Glyphosate 2020 – No public exposures

[1] Health impact, regulatory convention & the state of international scientific evidence

The ubiquity of glyphosate-based herbicides is of concern to public health experts internationally. In 2020, production of glyphosate is estimated to reach one million tonnes per year (Landrigan & Belpoggi, 2018). Glyphosate has been detected in rainfall in Canada, the USA and Argentina (Lupi, et al., 2019) and groundwater in New Zealand (Close & Humphries, 2019).

Has New Zealand risk assessed glyphosate?

No, the New Zealand Environmental Protection Authority (NZEPA) have never conducted a formal risk assessment of glyphosate. In 2015 the New Zealand Environmental Protection Authority (NZEPA) hired a toxicologist (Temple, 2016) to write a review, apparently in order to rebut the International Agency for Research on Cancer (IARC) finding that glyphosate and it's formulations probably caused cancer. The review used industry paid studies utilized in a European assessment which was also criticised (Portier, et al., 2016). NZEPA ignored formulation toxicity and the potential for oxidative stress to initiate disease. The review was criticised by senior New Zealand public health experts who requested that the NZEPA paper be withdrawn (Douwes, et al., 2018). The NZEPA has not responded to the paper by Douwes and colleagues.

What science is used to approve glyphosate and its formulations?

Conventionally, the chemical industry selects and supplies the data used in New Zealand authorisations and assessments. New Zealand conducts very few risk assessments, so authorisations are the main administrative pathway for approval of chemicals onto the local market. The NZEPA also depend on World Health Organisation and Food and Agriculture Organisation assessments by the Joint Meeting on Pesticide Residues (JMPR) – who also rely on industry data, usually unpublished. Independent scientists cannot scrutinise the data used by the JMPR to determine safety. JMPR processes are not democratically accountable.

An increasing body of evidence shows that data selected and supplied by industry is more likely to show safety, while data produced by independent scientists are likely to reveal a chemical substance is harmful (Michaels, 2020). European assessments are a little more rigorous and trustworthy, European assessors must consider formulation toxicity (rather than include but not base approvals around formulation toxicity), and a recent court case determined that private industry studies on glyphosate must not be censored from the public.

What is our daily permitted exposure of glyphosate?

The current permitted exposure levels (acceptable daily intake, or ADI) for New Zealand citizens is 0-1mg/kg bodyweight, based on a 1993 Monsanto study (Atkinson et al 1993b) that has never been published for scientific scrutiny (FAO-WHO, 2006). This study is based on safe exposures for an adult. Infant and childhood vulnerability are not considered.

Do the NZEPA know how much we are exposed to?

The NZEPA does not know how much glyphosate Kiwis are exposed to as blood or urine testing has never been undertaken. Because of the lack of data in New Zealand we must reference overseas data (this is commonly applied where there is undone science).

Many studies reveal glyphosate in urine samples (Gillezeau, et al., 2019; Brändli &

Reinacher, 2012). Children living near sprayed public parks have been found to have the same pesticides in their bodies that have been applied in neighbourhood parks. In one case, five year old Lilly was tested after her parents observed developmental delays, and laboratory tests identified high levels of glyphosate and 2,4-D (see image Great Plains Laboratories results) (Valdez, 2019).

New Zealand laboratories are expensive, which is a barrier to scientists who would like to test population exposures.

Further, while New Zealand used to collect and publish the tonnages of chemicals released into the environment, this activity was halted around 2010.

While glyphosate-based herbicides are a component of the herbicide mixtures sprayed down most roadsides and many drains in New Zealand, national regulatory responsibility does not extend to monitoring glyphosate in the environment. Scientists and regional councils do not commonly test for glyphosate because the test is prohibitively expensive. This is why the Soil and Health Association and Physicians and Scientists for Global Responsibility recently called for national environment standards to require monitoring of diffuse synthetic chemicals in freshwater, as the OECD suggests. National standards requiring national testing and publication of results would enable Kiwis to understand and advocate for restrictions on chemicals if they are accumulating in the environment (Soil and Health & PSGR, 2019).

The NZEPA claims to make cost-benefit analyses of glyphosate which entitle them to continue the authorisation, but unless tonnages and exposures are understood, and glyphosate is tested for in the environment, cost-benefit analysis cannot be claimed to be grounded on evidence (Douwes, et al., 2018).

Are the levels the public are commonly exposed to in the environment safe?

We can see that people are exposed from overseas studies. Levels in urine are very low, but scientists are increasingly concerned that these low, environmentally relevant levels, are harmful (Mesnage R. , Defarge, de Vendomois, & Seralini, 2015) (Myers, et al., 2016). Regulators have commonly relied on industry supplied data and

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Glyphosate Profile

Metabolite	Result ug/g creatinine	Reference Range
		LLOQ 75th 95th
Glyphosate	3.1	0.38 1.8 2.5

Glyphosate is the world's most widely produced herbicide. It is a broad-spectrum herbicide that is used in more than 700 different products for agriculture and forestry to home use. Glyphosate was introduced in the 1970s to kill weeds by targeting the enzymes that produce the amino acids tyrosine, tryptophan, and phenylalanine. Usage of glyphosate has since amplified, after the introduction of genetically modified (GMO) glyphosate-resistant crops.

Recent studies have discovered glyphosate exposure to be a cause of many chronic health problems. It can enter the body by direct absorption through the skin, by eating foods treated with glyphosate, or by drinking water contaminated with glyphosate. The World Health Organization International Agency for Research on Cancer published a summary in March 2015 that classified glyphosate as a probably carcinogen in humans. Possible cancers linked to glyphosate exposure include non-Hodgkin lymphoma, renal tubule carcinoma, pancreatic islet-cell adenoma, and skin tumors. Studies have also indicated that glyphosate disrupts the microbiome in the intestine, causing a decrease in the ratio of beneficial to harmful bacteria. The relationship between the microbiome of the intestine and overall human health is still unclear, but current research indicates that disruption of the microbiome could cause diseases such as autism, metabolic disorder, diabetes, depression, cardiovascular disease, and autoimmune disease.

Treatment of glyphosate toxicity should be centered on determining the route of introduction and avoiding future exposure. Glyphosate is readily metabolized in the body. However, a recent study found that glyphosate accumulates in mammalian bones. Another study found glyphosate to be detectable in mammalian intestine, spleen, liver, muscle, and kidney. Kidney impairment is common in regions where glyphosate may accumulate in ground water as metal chelates. The most effective way to reduce glyphosate exposure is to avoid living in areas where glyphosate is applied and to avoid eating GMO foods or animal products such as milk or meat for which GMO foods were used to feed the animals. Since glyphosate is now commonly combined with the weed killer 2,4-dichlorophenoxyacetic acid (2,4-D), testing for this chemical with the GPL-TOX test may wish to be considered also.

*LLOQ - Lower Limit of Quantitation

Testing performed by The Great Plains Laboratory, Inc., Lenexa, Kansas. The Great Plains Laboratory has developed and determined the performance characteristics of this test. The test has not been evaluated by the U.S. Food and Drug Administration. The FDA does not currently regulate such testing.

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guidelines that do not account for hormone level toxicity, nor mixture effects. Our hormones, (the endocrine system), works at parts per trillion (ppt), and parts per billion (ppb) – and exposures in the environment can be at this level.

Traditionally industry data has been supplied with dosage rates at parts per million rather than at lower levels such as the hormonal level. Today regulators accept data at ppt and ppb supplied by industry, but they are not reviewing the published scientific literature produced by independent scientists (Gasnier, et al., 2009; Székács & Darvas, 2018).

Regulatory guidelines are considered to be insensitive and increasingly irrelevant for understanding risk at environmentally relevant levels (Vandenberg, et al., 2017). Public health scientists are concerned that the guidelines chemical regulators use prevent them from finding harm from hormone responses at low levels of exposure (Trasande, et al., 2016; Myers, et al., 2009). This appears particularly relevant for glyphosate (Myers, et al., 2016).

Even if a study is supplied by industry at hormone levels, unless a formal risk assessment happens, it doesn't habitually kick the earlier studies that established the ADI, out of place.

Regulatory guidelines and conventions enable regulators to ignore published scientific literature. This is why the glyphosate ADI remains based on an entrenched, unpublished Monsanto 1993 study, despite a large amount of studies showing risk at much lower levels.

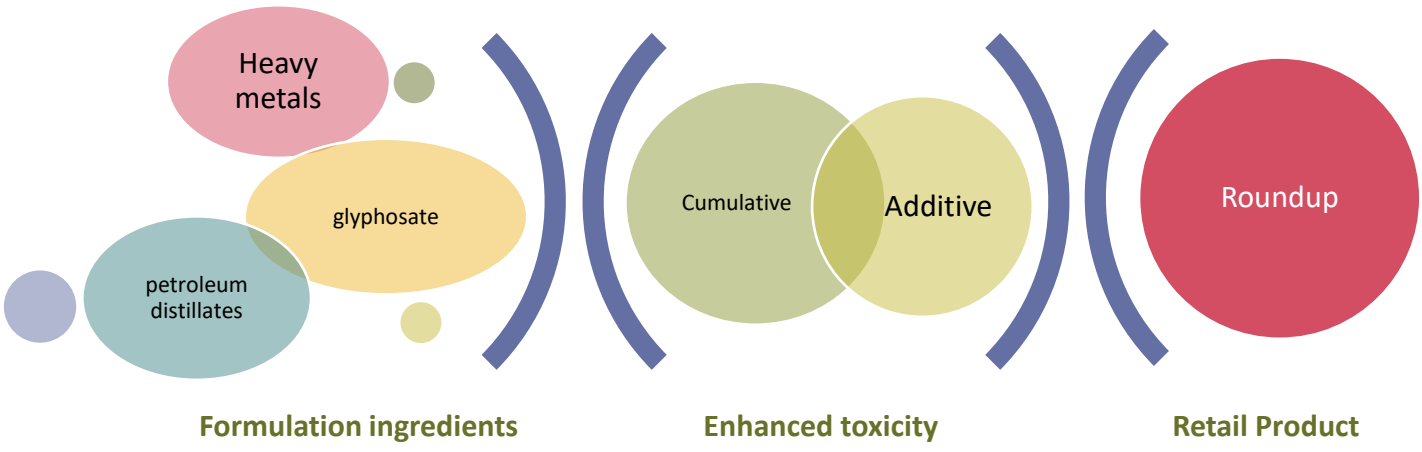
Is the glyphosate *formulation* toxicity different from *active ingredient* toxicity?

Glyphosate formulations applied to food crops; on roadsides and in parks are always more toxic than the single chemical glyphosate (Mesnage R. , Defarge, de Vendômois, & Séralini, 2014; Richard, Moslemi, Sipahutar, Benachour, & Seralini G.E., 2005; Myers, et al., 2016). However, the current approval of glyphosate is based on the toxicity of the single chemical – glyphosate. Single chemical approvals are increasingly criticised for being irrelevant to real world applications (Kortenkamp & Faust, 2018). It is now evident that glyphosate formulations can contain other pollutants, including heavy metals and petroleum products (Defarge, de Vendômois, & Séralini, 2018) that synergistically work together to make the formulation more toxic (Mesnage & Antoniou, 2018).

It's just cancer that is the problem, right?

Physicians and scientists continue to publish papers asking for glyphosate to be phased outInvalid source specified.. Mainstream discussion of glyphosate tends to restrict discussion to cancer. This is because of the 2015 IARC finding that glyphosate probably caused cancer (IARC Working Group, 2015).

The IARC finding initiated media controversy and regulators openly opposed the finding (Portier, et al., 2016). It is now evident that Monsanto initiated a political public relations storm to counteract the IARC finding, influence lawmakers, discredit journalists (Vainio, 2019) and maintain public doubt concerning the safety of glyphosate that might, in turn persuade regulators to restrict or ban the chemical.



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As of October 2019, lawsuits claiming glyphosate initiates cancer (primarily non-Hodgkins lymphoma) have grown to 42,700. Lawsuits have increased markedly followed three prominent court cases, the initial Johnson Trial, the Hardeman Trial, and the Californian Pilliod Trial. New Zealand incidence of non-Hodgkins lymphoma has increased significantly since glyphosate was introduced to the local market.

The evidence that glyphosate is carcinogenic continues to increase. A recent meta-study concluded that there is a 'compelling link' between glyphosate and NHL. Further, the study drew attention to the fact that immunosuppression, endocrine disruption and genetic alterations are commonly associated with NHL (Zhang, Rana, Taioli, Shaffer, & Sheppard, 2019).

The cancer-causing potential of glyphosate is a major concern. However, in addition to causing cancer, glyphosate and its more toxic commercial formulations have the potential to cause many other illnesses and comorbidities (multiple conditions). For example farmers with long term exposure to pesticides are more likely to have depression (Beard, et al., 2014) and prostate cancer and/or multiple myeloma (Stoop, 2018). It cannot be assumed that these illnesses occur separately.

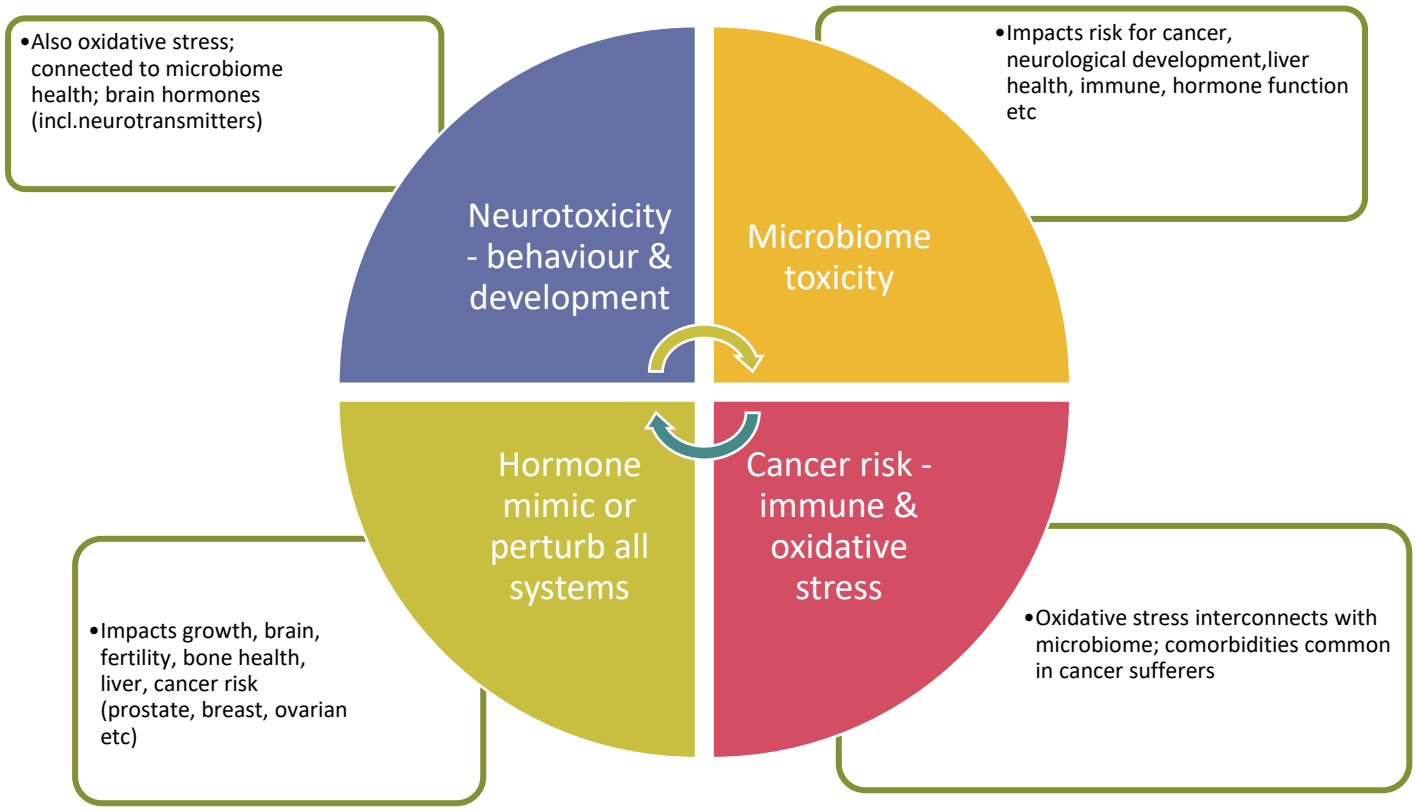
Neurotoxicity

Glyphosate travels across the blood-brain barrier. Studies indicate glyphosate can affect neuronal development, nerve cells, neurotransmitter systems which may increase risk of cognitive impairment including for ADHD, Parkinson's disease and mental health (Aitbali, et al., 2018) (Watts, et al., 2016, p. 34). Neurotransmitters affected by glyphosate include serotonin, dopamine and norepinephrine (Martínez, et al., 2018; Pu, et al., 2020). There is increasing evidence glyphosate exposures may contribute to autism spectrum disorder risk. (Ongono, Béranger, Baghdadli, & Mortamais, 2020; Pu, et al.).

There are now several studies linking glyphosate to autism risk (Rueda-Rufaza, Cruz, Roman, & Cardona, 2019; Von Ehrenstein, et al., 2019).

Hormone level toxicity

A large body of literature shows glyphosate herbicides damage/perturb hormone function. A 2005 study found that glyphosate altered a key enzyme responsible for hormone synthesis at levels 100 times lower than recommended in agriculture, and that the adjuvants added to the formulation amplified the toxic effects (Richard, Moslemi, Sipahutar, Benachour, & Seralini G.E., 2005). Since



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then public health scientists have uncovered many more ways glyphosate alters hormone function. New Zealander Dr Meriel Watts and colleagues noted that 'the implications of the endocrine-disrupting effects can be profound and far-reaching, involving a range of developmental impacts including sexual and other cell differentiation, bone metabolism, liver metabolism, lipid metabolism, reproduction, pregnancy, growth, brain and organ development, cognition, behaviour, and endocrine-related diseases such as breast, testicular and prostate cancer, neurodegenerative and metabolic disorders (diabetes, obesity)' (Watts, et al., 2016).

Glyphosate and its formulations appear to alter testosterone and estrogen production and the activity of the aromatase enzyme that synthesises estrogens. Glyphosate and Roundup can alter sperm counts and sperm motility and alter sexual development in females. Fertility is affected in males. Glyphosate formulations can impact hormonally related breast cell development. (Manservisi, et al., 2019) In fact, regulators have known Roundup damages semen quality since 1995 (Watts, et al., 2016). Despite studies showing harm, in 2006 international regulators confirmed that glyphosate herbicides could be sprayed on food crops, increasing levels across the world to permit this (Codex, 2019).

Science is revealing the reason why granddad might not have become sick from using toxic chemicals such as glyphosate, but why his grandchildren may be at greater risk. Heritable traits after the parent generation has been exposed can be passed down through sperm, epigenetically altering the genetic expression of unexposed children and grandchildren, predisposing them to disease. Epigenetic functioning often occurs at hormone level. Science now suggests that even if, for example the parent generation is exposed and unharmed, grandchildren and great-grandchildren may be at greater risk of diseases including obesity, kidney disease, prostate disease, ovarian disease and birth abnormalities (Kubsad, et al., 2019). Scientists are drawing attention to the potential for glyphosate to harm at the epigenetic level (Portier & Duforestel, 2020).

Organ toxicity

Low doses of Roundup harm the liver. The kidney and liver are target organs, glyphosate can bind nephrotoxic metals (Valcke, Levasseur, da Silva, & Wesseling, 2017; Vandenberg, et al., 2017).

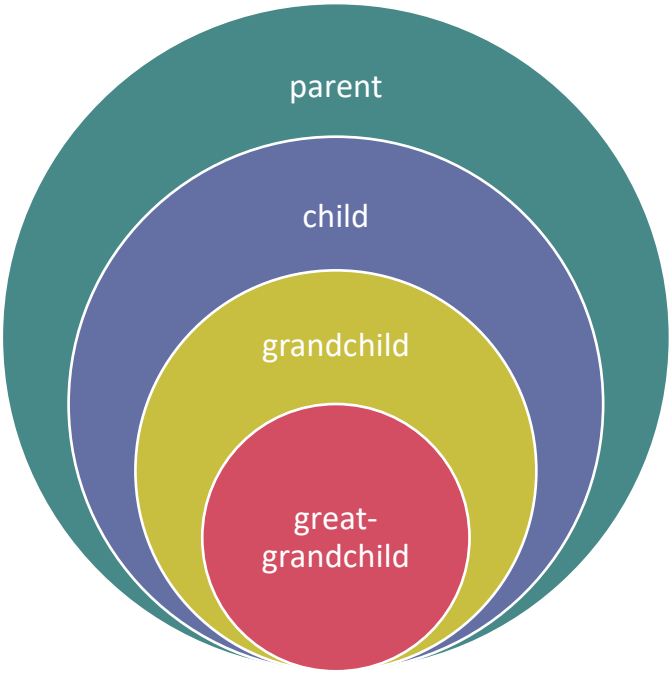
Miicrobiome toxicity

The microbiome is connected to biological health. Organ toxicity may be linked to risk of microbiome toxicity (Lozano, et al., 2018). Scientists have observed glyphosate exposure alters the microbiome. In the same study the scientists observed resultant 'despair behaviour' in rodents. Scientists theorise that breast cancer might be interrelated with microbiome function (Aitbali, et al., 2018).

A depleted or altered (dysbiotic) microbiome can induce immunosuppression (involved in cancer) chronic inflammation and increase pathogen susceptibility. Scientists have observed that glyphosate appears to inhibit growth of beneficial organisms while pathogenic bacteria are resistant to the molecule (Watts, et al., 2016, p. 18). The impact from glyphosate exposure can be gendered - different for males and females (Lozano, et al., 2018).

A recent study demonstrated glyphosate can alter the Firmicutes to Bacteroidetes ratio in mice microbiomes and induce anxiety and depression-like behaviours in mice. Alteration of this ratio is also associated with obesity and inflammation (Aitbali, et al., 2018).

It is well known that the endocrine system is connected to the microbiome, and breast cancer is



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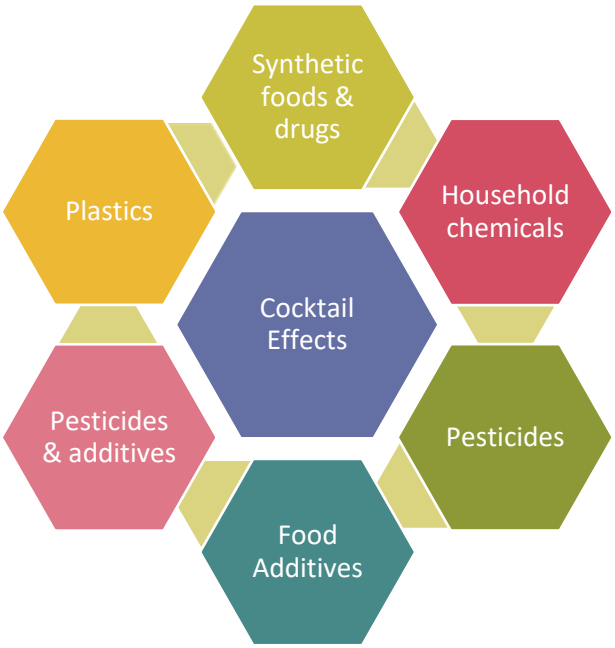
often modulated by hormone function. The intestinal tract is the organ exposed to the highest concentrations of glyphosate.

Recently scientists used a multi-omics approach integrating shotgun metagenomics and metabolomics to understand how glyphosate herbicides alter the rat gut microbiome.

The substance appeared to inhibit the shikimic acid pathway in gut bacteria, and formulation surfactants differently affected the microbiome. Changes observed were indicative of oxidative stress. Scientists consider that shifts in bacterial species could act as biomarkers of glyphosate-based herbicides exposure (Mesnage, et al., 2019).

Antibiotic resistance

Antimicrobial resistance appears to develop 100,000 times faster in the presence of glyphosate and/or dicamba. Low-level chemical exposures in food and in freshwater systems may be contributing to antibiotic resistance and pathogenic outbreaks. Low levels of glyphosate (and other herbicides), can change the way bacterial cells respond to antibiotics in such a way that can cause bacteria to be less susceptible to antibiotics. Environmentally relevant levels of herbicides (but also, the so-called inert or formulation ingredients in the commercial products) mimic antibiotics (with varying effect). Because herbicides are less toxic to the bacteria in question, there is greater capacity for resistant populations of pathogenic bacteria to arise (Kurenbach, et al., 2017; Kurenbach, Hill, Godsoe, van Hamelsveld, & Heinemann, 2018; Kubsad, et al., 2019). Bacteria that have traditionally degraded herbicides may also be the bacteria that possess the trait of antimicrobial resistance (Ramakrishnan, Venkateswarlu, Sethunathan, & Megharaj, 2019).



Glyphosate reduces nutrient availability and detoxification capacity

Glyphosate is a chelator and can bind mineral micronutrients, reducing their bioavailability for crop systems, and consequent availability in food (Krüger, et al., 2014). Glyphosate affects enzymes within the shikimate pathway that governs the production of aromatic amino acids. Phenylalanine, tyrosine, and tryptophan are aromatic amino acids. Glyphosate has been observed to interfere with cytochrome P450 enzymes. The degree to which this is a pathway to disease is contested (Mesnage & Antoniou, 2017).

Are mixtures unsafe?

'Synergistic effects from multiple chemical exposures often occur in populations (female, low-socioeconomic status, immigrant, children etc) least provisioned to defend against these chemicals—and with the least political and legal power to voice their injuries' (Arcuri & Hendlin, 2019).

Scientists and European regulators are increasingly worried the cocktail effect of chemical mixtures damage both human and environmental health. The European Environment Agency has expressed concern around the 'cocktail effect', 'whereby mixtures of single chemical substances that individually may be present at harmless concentrations can combine and pose a risk to health' (EEA, 2019).

Effects can be additive and/or synergistic and combinatory effects can result in harm occurring at levels much lower than the threshold levels considered by regulators to be safe (Kortenkamp A., 2014) (Kortenkamp & Faust, 2018). This further changes when exposures to infants and children are considered, due to their increased vulnerabilities.

Glyphosate is commonly applied as a chemical mixture in the New Zealand environment and cocktails of pesticides are in New Zealand rivers (Hageman, et al., 2019). It is rare that pesticides are

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detected as an isolated chemical. Heavy metals such as cadmium are commonly found in fertilisers, but are also in glyphosate formulations (Defarge, de Vendômois, & Séralini, 2018), and synergies may increase health risk. Because weeds may be resistant to glyphosate applicators commonly mix glyphosate formulations with other herbicides such as metsulfuron-methyl, or organosilicon surfactants. The mixture toxicity of these has never been assessed and while organosilicons are treated as harmless they are increasingly demonstrated to be toxic (Chen, Fine, & Mullin, 2018).

Testing of pesticides in food demonstrate mixtures of pesticides are commonly found in foods (FSANZ, 2019). Of course, environmental, including household and workplace exposures to other chemicals including personal care products, food ingredients, plastics, cleaning agents and air pollution increase lifetime exposures to chemical mixtures.

The complexity of the chemical cocktail challenge is arguably beyond New Zealand resourcing. A cohort of European scientists have recently produced a document intended to address this complexity: *Guidance on harmonised methodologies for human health, animal health, and ecological risk assessment of combined exposure to multiple chemicals* (More, et al., 2019).

Is drinking water safe?

Glyphosate degrades to the metabolite aminomethylphosphonic acid (AMPA). AMPA is similarly toxic but can exist in the environment for longer and accumulate. It is more likely to pollute drinking water. AMPA is more likely to accumulate where phosphates such as fertiliser runoff pollute drinking water sources. Source waters are not tested for chemical pollution in Aotearoa and testing of drinking water for pesticides including glyphosate is locally managed. It is difficult to understand if glyphosate and AMPA are regularly tested for, there is no central information source, and it is difficult to gauge if local testing methods reflect best international practice. There is no evidence AMPA can be removed by drinking water treatment plants in New Zealand. (Soil and Health & PSGR, 2019)

There is no requirement for authorities to monitor glyphosate in New Zealand drinking water as there is no established Maximum Acceptable Value (MAV).

Are children more at risk?

Unborn babies, infants and children are vastly more vulnerable than adults to chemical exposures, particularly at low doses that impact hormones responsible for growth and development (Landrigan & Goldman, 2011; Watts M. , 2013). Dr Meriel Watts in her book Poisoning our Future: Children and Pesticides, acknowledged 'data used to register pesticides utterly fails to reflect the reality of exposure of the unborn foetus or newly born child to low levels of endocrine disrupting pesticides' (Watts M. , 2013, p. 43). In a similar vein, Catherine Iorns has cited the gaps in risk assessment that currently exist in New Zealand regulation (Iorns, 2018).

Babies and children tend to have higher levels of pesticides including glyphosate than adults in biofluids (eg. urine and blood serum) (Gillezeau, et al., 2019). Babies and children are more exposed than adults because they (Watts M. , 2013):

- Consume proportionately more by bodyweight and consume more residues
- Are in places where exposures are more likely (eg. walking home from school along roadside drains, playing on grass)
- Breathe more (double adults), absorbing higher quantities of airborne pollutants
- Are born pre-polluted following maternal exposures to chemicals
- Consume breast milk contaminated via maternal body-burdens

Embryos, foetuses, infants and children are particularly vulnerable because detoxification pathways are not mature and so chemicals tend to accumulate in young bodies (Watts M. , 2013):

- Foetuses and infants can absorb more through lungs, skin and the gastrointestinal tract than adults
- The blood brain barrier is not fully developed until at 6 months of age
- Metabolic pathways are immature. Kidney, liver and enzyme systems are still developing, and so babies and children are less able to metabolise, detoxify and excrete chemicals.

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Additionally, unborn babies, infants and children have critical windows where they are much more vulnerable to chemical exposures (Watts M. , 2013):

- The embryo, foetus and newborn are at greatest risk as early interferences can lead to problems with growth, behaviour and increase risk for disease.
- Endocrine disrupting compounds may harm an infant and child but not an adult. Effects can continue long after exposures cease.
- The brain and nervous system are not fully developed until age 10-12 and neurotoxic chemicals can produce permanent damage.
- The respiratory system can be damaged.
- Immunotoxic chemicals can weaken the immune system and lead to asthma, hypersensitivity, reduced ability to protect against cancer and autoimmune diseases.

What about exposures in food?

Glyphosate is widely sprayed on oilseeds, cereal and legume crops and pastures and international guidelines inform individual country regulators. Cereal consumption in the South Island of New Zealand may be locally produced, but North Island wheat, for example is secured offshore, predominantly from Australia. Australian diet studies confirm glyphosate is widely present in cereals (FSANZ, 2019). Pet lovers may like to know that glyphosate is a pet food contaminant, and residues tend to correlate with fibre content which may arise from the cereal component in petfoods (Zhao, et al., 2018). Glyphosate can be largely avoided through an organic diet.

Imported foods from weaker regulatory regions are likely to have glyphosate in food, as these regions have not enacted rules or policies to prevent glyphosate being used as a desiccant, or pre-harvest spray to dry-down crops (such as cereals and lentils) before harvest, or they may produce genetically engineered soy, canola, sugar beet, corn and cotton products that are resistant to herbicides. Many genetically engineered crops are resistant to multiple herbicides (this is referred to stacked traits), and so many herbicides are sprayed across the growing season. Glyphosate is not the only herbicide contaminant. As well as pre-harvest glyphosate treatment, many cereal crops have additional insecticides and fungicides applied to them in addition to neonicotinoid seed treatments.

In Germany, glyphosate desiccation on cereal crops has reduced and the practice is to be banned (BC Legal, 2018). Urinary levels in Germany are low, and correlate with consumption of pulses and mushrooms (Soukup, et al., 2020).

An effective way to prevent unnecessary exposures to a wider public that might not be able to afford an organic diet would be to require the same standards as European markets and remove authorisations that permit food and feed crops to be sprayed with glyphosate-based herbicides.

These food products can contain glyphosate:

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Access their excellent Playbook here.

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