Glyphosate

Summary

Glyphosate is used widely in domestic and commercial weed killers. Some organisations, including the World Health Organisation, classify glyphosate as a probable human carcinogen, but this has been rejected by others, including the EU's European Chemicals Agency. Although scientific studies have linked glyphosate to cancers in humans and animals and a few studies conclude that glyphosate can act as an oestrogen mimic, no human study has shown glyphosate causes breast cancer. Should we worry about using weed killer containing glyphosate in the garden? Could glyphosate increase our risk of breast cancer? This briefing helps shed light on the science behind these concerns and tries to answer these questions.

What is glyphosate?

Glyphosate is a herbicide, used globally as a weed killer. It was developed and commercialised in 1974 in a formulation marketed as Roundup, by the agricultural company, Monsanto. Today, it is the active ingredient of more than 750 different broad-spectrum herbicides (1) and glyphosate-based formulations are the most commonly used and sold pesticides, worldwide.

Glyphosate is used in commercial formulations, which include other chemical additives that allow and enhance its efficiency as a weed killer, by improving the plant's ability to take up the herbicide and by promoting its toxicity. These additives are considered to be 'inert diluents' by manufacturers and are classified as confidential for regulatory purposes (2).

The global use of glyphosate has risen 15-fold since the introduction of glyphosate-resistant genetically modified (GM) crops in 1996 (3). Such crops now account for 56% of total glyphosate use, worldwide.

Glyphosate-based formulations are used in agriculture, forestry, aquatic environments and in urban and domestic settings.

Glyphosate use on GM crops

Glyphosate-resistant GM crops are genetically engineered to tolerate glyphosate. This means that when a crop is sprayed, the weeds around the crop die, but the crop is resistant and accumulates herbicide as it grows. Examples of GM crops include glyphosate-tolerant soybean, corn, cotton, sugar beet and canola (rape).

The cultivation of GM crops means glyphosate can be used at all stages of crop cultivation, including when a plant has germinated. As a consequence, concentrations and quantities of glyphosate-based herbicides in the United States (and elsewhere) are increasing, along with increasing plant residues (4). Furthermore, excessive use of glyphosate has resulted in the emergence of glyphosate-resistant weeds, especially where GM crops are grown (5). Currently, 34 different species of glyphosate-resistant weeds have been identified (6).

Glyphosate use in the UK

The commercial cultivation of glyphosate-tolerant GM crops within the European Union is not permitted. Nonetheless, glyphosate use in UK farming has increased by 400% in the last 20 years (7). Glyphosate-based herbicides are mainly applied after harvest, to prevent weeds infesting winter crops or after sowing before the new crop plants emerge. In the UK and some other European countries, notably Germany, glyphosate is also used before crop harvest (especially for wheat and oilseed rape) to control weeds (pre-harvest) and to speed up the maturation process of crops (dessication) (8).

Glyphosate contamination of food crops in the UK is common. For example, annual glyphosate residue testing in the UK by the Food Standards Agency has identified frequent contamination of bread (9); residues of glyphosate were found in 10-30% of grain-based samples from 2007–2013, at generally rising levels (10). Although maximum residue levels (10mg/kg) have never been exceeded, levels as high as 0.5mg/kg have been found.

Glyphosate is also used as a weed killer in parks and schools and along roadsides and railway tracks. It is used in domestic settings to clear gardens, patios and driveways of weeds. According to the Department of Environment Food and Rural Affairs it is the most commonly used herbicide in residential areas (11) and on arable land (12).

Why should we be concerned?

Glyphosate is widespread in the environment (13) and has been detected in air, soil and water, as well as in humans. Studies from Europe and the US routinely identify urinary glyphosate residues in humans, as a result of occupational use or dietary intake (14). A study just published by a German environmental organisation, the Heinrich Böll Foundation (15), reported urinary glyphosate residues in 99.6% of the 2,009 people monitored. A third of those had levels 10 to 42 times higher than what is currently considered a safe threshold of exposure (16).

There is strong evidence that glyphosate is carcinogenic (17) (see section on Glyphosate and Cancer) and some evidence that it acts as an oestrogen mimic at high concentration (18) and so may increase breast cancer risk for those exposed to unusually high levels; however, no such elevated risk is associated with everyday exposures (see section on Glyphosate and Breast Cancer). Glyphosate may also be associated with kidney disease (19) and other illness (20) (see section on other Health Effects).

Glyphosate commercial formulations can be up to 1000 times more toxic than glyphosate alone (21). Additives, including surfactants, which help glyphosate enter plant cells and are also toxic in their own right, have been shown to enhance glyphosate toxicity (22, 23). Some contaminants of glyphosate formulations, such as 1,4-dioxane, cause mammary, liver and nasal cancers in laboratory rodents (24). The French environment agency, ANSES, recently called for a review of glyphosate formulations, based on their concerns about the combined effects of additives in combination with glyphosate.

Glyphosate and cancer

The carcinogenicity of glyphosate is a controversial issue. While several reviews (e.g. 25) and the European Chemicals Agency (ECHA) (26) concluded that glyphosate is not a carcinogen, an

independent review carried out by the WHO's International Agency for Research on Cancer (IARC) classified glyphosate as a "probable human carcinogen" (2A group) (27). Evidence of carcinogenicity in humans was supported by a positive association between glyphosate exposure and Non-Hodgkin lymphoma subtypes, in three out of four studies, considered as reliable by the IARC review panel. The panel also concluded that glyphosate is genotoxic (damages genes) and linked glyphosate to dose-related increases in malignant tumours at multiple sites (including kidneys and liver) in laboratory animals. In June 2017, the state of California classified glyphosate as a substance "known to cause cancer" (28).

Glyphosate and breast cancer

To date, no study has demonstrated a causal link between glyphosate and breast cancer in humans. Results from the US Agricultural Health Study did not report an association between glyphosate and breast cancer among wives of private pesticide applicators from Iowa and North Carolina (29). However, these results should be analysed cautiously, as the control population (farmers and their spouses who had never applied glyphosate) was likely to have been exposed through environmental contamination. Indeed, another study examining urinary levels of glyphosate metabolites of Iowa farmers and their families found similar levels in family members from both farming and non-farming households (30). Monitoring of human body fluids for glyphosate and its metabolites in such human population studies would generate more accurate results.

Only one long term study has been carried out into the possible association between glyphosate and mammary tumours in animals. This study, which used environmentally relevant concentrations of a glyphosate-based herbicide (31), reported a significant increase in the incidence of mammary tumours.

A recently published study (32) found that glyphosate is oestrogenic (can act as an oestrogen mimic), but only at relatively high concentrations. This suggests that humans exposed to glyphosate at typical exposure levels would not have an increased risk of breast cancer as a result of its oestrogenic effects. The researchers used several techniques to demonstrate this and their results are consistent with those obtained from the US Environmental Protection Agency's endocrine disruptor screening programme (33). The finding is in contrast to that of a previous study (34), which reported that glyphosate could activate the oestrogen receptor with similar potency to natural oestrogen (in other words, was a strong oestrogen mimic), a result that has not been repeated by other researchers.

No additives found in glyphosate-based herbicides have been shown to be oestrogenic (35). Previous studies have demonstrated that certain additives, including polyethoxylated tallowamine (POEA), can inhibit aromatase (an enzyme involved in sex hormone synthesis) and is toxic to cells (36). In July 2016, EU member states agreed to ban the use of POEA from glyphosate-based products (37).

In conclusion, current evidence suggests that exposure to glyphosate and glyphosate formulations through ordinary domestic usage and dietary intake would not increase breast cancer risk as a result of oestrogenic effects. However, exposure to high concentrations of glyphosate is likely to have oestrogenic effects, which suggests those who are acutely exposed - perhaps through their

occupation - may be at increased risk of breast cancer. More studies are needed to understand fully the role of glyphosate in breast cancer risk, in particular those involving occupational exposures, as well as the potential impact of long term chronic exposures, especially to mixtures of glyphosate-containing herbicides and other potentially harmful endocrine disrupting chemicals.

Other health effects

In addition to a link to Non-Hodgkin lymphoma, glyphosate has been associated with chronic kidney disease, following exposure to contaminated drinking water or herbicide spray (38). A recent study confirmed liver and kidney damage in animals following long term consumption of a very low dose of the glyphosate-based herbicide, Roundup (39). Further detrimental human health effects have been proposed, based on animal and in vitro studies, including liver disease, reproductive disorders, neurotoxicity, cardiovascular problems and allergies (see review, 40). Further evidence is needed to confirm whether or not glyphosate or its formulations are responsible for such effects.

What is the current regulatory position?

Pesticides such as glyphosate must be approved for use in the EU by the European Commission, according to the EU plant protection products regulation [Regulation: (EC) No 1107/2009]. In June, 2016, the EU licence for glyphosate use expired, and a temporary renewal was granted (for 18 months), following a lack of consensus by EU member states. In November 2015 a European Food Safety Authority (EFSA) assessment concluded that glyphosate is "unlikely to pose a carcinogenic hazard to humans" (41). This is significant as the 2009 EU pesticides regulation (Regulation 1107/2009; Annex II, 3.6.3) forbids active substances which can cause cancer from being used as pesticides. EFSA's conclusion was based on work done by the German Federal Risk Assessment institute, BfR, and is counter to IARC's findings that glyphosate is a "probable human carcinogen". The BfR report focused on studies which evaluated the effects of glyphosate alone, not its formulations, which are likely to be more toxic (42). The EFSA report has been questioned by over 90 leading scientists from around the world, who wrote an open letter to the European Health and Food Safety Commissioner, Vytenis Andriukaitis, challenging EFSA's decision and questioning the BfR report's credibility (43, 44).

An evaluation of glyphosate by the European Chemicals Agency (ECHA) in the context of the European legislation on classification, labelling and packaging was published in March 2017 (45). It concluded that "the available scientific evidence did not meet the criteria to classify glyphosate as a carcinogen, as a mutagen or as toxic for reproduction", paving the way for glyphosate re-authorisation. The proposal to re-approve glyphosate for use in the EU for a further 10 years will be decided on in November, 2017.

Some regional and national authorities have already banned or restricted glyphosate use. In 2015, Sri Lanka banned all use of glyphosate, due to its links with kidney disease (46), although this ban may be partially relaxed to allow use in tea plantations (47). In France, restrictions are in place on sales to the public and by 2020 the sale of glyphosate intended for public use will be banned and the Netherlands has also banned non-commercial use of glyphosate (48). In the UK several city councils, including Edinburgh, Brighton and Hove, Shaftsbury, Glastonbury, and the London

Borough of Hammersmith and Fulham have phased out glyphosate use on council land and in open spaces (49).

Concluding remarks

At present there is no strong evidence to suggest glyphosate or weed killers that contain glyphosate increase breast cancer risk in the general population. Glyphosate is a weak oestrogen mimic so may increase risk in those that are exposed to high concentrations over prolonged periods - for example occupational exposures amongst glyphosate applicators - although it's important to remember that no human studies support this. Currently, there is no evidence that members of the general population exposed to glyphosate as a result of dietary intake or domestic use are at an increased risk of breast cancer due to its oestrogenic effects. However, there is some evidence that glyphosate increases the risk of non-Hodgkin's lymphoma and may be responsible for human kidney disease and other illnesses. More research is needed to understand more clearly the role of glyphosate in cancers and other diseases. Although current research suggests that glyphosate does not increase breast cancer risk as a result of its oestrogenic effects, there is evidence it is harmful to the environment and is a human carcinogen. Breast Cancer UK will continue to follow glyphosate research closely and if new data suggest it may be associated with increased breast cancer risk we will update this brief accordingly.

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Please see here for a list of references cited. You can download a pdf of our glyphosate background briefing here.