Time for the end of GM/GE herbicide tolerant crops?

EXECUTIVE SUMMARY

A report by GeneWatch UK

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Executive Summary

In countries growing genetically modified (GM) crops, the adoption of GM crops which are tolerant to weedkillers is reaching saturation. These herbicide-tolerant (HT) GM crops have been genetically engineered so they can be blanket-sprayed with the associated herbicides, with the aim of killing weeds whilst the crop still grows. They were first grown commercially in 1996, when they were introduced by the US company Monsanto (now owned by Bayer). Monsanto's glyphosate-based weedkiller has the brand-name RoundUp, hence the first GM generation of herbicide-tolerant crops are tolerant to glyphosate and are known as 'RoundUp Ready' (RR) crops.

Herbicide-tolerant GM crops, which include an herbicide-tolerant trait alone or in combination with other traits, account for around 88% of the land area planted with GM crops worldwide (ISAAA, 2019a). Because cotton grown in India and China accounts for most non-HT GM crops, HT crops account for virtually all the GM crops grown for use in food or feed. This reality is in sharp contrast to GM industry PR which acts as a distraction by emphasising potential new traits, including GM crops that tolerate flooding or drought, which were first promised more than 40 years ago but have not been delivered. Since 1996, most herbicide-tolerant GM crops have been RR crops which are genetically engineered to be tolerant to glyphosate, but this has recently been changing with increasing areas planted with new HT crops which are tolerant to additional herbicides, such as dicamba and 2,-4,D. These crops are mainly grown in North and South America, with the USA, Brazil and Argentina growing the largest quantities.

The aim of this report is to look at the economic, environmental and social impacts of growing RR crops and newer HT crops. This report reviews more than 25 years of experience with this technology.

We conclude that the cultivation of GM HT crops may be regarded as a temporary aberration, rather than the revolution originally proclaimed by the proponents of these crops. The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods. It is particularly important that RR crops are not pushed into new countries which have so far avoided stepping onto the "transgenic treadmill", in which farmers are locked in to paying for ever more expensive seeds and herbicides. In seeking to expand markets for RR crops into new countries, the industry is dumping a failed technology on them.

Blanket spraying of RR crops with weedkiller leads to resistant weeds

RR crops are designed to make farming practices easier in that they allow farmers to apply the weedkiller glyphosate during the cropping season without risking harm to their crops, which are genetically engineered to be tolerant to it. This has led to an unprecedented increase in the use of glyphosate (Powles & Preston, 2006; Duke & Powles, 2008; Grube et al 2011; Vivian et al. 2013; Benbrook, 2016; Myers et al., 2016).

Initial benefits for farmers adopting RR crops have vanished with the emergence of glyphosate resistant (GR) weeds, sometimes known as 'superweeds' (Vila-Aiub et al. 2007, 2008; Cerdeira et al. 2011; Benbrook, 2012a; Allison, 2015; Zhou et al., 2015;

Duke et al., 2018). Such weeds have evolved because RR crops allow farmers to blanket spray their crops with the weedkiller glyphosate instead of using a mix of approaches to tackling weeds, including crop rotation. Since GR weeds are no longer affected by spraying with glyphosate, they require the use of additional weedkillers or pulling up by hand (Caulcutt, 2009; Zhou et al., 2015). With 55 evolved GR weed species already known worldwide (Heap, 2021), and new GR weed species evolving at an increasing rate, RR technology is becoming obsolete. GR weeds are common in all RR crop producing countries and these are also the countries with the greatest area infested with GR weeds (Heap, 2021; Heap and Duke, 2018; Alcántara de la Cruz et al., 2020; Yanniccari et al., 2021; Pannell et al., 2017). RR crop cultivation is leading to increased herbicide application, thus adding costs for farmers, and increasing risks to the environment and human health. On the two most important GM crops in the US, corn and soybean, the total applied toxicity of pesticides (not just glyphosate) has increased along with increasing GM adoption, notably since 2008 as GR weeds became a greater problem (Schulz et al., 2021).

In response to the problem of glyphosate resistant weeds, the industry has developed new GM herbicide tolerant crops which are resistant to additional weedkillers, such as 2,4-D and dicamba, as well as glyphosate. Such crops exacerbate concerns about adverse environmental impacts, pesticide residues in the food chain, and the future evolution of weeds which will become resistant to multiple herbicides (Mortensen et al. 2012, Roseboro, 2012).

Patents and monopolies add further costs and prevent seed saving

Just four large firms (Bayer, Corteva, ChemChina-Syngenta, and BASF) control around 70% of the global pesticides market and 60% of the global seed market (Clapp, 2021). Patents on GM seeds give companies monopoly control and allow them to prevent seed saving. This, along with market concentration in the industry, has led to significant increases in seed prices, with high premiums for GM seeds and restrictions on the non-GM varieties available on the market in some countries (Mascarenhas & Busch, 2006; Howard, 2009; Zilberman et al. 2010; Benbrook, 2012a; Filomeno, 2013; Benbrook, 2018; Brunharo et al., 2022). Farmers buying RR seeds are locked into a “transgenic treadmill” in which they are forced to pay for hikes in seed prices and for increasing amounts of herbicides and labour to tackle weed resistance (Binimelis et al., 2009; Mortensen et al., 2012).

RoundUp Ready crops do not have higher yields

Most farmers growing RR crops have adopted RR crop technology in the hopes of increasing their yields (Fernandez-Cornejo et al., 2014). However, there are no RR crops available today that increase the yield potential of a hybrid variety: any benefit to yields arises only if these crops improve weed control (Gurian-Sherman, 2009; Nolan & Santos, 2012; Bruns, 2014). A global meta-analysis of studies by Areal et al. (2013) reports no significant differences in yields between RR and conventional crops. Yield data from North America and Western Europe shows that Western Europe, where to date no herbicide tolerant resistant crops are grown, had a greater yield increase between 1961 and 2010 than North America for oil seed rape and maize (which are predominantly RR crops in North America) and that overall yields were similar or higher in Europe than in the USA (Hilbeck et al. 2013; Heinemann et al., 2014a, 2014b). There is also some evidence that supressed plant defence and enhanced disease susceptibility caused by glyphosate may have a negative impact on RR plants, through adverse effects on beneficial soil micro-organisms and plant nutrient uptake (Sanogo et al., 2000; King et al., 2001; Eker et al., 2006; Bellaloui et al. 2008; Bott et al., 2008; Johal and Huber, 2009; Zobiole et al., 2010a&b, 2011, 2012; Freitas-Silva et al., 2021).

Demand for non-GM seeds and ingredients is increasing

Farmers worldwide also need to consider the demand for non-GM ingredients, which is forecast to grow significantly (Mordor Intelligence, n.d.; Grand View Research, 2019; Fortune Business Insights, 2022).

Demand for animal feed that is segregated as non-GM has grown, particularly in Europe (Tillie & Rodríguez-Cerezo, 2015), where price premiums for non-GM crops reflect the preference of European consumers for non-GM products (Gaitán-Cremaschi et al., 2015; Fortune Business Insights, 2022). By 2021, around 60-70% of all milk egg, poultry and meat production in Germany was certified according to the GM-free VLOG standard (Southey, 2021). Brazil has increased its import share faster in countries with a strong non-GM preference versus other countries. This is explained statistically by Brazil's level of non-GM soybean production rather than by changes in prices. Garrett et al. (2013) find that the Netherlands, Italy, Spain, and Belgium increased imports from Brazil and simultaneously decreased imports from the United States, even as Brazil's currency increased in value in the late 2000s, which should have made Brazilian soybean producers less competitive than their North American counterparts on a pure cost basis. The South American non-GMO food market continues to grow, with Brazil expected to have the biggest market (Fortune Business Insights, 2022). Among US farmers, interest in growing non-GM varieties reportedly started increasing around 2014, with seed companies reporting strong demand for non-GM seed sales and some even reporting they had sold out of non-GM seeds due to the rapidly increasing demand (Bunge, 2015; Roseboro, 2015b; Doering, 2015; Kuphal, 2017). Retail sales of products verified by the Non-GMO Project, based in North America, rose dramatically from $248.8 million in 2010 to $8.5 billion in 2014 and 13.5 billion in 2015, with sales now over $26 billion (Non-GMO Project, 2014; 2015; 2022). However, the non-GM corn and soybean supply in the U.S. remains relatively small (Twellman, 2021).

Growing GM crops risks expensive contamination incidents

Cultivation of RR crops risks GM contamination of non-GM food and feed supplies (Price & Cotter, 2014). Contamination risks arise due to cross-pollination of non-GM crops and co-mingling of seeds or grains during harvest, transportation, storage, processing and distribution (Sohn et al., 2021). These risks cannot be eliminated through technical measures (Binimelis, 2008; Paull, 2018; Lu et al., 2019) and this causes legal and economic uncertainties for farmers, because contaminated crops have lower value (due to consumers' preference for non-GM crops) and may be rejected completely by some markets (e.g. organic markets, or any market where the GM crop has not been authorised by regulators).

Attempts to allow GM and non-GM crops to be grown together in a given country or region (known as "co-existence") creates tensions among neighbouring farmers because of the risk of GM contamination. Every actor and level of a supply chain will be economically affected under a coexistence scenario and costs of coexistence of GM and non-GM agricultural production systems are influenced by multiple factors (Gabriel & Menrad, 2015). At the producer level they include costs for cleaning of machinery and equipment, buffer zones of uncultivated land around the edge of non-GM fields, monitoring costs such as testing of seeds or crops and building additional farm storage facilities. For processors, costs to prevent contamination include: costs for testing of the incoming commodity as well as the produced outgoing goods, greater transportation distances to the next GM or non-GM plant respectively, building of additional storage facilities, complete second production line in an existing plant, cleaning or flushing of repositories, investment in additional personnel and equipment and in training programs for workers (Gabriel & Menrad, 2015). According to this study, the total additional costs of coexistence and implemented product segregation systems can amount up to 14% of the total product turnover at the gates of rapeseed oil mills or companies processing maize starch, respectively. In Switzerland, where GM crops are not grown, estimated coexistence measures if they were introduced could amount to up to 5-20% of the total costs for conventional production (Albisser Vögeli et al., 2011). The costs to prevent GM contamination are likely to be especially high for organic producers, since global organic farming standards do not allow GMOs in either seed or food (IFOAM, 2002).

Thus, allowing GM cultivation increases the cost of food supplies, because of the added costs of segregation. In countries where GM crops are grown, non-GM farmers, including organic farmers, bear risks and costs associated with protecting their crops from GM contamination and certifying their supply chain as GM-free for consumers.

When coexistence measures fail, contamination incidents can lead to the destruction of crops or entire fields (Furst, 1999; Smyth et al., 2002) and the rejection of shipments, product recalls and loss of markets (Ryan & Smyth, 2012; Smyth et al., 2002; Schaefer & Carter, 2015; USDA NASS, 2015; Reuters, 2016c), with multi-million dollar economic impacts.

GM contamination can also have environmental implications and risk the loss of local varieties of seed. Glyphosate tolerance, and other GM traits, can spread from GM maize to maize landraces, as has happened in Brazil (Fernandes et al., 2022). Maize is mainly produced by smallholders in Mexico, using landraces that are very well adapted to the local growth conditions. Contamination of these landraces, could threaten preservation of this very important maize genetic diversity (Snow, 2009). GM transgenes are already present in at least some maize landraces in Mexico (Piñeyro-Nelson et al., 2009; Quist & Chapela, 2001; Snow, 2009). Wild populations of the most widely cultivated cotton species in the world, *Gossypium hirsutum*, have also been contaminated by GM varieties, the majority of which are geographically located over 300 km away from all wild cotton populations (Wegier et al., 2011). In Spain, GM contamination of organic maize led to the loss of farmers' maize varieties adapted to the local climate (Cipriano et al., 2006). Such events could limit the future availability of high-value germplasm in breeding programs (Burgeff et al., 2014).

Impact of RR crops on farmers' choice, land rights and indebtedness

Patents on GM crops lead to restricted access to breeding material for farmers and breeders and thus hinder innovation in plant breeding and impede farmers' freedom of choice. In countries adopting GM crops the maize seed market is more concentrated with fewer available maize cultivars for farmers than in non-adopting countries, where it has become more difficult to find non-GM seeds (Roseboro, 2008; Hilbeck et al., 2013; Burgeff et al., 2014). In the USA, rising input costs, volatile production values, and rising land rents have left farmers with unprecedented levels of farm debt, low on-farm incomes, and high reliance on federal programs (Burchfield et al., 2022). Subsidies are largely directed at commodity production, including soy and corn, which are typically GM crops, and for which per acre costs tripled between 1990 and 2020.

Impacts of RR crop cultivation on smallholders in South America and elsewhere include land conflicts and the intensification of agro-industrial practices, including greater use of herbicides, increased farm sizes, land use changes and deforestation, seed price hikes, and the expansion of monocultures and indebtedness (Lapegna, 2013; Garrett and Rausch, 2016; Goldfarb and van der Haar, 2016; Leguizamón, 2016; McKay and Colque, 2016; Elgert, 2016; MASIPAG, 2013; Phélinas and Choumert, 2017; Schmidt et al., 2022; Dreoni et al., 2022).

RR crops have negative environmental impacts

The widespread adoption of RR crops in North and South America has contributed significantly to an increased environmental presence of glyphosate-based herbicides and their primary break-down product, AMPA, in rain, streams, rivers, lakes, ponds, wetlands, soil water, ground water, plants, soil, dust and sediment (Battaglin et al. 2005, 2014; Struger et al. 2008; Chang et al., 2011; Bohm et al., 2014; Majewski et al., 2014; Bento et al., 2016; Mamy et al., 2016; Bonansea et al., 2017; Alonso et al., 2018; Fernandes et al., 2019; Zheng et al. 2018; Clasen et al. 2019; Iturburu et al., 2019; Lupi et al., 2019; Lutri et al., 2020; Maggi et al., 2020; Medalie et al., 2019; Montiel-León et al., 2019; da Silva et al., 2021; Barbosa Lima et al., 2021; Botten et al., 2021; Brovini et al. 2021a,b; Cristofaro et al., 2021; Ramirez Haberkon et al., 2021; Carretta et al., 2022).

Negative environmental impacts due to growing herbicide-tolerant GM crops, including RR crops, include:

- impacts on farmland diversity of weeds, insects and birds through loss of important habitats due to blanket spraying of these crops with herbicide (Burke, 2003; Burke, 2005; Firbank et al., 2003; Gibbons et al., 2006; Cederlund, 2017; Pereira et al., 2018a, 2020);
- chronic toxicological effects of glyphosate and its metabolites on annelids (earthworms), arthropods (crustaceans and insects), molluscs, echinoderms, fish, reptiles, amphibians, birds, mammals, and non-target plants (Santadino et al., 2014; Zaller et al. 2014; Gaupp-Berghausen et al. 2015; Domínguez et al., 2016; Kissane & Shephard, 2017; Gill et al., 2018; Odetti et al., 2020; Ruuskanen et al., 2020a,b,c; Singh et al., 2020; Barbosa Lima et al. 2021);
- negative effects on pollinators, such as bees, including damage to habitat and ecosystems; toxicity; and effects on their behaviours, growth and development, metabolic processes, and immune defence (Fuchs et al., 2021; Strandberg et al., 2021; Battisti et al., 2021; Tan et al., 2022);
- toxic and chronic sub-lethal effects of glyphosate-based weedkillers on aquatic species including tadpoles, frogs, snails, crayfish, molluscs, crabs, fish, fresh-water fleas and corals (Relyea, 2005a,b and c; Pérez et al., 2012; Cuhra el al., 2013, 2014, 2015; Avigliano et al. 2014a,b; Gonçalves et al., 2019; Hendlin et al., 2020; Herek et al., 2021; Matozzo et al. 2020; Mohapatra et al., 2021; Moutinho et al., 2020; Riaño et al. 2020; Slaby et al., 2020; Suppa et al., 2020; Babalola et al., 2021; Le Du-Carrée et al., 2021, 2022; Ramsdorf et al., 2021; Rodríguez et al., 2021; Sánchez et al., 2021; Santos-Silva et al., 2021; Tresnakova et al., 2021; de Maria et al., 2021, 2022; Jia et al. 2022; Liu et al., 2022b; Pompermaier et al., 2022; Zhou et al., 2022); and
- adverse impacts of glyphosate-based herbicides on soil biota: such as effects on soil microbial communities (Jaworski, 1972; Schulz et al., 1985; Moorman et al., 1992; Dick and Quinn, 1995; Kremer and Means 2009; Nye et al., 2014; Newman et al., 2016); and impacts on overall ecosystem functioning, including interactions of crops with fungi and soil-borne pathogens (Johal &

Rahe 1984; Sanogo et al., 2000, 2001; Larson et al., 2006; Krzysko-Lupicka and Sudol, 2008; Johal and Huber, 2009; Kremer and Means, 2009; Zobiole et al., 2011; Lu et al., 2018; Martinez et al., 2018; Yang et al., 2020; Hertel et al. 2021, Van Bruggen et al, 2021; Vázquez et al., 2021; Chávez-Ortiz et al., 2022).

One important example of the effects of habitat loss is a major contribution to the dramatic decline in populations of the Monarch butterfly in the USA. Although other factors (such as climate change and deforestation) play a role, this decline is associated with the loss of the milkweed habitat where the butterflies lay their eggs, caused by blanket spraying the weedkiller glyphosate on RR crops (Hartzler, 2010; Zalucki & Lammers 2010; Brower et al., 2012; Pleasants & Oberhauser, 2012; Fallon, 2014; Flockhart et al., 2014; Vidal & Rendón-Salinas, 2014; Stenoien et al., 2016; Pleasants, 2017; Pleasants et al., 2016, 2017; Thogmartin et al., 2017; Belsky & Joshi, 2018; Malcolm, 2018; Taylor et al., 2020).

Glyphosate-contaminated runoff also likely contributes to harmful incidences of algal bloom in lakes (Dabney & Patiño, 2018; Berman et al., 2020).

In glyphosate-based herbicide formulations, glyphosate is the active ingredient that is supposed to kill the target weeds. Those formulations also contain various adjuvants, the so-called inert ingredients, including surfactants such as polyethoxylated tallow amine (POEA) which is found in Roundup. However, ecotoxicological assessment of pesticides usually focuses on the effects of the active ingredient, such as glyphosate, rather than on commercial formulations like Roundup (Cox & Surgan, 2006; Pereira et al., 2009; Mesnage & Antoniou, 2018; Sprinkle & Payne-Sturges, 2021; Martins-Gomes et al., 2022). This is a major issue of concern because many studies find that commercial formulations are significantly more toxic than glyphosate alone, particularly to aquatic organisms (Mitchell et al., 1987; Servizi et al. 1987; Mann & Bidwell, 1999; Perkins et al. 2000; Marc et al., 2002; Everett & Dickerson, 2003; Tsui & Chu, 2003, 2004; Howe et al., 2004; Cedergreen & Streibig, 2005; Brausch et al. 2007; Brausch & Smith, 2007; Pereira et al. 2009; Moore et al. 2012; Vincent & Davidson, 2015; Bach et al., 2016; Rissoli et al., 2016; Janssens & Stoks, 2017; de Brito Rodrigues et al., 2019; Mesnage et al. 2019; Bednářová et al., 2020; Le Du-Carrée et al., 2022; Sabio y García et al., 2022).

In South America, there have also been significant changes in land use to create large-scale RR soybean farms, for example in the Rolling Pampas in Argentina and the Cerrado in Brazil, with serious negative impacts on biodiversity and water-balance (De la Fuente et al. 2006, 2010; Martinelli et al., 2010; Hayhoe et al., 2011; Macedo et al., 2013; Neill et al., 2013; Redo et al. 2013; Eloy et al. 2016; de Groot et al., 2021).

An additional issue with RR crops is that they may contribute to the development and spread of antibiotic resistant bacteria, which can make it difficult to treat human and animal bacterial infections. Some RR crops contain antibiotic resistant marker genes, which might be able to spread into the environment (Chen et al., 2012). Exposure to sub-lethal levels of the herbicide Roundup has been linked to a change in susceptibility of bacteria to antibiotics, significantly increasing the concentration of two antibiotics (kanamycin and ciprofloxacin) necessary to kill gut bacteria associated with food poisoning, *Escherichia coli* and *Salmonella enterica* (Kurenbach et al., 2015). This research suggests that spraying RR crops with RoundUp might contribute to the development of antibiotic resistant bacteria in the environment, with major implications for human and animal health (Van Bruggen et al., 2018; Raoult et al., 2021; Liao et al., 2021; da Costa et al., 2021; Daisley et al., 2022).

RR crops pose unknown risks to human health

There are significantly higher levels of glyphosate and AMPA residues in RR soybeans compared to conventionally grown or organic soybeans (Arregui et al., 2004; Bøhn et al., 2014; Bohm et al., 2014). Bøhn & Millstone (2019) estimate that glyphosate-tolerant soybeans produced on commercial farms in the USA, Brazil and Argentina accumulate in total an estimated 2,500–10,000 metric tonnes of glyphosate per year, which enter global food chains. Glyphosate has been detected in a wide variety of foods, including soy-based infant formula and honey: dietary exposure levels are generally (but not always) below permitted limits (Rodrigues & de Souza, 2018; Bøhn & Millstone, 2019; Xu et al., 2019; de Souza et al., 2021; Rodrigues et al., 2020; Louie et al., 2021; Viljoen et al., 2021). However, regulatory limits vary in different countries, there is a lack of transparency about how they are set, and some researchers believe that the risks to human health could still be underestimated (Marino et al., 2021).

Krüger et al. (2014a) showed that glyphosate that accumulates in feed can be consumed by animals and be detected in their organs and urine. Subsequently, glyphosate has been detected in the urine of adults and children, both within and outside agricultural communities (Gillezeau et al., 2020; Ferreira et al., 2021; Lozano-Kasten et al., 2021; Grau et al., 2022; Nomura et al., 2022). Farmers and other operators can be directly exposed to glyphosate-based formulations when they are spraying it onto their fields (Acquavella et al., 2004; Mesnage et al., 2012). Children may also be exposed to glyphosate-contaminated breast milk. Glyphosate was detected in all breast milk samples taken from mothers in a study in Brazil, undertaken at the peak of glyphosate application in corn and soy crops (Camiccia et al., 2022). Regulators do not currently routinely monitor levels of glyphosate in food and have not investigated reports that glyphosate may be detected in human urine samples and breast milk as a result of its presence in the food chain. Some studies suggest that spraying with glyphosate-based weedkillers may also adversely affect the nutrient composition of soybeans (Zobiole et al., 2010b,c; Bellaloui et al., 2008).

As discussed above, Roundup formulations are a mixture of glyphosate and other chemicals that have been shown to increase the toxicity of glyphosate to aquatic organisms. Many toxicological studies conducted with human, mouse and rat cells confirm these findings and suggest that looking at the effects of glyphosate alone is insufficient for a comprehensive assessment of the possible risks to human health resulting from growing and consuming RR crops (Benachour et al., 2007; Benachour & Séralini, 2009; Clair et al., 2012; Gasnier et al., 2009; Mesnage et al., 2013, 2014; Moore et al., 2012; Richard et al., 2005; Walsh et al., 2000; Young et al., 2015; Chłopecka et al., 2017; Vanlaeys et al., 2018; Dedeke et al., 2018; Defarge et al., 2018). However, regulators only consider the effects of glyphosate alone (Mesnage et al., 2019).

In March 2015, the World Health Organisation (WHO)'s cancer agency, the International Agency for Research on Cancer (IARC), classified glyphosate as "probably carcinogenic to humans" (Guyton et al., 2015). As a consequence, many countries and regions have restricted the use of glyphosate (Where is Glyphosate Banned?, 2022). Subsequent reviews of the evidence have confirmed that chronic exposure to glyphosate causes a variety of tumours in rats and mice, and that there is clear evidence of glyphosate toxicity in studies using human cells (Agostini et al., 2020; Portier, 2020).

Research in Sri Lanka and elsewhere suggests a possible link between simultaneous exposure to glyphosate and toxic heavy metals, and chronic kidney disease, with other factors (such as exposure to high temperatures and other pollutants) perhaps playing a role (Jayasumana et al., 2014, 2015; Gunatilake et al., 2019; Herrera-Valdés et al., 2019; Babich et al., 2020; Abdul et al., 2021; Upamalika et al., 2022).

There is evidence that glyphosate may act as an endocrine disrupting chemical (EDC) i.e. a chemical that interferes with female and male sex hormones (Richard et al., 2005; Benachour et al., 2007; Gasnier et al., 2009; Romano et al., 2010; Clair et al., 2012; Thongprakaisang et al., 2013; Abarikwu et al., 2015; Guerrero Schimpf et al., 2017; Varayoud et al., 2017; Anifandis et al., 2017, 2018; Cai et al., 2017; Ingaramo et al., 2017, 2020, 2022; Owagboriaye et al., 2017; Lorenz et al., 2020; Kaboli Kafshgiri et al., 2021; Lesseur et al., 2021; Milesi et al., 2021; Mohammadi et al., 2021; Muñoz et al., 2021; Serra et al., 2021; Zhao et al., 2021). Endocrine disrupters can lead to negative impacts on male and female reproductive health, even at very low doses. These effects are not adequately regulated (Kalofiri et al., 2021). Two small studies have found that glyphosate exposure (measured in urine) in pregnancy is correlated with shortened pregnancy lengths (Parvez et al., 2018; Silver et al., 2021).

Other researchers suggest that glyphosate could affect gut bacteria, killing beneficial bacteria and allowing harmful ones to cause disease (Krüger et al., 2013; Shehata et al., 2013; Pu et al., 2020, 2021; Barnett et al., 2022).

Working with glyphosate and glyphosate spray drift can affect farm workers, bystanders and people living in the surrounding area.

In the Ontario Farm Family Health Study, Arbuckle et al. (2001) observe moderate increases in risk of early abortions for preconception exposures to any herbicide, and for late abortions, preconception exposure to glyphosate is associated with elevated risk. In the same study, Savitz et al. (1997) find that combinations of farm activities using a variety of chemicals, including glyphosate, are associated with an increased risk of miscarriage in the wives of exposed farm workers. In the Red River Valley, Minnesota, USA, Garry et al. (2002) find that exposure to glyphosate is associated with an increased risk of neurobehavioral developmental effects. In the Agricultural Health Study in Iowa and North Carolina, Hoppin et al. (2008) find an increased risk of atopic asthma in farm women using glyphosate and a number of other pesticides, and Hoppin et al. (2016) find an increased risk of allergic and non-allergic wheeze in male farm workers using glyphosate and some other pesticides. In the same study, Slager et al. (2009) find an increased risk of rhinitis in farm workers who had used glyphosate in the past year.

Aerial application (spraying from planes) increases the risk of accidental exposure of neighbouring inhabitants (Schiesari and Grillitsch, 2010; Pignati et al., 2007). Epidemiological studies and reports of interviews with local people cannot prove cause and effect, nevertheless there are numerous and widespread reports of glyphosate poisonings due to aerial spraying of RR soybeans in Latin America (Benítez-Leite et al., 2007; Oliva et al., 2008; Berger and Ortega, 2010; Sineiro and Berger 2012; Rigotto et al., 2014; Oliveira et al., 2014; Silva et al., 2015; Elgert, 2016; Lapegna, 2016; Dias et al., 2020; Longhi & Bianchi, 2020). Reported effects, according to people living in sprayed areas, include vomiting, diarrhoea, respiratory problems, skin rashes, cancer, infertility, pregnancy problems, and birth defects (PAN Asia & Pacific, 2008 & 2012).

RR crops do not help to feed the world or tackle climate change

The primary reasons for hunger are poverty and lack of access to affordable food (Tscharntke et al., 2012). Conflict, weather extremes and economic shocks were the main drivers behind food insecurity in 2021, with poverty and inequality as underlying causes (EU/FAO/WFP, 2022).

RR crops are currently produced mainly for use in animal feed (soya and maize/corn) or in biofuels (corn ethanol) or fabric (cotton). Soybean and maize (corn) are the top two GM crops grown by area, the majority of which are Roundup Ready. Most soy (around 75% measured by weight in 2018) is fed to animals in livestock production systems, with around 3.8% going to biofuels and other industrial applications, and only 19.2% to direct human consumption as food (mainly as soybean oil) (Fraanje & Garnett, 2020). Similarly, around 74% of the global maize production is used for animal feed (Cassidy et al., 2013). In the U.S., 40% of the maize harvest was processed to ethanol in 2014 (Ranum et al., 2014). In 2014, production and use of corn ethanol resulted in 27 billion kg more carbon emissions than if conventional gasoline were used according to calculations by the Environmental Working Group (Cassidy, 2015a). This is because converting rainforests, peatlands, savannas, or grasslands to produce food crop–based biofuels in Brazil, Southeast Asia, and the United States releases 17 to 420 times more carbon dioxide than the annual greenhouse gas (GHG) reductions that these biofuels would provide by displacing fossil fuels (Fargione et al., 2008).

Shifting crop calories used for animal feed and biofuels to direct human consumption could, according to Cassidy et al. (2013), potentially feed an additional 4 billion people and in the U.S. alone an additional 1 billion people. Further, tackling food waste can also play a major role: many crop calories are lost during food production, transport and storage as well as in retail facilities, restaurants and at private households etc. (FAO, 2011).

It is questionable whether sparing land for nature needs higher intensity of farming to produce adequate food (Tscharntke et al., 2012). Strategies to increase yields without explicitly considering the actual and potential cost of biodiversity losses can compromise ecosystem functionality and resilience in agriculture. Rather, food security and food sovereignty need to increase in areas where the hungry live, based on robust, eco-efficient approaches. Smarter resource use, improving livelihoods of small-scale farmers, reducing food waste and small changes in diets, such as reducing meat consumption or swapping from grain-fed beef to chicken or grass-fed beef, have the potential to double calorie availability (Cassidy 2015b).

Further, in the case of RR crops, yields have not increased compared to non-GM crops (Areal et al., 2013). Cultivation of RR crops has led to significant expansion of intensive agricultural monocultures into previously diverse ecosystems (Oliveira and Hecht, 2016) and production of non-GM soybean meal has been found to be more sustainable than GM soy production (Ortega et al. 2005; Gaitán-Cremaschi et al., 2015).

Some authors have argued that the use of no-till agriculture (i.e. farming without disturbing the soil through ploughing), in combination with RR crops, has helped to mitigate climate change by keeping carbon in the soil: however, in a 41 year experiment in France, no-till agriculture led to no increase in soil organic carbon (Powlson et al., 2014). In addition, whilst the use of no-till increased in the United States from 1998 to 2016, it then shrank again, although herbicide-tolerant GM corn and soybeans still dominate the market (Yu et al., 2020). This is likely at least partly due to the increasing presence of glyphosate-resistant weeds, which have led to a return to ploughing.

Industry responses to glyphosate-resistant weeds are not sustainable

The industry's answer to the development of GR weeds is mainly herbicide-centric and includes a) developing herbicide tolerant (HT) crops with enhanced tolerance to glyphosate (allowing higher application rates), b) increasing the herbicide platform used on RR crops to include additional herbicides (e.g. in seed treatments and tank mixes); and c) developing new HT crops with tolerance to additional herbicides (Desquilbet et al. 2019).

Another aspect of the industry response is the use of other (supposedly beneficial, but likely ineffective) traits as a 'Trojan Horse' to smuggle herbicide tolerant GM traits into new crops and markets. These include HB4 GM wheat, developed by Bioceres, which is tolerant to glufosinate, but is being promoted for its supposedly drought tolerant properties (Paixão, 2020; Little, 2022); camelina (a plant also known as 'false flax') with herbicide-tolerance combined with altered oil content (Yield10 Bioscience, 2022, ACRE, 2019); and drought-tolerant GM maize for Africa, which is also being stacked with glyphosate-tolerance in some cases (African Centre for Biodiversity, 2021). These projects are consistent with the industry's awareness that, although RoundUp Ready crops are failing, there may still be opportunities to profit from expanding into new geographic areas and/or new crops before resistant weeds take hold (Green & Siehl, 2021). This PR strategy acts as a distraction from the negative consequences of growing HT GM crops, and as a means to attempt dump failing HT traits onto new markets.

Increased spraying of tank mixes of multiple weedkillers has led to grower weed control costs tripling in the USA (Vivian et al, 2013; Evans et al. 2016; Myers et al., 2016; Pratt, 2016a; Duke et al., 2018). The total applied toxicity of pesticides (not just glyphosate) has increased significantly since 2008 (Schulz et al., 2021). A 2015 survey conducted in 17 states in Brazil, revealed that 97% of respondents used tank mixtures by this date, usually with 2 to 5 products at the highest recommended doses (Gazziero 2015). A major problem remains the inadequate examination by regulators of the effects of mixtures of herbicides on human health and the environment (Sprinkle & Payne-Sturges, 2021). In addition, weeds are becoming resistant to multiple different herbicides (e.g. Benoit et al., 2020).

The US Department of Agriculture (USDA) argues that GM maize and soybeans with resistance to multiple herbicides will become the norm in future (Nandula, 2019). GM soybeans and maize with resistance to dicamba and 2,4-D are already on the market, and these are being stacked with existing GM resistance traits (to glyphosate and/or glufosinate) or other herbicides (such as isoxaflutole). In the USA, in crop year 2018, around three quarters of the soybean seed offered to farmers expressed the glyphosate-resistance gene, plus either dicamba or 2,4-D resistance genes (Benbrook, 2018). In 2019, Monsanto (now owned by Bayer) filed a petition with the USDA for determination of nonregulated status of a genetically engineered corn variety resistant to five active ingredients: glyphosate, glufosinate, dicamba, 2,4-D and quizalofop (Monsanto, 2019). These herbicide tolerant GM crops allow farmers to apply additional herbicides such as 2,4-D, dicamba, isoxaflutole or glufosinate during the whole cropping season at high rates, with the risk of detrimental effects to the environment and human health. For example:

- isoxaflutole is known to persist in the environment and to leach into and accumulate in ground- and surface waters (US EPA, 1998);

- an association between increasing 2,4-D application and human urine concentrations has already been reported (Freisthler et al., 2022); 2,4-D is classified as possibly carcinogenic by the WHO (IARC, 2018); 2,4-D is reported to be toxic to a variety of organisms, including fish, amphibians, insects, earthworms and rodents (Islam et al., 2018; da Silva et al., 2022);
- dicamba is a suspected endocrine disruptor (Zhu et al. 2015); and
- glufosinate is classified as a known or presumed reproductive toxicant and is no longer authorised for use in the EU (EFSA, 2017; European Commission, n.d.).

Moreover, 2,4-D and dicamba are prone to drift (risking damage to other farmers' crops, as well as the environment) (Murschell & Farmer, 2019; Lerro et al., 2020; Soltani et al., 2020) and it has been shown that repeated herbicide drift exposure can rapidly select for weed resistance (Vieira et al. 2020; Comont et al., 2020). Dicamba-resistant, 2,4-D resistant and glufosinate-resistant Palmer Amaranth (pigweed) have already been identified in the USA (Kumar et al, 2019; Unglesbee, 2020b; Unglesbee, 2021a). This circular process of the evolution of resistant weeds and the subsequent development of the next generation of transgenic crops, that allow for an intensified use of herbicides and thus favour the emergence of another round of resistant weeds, has been called the "transgenic treadmill" (Binimelis et al., 2009; Mortensen et al., 2012).

RR GM crops, and newer HT GM crops, use a method of genetic engineering known as transgenesis, which involves transferring new DNA from another species into plant cells (known as 'transgenes'). Newer genetic engineering techniques, using a variety of methods called 'gene editing', may allow new herbicide-tolerant GM crops to be produced which rely on mutating the crop's own genes and not on introducing foreign genes into the genome of a crop. There is commercial interest in this approach because such crops may be deregulated in some countries, so that environmental risk assessments and food labelling may not be required before they can be marketed. In particular, 'base editing' and 'prime editing' techniques can be used to mutate DNA without the need for donor DNA, although these methods are not currently efficient (Tang et al., 2020). Crops that have been gene edited to include herbicide tolerant traits remain at the experimental stage, but include wheat, rice, maize, soybean, potato, rapeseed (canola), flax, cassava, watermelon and tomato (Gosavi et al., 2022). The problems associated with existing HT GM crops will not be avoided by using gene editing techniques, since all these experimental crops are genetically engineered to withstand blanket spraying with the associated herbicides.

Lawsuits

There have been numerous lawsuits relevant to the cultivation of GM herbicide-tolerant crops in the United States.

One set of lawsuits relates to claims that exposure to glyphosate causes cancer and environmental harm. Following the IARC's classification of glyphosate as a "probable human carcinogen", in March 2015, numerous lawsuits were filed alleging that past use of Monsanto's Roundup herbicide had contributed to the plaintiffs' development of non-Hodgkin lymphoma (NHL). Three lawsuits were heard before a jury and resulted in victories for the plaintiffs. In June 2022, the U.S. Supreme Court rejected Bayer's bid to dismiss these legal claims by customers and left in place the lower court decision that upheld $25 million in damages awarded to one California resident (Hurley, 2022). In July 2021, Bayer (which bought Monsanto in 2018) took an additional litigation provision of $4.5 billion for this case, on top of $11.6 billion that the company previously set aside for settlements and litigation (Hurley, 2022). In addition, in a case brought by farmers and environmental groups, the 9th Circuit Court of Appeals in California determined in June 2022 that the EPA did not adequately consider whether glyphosate causes cancer and threatens endangered species, and ordered it to look again at the risks it poses (Stempel, 2022).

Another set of lawsuits relates to crop damage caused by farmers spraying dicamba or 2,4-D on to GM crops resistant to these herbicides. In particular, Elmore (2022) describes how, in 2021, thousands of U.S. growers reported to the Environmental Protection Agency (EPA) that dicamba sprayed by other farmers on dicamba-resistant GM crops damaged crops in fields all over the country. In February 2020, Bader Farms won the first dicamba lawsuit and was awarded U.S. $15 million in damages, plus U.S. $250 million in punitive damages. The jury also found Monsanto and BASF had engaged in a joint venture and conspiracy, knowingly risking widespread crop damage in order to increase their own profits (Davies, 2020; Gillam 2020b). In June 2020, the Ninth Circuit's three-judge panel unanimously vacated EPAs approval of dicamba based herbicides (National Family Farm Coalition v. USEPA, 2020; Unglesbee, 2020f). However, these were subsequently re-registered. In 2022, the federal judge considering a case against the EPA in the U.S. District Court for the District of Arizona ordered that the EPA should file a report on the status of its ongoing evaluation of its options for addressing future dicamba-related incidents (Unglesbee, 2022a). The environmental and farming organisations involved subsequently asked court to lift a stay and expedite their lawsuit demanding EPA vacate its 2020 dicamba herbicide registrations (Unglesbee, 2022b). Despite these developments, the companies involved aim to commercialise new dicamba tolerant traits, some with tolerances against four or five active ingredients (Unglesbee, 2020n).

Alternatives

The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods. It is now widely recognised that herbicide dependency must be reduced (Harker et al., 2017; Beckie et al., 2019b).

Viable alternatives include:

- Increased use of agro-ecological methods, for conventional as well as organic farming, including crop rotations;
- Further development and implementation of spot spraying and precision weeding to target and reduce the use of herbicides and/or technologies to limit weed seed production during the grain harvest (Quartz, 2015; Guardian, 2015; Horticulture Week, 2015; Gonzalez-de-Santos et al., 2017; Walsh et al., 2017; Beckie et al., 2019b; Oliver, 2020; Belton, 2021; Peters, 2021).

Even advocates of GM crops now accept that RR crops – the main GM crops that are grown today - are not the future of agriculture. Former UK Life Sciences Minister, George Freeman MP (Minister for Science, Research and Innovation until July 2022) stated: "*The first generation, if you like 'GM1.0', was very crude, particularly the original Monsanto monoculture model: "Spray everything that dies apart from the thing we have protected." I do not think anyone thinks that is a particularly progressive way of doing 21st century agriculture…*" (House of Commons Science and Technology Committee, 2016). Former senior scientists at DuPont and Corteva

Agriscience conclude a recent book chapter, "*Today, glyphosate-based crop systems are still mainstays of weed management, but they cannot keep up with the capacity of weeds to evolve resistance. Growers desperately need new technologies, but no technology with the impact of glyphosate and GR crops is on the horizon. Although the expansion of GR crop traits is possible into new geographic areas and crops such as wheat and sugarcane and could have high value, the Roundup Ready® revolution is over*" (Green & Siehl, 2021).

There are significant opportunity costs associated with investing in 'next-generation' HT crops which are tolerant to more herbicides but which will not solve the long-term problem of resistant weeds and will continue to pose risks to human health and the environment. Investing in alternatives means a supporting a paradigm shift towards using less herbicide, not more, to the benefit of farmers, human health and the environment. It is particularly important that RR crops are not pushed into new countries which have so far avoided stepping onto the "transgenic treadmill".

Recommendations

GeneWatch calls for an end to the cultivation of herbicide-tolerant (HT) GM crops, including RoundUp Ready (RR) crops and 'next-generation' GM crops that are tolerant to more than one weedkiller. Protecting the environment and human health should be a priority.

The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods.

Governments of countries where RR crops are grown should urgently develop phase-out plans for this technology and publish these for public consultation and debate.

Governments should also end subsidies for maize (corn) to be used as biofuels (corn ethanol), rather than as food.

Governments of countries where RR crops are not currently grown (for example in Europe, most of Africa and Asia, parts of Latin America and New Zealand) should maintain their *de facto* bans on this technology.

In addition:

- Food retailers should require non-GM feed for meat and dairy products, to seek to minimise environmental damage in countries where GM HT crops are grown. At minimum, labelled non-GM-fed meat and dairy products should be available to allow consumers to choose to eat such products.
- In the United States, GM food products should be labelled and food manufacturers should seek to avoid using ingredients from GM HT crops.

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