM, Grisolia CK. Mutagenicity and genotoxicity in gill erythrocyte cells of Poeciliareticulata exposed to a glyphosate formulation. Bull Environ Contam Toxicol. 2013 Nov;91(5):583-7. doi: 10.1007/s00128-013-1103-7. Epub 2013 Sep 17.

Male guppies exposed to Roundup showed a poorer sperm quality, measured as reduced plasmatic membrane integrity, mitochondrial functionality, DNA integrity, motility, motility period and concentration of spermatic cells, than those kept under control condition (no Roundup addition to the water).
Harayashiki CA, Varela AS Jr, Machado AA, Cabrera Lda C, Primel EG, Bianchini A, Corcini CD. Toxic effects of the herbicide Roundup in the guppy Poecilia vivipara acclimated to fresh water. Aquat Toxicol. 2013 Oct 15;142-143:176-84. doi: 10.1016/j.aquatox.2013.08.006. Epub 2013 Aug 21.

Different formulations of pesticides can create a cocktail effect and increase the genotoxic impact of pesticides and pesticide mixtures. For example atrazine and glyphosate enhanced cytogenic activities.
Roustan A, Aye M, De Meo M, Di Giorgio C. Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation products before and after photoactivation. Chemosphere. 2014 Aug;108:93-100. doi: 10.1016/j.chemosphere.2014.02.079. Epub 2014 Apr 12.

Significant ($p < 0.01$) genetic damage was observed in vivo and in vitro in all cell types and organisms tested. Glyphosate is genotoxic in the cells and organisms studied at concentrations of 0.7-7 µM.
Alvarez-Moya C, Silva MR, Ramírez CV, Gallardo DG, Sánchez RL, Aguirre AC, Velasco AF. Comparison of the in vivo and in vitro genotoxicity of glyphosate

isopropylamine salt in three different organisms. Genet Mol Biol. 2014 Mar;37(1):105-10. Epub 2013 Feb 28.

3. Glyphosate is a hormone-damaging endocrine disruptor at levels not studied in risk assessment

In these studies, Roundup is shown to disrupt the way we make our sex hormones. It reduces testosterone levels as well as increases levels of aromatase, an enzyme complex that converts testosterone into oestrogen and altered hormones that affect growth, sexual development and reproduction.

The following quote can be attributed to Benachour et al 2007 – however in numerous cases this quote expresses the findings of study authors: *Effects are more dependent on the complete formulation they are contained in than glyphosate alone. Chemical mixtures in formulations appear to be underestimated regarding their toxic or hormonal impact.*[22]

Roundup may effect human reproduction and fetal development. Human cell endocrine disruption was detected at 0.5ppm. Aromatase transcription and activity were disrupted from 10 ppm. Cytotoxic effects started at 10 ppm and DNA damages at 5 ppm.

Gasnier C, Dumont C, Benachour N, Clair E, Chagnon MC, Séralini GE. Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology. 2009 Aug 21;262(3):184-91. doi: 10.1016/j.tox.2009.06.006. Epub 2009 Jun 17.

[22] Benachour N, Sipahutar H, Moslemi S, Gasnier C, Travert C, Séralini GE. Time and dose-dependent effects of roundup on human embryonic and placental cells. Arch Environ Contam Toxicol. 2007 Jul;53(1):126-33. Epub 2007 May 4.

Glyphosate caused the dysregulation of genes in human breast cancer cells grown in the laboratory in vitro. Roundup was able to replace and work synergistically with estrogen. This demonstrates the strong potential endocrine disruption by glyphosate in this hormonal system.
Hokanson R, Fudge R, Chowdhary R, Busbee D. Alteration of estrogen-regulated gene expression in human cells induced by the agricultural and horticultural herbicide glyphosate. Hum Exp Toxicol. 2007;26:747-752. doi:10.1177/0960327107083453.

At environmentally relevant concentrations, this study demonstrated that glyphosate is toxic to human placental JEG3 cells, and the effect was increased with concentration and time or in the presence of Roundup adjuvants. This study additionally concluded that glyphosate based herbicides affect the endocrine system as GBH disrupt aromatase activity and mRNA levels.
Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini GE. Differential effects of glyphosate and Roundup on human placental cells and aromatase. Env Health Perspect. 2005;113:716-20

Glyphosate is less toxic than Roundup. Glyphosate and Roundup caused cell death which resulted in decreased progesterone levels in vitro. Endocrine disruption did not precede cytotoxicity. The lowest toxic level was found to be 720ug/L, lower than the Australian drinking water guideline (1mg/L).
Young F, Ho D, Glynn D, Edwards V. Endocrine disruption and cytotoxicity of glyphosate and roundup in human Jar cells in vitro. Integrative Pharmacology, Toxicology and Genotoxicology 2015, 1, 12-19 doi: 10.15761/IPTG.1000104

These results suggest that maternal exposure to glyphosate disturbed the masculinization process and promoted behavioural changes and histological and endocrine problems in reproductive parameters. Romano MA, Romano RM, Santos LD, Wisniewski P, Campos DA, de Souza PB, Viau P, Bernardi MM, Nunes MT, de Oliveira CA. Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression. Archives of Toxicology 2011, Nov 26.

The deleterious effects are not proportional to glyphosate concentrations but rather depend on the nature of the other ingredients in the compound. Ingredients called AMPA and POEA separately and together damage cell membranes like Roundup, but at different concentrations. Their mixtures are generally even more harmful with glyphosate POEA changes human cell permeability and amplifies the toxicity of glyphosate.
Benachour N and Séralini G-E. Glyphosate formulations Induce Apoptosis and Necrosis in Human Umbilical, Embryonic, and Placental Cells. Chem. Res. Toxicol. 2009, 22 (1), pp 97–105

At low concentrations below that permitted in drinking water (ppb), glyphosate is estrogenic and induces hormone-dependent breast cancer growth.
Thongprakaisang S,Thiantanawat A,Rangkadilok N,Suriyo T,Satayavivad J. Glyphosate induces human breast cancer cells growth via estrogen receptors. Food Chem Toxicol.2013, 59C, 129-136
http://www.ncbi.nlm.nih.gov/pubmed/23756170

Hormone disruption depends on your gender. This rodent study of Roundup at low levels showed that estrogen dependent mammary tumours developed in exposed females while liver pathologies predominated in

exposed males. 2-year period of exposure. This study was not a carcinogenicity study – mammary tumours were not expected.
Séralini G-E, Clair E, Mesnage R, Gress S, Defarge N, Malatesta M, Hennequin D, de Vendômois J-S. Re-published: Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize Environmental Sciences Europe 2014, 26, 14 http://www.enveurope.com/content/26/1/14

4. Glyphosate contributes to infertility, birth defects & negative impacts on the reproductive system

Roundup causes malformations in frog and chicken embryos at doses much lower than those used in agricultural spraying. The malformations mostly affected the skull, face, midline, and developing brain and spinal cord.
Paganelli, A., Gnazzo, V. et al. 2010. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling. Chem Res Toxicol 23(10): 1586–1595.

Glyphosate can affect sperm motility and the motility period, but also impact DNA.
Lopes FM, Varela Junior AS, Corcini CD, da Silva AC, Guazzelli VG5, Tavares G, da Rosa CE. Effect of glyphosate on the sperm quality of zebrafish Danio rerio. Aquat Toxicol. 2014 Oct;155:322-6. doi: 10.1016/j.aquatox.2014.07.006. Epub 2014 Jul 12.

The commercial formulation of glyphosate could be a potent endocrine disruptor, causing disturbances in the reproductive development of rats if exposed during the puberty period.
Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide glyphosate

alters testosterone levels and testicular morphology. Arch Toxicol. 2010 Apr;84(4):309-17. doi: 10.1007/s00204-009-0494-z. Epub 2009 Dec 12.

Glyphosate may disrupt the hormonal system controlling reproduction.

Avigliano L, Alvarez N, Loughlin CM, Rodríguez EM. Effects of glyphosate on egg incubation, larvae hatching, and ovarian rematuration in the estuarine crab Neohelice granulata. Environ Toxicol Chem. 2014 Aug;33(8):1879-84. doi: 10.1002/etc.2635. Epub 2014 Jun 30.

Glyphosate may affect reproduction in female fish.

Armiliato N, Ammar D, Nezzi L, Straliotto M, Muller YM, Nazari EM. Changes in ultrastructure and expression of steroidogenic factor-1 in ovaries of zebrafish Danio rerio exposed to glyphosate. J Toxicol Environ Health A. 2014;77(7):405-14. doi: 10.1080/15287394.2014.880393.

Glyphosate can also alter pollination patterns, change geneflow and affect male fertility in plant species.

Londo JP, McKinney J, Schwartz M, Bollman M, Sagers C, Watrud L. Sub-lethal glyphosate exposure alters flowering phenology and causes transient male-sterility in Brassica spp. BMC Plant Biol. 2014 Mar 21;14:70. doi: 10.1186/1471-2229-14-70.

Roundup may contribute to Sertoli cell disruption in spermatogenesis that could have an impact on male fertility.

de Liz Oliveira Cavalli VL, Cattani D, Heinz Rieg CE, Pierozan P, Zanatta L, Benedetti Parisotto E, Wilhelm Filho D,Mena Barreto Silva FR, Pessoa-Pureur R, Zamoner A. Roundup disrupts male reproductive functions by triggering calciummediated cell death in rat testis and Sertoli cells. Free Radic Biol Med. 2013 Dec;65:335-46. doi: 10.1016/j.freeradbiomed.2013.06.043. Epub 2013 Jun 29.

At doses higher than human exposure levels, glyphosate-based herbicides, in this instance Roundup, induced adverse reproductive effects on male offspring rats: a decrease in sperm number and sperm production during adulthood, an increase in the percentage of abnormal sperms and a dose-related decrease in the serum testosterone level at puberty, and signs of individual spermatid degeneration during both periods.

Dallegrave E, Mantese FD, Oliveira RT, Andrade AJ, Dalsenter PR, Langeloh A. Pre- and postnatal toxicity of the commercial glyphosate formulation in Wistar rats. Arch Toxicol. 2007 Sep;81(9):665-73. Epub 2007 Jul 19.

A study showing shrimp offspring vulnerable at .0011ppm

Arun Kumar MS* and A Jawahar Ali Effect of two organophosphorus pesticides on the reproductive bionomics of freshwater fairy shrimp streptocephalus dichotomus International Journal of Bioassays, Vol 3, No 09 (2014)

5. Glyphosate contributes to digestive illness, gut disruption & nutrient deficiencies

Roundup has been found to destroy or damage epithelial cells, and may disrupt our gut wall. As an organic phosphate chelator it immobilises essential nutrients, reducing nutrient availability. Glyphosate disrupts an essential plant based pathway that makes essential amino acids phenylalanine, tyrosine, and tryptophan.[23] Until recently, science was not aware this pathway was contained within the gut bacteria. [24]

[23] Herrmann, K.M.; Weaver, L.M. The shikimate pathway. Annu. Rev. Plant. Physiol. Plant. Mol. Biol. 1999, 50, 473–503

[24] Moco, S.; Martin, F.-P.J.; Rezzi, S. Metabolomics view on gut microbiome modulation by polyphenol-rich foods J. Proteome Res. 2012, 11, 4781–4790.

This study demonstrated that low concentrations of Roundup negatively impacted the gastrointestinal bacteria of poultry in vitro. The researchers presented evidence that highly pathogenic bacteria resisted glyphosate. Beneficial bacteria were moderately to highly susceptible to it with the result that serious pathogens could not be kept in control.
Shehata AA, Schrodl W, Aldin AA, Hafez HM, Kruger M. The effect of glyphosate on potential pathogens and beneficial members of poultry microbiota in vitro. Curr Microbiol 2012. doi:10.1007/s00284-012-0277-2.

This report observed 'the toxicity of glyphosate to the most prevalent Enterococcus spp. in the gastro-intestinal tract. Ingestion of this herbicide could be a significant predisposing factor that is associated with the increase in C. botulinum mediated diseases in cattle.'

Krüger M, Shehata AA, Schrödl W, Rodloff A. Glyphosate suppresses the antagonistic effect of Enterococcus spp. on Clostridium botulinum. Anaerobe 2013;20:74–78.

Ganal, S.C.; Sanos, S.L.; Kallfass, C.; Oberle, K.; Johner, C.; Kirschning, C.; Lienen-klaus, S.; Weiss, S.; Staeheli, P.; Aichele, P.; et al. Priming of natural killer cells by nonmucosal mononuclear phagocytes requires instructive signals from commensal microbiota. Immunity 2012, 37, 171–186.
Hashimoto, T.; Perlot, T.; Rehman, A.; Trichereau, J.; Ishiguro, H.; Paolino, M.; Sigl, V.; Hanada, T.; Hanada, R.; Lipinski, S. et al. ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. Nature 2012, 487, 477–483. (The same with ref.160)
Littman, D.R.; Pamer, E.G. Role of the commensal microbiota in normal and pathogenic host immune responses. Cell. Host Microbe 2011, 10, 311–323

Samsel & Seneff postulated that that glyphosate formulations impairs important cytochrome P450 enzymes required for detoxifying environmental toxins (xenobiotics) and activating vitamin D3 (in the liver).
Samsel A, Seneff S. Glyphosate's suppression of cytochrome P450 enzymes and amino acid biosynthesis by the gut microbiome: Pathways to modern diseases. Entropy 2013;15:1416-1463.

This study considered that the ability of glyphosate to impact gut bacteria and make key nutrients unavailable results in deficiencies connected to many modern diseases.
Samsel A, Seneff S. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. Interdiscip. Toxicol. 2013;6(4):159-184. doi:10.2478/intox-2013-0026.

The aim of Clair et al 2012 was to shed light on the real impact on biodiversity and ecosystems of Roundup(®), a major herbicide used worldwide, and the glyphosate it contains, by the study of their effects on growth and viability of microbial models, namely, on three food microorganisms (Geotrichum candidum, Lactococcus lactis subsp. cremoris and Lactobacillus delbrueckii subsp. bulgaricus) widely used as starters in traditional and industrial dairy technologies. **The presented results evidence that Roundup(®) has an inhibitory effect on microbial growth and a microbicide effect at lower concentrations than those recommended in agriculture.** Interestingly, glyphosate at these levels has no significant effect on the three studied microorganisms. Our work is consistent with previous studies which demonstrated that the toxic effect of glyphosate was amplified by its formulation adjuvants on different human cells and other eukaryotic models.

Emilie Clair, Laura Linn, Carine Travert, Caroline Amiel, Gilles-Eric Séralini, Jean-Michel Panoff. Effects of Roundup(®) and Glyphosate on Three Food

Microorganisms: Geotrichum candidum, Lactococcus lactis subsp. cremoris and Lactobacillus delbrueckii subsp. bulgaricus. Curr Microbiol. 2012 Feb 24. Epub 2012 Feb 24. PMID: 22362186

6. Glyphosate-based herbicides can exert worrying effects on antibiotics

"We found that exposure to some very common herbicides can cause bacteria to change their response to antibiotics. They often become antibiotic resistant, but we also saw increased susceptibility or no effect. In most cases, we saw increased resistance even to important clinical antibiotics." - Prof. J Heinemann.
Kurenbach B, Marjoshi D, Amábile-Cuevas CF, Ferguson GC, Godsoe W, Gibson P, Heinemann JA. 2015. Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in Escherichia coli and Salmonella enterica serovar Typhimurium. mBio 6(2):e00009-15. doi:10.1128/mBio.00009-15.

Note: Herbicide concentrations needed to invoke the maximal response were above current food maximum residue levels but within application levels for all herbicides.

7. Glyphosate is neurotoxic at sub-lethal concentrations

There have been two published cases of Parkinsons Disease related to glyphosate exposure:

Barbosa ER, Leiros da Costa MD, Bacheschi LA, Scaff M, Leite CC. Parkinsonism after glycine-derivate exposure. Movement Disorders 2001 16, 565-8. 116.

Potrebić O, Jović-Stosić J, Vucinić S, Tadić J, Radulac M.[Acute glyphosate-surfactant poisoning with neurological sequels and fatal outcome]. Vojnosanit Pregl 2009, 66, 758-62.

The results demonstrated that Roundup might lead to excessive extracellular glutamate levels and consequently to glutamate excitotoxicity and oxidative stress in rat hippocampus. The study authors cautioned: 'exposure to environmental toxicants during pregnancy and suckling periods has the potential to affect embryo and fetal development.' Cattani D, de Liz Oliveira Cavalli VL , Heinz Rieg CE, Domingues JT, Dal-Cim T, Tasca CI, Mena Barreto Silva FR, Zamoner A. Mechanisms underlying the neurotoxicity induced by glyphosate based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity. Toxicology. 2014 Jun 5;320:34-45. doi: 10.1016/j.tox.2014.03.001. Epub 2014 Mar 15.

This paper evidenced both the role of the oxidative stress as a mechanism of action, and the potential additive effects of a simultaneous exposure to more than one compound. In addition, results suggest a potential contribution of pesticide mixtures to some neurodegenerative diseases.

Astiz M, de Alaniz MJ, Marra CA. Antioxidant defense system in rats simultaneously intoxicated with agrochemicals. Environ Toxicol Pharmacol. 2009b, 28, 465-73.

Glyphosate appears to negatively impact an area of the brain called the substanta nigra at low dose (sub-lethal) levels over a long time period. A DNA fragmentation pattern in the brain and liver was observed.
Astiz M, de Alaniz MJ, Marra CA. Effect of pesticides on cell survival in liver and brain rat tissues. Ecotoxicol Environ Saf 2009a, 72, 2025-32. Epub 2009 Jun 2.

Glyphosate reduces dopamine levels, causes hypoactivity & can alter dopamine receptor functioning in the brain.
Hernández-Plata I, Giordano M, Díaz-Muñoz M, Rodríguez VM. The herbicide glyphosate causes behavioral changes and alterations in dopaminergic markers in male Sprague-Dawley rat. Neurotoxicology. 2015, 46, 79-91. doi: 10.1016/j.neuro.2014.12.001.

Glyphosate activates cell pathways implicated in neurodegenerative diseases.
Gui YX, Fan XN, Wang HM, Wang G, Chen SD. Glyphosate induced cell death through apoptotic and autophagic mechanisms. Neurotoxicology and Teratology 2012, Apr 4.

Treatment of rats at low doses induced oxidative stress (OS) in liver and brain. Treatment resulted in loss of mitochondrial transmembrane potential and cardiolipin content, especially in the substantia nigra.
Astiz M, de Alaniz MJ, Marra CA. Effect of pesticides on cell survival in liver and brain rat tissues. Ecotoxicol Environ Saf. 2009 Oct;72(7):2025-32. doi: 10.1016/j.ecoenv.2009.05.001. Epub 2009 Jun 2.

Glyphosate inhibits AChE – a critical enzyme in brain functioning.
AChE inhibitors (like organophosphates) are considered potent nerve agents.

Glyphosate was never considered to be a toxic AChE inhibitor and was considered a less toxic organophosphate phosphanoglycine. New science demonstrates glyphosate is an inhibitor.

Glyphosate changed AChE activity, metabolic parameters and TBARS production at environmentally relevant concentrations (0.2 or 0.4mg/l for 96 hours).

Glusczak L, Miron Ddos S, Moraes BS, Simões RR, Schetinger MR, Morsch VM, Loro VL. Acute effects of glyphosate herbicide on metabolic and enzymatic parameters of silver catfish (Rhamdia quelen). . Laboratório de Bioquímica Adaptativa, Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, Brazil. 2007. Comp Biochem Physiol C Toxicol Pharmacol. 2007, 146, 519-24.

These results indicate that AChE-a neurotoxicity biomarker-in a species of fish may be affected by exposure to environmentally relevant concentrations of glyphosate.

Menéndez-Helman RJ, Ferreyroa GV, dos Santos Afonso M, Salibián A. Glyphosate as an acetylcholinesterase inhibitor in Cnesterodon decemmaculatus. Bull Environ Contam Toxicol. 2012 Jan;88(1):6-9. doi: 10.1007/s00128-011-0423-8. http://link.springer.com/article/10.1007%2Fs00128-011-0423-8#page-2

In this study glyphosate affected enzyme activity of mussel and fish species.

Sandrini JZ, Rola RC, Lopes FM, Buffon HF, Freitas MM, Martins Cde M, da Rosa CE. Effects of glyphosate on cholinesterase activity of the mussel Perna perna and the fish Danio rerio and Jenynsia multidentata: In vitro studies. Aquat Toxicol. 2013 Apr 15;130-131:171-3. doi: 10.1016/j.aquatox.2013.01.006. Epub 2013 Jan 18.

AChE activities decreased significantly and markedly with herbicide concentration – this study indicates the potential of glyphosate based herbicides to disrupt ecological communities near areas where herbicides are applied.

Ruamthum W, Visetson S, Milne JR, Bullangpoti V. Effect of glyphosate-based herbicide on acetylcholinesterase activity in tadpoles, Hoplobatrachus rugulosus. Commun Agric Appl Biol Sci. 2011;76(4):923-30. Department of Zoology, Faculty of Science, Kasetsart University, 50 Phahon Yothin Road, Chatuchak, Bangkok 10900, Thailand. rwatchar@su.ac.th

8. How glyphosate affects organs: from damaged kidneys to arrhythmia

Ultra low doses of Roundup over the long term can result in liver and kidney damage with potential significant health implications for animal and human populations. This study detected alterations in gene function that were consistent with fibrosis (scarring), necrosis (areas of dead tissue), phospholipidosis (disturbed fat metabolism), and damage to mitochondria (the centres of respiration in cells).
Robin Mesnage, Matthew Arno, Manuela Costanzo, Manuela Malatesta, Gilles-Eric Séralini and Michael N. Antoniou Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure. Environmental Health (2015) 14:70

Scientists consider the chelating action of glyphosate may play a role in development of kidney disease – chelating with metals in hard water and acting as a shield, protecting metals from metabolism by the liver.
Jayasumana C, Gunatilake S, Senanayake P. Glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka? Int J Environ Res Public Health. 2014 Feb 20;11(2):2125-47. doi: 10.3390/ijerph110202125.

Researchers have observed an increased incidence of arrhythmias at different doses of Roundup with unknown adjuvants (while glyphosate by itself did not have the same effects).
Gress S, Lemoine S, Puddu PE, Séralini GE, Rouet R. Cardiotoxic Electrophysiological Effects of the Herbicide Roundup® in Rat and Rabbit Ventricular Myocardium In Vitro. Cardiovasc Toxicol. October 2015, Volume 15, Issue 4, pp 324-335.

One hundred patients developed severe effects and 146 patients died following oral glyphosate exposure to 2,186 patients. Shock and respiratory failure accounted for most fatalities.
Chen YJ, Wu ML, Deng JF, Yang CC. The epidemiology of glyphosate-surfactant herbicide poisoning in Taiwan, 1986-2007: a poison center study. Clin Toxicol (Phila). 2009 Aug;47(7):670-7. doi: 10.1080/15563650903140399.

9. Glyphosate's off-target adverse effects: From pollinators to skinks

Bees
María Sol Balbuena, Léa Tison, Marie-Luise Hahn, Uwe Greggers, Randolf Menzel and Walter M. Farina. Effects of sublethal doses of glyphosate on honeybee navigation. J Exp Biol 2015 218:2799-2805.

Glyphosate can disrupt learning behaviours in honeybees and severely impair long-term colony performance. Glyphosate at concentrations found in agro-ecosystems due to standard spraying can reduce sensitivity to nectar reward and impair associative learning in honeybees.
Herbert LT, Vázquez DE, Arenas A, Farina WM. Effects of field-realistic doses of glyphosate on honeybee appetitive behaviour. J Exp Biol. 2014 Oct 1;217(Pt 19):3457-64. doi: 10.1242/jeb.109520. Epub 2014 Jul 25.

Honey bee carotenoid-retinoid system may be altered by sub-lethal field-realistic doses of herbicides.
Helmer SH, Kerbaol A, Aras P, Jumarie C, Boily M. Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera). Environ Sci Pollut Res Int. 2015 Jun;22(11):8010-21. doi: 10.1007/s11356-014-2879-7. Epub 2014 Apr 15.

But industry studies tell us there is nothing to worry about:

Levine et al found there were no significant effects from glyphosate observed in brood survival, development, and mean pupal weight. Additionally, there were no biologically significant levels of adult mortality observed in any glyphosate treatment group. Thompson HM, Levine SL (Monsanto), Doering J (Feinchemie), Norman S (DowAgrosciences), Manson P (Cheminova), Sutton P (Syngenta), von Mérey G. Evaluating exposure and potential effects on honeybee brood (Apis mellifera) development using glyphosate as an example. Integr Environ Assess Manag. 2014 Jul;10(3):463-70. doi: 10.1002/ieam.1529. Epub 2014 May 19.

Skinks

The New Zealand Department of Conservation recommend in the paper 'The effect of glyphosate herbicides on lizards' that herbicides be used with caution in areas that are inhabited by rare or threatened lizard species. DOC noted that research regarding chemical toxicity to reptile populations has been neglected due to a lack of regulatory requirements.
Weir, S. M., Suski, J. G., & Salice, C. J. (2010). Ecological risk of anthropogenic pollutants to reptiles: Evaluating assumptions of sensitivity and exposure. Environmental Pollution, 158(12), 3596-3606

An unpublished short term laboratory study found that glyphosate formulations altered skinks' thermoregulatory behaviour and may have caused slower sprint speeds.

Carpenter, J. K. (2013). Evaluating the effect of glyphosate formulations on the New Zealand common skink (Oligosoma polychroma) (Honours thesis). Victoria University of Wellington, Wellington.

10. Roundup is more toxic than glyphosate alone. 'Inert' adjuvants (ingredients) are not inert

Risk assessment failure: Roundup has *never* been tested for long-term toxicity in animals for regulatory purposes; only glyphosate alone has been tested.

Roundup is 1,000 times more toxic than glyphosate alone according to time of exposure according to this study below. This study demonstrated a time-amplifying effect: the differential toxicity between the principal ingredient glyphosate and the full formulation Roundup increased by 5 times in 72 h. See Figure 3 on page 130.

Benachour N, Sipahutar H, Moslemi S, Gasnier C, Travert C, Séralini GE. Time- and dose-dependent effects of roundup on human embryonic and placental cells. Arch Environ Contam Toxicol. 2007 Jul;53(1):126-33. Epub 2007 May 4.

Kwiatkowska M, Paweł J, Bukowska B. Glyphosate and its formulations--toxicity, occupational and environmental exposure. Med Pr. 2013;64(5):717-29.

Nine different glyphosate formulations were found to be more toxic than glyphosate alone. The ethoxylated adjuvant POEA-15 was found toxic, affecting cellular respiration and membrane integrity at 1-3ppm
Mesnage R, Bernay B, Séralini GE. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology. 2013 Nov 16;313(2-3):122-8. doi: 10.1016/j.tox.2012.09.006. Epub 2012 Sep 21.

Herbicide Roundup GT+ (450g/L Glyphosate) was found to be 125 times more toxic than the active chemical. In this study, eight formulations out of nine were up to 1000 times more toxic than their active ingredients.

Mesnage R, Defarge N, de Vendômois JS, Séralini GE. Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. BioMed Research International Volume 2014 (2014), Article ID 179691, 8 pages http://dx.doi.org/10.1155/2014/179691

A POEA surfactant system was found to be toxic to embryo larval development and toxic to the metamorphosis process.

Mottier A, Pini J, Costil K. Effects of a POEA surfactant system (Genamin T-200(®)) on two lifestages of the Pacific oyster, Crassostrea gigas. J Toxicol Sci. 2014 Apr;39(2):211-5.

Surfactants help disrupt the integrity of the cellular barrier to enable glyphosate uptake. The surfactant and glyphosate together are cytotoxic.

Kim YH, Hong JR, Gil HW, Song HY, Hong SY. Mixtures of glyphosate and surfactant TN20 accelerate cell death via mitochondrial damage-induced apoptosis and necrosis. Toxicol In Vitro. 2013 Feb;27(1):191-7. Marine Pollution Bulletin Volume 85, Issue 2, 30 August 2014, Pages 385–390 doi: 10.1016/j.tiv.2012.09.021. Epub 2012 Oct 23.

Roundup has a higher toxicity to acquatic life than glypghosate by itself when used to control lake weed

D Williams, R A Mascarenhas and S Lewis Herbicides for Use in or Near the Aquatic Environment: Priorities for Environmental Quality Standard Development R&D Technical Report, The Environment Agency

11. Glyphosate's effect on groundwater

Traditionally we said because it binds, glyphosate doesn't enter groundwater – we know now it is persistent and it leaches into groundwater.

Despite low mobility in soils, glyphosate does not fully break down before reaching groundwater.
Sanchís J, Kantiani L, Llorca M, Rubio F, Ginebreda A, Fraile J, Garrido T, Farré M. Determination of glyphosate in groundwater samples using an ultrasensitive immunoassay and confirmation by on-line solid-phase extraction followed by liquid chromatography coupled to tandem mass spectrometry. Anal Bioanal Chem. 2012 Mar;402(7):2335-45. doi: 10.1007/s00216-011-5541-y. Epub 2011 Nov 20.

Wide ranging detection of glyphosate in surface soils, deeper layers and streamwater resulted in the study authors cautioning re. vertical transport trough soil profile with the possibility of reaching groundwater.
Lupi L, Miglioranza KS, Aparicio VC, Marino D, Bedmar F, Wunderlin DA. Occurrence of glyphosate and AMPA in an agricultural watershed from the southeastern region of Argentina. Sci Total Environ. 2015 Dec 1;536:687-94. doi: 10.1016/j.scitotenv.2015.07.090. Epub 2015 Aug 4.

This study demonstrates glyphosate is moderately persistent in the marine water under low light conditions and is highly persistent in the dark.
Mercurioa P, Florita Flores F, Muellera JF, Carter S, Negri A P. Glyphosate persistence in seawater doi:10.1016/j.marpolbul.2014.01.021

This study demonstrated that glyphosate is more mobile and occurs more widely in the U.S. environment than was previously thought.
Brauman, K. A.; Flörke, M.; Mueller, N. D.; Foley, J. A. Widespread Occurrence

of Glyphosate and its Degradation Product (AMPA) in U.S. Soils, Surface Water, Groundwater, and Precipitation, 2001-2009. American Geophysical Union, Fall Meeting 2011, abstract #H44A-08

12. We don't know the safe level. Neither glyphosate nor Roundup have ever been assessed by regulators at sub-lethal concentrations.

Mesnage et al 2015 'reviewed the toxic effects of glyphosate based herbicidesmeasured below regulatory limits by evaluating the published literature and regulatory reports. We reveal a coherent body of evidence indicating that glyphosate-based herbicides could be toxic below the regulatory lowest observed adverse effect level for chronic toxic effects. It includes teratogenic, tumorigenic and hepatorenal effects. They could be explained by endocrine disruption and oxidative stress, causing metabolic alterations, depending on dose and exposure time. Some effects were detected in the range of the recommended acceptable daily intake. Toxic effects of commercial formulations can also be explained by glyphosate-based herbicide adjuvants, which have their own toxicity, but also enhance glyphosate toxicity. These challenge the assumption of safety of glyphosate-based herbicide at the levels at which they contaminate food and the environment, albeit these levels may fall below regulatory thresholds. Neurodevelopmental, reproductive, and transgenerational effects of glyphosate-based herbicide must be revisited, since a growing body of knowledge suggests the predominance of endocrine disrupting mechanisms caused by environmentally relevant levels of exposure.'

Dr Robin Mesnage commented:

"This is the first independent systematic and peer-reviewed review to balance the dozens of Monsanto-sponsored reviews of Roundup and glyphosate toxicity, which have concluded that these substances are safe to use. Our

review shows that there is a coherent body of evidence showing that toxic effects can occur below regulatory safety limits.

R. Mesnage, N. Defarge, J. Spiroux de Vendômois, G.E. Séralini. Potential toxic effects of glyphosate and its commercial formulations below regulatory limits. Food and Chemical Toxicology (2015), doi: 10.1016/j.fct.2015.08.012

This significant study concluded that that glyphosate and Roundup toxicity to aquatic invertebrates has been underestimated and that current European Commission and US EPA toxicity classification of these chemicals needs to be revised.

'Significant reduction of juvenile size was observed even in the lowest test concentrations of 0.05 mg a.i./l, for both glyphosate and Roundup. At 0.45 mg a.i./l, growth, fecundity and abortion rate was affected, but only in animals exposed to Roundup. At 1.35 and 4.05 mg a.i./l of both glyphosate and Roundup, significant negative effects were seen on most tested parameters, including mortality. D. magna was adversely affected by a near 100 % abortion rate of eggs and embryonic stages at 1.35 mg a.i./l of Roundup.'

Cuhra M, Traavik T, Bøhn T. Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna. Ecotoxicology. 2013 Mar;22(2):251-62. doi: 10.1007/s10646-012-1021-1. Epub 2012 Dec 6.

Further Notes:

1. **Rats are a good cancer model for humans.**

In a well-designed study, rats are a good cancer model: the Sprague-Dawley rat commonly used in toxicological studies have similar likelihood of cancer from chemical exposure as humans have.

Soffritti M, Belpoggi F, Degli Esposti D. Cancer prevention: The lesson from the lab. In: Biasco G, Tanneberger S, eds. Cancer Medicine at the Dawn of the 21st Century: The View from Bologna. Bologna: Bononia University Press; 2006:49-64.

2. **NZ's EPA uses industry studies to say glyphosate is safe, which means that there is no New Zealand testing for glyphosate in food and water.**

The New Zealand Total Diet Study did not test for glyphosate (2009)

National Survey of pesticides in groundwater does not test for glyphosate (2010)

National Programme for the Monitoring and Surveillance of Chemical Residues and Contaminants in milk does not list glyphosate

3. **Definitions**

Cytotoxicity & Genotoxicity:
http://www.researchgate.net/post/What_is_the_main_difference_between_cytotoxicity_and_genotoxicity

Generally and depending on the agent, a cytotoxic agent may be genotoxic (causing DNA damage), mutagenic (causing gene mutation) or it may be harmful for cell organelles (e.g. cell membrane) or it may even be teratogenic. Therefore, not every cytotoxic agent is genotoxic. A genotoxic substance will induce DNA damage at non-cytotoxic concentrations.

Genotoxicity describes the property of chemical agents that damages the genetic information within a cell causing mutations, which may lead to cancer or birth defect.

While genotoxicity is often confused with mutagenicity, all mutagens are genotoxic, however, not all genotoxic substances are mutagenic. However, cytotoxicity is the quality of being toxic to cells in general without necessarily affecting the genome.

4. Further reading

Institute of Science in society: Banishing Glyphosate. September 2015.

DetoxProject.org cancer hormone hacking

Roundup and birth defects: Is the public being kept in the dark? © Earth Open Source, 2011. Antoniou M et al.