Cancer Association of South Africa (CANSA)

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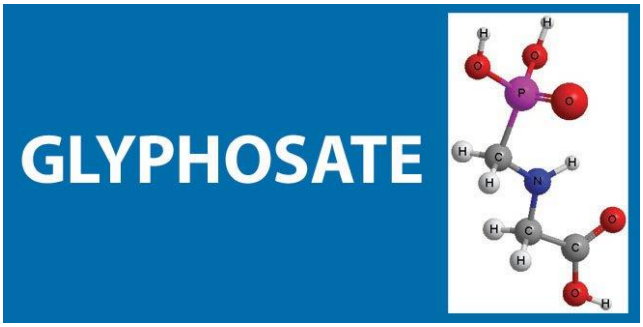
Fact Sheet and Position Statement on Glyphosate

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.
(Scientific Committees).

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.
(Glyphosate Facts).

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).

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.
(EPA Technical Sheet).

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.
(The Times).

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.

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.

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.

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).

Statement of Concern Over Glyphosate

Animal and epidemiology studies published in the last decade, point to the need for a fresh look at glyphosate toxicity. Furthermore, the World Health Organization's International Agency for Research on Cancer (IARC) recently concluded that glyphosate is "probably carcinogenic to humans". In response to changing glyphosate-based herbicides (GBH) use patterns and advances in scientific understanding of their potential hazards, the researchers have produced a Statement of Concern drawing on emerging science relevant to the safety of GBHs. Their Statement of Concern considers current published literature describing GBH uses, mechanisms of action, toxicity in laboratory animals, and epidemiological studies. It also examines the derivation of current human safety standards.

The researchers concluded that:

(1) GBHs are the most heavily applied herbicide in the world and usage continues to rise;

(2) Worldwide, GBHs often contaminate drinking water sources, precipitation, and air, especially in agricultural regions;

(3) The half-life of glyphosate in water and soil is longer than previously recognised;

(4) Glyphosate and its metabolites are widely present in the global soybean supply;

(5) Human exposures to GBHs are rising;

(6) Glyphosate is now authoritatively classified as a probable human carcinogen;

(7) Regulatory estimates of tolerable daily intakes for glyphosate in the United States and European Union are based on outdated science.

The researchers offer a series of recommendations related to the need for new investments in epidemiological studies, biomonitoring, and toxicology studies that draw on the principles of endocrinology to determine whether the effects of GBHs are due to endocrine disrupting activities. They suggest that common commercial formulations of GBHs should be prioritised for inclusion in government-led toxicology testing programs such as the U.S. National Toxicology Program, as well as for biomonitoring as conducted by the U.S. Centers for Disease Control and Prevention.

The following recommendations are offered by the researchers to further improve the predictive capability regarding glyphosate risks:

1. Scientists independent of the registrants should conduct regulatory tests of GBHs that include glyphosate alone, as well as GBH-product formulations. [Note: in the latest glyphosate regulatory assessment process by the German Federal Institute for Risk Assessment, the description and assessment of studies was provided by the Glyphosate Task Force, a group of 25 agrochemical companies that combined resources to jointly apply for renewal of registrations for this herbicide within Europe. By way of contrast, in order to avoid conflicts of interests, the Glyphosate Task Force was restricted to a role of observer to the evaluation of data by independent scientists at the recent WHO IARC evaluation of glyphosate's carcinogenic potential].

2. Epidemiological studies are needed to improve knowledge at the interface of GBH uses, exposures, and human-health outcomes.

3. Biomonitoring studies examining reference populations like the U.S. CDC's NHANES program should examine human fluids for glyphosate and its metabolites.

4. More comprehensive toxicity experiments are needed including those using “two hit” study designs, which examine early life exposures to GBHs followed by later-life exposures to chemical or other environmental stressors.

5. Because GBHs are potential endocrine disruptors, future studies should incorporate testing principles from endocrinology.

6. Future studies of laboratory animals should use designs that examine the full lifespan of the experimental animal, use multiple species and strains, examine appropriate numbers of animals, and carefully avoid contaminating GBH and other pesticides within control feeds and drinking water.

7. GBHs should be prioritised by the U.S. National Toxicology Program for safety investigations, including tests of glyphosate and common commercial formulations.

(Meyers, et al., 2016).

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.

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

CANSA, therefore 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)

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:

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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