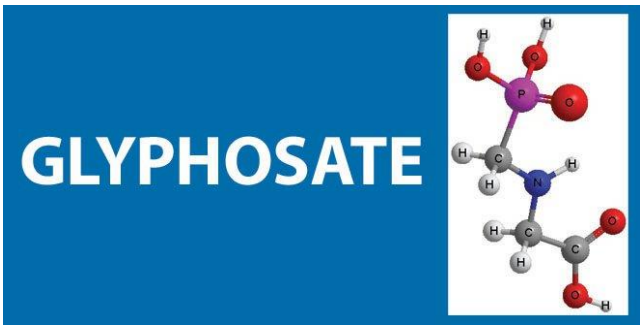
Cancer Association of South Africa (CANSA)

Fact Sheet and Position Statement on Glyphosate

Introduction

Glyphosate (*N*-(phosphonomethyl)glycine) is a broad-spectrum systemic herbicide used to kill weeds, especially annual broadleaf weeds and grasses known to compete with commercial crops grown around the globe.



[Picture Credit: Glyphosate]

Glyphosate was discovered to be a herbicide by a Monsanto chemist, Jon E Franz, in 1970. Monsanto brought glyphosate to market in the 1970s under the trade name 'Roundup'. Monsanto's last commercially relevant United States patent expired in 2000. Various international companies have since started manufacturing and distributing products containing glyphosate.
(Wikipedia; China Research & Intelligence; Reuters).

IARC Classification of Glyphosate

Glyphosate is the world's most widely produced herbicide, by volume. It is used extensively in agriculture and is also found in garden products in many countries. The chemical is an ingredient in a weed killer product, and glyphosate has become more popular with the increasing market share of crops that are genetically engineered to be tolerant to the herbicide.

The International Agency for Research on Cancer (IARC) regularly reviews the carcinogenicity of industrial chemicals, foodstuffs and even jobs. On 20 March, 2015, a panel of international experts convened by the Agency reported the findings of a review of five agricultural chemicals in a class known as organophosphates. A summary of the study was published in *The Lancet Oncology.*

Two of the pesticides - tetrachlorvinphos and parathion - were rated as "possibly carcinogenic to humans", or Group 2B. Three chemicals - malathion, diazinon and glyphosate - were rated as "probably carcinogenic to humans", labelled Group 2A (Nature).

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IARC Classification of Carcinogens (Cancer Causing Agents)
Compounds or physical factors assessed by IARC (International Agency for Research on Cancer) are classified in four groups based on the existing scientific evidence for carcinogenicity (cancer causing ability).

Group 1:
"Carcinogenic to humans" - there is sufficient evidence to conclude that it can cause cancer in humans.

Group 2A:
"Probably carcinogenic to humans" - there is strong evidence that it can cause cancer in humans, but at present it is not conclusive.

Group 2B:
"Possibly carcinogenic to humans" - there is some evidence that it can cause cancer in humans but at present it is far from conclusive.

Group 3:
"Unclassifiable as to carcinogenicity in humans" - there is no evidence at present that it causes cancer in humans.

Group 4:
"Probably not carcinogenic to humans" - there is strong evidence that it does not cause cancer in humans.

Monsanto Disputes the IARC Classification of Glyphosate
The Monsanto Glyphosate Task Force does not accept the recent classification of glyphosate by the International Agency for Research on Cancer (IARC) as a Group 2A carcinogen. They claim serious deficiencies in terms of methodological approach as well as the overall conclusion.

Possible Reasons Why the International Agency on Research in Cancer (IARC) Reached a Different Conclusion on Glyphosate
There are several possible reasons why the IARC has reached a different conclusion on the safety of glyphosate compared to other internationally recognised bodies:

- The IARC only considered documents on the safety of glyphosate that are available in the public domain. Compared to this, other bodies have also taken proprietary documentation provided by the herbicide developer and not available in the public domain into account
- The IARC considered the safety of glyphosate in formulation, which includes surfactants. Compared to this, regulatory bodies assessed the safety of pure glyphosate and not in formulation

- Safety assessment of glyphosate and glyphosate tolerant crops is evaluated separately and not in combination by regulatory authorities

Since the commercialisation of herbicide tolerant crops, independent research has generated previously unknown information regarding the application of glyphosate on maize and soybean crops:

- Glyphosate is present in the grain of herbicide tolerant crops treated with glyphosate
- Glyphosate is not removed from food during processing
- Low concentrations of glyphosate in formulation have been found to have genotoxic effects in mammalian cells *in vitro*

(Koortzen, 2017).

Health Effects of Pure Glyphosate versus Glyphosate in Formulation

The commercial formulation of glyphosate contains surfactants which enhance its herbicidal properties. These surfactants facilitate absorption and increase the degree of rainfastness of the herbicide and ensure that it is not washed off by rain or during irrigation (Duke, *et al.,* 2003).

The United States of America Environmental Protection Agency (EPA) does not require safety testing of the surfactants used in pesticides, since they are considered to have no pesticidal properties (Herzfeld and Sargent, 2012). As a result of this, there are no standards on the composition and safety of the non-pesticidal ingredients of pesticide formulations worldwide (Herzfeld and Sargent, 2012).

Several studies, reports and reviews on the safety of pure glyphosate have concluded that it is safe for humans if applied at the correct agricultural concentration (Williams, *et al.,* 2000). The acute toxicity of glyphosate and its major metabolite aminomethylphosphonic acid (AMPA) has been tested in animal feeding trials and no adverse effects have been found (Williams, *et al.,* 2000; Williams *et al.,* 2012). Furthermore, in 1993, the Environmental Protection Agency (EPA) classified both glyphosate and AMPA in Category E, which is described as "Evidence of Non-carcinogenicity", based on the lack of convincing evidence of carcinogenicity in numerous studies (EPA, 1993). In 1994, the World Health Organization (WHO) reaffirmed the findings that there was no evidence that glyphosate and AMPA were harmful to humans and that both glyphosate and AMPA had negligible levels of acute toxicity (World Health Organization, 1994).

In contrast to studies on pure glyphosate, several studies on glyphosate in formulation (glyphosate with surfactants) have reported toxicity and carcinogenicity. A study by Gasnier, *et al.* (2009) demonstrated that glyphosate in formulation at 5 ppm (5 mg/kg) had toxic effects and resulted in cell death of human liver, umbilical cord and placental cells within 24 hours of exposure. They also indicated that glyphosate in formulation at 0.5 ppm (0.5 mg/kg) caused endocrine disruption in human liver cells within 24 hours of exposure.

A more recent study by Belle, *et al.* (2012) determined that 8mM (1,300 mg/kg) of glyphosate in formulation inhibited the cell replication of human embryonic cells within 24 hours of exposure. Belle, *et al.* (2012) concluded that the concentration of glyphosate in formulation used in their study was far below the prescribed concentration of 40 mM recommended for herbicide application during agricultural practice.

A study by Koller, *et al.* (2012) found that glyphosate in formulation at 10 mg/L to 20 mg/L (5.7 mg/kg to 11.4 mg/kg), caused DNA damage and at 40 mg/L (22 mg/kg) caused membrane damage and mitochondrial impairment in human epithelial cells.

A study by Young, *et al.* (2015) demonstrated that glyphosate in formulation was cytotoxic to human placenta cells at concentrations ranging from 0.005 mM to 0.008 mM (0.85 mg/kg to 1.35 mg/kg). They confirmed that the surfactants within the glyphosate formulation had a major effect on the toxicity of the herbicide and demonstrated that glyphosate in formulation exhibited similar toxicity at a concentration of 2 000 times lower than pure glyphosate. Furthermore, Belle, *et al.* (2012) suggested that glyphosate on its own should not be considered a herbicide, since without surfactants it is not permeable and cannot be absorbed by plant cells.

A study by Alvarez-Moya, *et al.* (2014) reported that glyphosate in formulation at a concentration of 0.12 mg/L (0.069 mg/kg) caused DNA damage in human lymphocytes.

A further study by Roustan, *et al.* (2014) indicated that glyphosate in formulation induced chromosomal breakage in hamster ovary cells at a concentration of only 0.01 mg/L (0.006 mg/kg). Similar results were found in fish by Moreno, *et al*. (2014) indicating that glyphosate in formulation caused DNA strand breaks in liver and gill cells at a concentration of 0.058 mg/L (0.033 mg/kg). DNA and chromosomal damage leads to an increased mutation rate and subsequently an increased risk for developing cancer.

Currently the only cancer in humans with a significant link to glyphosate is Non-Hodgkin's lymphoma (IARC, 2015). Case-control studies from the USA and Sweden reported a statistically significant increased risk for Non-Hodgkin's lymphoma associated with glyphosate exposure (Hardell ,*et al.,* 2002; De Roos, *et al.,* 2003; Eriksson, *et al.,* 2008; Orsi, *et al.,* 2009).

Animal studies have indicated that continuous exposure to glyphosate resulted in a significant increase in the risk for pancreatic islet cell adenoma, renal tubule carcinoma, hepatocellular adenoma and thyroid C cell adenoma in male and female mice (Environmental Protection Agency, 1986; Environmental Protection Agency, 1991). Thus as a result, the IARC has concluded that there is limited evidence of carcinogenicity in humans and convincing evidence of carcinogenicity in animals as a result of exposure to glyphosate.

Williams, *et al.* (2012) argued that safety studies on glyphosate in formulation are irrelevant since glyphosate toxicity is as a result of "surfactants present in the formulation" and not due to glyphosate itself. Viljoen (2013) suggested that the argument of Williams, *et al.* (2012) was "irrelevant, since it is the formulation that is being applied to the plant in practice and it is part of the herbicide complex of chemicals taken up by the plant".

Meftaul, I.M., Venkateswarlu, K., Dharmarajan, R., Annamalai, P., Asaduzzaman, M., Parven, A. & Megharaj, M. 2020.
"Glyphosate, introduced by Monsanto Company under the commercial name Roundup in 1974, became the extensively used herbicide worldwide in the last few decades. Glyphosate has excellent properties of fast sorption in soil, biodegradation and less toxicity to nontarget organisms. However, glyphosate has been reported to increase the risk of cancer, endocrine-disruption, celiac disease, autism, effect on erythrocytes, leaky-gut syndrome, etc. The reclassification of glyphosate in 2015 as

'probably carcinogenic' under Group 2A by the International Agency for Research on Cancer has been broadly circulated by anti-chemical and environmental advocacy groups claiming for restricted use or ban of glyphosate. In contrast, some comprehensive epidemiological studies involving farmers with long-time exposure to glyphosate in USA and elsewhere coupled with available toxicological data showed no correlation with any kind of carcinogenic or genotoxic threat to humans. Moreover, several investigations confirmed that the surfactant, polyethoxylated tallow amine (POEA), contained in the formulations of glyphosate like Roundup, is responsible for the established adverse impacts on human and ecological health. Subsequent to the evolution of genetically modified glyphosate-resistant crops and the extensive use of glyphosate over the last 45 years, about 38 weed species developed resistance to this herbicide. Consequently, its use in the recent years has been either restricted or banned in 20 countries. This critical review on glyphosate provides an overview of its behaviour, fate, detrimental impacts on ecological and human health, and the development of resistance in weeds and pathogens. Thus, the ultimate objective is to help the authorities and agencies concerned in resolving the existing controversies and in providing the necessary regulations for safer use of the herbicide. In our opinion, glyphosate can be judiciously used in agriculture with the inclusion of safer surfactants in commercial formulations sine POEA, which is toxic by itself is likely to increase the toxicity of glyphosate."

Opinion on Glyphosate by an Expert Panel of Scientists

In 2015, the International Agency for Research on Cancer (IARC) published a monograph concluding there was strong evidence for genotoxicity of glyphosate and glyphosate formulations and moderate evidence for genotoxicity of the metabolite aminomethylphosphonic acid (AMPA).

These conclusions contradicted earlier extensive reviews supporting the lack of genotoxicity of glyphosate and glyphosate formulations. The IARC Monograph concluded there was strong evidence of induction of oxidative stress by glyphosate, glyphosate formulations, and AMPA.

An Expert Panel (Brusick, *et al*., 2016) reviewed the genotoxicity and oxidative stress data considered in the IARC Monograph, together with other available data not considered by IARC. The Expert Panel defined and used a weight of evidence (WoE) approach that included ranking of studies and endpoints by the strength of their linkage to events associated with carcinogenic mechanisms.

Importantly, the Expert Panel concluded that there was sufficient information available from a very large number of regulatory genotoxicity studies that should have been considered by IARC. The WoE approach, the inclusion of all relevant regulatory studies, and some differences in interpretation of individual studies led to significantly different conclusions by the Expert Panel compared with the IARC Monograph.

The Expert Panel concluded that glyphosate, glyphosate formulations, and AMPA do not pose a genotoxic hazard and the data do not support the IARC Monograph genotoxicity evaluation. With respect to carcinogenicity classification and mechanism, the Expert Panel concluded that evidence relating to an oxidative stress mechanism of carcinogenicity was largely unconvincing and that the data profiles were not consistent with the characteristics of genotoxic carcinogens.
(Brusick, *et al*., 2016).

Muñoz, J.P., Bleak, T.C. & Calaf, G.M. 2021.
"Glyphosate is a large-spectrum herbicide that was introduced on the market in 1974. Due to its important impact on the crop industry, it has been significantly diversified and expanded being considered the most successful herbicide in history. Currently, its massive use has led to a wide environmental diffusion and its human consumption through food products has made possible to detect it in urine, serum, and breast milk samples. Nevertheless, recent studies have questioned its safety and international agencies have conflicting opinions about its effects on human health, mainly as an endocrine-disrupting chemical (EDC) and its carcinogenic capacity. Here, we conduct a comprehensive review where we describe the most important findings of the glyphosate effects in the endocrine system and asses the mechanistic evidence to classify it as an EDC. We use as guideline the ten key characteristics (KCs) of EDC proposed in the expert consensus statement published in 2020 (La Merrill et al., 2020) and discuss the scopes of some epidemiological studies for the evaluation of glyphosate as possible EDC. We conclude that glyphosate satisfies at least 8 KCs of an EDC, however, prospective cohort studies are still needed to elucidate the real effects in the human endocrine system."

Wieslenburger, D.D. 2021.
"Glyphosate-based formulations (GBFs), such as Roundup, are the most heavily used herbicides in the world. In 2015, the International Agency for Research on Cancer (IARC) concluded that glyphosate and GBFs are probably carcinogenic to humans (group 2A), mainly for non-Hodgkin lymphoma (NHL). However, this finding has been controversial, and most pesticide regulatory agencies have not followed their lead. The purpose of this review was to examine the scientific literature linking exposure to glyphosate and GBFs to the development of NHL, with emphasis on new findings since publication of the IARC report. The epidemiologic studies provide ample evidence for an association between exposure to GBFs and an increased risk of NHL. Animal studies have shown that glyphosate is carcinogenic in rodents and causes NHL in mice. Mechanistic studies have demonstrated that glyphosate and GBFs are genotoxic to human lymphocytes, the normal cell of origin of NHL, both in vitro and in vivo. Genotoxic and other biological effects have also been shown in various animal and cell models with these agents even at low doses. A novel mechanism underlying the specificity of glyphosate for NHL, that is upregulation of the B-cell genome mutator enzyme activation-induced cytidine deaminase, has recently been demonstrated. These findings were evaluated holistically using the guidelines for evaluation of general causation set forth by Bradford Hill. This evaluation provides coherent and compelling evidence that glyphosate and GBFs are a cause of NHL in humans exposed to these agents. These findings should prompt new reviews by pesticide regulatory agencies around the world."

Meloni, F., Satta, G., Padoan, M., Montagna, A., Pilia, I., Argiolas, A., Piro, S., Magnani, C., Gambelunghe, A., Muzi, G., Ferri, G.M., Vimercati, L., Zanotti, R., Scarpa, A., Zucca, M., De Matteis, S., Campagna, M., Miligi, L. & Cocco. P. 2021.
Background: The International Agency for Research on Cancer (IARC) recently classified glyphosate, the most used herbicide worldwide, as a probable human carcinogen. We inquired into the association between occupational exposure to glyphosate and risk of lymphoma subtypes in a multicenter case-control study conducted in Italy.
Methods: The Italian Gene-Environment Interactions in Lymphoma Etiology (ItGxE) study took place in 2011-17 in six Italian centres. Overall, 867 incident lymphoma cases and 774 controls participated in the study. Based on detailed questionnaire information, occupational experts classified duration, confidence, frequency, and intensity of exposure to glyphosate for each study subject. Using

unconditional regression analysis, we modelled risk of major lymphoma subtypes associated with exposure to glyphosate adjusted by age, gender, education, and study centre.
Results: Very few study subjects (2.2%) were classified as ever exposed to glyphosate. Risk of follicular lymphoma (FL) was elevated 7-fold in subjects classified as ever exposed to glyphosate with medium-high confidence, 4.5-fold in association with medium-high cumulative exposure level, 12-fold with medium-high exposure intensity, and 6-fold with exposure for 10 days or more per year. Significant upward trends were detected with all the exposure metrics, but duration. The overall p-value for an upward trend with four independent metrics was 1.88×10^{-4}. There was no association with risk of lymphoma (any subtype), Non Hodgkin Lymphoma, B-cell lymphoma, or the major lymphoma subtypes other than FL.
Conclusions: Our findings provide limited support to the IARC decision to classify glyphosate as Group 2A human carcinogen.

Glyphosate (Roundup) to be Removed from United States Garden Shelves from 2023
The following article was:
Posted on 29th July 2021 by Sustainable Pulse.

Bayer Confirms End of Sale of Glyphosate-Based Herbicides for US Lawn & Garden Market

Posted on Jul 29 2021 - 6:54pm ***by*** Sustainable Pulse
Bayer have announced that they will no longer sell glyphosate-based herbicides to U.S. gardeners as of 2023, following the costly litigation battle over their cancer causing weedkiller Roundup.

Bayer Monsanto stated Thursday that "the company and its partners will replace its glyphosate-based products in the U.S. residential Lawn & Garden market with new formulations that rely on alternative active ingredients beginning in 2023, subject to a timely review by the U.S. Environmental Protection Agency (EPA) and state counterparts….."
"As the vast majority of claims in the litigation come from Lawn & Garden market users, this action largely eliminates the primary source of future claims beyond an assumed latency period. There will be no change in the availability of the company's glyphosate formulations in the U.S. professional and agricultural markets," Bayer continued.
Sustainable Pulse and Detox Project Director, Henry Rowlands, commented on Bayer's announcement; "It is a great victory in a small battle for the removal of glyphosate from the Lawn & Garden market, however this is just part of a much larger War. We must all remember that this will not stop glyphosate being sprayed in parks, schools and on our food crops in ever greater amounts across the U.S. and the world. It is time to phase the chemical
In the company's announcement on Thursday they also revealed an extra provision of $4.5 Billion adding on to their previous agreement of $10.9 Billion to sufferers of Non-Hodgkin's

lymphoma, which is caused by the use of their Roundup weedkiller; "Bayer is also prepared …….to manage anticipated claims, through settlement and litigation, to ultimately bring an end to this litigation. For this second scenario, the company posts an additional provision of a gross amount of 4.5 billion U.S. dollars (3.8 billion euros), i.e. before tax and discounting in the second quarter 2021, reflecting the company's potential long-term exposure."
"Moreover, the company will engage in discussions with EPA about Roundup™ labels with the goal of providing more information to users about the science as an additional element towards ensuring even more informed purchasing and application decisions," Bayer concluded.

Usage Patterns of Glyphosate
Glyphosate is a non-selective herbicide registered for use on many food and non-food crops as well as non-crop areas where total vegetation control is desired. When applied at lower rates, it serves as a plant growth regulator. The most common uses include control of broadleaf weeds and grasses in:

- hay/pasture
- soybeans
- field corn
- ornamentals
- lawns
- turf
- forest plantings
- greenhouses
- rights-of-way.

Glyphosate is among the most widely used pesticides/herbicides by volume. In 1986, an estimated 3 000 000kg of glyphosate was used in the United Sates. Usage in 1990 was estimated to be 5 000 000kg. It ranked eleventh among conventional pesticides/herbicides in the US during 1990/91. In recent years, 13 to 20 million acres were treated with 9 million kilograms annually. Glyphosate is generally sold as the isopropylamine salt and applied as a liquid foliar spray.
(EPA Technical Sheet).

Release Patterns of Glyphosate
Glyphosate is released to the environment in its use as a herbicide for controlling woody and herbaceous weeds on forestry, right-of-way, cropped and non-cropped sites. These sites may be around water and in wetlands. It may also be released to the environment during its manufacture, formulation, transport, storage, disposal and clean-up, and from spills. Since glyphosate is not a listed chemical in the Toxics Release Inventory, data on releases during its manufacture and handling are not available.

Environmental Fate of Glyphosate
Glyphosate is most often applied as a spray of the isopropylamine salt and is removed from the atmosphere by gravitational settling. After glyphosate is applied to forests, fields, and other land by spraying, it is strongly adsorbed in the soil where it remains in the upper layers. It has a low propensity for leaching. Iron and aluminium clays and organic matter tend to adsorb more glyphosate than sodium and calcium clays. Glyphosate readily binds to kaolinite, illite, bentonite, charcoal and muck but not to ethyl cellulose.

Glyphosate readily and completely biodegrades in soil even under low temperature conditions. The average half-life of glyphosate in soil is about 60 days.

Biodegradation in foliage and litter is somewhat faster, although, in field studies, residues are often found the following year. Glyphosate may enter aquatic systems through accidental spraying, spray drift, or surface runoff. It dissipates rapidly from the water column as a result of adsorption and possibly biodegradation.

[Picture Credit: Glyphosate Spraying]

The half-life of glyphosate (the time required for half of the compound to dissipate or degrade) varies, depending on conditions. For example, a Monsanto study conducted at eight sites across the U.S. in 1992-1993 produced a range of half-lives, some short (1.7, 7.3, 8.3 days) and some longer, up to 141.9 days at one site in Iowa (Oppenhuizen 1993).

The average half-life of glyphosate at the eight study sites was about 40 days, a moderately rapid rate compared with degradation of other compounds. The variability in rates of glyphosate degradation is believed to be due to the varying microbial activity and extent of soil-binding at the different study sites. Half-life is related to soil persistence, but the two terms are not interchangeable. A half-life of 32 days means that half of the residues initially present will have dissipated or degraded in 32 days. However, this does not mean that all of the compound will be gone in 64 days.

Detectable levels can be present even after 3 to 4 half-lives, but the concentration in soil will be very low and the residues will be tightly bound to soil particles. Detection of glyphosate at very low levels 3 years after application has been reported in a study conducted in subarctic forest soils in Sweden (Torstensson, *et al*., 1989), but was attributed to the lack of microbial activity during winter months and to the gradual release of small amounts of adsorbed glyphosate from treated vegetation residues, rather than an insufficient capacity of the soils to degrade glyphosate. Microbes, even if frozen for several months a year, eventually will degrade the glyphosate in soil.

The bioconcentration factor (BCF) of glyphosate in fish following a 10-14 day exposure period was 0.2 to 0.3. Occupational workers and home gardeners may be exposed to glyphosate by inhalation and dermal contact during spraying, mixing, and clean-up. They may also be exposed by touching soil and plants to which glyphosate was applied. Occupational exposure may also occur during glyphosate's manufacture, transport, storage, and disposal. (Monsanto; EPA Technical Sheet).

Glyphosate Use in South Africa

The weed killer, glyphosate, is widely used in South Africa and has been found in bread flour and maize meal.

In South Africa, the use of glyphosate - an active ingredient in certain herbicides, which is used on genetically modified crops - has been growing. According to the African Centre of Biodiversity, half of

South Africa's maize crop and 100% of the soya crop is genetically modified, meaning it has to be grown with the use of glyphosate.

According to Christo Joubert, from the Market Economic Research Centre at the National Agricultural Marketing Council, South Africa consumes nearly 27 000 tons of maize daily. It is unclear what portion of this is genetically modified maize.

In 2012, the African Centre for Biodiversity conducted a study of glyphosate levels in maize and soya in South Africa. It found traces of glyphosate, but it was below the maximum residue levels permitted. What concerned the organisation was that it had to get the tests done in France because none of the laboratories in South Africa could perform the analyses.

Rhodes University tested the effect of glyphosate on aquatic animals. The herbicide is known to affect the embryonic development of frogs. Professor Tally Palmer, of the Rhodes Institute for Water Research, said glyphosate was used to control a number of aquatic weeds. However, to test the amount of glyphosate in South Africa's waterways would be expensive.

The South African Consumer Protection Act requires all food containing 5% or more genetically modified content to be labelled.

According to a Report "Assessing the Value of Glyphosate in the South African Agricultural Sector" by the Department of Agricultural Economics, Extension and Rural Development, University of Pretoria, glyphosate was used in South Africa during 2012 for the following:

- Maize
- Wheat
- Soybeans
- Citrus
- Forestry
- Wine grapes
- Table grapes
- Sugarcane
- Sorghum
- Pome fruits (apples and pears)
- Sunflower seed
- Barley
- Pastures
- Nuts
- Stone fruit (e.g. peaches and prunes)
- Ground nuts

According to the aforementioned Report, a total of 23 253 million litres of glyphosate at a cost of R1 008,9 million was used in South Africa during 2012.

For a response by the South African Department of Agriculture, Forestry & Fisheries on Glyphosate Carcinogen Classification by IARC, please refer to Annexure A.

Detection of Glyphosate in Herbicide Tolerant Maize and Herbicide Tolerant Soybean

Glyphosate in formulation is applied to genetically modified and herbicide tolerant (GM HT) crops one to three times during the growing season to control weeds (Krüger, *et al.,* 2014a). After application, glyphosate is absorbed and distributed to all parts of the HT plant tissue (Duke, *et al.,* 2003; Robinson, 2009). When glyphosate was initially applied in agriculture it was not known that it would later be detected in the grain of HT crops. Published data on glyphosate residue in HT crops is sparse (Benbrook, 2016). However, studies have detected glyphosate in HT maize from the USA as well as HT soybean from the USA and Argentina (Reddy *et al.,* 2004).

According to Koortzen (2017) glyphosate was detected in both herbicide tolerant (HT) maize and HT soybean in South Africa. A total of 81 food products were selected from retail outlets including Pick 'n Pay, Shoprite, Checkers, Spar, Dischem and Woolworths according to product availability during 2015. Products were selected to include as many different product brands as possible.

During sampling, only products which contained maize and/or soybean as the major constituent in raw or processed form were selected. Products were arranged into three categories using their ingredients list as a guideline showing both soybean and maize as a primary constituent:

- samples containing maize
- samples containing soybean
- samples containing both maize and soybean

The texturised soy protein products and corn-soy blends listed both maize and soybean as a primary constituent and were tested for both HT maize and soybean events.

For soybean, infant milk and soy flour, only one brand was commercially available.

Eighty-one off-the-shelf maize and soybean food products were tested for glyphosate. Of these products, 57 indicated maize as a primary constituent, 11 specified soybean as a primary constituent, while 13 contained both maize and soybean as a primary constituent (corn-soy blends and texturized soy protein products).

- Of all the products tested, 54 (66.70%) contained glyphosate in a range of 27 to 2,257 parts per billion (ppb) (0.027 to 2.26 mg/kg).

- Of the 57 maize products, 30 (52.63%) contained glyphosate in a range of 27 to 95 ppb (0.027 to 0.095 mg/kg).

- All 11 soybean products contained glyphosate in a range of 27 to 142 ppb (0.027 to 0.142 mg/kg).

- Of the six corn-soy blends, all tested positive for glyphosate in a range of 43 to 65 ppb (0.043 to 065 mg/kg).

- All seven texturized soy protein products tested positive for glyphosate in a range of 41 to 2,257 ppb (0.041 to 2.26 mg/kg).

These findings confirm that glyphosate is present in South African food products containing maize and soybean.

Maize is the primary staple and soybean an important source of protein in South Africa. A study by Payne (2011) suggested that approximately 500g of maize meal is consumed daily by adults (age 18 to 65) in poor households. Based on this, it is estimated that 182kg of maize meal is consumed per person annually and approximately 8 601 kg over the average adult lifespan (age 18 to 65).

Considering that the level of glyphosate detected in maize meal, in the study by Koortzen (2017), ranged from 0.027 to 0.093 mg/kg, the total exposure to glyphosate would be approximately 5 mg to 17 mg annually and approximately 240 mg to 806 mg over the average adult lifespan (age 18 to 65).

A recent report by the National Agricultural Marketing Council of South Africa (NAMC) indicated that texturised soy protein was the major soybean food product consumed in South Africa, accounting for approximately 52% of the soybean food market (NAMC, 2011).

In the absence of an estimation of the daily intake of soybean per adult individual in South Africa, the serving suggestion was used to calculate the maximum potential consumption. Based on this, it is estimated that 54.8 kg of texturized soy protein is in theory consumed per person annually and approximately 2,575.6 kg (54.8 x 47 years) over the adult lifespan (age 18 to 65). Considering that the level of glyphosate detected in texturised soy protein products, in the study by Koortzen (2017), ranged from 0.041 to 2.257 mg/kg, the total exposure to glyphosate would be approximately 2,2mg to 123.7mg annually and approximately 105,6mg to 5 813,1mg over the average adult lifespan (age 18 to 65). His study suggests that the consumption of maize and soybean food products does expose South Africans to glyphosate but at low levels.

In recent years, several *in vitro* studies on human cell lines have reported that glyphosate in formulation exhibits toxicity at low concentrations. These findings include human cell death at 5 mg/kg as well as DNA damage and endocrine disruption at concentrations ranging from 0.006 mg/kg to 0.5 mg/kg. Taking this into account, the levels of glyphosate detected in the maize and soybean products in this study cannot be summarily considered to have no effect.

Although pure glyphosate may be considered, the effect of exposure to glyphosate in formulation found at low levels in maize meal, and consumed daily in South Africa, warrants further research.

Glyphosate in Processed Food Products and Water

Various countries including South Africa have established routine monitoring of pesticides in food. However, this is mostly aimed at fresh fruit, vegetables and grain (Swanepoel, 2014). Limited research has been conducted on the presence of glyphosate in processed foods. Nonetheless, recent studies have detected glyphosate in various processed food products (McQueen, *et al.,* 2012; Swanepoel, 2014; Rubio, *et al.,* 2014).

In 2014, 15.4% (30 out of 195) of bread samples from the United Kingdom (UK) were found to contain glyphosate at concentrations of up to 0.100 mg/kg (PRIF, 2015). Similarly, a study by Swanepoel (2014) in South Africa confirmed that glyphosate was present in 88.0% (seven out of eight) of white bread samples tested but did not specify the concentrations of glyphosate detected.

Glyphosate in Animal Tissue and Excretions

Several studies have tested the fate of glyphosate in animals including humans. Research on laboratory animals has confirmed the absorption of glyphosate within the gastrointestinal tract after being fed glyphosate treated feed. Animal feeding studies have also confirmed the distribution of

absorbed glyphosate to the tissue of all major organs, blood and bone (Brewster, *et al.,* 1991; Krüger, *et al.,* 2014).

According to Koortzen (2017), although not proven, the possibility of glyphosate bio-accumulation within animal tissue cannot be ignored. It has been suggested that ingested glyphosate is rapidly excreted from the body by means of urine and faeces (Brewster, *et al.,* 1991). However, it is not known whether the glyphosate absorbed in organ tissue follows the same excretion rate. Furthermore, the detection of glyphosate in animal tissue as a result of being fed glyphosate treated feed indicates that it is transferred within the food chain.

Studies on the fate of glyphosate in humans are limited to urine testing. Studies have confirmed that glyphosate is detectable in the urine of humans from farming and urban communities in the USA and Europe. One of the earliest studies testing for glyphosate in human urine was done by Acquavella, *et al.* (2004). They tested urine samples of 127 individuals from farms in the USA and reported that sixty percent had detectable levels of glyphosate with concentrations of up to 233 µg/L (0.133 mg/kg). It was suggested that the glyphosate in the urine samples was as a result of occupational exposure during agricultural application.

A similar study by Curwin, *et al.* (2007) analysed the urine samples of individuals from farming communities in USA and as a control group, used urine samples of individuals from non-farming communities. They reported that glyphosate was detected in the majority of samples (60% of adults and 80% of children) with concentrations of up to 18 µg/L (0.010 mg/kg) and that there was no significant difference in urinary glyphosate concentration between individuals from farming or non-farming communities. Their findings suggest that other sources of glyphosate exposure should be considered as non-farming individuals are not exposed to glyphosate as a result of occupational application.

Several studies have confirmed the presence of glyphosate in grain (Food and Agricultural Organization of the United Nations (AFO), 2005, Then, 2013, Bøhn, *et al.,* 2014), processed food (Rubio *et al.,* 2014; Swanepoel, 2014), animal tissue (Krüger, *et al.,* 2014 a/b) and water (Battaglin, *et al.,* 2014) which all contribute substantially to the human diet. These findings suggest that diet may contribute a greater role in exposing individuals to glyphosate than initially thought. Furthermore, considering the results from animal studies detecting glyphosate in the tissue of all major organs after being fed glyphosate treated feed (Brewster, *et al.,* 1991; Krüger, *et al.,* 2014), it can be argued that a similar result may be expected in human tissue.

Glyphosate Poisoning

Glyphosate is used extensively as a non-selective herbicide by both professional applicators and consumers and its use is likely to increase further as it is one of the first herbicides against which crops have been genetically modified to increase their tolerance. Commercial glyphosate-based formulations most commonly range from concentrates containing 41% or more glyphosate to 1% glyphosate formulations marketed for domestic use.

They generally consist of an aqueous mixture of the isopropylamine (IPA) salt of glyphosate, a surfactant, and various minor components including anti-foaming and colour agents, biocides and inorganic ions to produce pH adjustment.

The mechanisms of toxicity of glyphosate formulations are complicated. Not only is glyphosate used as five different salts but commercial formulations of it contain surfactants, which vary in nature and concentration. As a result, human poisoning with this herbicide is not with the active ingredient alone but with complex and variable mixtures.

It is difficult to separate the toxicity of glyphosate from that of the formulation as a whole or to determine the contribution of surfactants to overall toxicity.

Experimental studies suggest that the toxicity of the surfactant, polyoxyethyleneamine (POEA), is greater than the toxicity of glyphosate alone and commercial formulations alone. There is insufficient evidence to conclude that glyphosate preparations containing POEA are more toxic than those containing alternative surfactants. Although surfactants probably contribute to the acute toxicity of glyphosate formulations, the weight of evidence is against surfactants potentiating the toxicity of glyphosate.

Accidental ingestion of glyphosate formulations is generally associated with only mild, transient, gastrointestinal features. Most reported cases have followed the deliberate ingestion of the concentrated formulation of 41% glyphosate as the IPA salt and 15% POEA.

There is a reasonable correlation between the amount ingested and the likelihood of serious systemic sequelae or death. Advancing age is also associated with a less favourable prognosis. Ingestion of >85 mL of the concentrated formulation is likely to cause significant toxicity in adults:

- Gastrointestinal corrosive effects, with mouth, throat and epigastric pain and dysphagia are common
- Renal and hepatic impairment are also frequent and usually reflect reduced organ perfusion
- Respiratory distress, impaired consciousness, pulmonary oedema, infiltration on chest x-ray
- Shock
- Arrhythmias
- Renal failure requiring haemodialysis
- Metabolic acidosis and hyperkalaemia may supervene in severe cases.
- Bradycardia and ventricular arrhythmias are often present pre-terminally

Dermal exposure to ready-to-use glyphosate formulations can cause irritation and photo-contact dermatitis has been reported occasionally; these effects are probably due to the preservative Proxel (benzisothiazolin-3-one). Severe skin burns are very rare.

Inhalation is a minor route of exposure but spray mist may cause oral or nasal discomfort, an unpleasant taste in the mouth, tingling and throat irritation.
Eye exposure may lead to mild conjunctivitis, and superficial corneal injury is possible if irrigation is delayed or inadequate.

Management is symptomatic and supportive, and skin decontamination with soap and water after removal of contaminated clothing should be undertaken in cases of dermal exposure.
(Bradberry, Proudfoot & Vale, 2004).

Health Effects of Glyphosate

The World Health Organization (WHO) study, published in the journal *The Lancet Oncology*, said there was limited evidence that the herbicide caused non-Hodgkin's lymphoma in humans, although there was sufficient evidence that it caused cancer in animals. Non-Hodgkin's lymphoma is a cancer that attacks the lymphocytes that form part of the immune system. The study found that glyphosate had been detected in the blood and urine of agricultural workers, suggesting absorption.

Endocrine Disruptive Activity and Toxicity of Glyphosate-based Herbicides - according to a study by Gasnier, *et al*., (2009), glyphosate-based herbicides are the most widely used across the world; they are commercialised in different formulations. Their residues are frequent pollutants in the environment. In addition, these herbicides are spread on most eaten transgenic plants, modified to tolerate high levels of these compounds in their cells. Up to 400 ppm of their residues are accepted in some feed. The researchers exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic *in vivo* regulatory studies. They measured cytotoxicity with three assays (Alamar Blue, MTT, ToxiLight), plus genotoxicity (comet assay), anti-estrogenic (on ERalpha, ERbeta) and anti-androgenic effects (on AR) using gene reporter tests. The researchers also checked androgen to oestrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24h. These effects were more dependent on the formulation than on the glyphosate concentration.

First, the researchers observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in MDA-MB453-kb2 cells for the most active formulation (R400), then from 2 ppm the transcriptional activities on both oestrogen receptors were also inhibited on HepG2. Aromatase transcription and activity were disrupted from 10 ppm.

Cytotoxic effects started at 10 ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered.

Glyphosate Exposure and Breast Cancer – according to Thongprakaisang, *et al*., (2013) glyphosate is an active ingredient of the most widely used herbicide and it is believed to be less toxic than other pesticides. However, several recent studies showed its potential adverse health effects to humans as it may be an endocrine disruptor. This study focused on the effects of pure glyphosate on oestrogen receptors (ERs) mediated transcriptional activity and their expressions. Glyphosate exerted proliferative effects only in human hormone-dependent breast cancer, T47D cells, but not in hormone-independent breast cancer, MDA-MB231 cells, at 10^{-12} to 10^{-6}M in oestrogen withdrawal condition. The proliferative concentrations of glyphosate that induced the activation of oestrogen response element (ERE) transcription activity were 5-13 fold of control in T47D-KBluc cells and this

activation was inhibited by an oestrogen antagonist, ICI 182780, indicating that the estrogenic activity of glyphosate was mediated via ERs. Furthermore, glyphosate also altered both ERα and β expression. These results indicated that low and environmentally relevant concentrations of glyphosate possessed oestrogenic activity. Glyphosate-based herbicides are widely used for soybean cultivation, and the results also found that there was an additive oestrogenic effect between glyphosate and genistein, a phytoestrogen in soybeans. However, the researchers suggest that these additive effects of glyphosate contamination in soybeans need further animal study.

Franke, A.A., Li, X., Shvetsov, Y.B. & Lai, J.F. 2021.
"Breast cancer is the most commonly diagnosed female cancer and the second leading cause of death in women in the US, including Hawaii. Accumulating evidence suggests that aminomethylphosphonic acid (AMPA), the primary metabolite of the herbicide glyphosate-a probable human carcinogen, may itself be carcinogenic. However, the relationship between urinary AMPA excretion and breast cancer risk in women is unknown. In this pilot study, we investigated the association between pre-diagnostic urinary AMPA excretion and breast cancer risk in a case-control study of 250 predominantly postmenopausal women: 124 cases and 126 healthy controls (individually matched on age, race/ethnicity, urine type, date of urine collection, and fasting status) nested within the Hawaii biospecimen subcohort of the Multiethnic Cohort. AMPA was detected in 90% of cases and 84% of controls. The geometric mean of urinary AMPA excretion was nearly 38% higher among cases vs. controls (0.087 vs 0.063 ng AMPA/mg creatinine) after adjusting for race/ethnicity, age and BMI. A 4.5-fold higher risk of developing breast cancer in the highest vs. lowest quintile of AMPA excretion was observed ($OR_{Q5\ vs.\ Q1}$: 4.49; 95% CI: 1.46-13.77; p_{trend} = 0.029). To our knowledge, this is the first study to prospectively examine associations between urinary AMPA excretion and breast cancer risk. Our preliminary findings suggest that AMPA exposure may be associated with increased breast cancer risk; however, these results require confirmation in a larger population to increase study power and permit careful examinations of race/ethnicity differences."

Cytotoxic and Genotoxic Properties of Glyphosate – according to Koller, *at al*., (2012), Glyphosate (G) is the largest selling herbicide worldwide; the most common formulations (Roundup, R) contain polyoxyethyleneamine as main surfactant. Recent findings indicate that G exposure may cause DNA damage and cancer in humans. The aim of this investigation was to study the cytotoxic and genotoxic properties of G and R (UltraMax) in a buccal epithelial cell line (TR146), as workers are exposed via inhalation to the herbicide. R induced acute cytotoxic effects at concentrations > 40 mg/l after 20 min, which were due to membrane damage and impairment of mitochondrial functions. With G, increased release of extracellular lactate dehydrogenase indicative for membrane damage was observed at doses > 80 mg/l. Both G and R induced DNA migration in single-cell gel electrophoresis assays at doses > 20 mg/l. Furthermore, an increase of nuclear aberrations that reflect DNA damage was observed. The frequencies of micronuclei and nuclear buds were elevated after 20-min exposure to 10-20 mg/l, while nucleoplasmatic bridges were only enhanced by R at the highest dose (20 mg/l). R was under all conditions more active than its active principle (G). Comparisons with results of earlier studies with lymphocytes and cells from internal organs indicate that epithelial cells are more susceptible to the cytotoxic and DNA-damaging properties of the herbicide and its formulation. Since the researchers found genotoxic effects after short exposure to concentrations that correspond to a 450-fold dilution of spraying used in agriculture, their findings indicate that inhalation may cause DNA damage in exposed individuals.

Teratogenic, Tumorigenic and Hepatorenal Effects of Glyphosate – According to Mesnage, *et al*., (2015), glyphosate-based herbicides (GlyBH), including Roundup, are the most widely used pesticides worldwide. Their uses have increased exponentially since their introduction on the market. Residue levels in food or water, as well as human exposures, are escalating. The researchers reviewed the toxic effects of GlyBH measured below regulatory limits by evaluating the published literature and regulatory reports. Their research reveals a coherent body of evidence indicating that GlyBH could be toxic below the regulatory lowest observed adverse effect level for chronic toxic effects. It includes teratogenic, tumorigenic and hepatorenal effects. This 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 GlyBH adjuvants, which have their own toxicity, but also enhance glyphosate toxicity. These challenge the assumption of safety of GlyBH 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 GlyBH must be revisited, since a growing body of knowledge suggests the predominance of endocrine disrupting mechanisms caused by environmentally relevant levels of exposure.

Glyphosate Poisoning and Acute Pulmonary Oedema – According to a study by Thakur, *et al.*, (2014), GlySH-surfactant herbicide (GlySH), one of the most commonly used herbicides worldwide, has been considered as minimally toxic to humans. However, clinical toxicologists occasionally encounter cases of severe systemic toxicity. The US Environmental Protection Agency (EPA) states that 'GlySH' is of relatively low oral and acute dermal toxicity. It does not have anticholinesterase effect and no organophosphate-like central nervous system (CNS) effects. The clinical features range from skin and throat irritation to hypotension and death. Severe GlySH-surfactant poisoning is manifested by gastroenteritis, respiratory disturbances, altered mental status, hypotension refractory to the treatment, renal failure, and shock. GlySH intoxication has a case fatality rate 3.2-29.3%. Pulmonary toxicity and renal toxicity seem to be responsible for mortality. Metabolic acidosis, abnormal chest X-ray, arrhythmias, and elevated serum creatinine levels are useful prognostic factors for predicting GlySH mortality. There is no antidote and the mainstay of treatment for systemic toxicity is decontamination and aggressive supportive therapy. The researchers report a case of acute pulmonary oedema, which is a rare but severe manifestation of oral GlySH poisoning, where the patient survived with aggressive supportive therapy.

Glyphosate and Chronic Kidney Disease in Sri Lanka – According to Jayasumana, *et al.,* (2014), the current chronic kidney disease epidemic, the major health issue in the rice paddy farming areas in Sri Lanka has been the subject of many scientific and political debates over the last decade. Although there is no agreement among scientists about the aetiology of the disease, a majority of them has concluded that this is a toxic nephropathy. None of the hypotheses put forward so far could explain coherently the totality of clinical, biochemical, histopathological findings, and the unique geographical distribution of the disease and its appearance in the mid-1990s. A strong association between the consumption of hard water and the occurrence of this special kidney disease has been observed, but the relationship has not been explained consistently. Here, the researchers have hypothesised the association of using glyphosate, the most widely used herbicide in the disease endemic area and its unique metal chelating properties. The possible role played by glyphosate-metal complexes in this

epidemic has not been given any serious consideration by investigators for the last two decades. Furthermore, it may explain similar kidney disease epidemics observed in Andra Pradesh (India) and Central America. Although glyphosate alone does not cause an epidemic of chronic kidney disease, it seems to have acquired the ability to destroy the renal tissues of thousands of farmers when it forms complexes with a localised geo-environmental factor (hardness) and nephrotoxic metals.

Glyphosate, DNA Damage and Cancer – According to Swanson, *et al*., (2014), a huge increase in the incidence and prevalence of chronic diseases has been reported in the United States (US) over the last 20 years. Similar increases have been seen globally. The herbicide glyphosate was introduced in 1974 and its use is accelerating with the advent of herbicide-tolerant genetically engineered (GE) crops. Evidence is mounting that glyphosate interferes with many metabolic processes in plants and animals and glyphosate residues have been detected in both.

Glyphosate disrupts the endocrine system and the balance of gut bacteria, it damages DNA and is a driver of mutations that lead to cancer.

In the present study, US Government databases were searched for GE crop data, glyphosate application data and disease epidemiological data. Correlation analyses were then performed on a total of 22 diseases in these time-series data sets. The Pearson correlation coefficients are highly significant (< 10-5) between glyphosate applications and hypertension (R = 0.923), stroke (R = 0.925), diabetes prevalence (R = 0.971), diabetes incidence (R = 0.935), obesity (R = 0.962), lipoprotein metabolism disorder (R = 0.973), Alzheimer's (R = 0.917), senile dementia (R = 0.994), Parkinson's (R= 0.875), multiple sclerosis (R = 0.828), autism (R = 0.989), inflammatory bowel disease (R = 0.938), intestinal infections (R = 0.974), end stage renal disease (R = 0.975), acute kidney failure (R = 0.978), cancers of the thyroid (R = 0.988), liver (R = 0.960), bladder (R = 0.981), pancreas (R = 0.918), kidney (R = 0.973) and myeloid leukaemia (R = 0.878).

The Pearson correlation coefficients are highly significant (< 10-4) between the percentage of GE corn and soy planted in the US and hypertension (R = 0.961), stroke (R = 0.983), diabetes prevalence (R = 0.983), diabetes incidence (R = 0.955), obesity (R = 0.962), lipoprotein metabolism disorder (R = 0.955), Alzheimer's (R = 0.937), Parkinson's (R = 0.952), multiple sclerosis (R = 0.876), hepatitis C (R = 0.946), end stage renal disease (R = 0.958), acute kidney failure (R = 0.967), cancers of the thyroid (R = 0.938), liver (R = 0.911), bladder (R = 0.945), pancreas (R = 0.841), kidney (R = 0.940) and myeloid leukaemia (R = 0.889). The significance and strength of the correlations show that the effects of glyphosate and GE crops on human health should be further investigated.

Glyphosate and Non-Hodgkin's Lymphoma

Kabat, G., Price, W.J. & Tarone, R.E. 2021.

Purpose: A recent meta-analysis of five case-control studies and one cohort study reported that exposure to glyphosate was associated with increased risk of non-Hodgkin's lymphoma (NHL). The meta-analysis was based on estimates of risk from the included studies at the highest reported exposure level obtained from analyses with the longest lag period. The extent to which the summary estimate depends upon the exposure definitions and assumed latency period is uncertain.

Methods: We carried out sensitivity analyses to determine how the definition of exposure and the choice of latency period affect the summary estimate from meta-analyses of the 6 studies included in

the recent meta-analysis. We also conducted a meta-analysis of ever-exposure to glyphosate incorporating the most updated results from the case-control studies.
Results: The summary estimates of risk varied considerably depending on both the assumptions about exposure level and latency. Using the highest reported exposure levels, evidence of an association between glyphosate and NHL was strongest when estimates from analyses in the cohort study with a 20-year lag [RR = 1.41 (95% CI 1.13-1.76)] and a 15-year lag [RR = 1.25 (95% CI 1.01-1.25)] were included. In our meta-analysis of ever-exposure with no lag period, the summary relative risk with updated estimates was 1.05 (95% CI 0.87-1.28).
Conclusion: The results of meta-analyses of glyphosate exposure and NHL risk depend on assumptions made about both exposure level and latency period. Our results for ever-exposure are consistent with those of two recent meta-analyses conducted using somewhat different study inclusion criteria.

Carcinogenicity (cancer causing ability) of Glyphosate) – Evaluation of glyphosate by the International Agency for Research on Cancer (IARC) resulted in glyphosate being classified as probably carcinogenic to humans (Group 2A) which means:

- There is LIMITED evidence in humans for the carcinogenicity (cancer causing ability) of glyphosate. A positive association has been observed for non-Hodgkin's lymphoma.

- There is SUFFICIENT evidence in experimental animals for the carcinogenicity (cancer causing ability) of glyphosate (IARC).

Staying Safe with Glyphosate
Many chemicals used every day can pose a risk to people or the environment. One can protect oneself, others, and the environment by following the following recommendations for using and storing glyphosate.

Using glyphosate safely – when using any chemical, one should commence by reading the label. This will inform one of the specific potential risks for the product, and how one can reduce these risks. There are some practices that one should follow any time one uses any product containing glyphosate.

Before spraying – the following are of importance:

Read all instructions on the label and follow them
Make sure of using the right product for the job
Confirm that the spray area is not close to water, such as streams, rivers, lakes of ponds
Check the weather forecast to make sure no rain is predicted for at least 24 hours
Avoid spraying when it is windy
Follow the label advice with special reference to the need for protective clothing and adhere to the advice provided

After spraying – follow the suggestions:

- Wash hands and face
- Change clothing and wash the used clothing
- Keep children and pets away until the spray has dried, or for the amount of time stated on the label
- Follow the instructions on the label on how to safely dispose of any unused product

Storing glyphosate safely – one should follow the following simple recommendations to protect oneself, others, and the environment:

- Keep glyphosate-containing chemicals locked up and out of reach of children and pets
- Store the product in its original container
- Make sure that all text on the outside of the container remains legible
- Make sure it is kept far away from food, including pet food
- Dispose of empty herbicide containers and unused herbicides properly
- Check the label instructions and use-by date before each re-use.

Countries that have Banned Glyphosate

Germany's agricultural minister, Julia Kloeckner, announced that she was finalizing a draft regulation to end the use of glyphosate, the world's most heavily used herbicide in history. Glyphosate is the key active ingredient in Monsanto's Roundup weedkiller.

According to Baum, Hedlund, Aristei & Goldman, a United States law firm representing hundreds of plaintiffs suing Monsanto for allegedly causing their cancer, the following countries have banned or placed restrictions on the use of glyphosate:

Belgium
Bermuda
Colombia
The Netherlands
Sri Lanka
El Salvador
Middle Eastern countries including Saudi Arabia, Kuwait, Qatar, Bahrain, Oman and the United Arab Emirates
France

CANSA's Position on Glyphosate

The Cancer Association of South Africa (CANSA) accepts the International Agency for Research on Cancer (IARC) classification of glyphosate as probably carcinogenic to humans (a Group 2A Carcinogen).

CANSA accepts the finding of a positive association between glyphosate exposure and non-Hodgkin's Lymphoma.

CANSA further accepts research results that indicate that glyphosate could be responsible (among others) for:

- Endocrine disruption
- Increasing risk of breast and other cancers, including non-Hodgkin's Lymphoma
- Cytotoxic changes (toxic changes to living cells)
- Genotoxic changes (ability to cause damage to the genetic information within a cell causing mutations, which may lead to cancer)
- Teratogenic changes (capable of forming or tending to form tumours)
- Pulmonary oedema (excess fluid in the lungs) in exposed individuals

And that glyphosate in formulation has been detected in maize and soybean products in South Africa, and that there is sufficient evidence that glyphosate in formulation at low levels are found in tissue of humans and animals,

CANSA advocates that:

- The Department of Agriculture, Forestry and Fisheries should re-examine the conditions of approval of glyphosate in South Africa
- The National Department of Health investigate the health implications of glyphosate exposure in South Africa with a view of instituting control measures over its free availability
- Glyphosate exposure to humans, animals and the environment must be limited as far as possible
- The indiscriminate spraying of glyphosate on unwanted plants (e.g. cannabis) in rural areas must be discontinued as this indiscriminate spraying results in the destruction of cultivated fields of rural inhabitants which deprives them of self-sufficiency as far as food production is concerned
- Sufficient and adequate protective clothing and protective devices must be provided to workers who may be exposed to glyphosate
- No planting of edible crops should take place on soil sprayed with glyphosate until laboratory results indicate that the soil is totally free from any glyphosate residue
- All individuals who work with, or handle, glyphosate must be informed of the potential dangers of glyphosate and be instructed on its safe handling
- The public must be informed of the classification of glyphosate by the International Agency for Research on Cancer (IARC) as a probable carcinogen to humans (Group 2A)
- Additional research must be conducted on the environmental and health effects of glyphosate in formulation within the South African context.

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet and Position Statement, neither it, nor any contributor(s) to this Fact Sheet and Position Statement can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet and Position Statement.

ANNEXURE A

The Response of the South African Department of Agriculture, Forestry & Fisheries on Glyphosate Carcinogen Classification by IARC

In a Media Release dated 22 May 2015, The Department of Agriculture, Forestry & Fisheries, stated the following:

agriculture, forestry & fisheries
Department:
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA

Media Release
22 May 2015

The Department of Agriculture, Forestry and Fisheries' Response on Glyphosate Carcinogen Classification

In its recent evaluation in March 2015, the International Agency for Research on Cancer (IARC), as the specialised cancer agency of the World Health Organization (WHO), came to the conclusion that there

is limited evidence of possible carcinogenicity associated with glyphosate, which could result in non-Hodgkin lymphoma in humans. The IARC concluded that glyphosate should now be classified as a carcinogenic substance in Group 2A which means that it is probably carcinogenic to humans. This is based on evidence from animal-based experimentation. Following the publication of the report in the Lancet Journal on 20 March 2015 by the IARC, there have been public concerns raised about human exposure to glyphosate as "probably carcinogenic to humans.''

Glyphosate is a broad-spectrum herbicide, and works by inhibiting an enzyme found in plants. There are about 100 products containing glyphosate currently registered for use in South Africa. Glyphosate has been registered for use in South Africa and all over the world for over 40 years.

All glyphosate-based products that are registered for use in South Africa have been through a robust chemical risk assessment process. Based on current risk assessments, glyphosate poses a minimal risk to users and the general public, provided it is used according to label instructions and safety statements. This is in agreement with other risk assessments conducted by the United States Environmental Protection Agency (US EPA), Australian Pesticides and Veterinary Medicines Authority (APVMA), and the European Food Safety Authority (EFSA).

Department of Agriculture, Forestry and Fisheries (DAFF) Action

The DAFF, however, takes the IARC's findings very seriously and will examine the data and assessment done for the IARC classification and determine whether any regulatory action is necessary.

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