Roundup – Is it safe?

Special briefing

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This briefing summarises the key findings of recently published research on the toxicity of the herbicide Roundup used on GM crops and explains how the regulatory system fails to provide the level of protection required to protect human health.

Background

Roundup is the world's best selling herbicide (weed killer). Its active ingredient is glyphosate, which was developed by Monsanto. Glyphosate-based herbicides are highly effective at destroying weeds because they are taken up by the plant so that the whole plant is killed. Roundup is the brand name for Monsanto products containing glyphosate mixed with other chemicals, or adjuvants, which allow the product to stick to the leaves or other parts of the plant and help the active ingredients to enter the plant cells. Several different versions of Roundup/glyphosate herbicides are produced based on different formulations containing "commercially sensitive" (ie, secret) mixtures of adjuvants. When absorbed by plants, glyphosate is transformed into its metabolite aminomethylphosphonic acid (AMPA). Glyphosate-based herbicides are also made by other companies using different formulations, as Monsanto's patent on glyphosate expired in 2000.

New Evidence on Roundup Toxicity

Recently published research[i] shows that a number of formulations of Roundup are generally more toxic to human umbilical, embryonic, and placental cells than either glyphosate on its own, its metabolite (AMPA) or one commonly used adjuvant (POEA). The Roundup formulations caused "total cell death within 24 hours, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis" (ie, cell death).

The researchers concluded that the presence of adjuvants changes the permeability of human cells to Roundup and amplifies the toxicity of glyphosate*: "…the proprietary mixtures available on the market could cause cell damage and even death around residual levels to be expected, especially in food and feed derived from R (Roundup) formulation-treated crops."*

In these experiments, Roundup obtained from stores was diluted by 100,000 times – far below the concentrations used when the chemical is sprayed on GM herbicide resistant crops designed to be used with Roundup and equivalent to the levels likely to be found in residues in food and animal feed made from such "Roundup Ready" crops.

In other words, the research found that in the laboratory, formulations of Roundup were more able to penetrate human cells and kill them than glyphosate alone or the individual chemicals added to make it an effective weedkiller (see footnote[1]) (see Figure1 below). These findings are significant in that they may alter Roundup's toxicity profiles for farmers and bystanders and via residues in food or feed.

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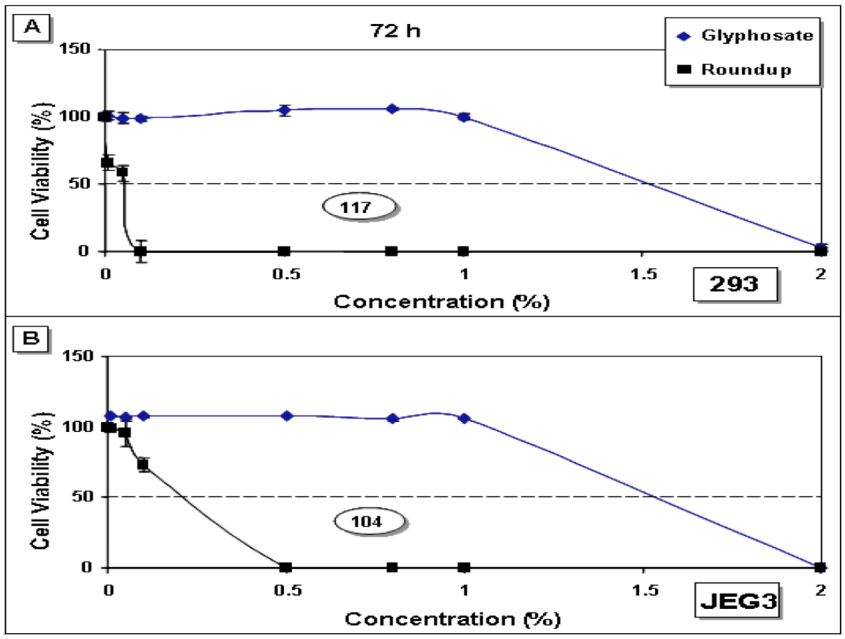
[1] **Glyphosate – Mode of Action**

Glyphosate kills plants by inhibiting the EPSP (5-enoylpyruvylshikimate-3-phosphate synthase) synthase enzyme. EPSPS is a key enzyme in the shikimate biosynthetic pathway and its disruption, which leads to depletion of chemicals vital to protein synthesis and plant growth such as aromatic amino acids, auxins, folic acids and lignin.

Figure 1 showing the difference in toxicity to human umbilical, embryonic, and placental cells between Roundup and Glyphosate



Source: CRIIGEN presentation 2009

Equally importantly, Roundup or other herbicide formulations are never tested in long-term *in vivo* tests in mammals in order to gain approval by regulatory authorities – safety tests are only undertaken on individual components of the mixtures that are sold.

Roundup Residues

The use of Roundup on food and feed crops means that residues of glyphosate and other chemicals used in the various formulations will be found in our food. Indeed the maximum residue levels (MRL) permitted in food and feed products were raised 200 times compared to levels previously permitted[ii] at the time GM soya crops were approved. Not all soya products have a MRL for glyphosate. In 1999, UK Minister Jeff Rooker made it clear that residues were likely to be found in RR soya:

> *"Experimental studies indicate that two major residues may be found in glyphosate treated soya. The residues concerned are glyphosate itself and its metabolite aminomethylphosphonic acid (AMPA). These two residues occur in both conventionally bred soya and genetically modified (GM) glyphosate tolerant soya. However, the levels of the metabolite AMPA are generally higher in GM crop[iii]."*

In recent years, UK sampling of food for glyphosate residues has been largely confined to cereals, bread and flour. It is regularly detected:

- Out of 466 bread and flour samples tested between 2006 and 2008, 27% contained glyphosate residues in the range 0.1-3.8mg/kg (parts per million).
- In 2006, residues of glyphosate in tofu and soya pieces were reported. The country of origin or type soya used as the raw ingredients are not recorded. However, 6 out of 8 samples of tofu/soya pieces originating from Brazil (where GMRR soya is cultivated) contained glyphosate, with the highest level recoded being 1.1mg/kg (parts per million). AMPA residues were not reported.
- No glyphosate residues were found in 60 samples of EU manufactured soya milk in 2006, but again the raw ingredients were of unknown origin.

At the time of writing, no data on the presence of glyphosate or AMPA in animal feed or animal products fed on glyphosate-contaminated feed in the UK has been published by the Pesticides Residues Committee, even though it is reasonable to assume such residues are there given the current reliance on GM in animal feed.

Roundup and GM crops

One of the main drivers for the development of GM crops was Monsanto's need to increase Roundup sales in a way that outmanoeuvred their competitors, at least for the duration of a patent. The discovery of a gene in a soil bacterium resistant to the way glyphosate works (see mode of action footnote above) enabled the company to use genetic engineering to produce Roundup-tolerant varieties of soya beans, maize, cotton and oilseed rape, which are marketed as RR (Roundup Ready) crops. Roundup can be spayed on the growing RR crop leaving it unharmed but killing all weeds and other plants around it. Monsanto were thus able to sell seeds and herbicide in contractually-binding packages to farmers, guaranteeing growing sales of Roundup plus additional revenues from the sale of the RR seeds.

As a result, Roundup remains the world's best-selling herbicide, and Monsanto have become a major player in the global seed industry. Following RR crop introductions in the USA, glyphosate use grew 15 fold in the period 1994 to 2005, and a further 28% in the following year. Similar trends have followed the introductions of RR soya in Argentina and Brazil. Roundup sales are essential for Monsanto's strength – sales were 48% of the total corporate sales in the first quarter of 2008[iv].

Roundup Ready crops dominate the sales of GM varieties. RR soya is by far and away the largest selling of GM crop and is grown in the USA, Canada, Argentina, Brazil and Paraguay[v], Uruguay, Chile and Bolivia, and South Africa have also recently started to grow RR soya on a smaller scale. Other RR crops are mainly grown in the USA and Canada. None have been commercially grown in Europe or Asia.

In the EU, RR soya and RR maize are mainly imported for animal feed, and some RR soya cooking oil is sold (mainly to the catering industry).

In the UK, Roundup and other glyphosate herbicides are used extensively to provide blanket control of weeds (eg, clearing a field for ploughing or direct sowing of seeds), for the desiccation of oilseed rape and cereal crops prior to harvest and to control urban weeds and, in particular, Japanese knotweed, by local authorities and other public/charitable bodies.

Safety assessments of Pesticides and GM Crops

EU approvals for GM herbicide tolerant crops involve two completely separate regulatory processes:

1) The GMO approvals are under Directive 2001/18 and Regulation 1829/03.
2) The use of Roundup is covered by the Plant Protection Products Directive 91/414, and other regulations.

In the case of imports of RR soya for food or feed, only the GMO regulations apply. If RR soya were to be given approval for cultivation in the EU, approval for using Roundup (glyphosate) on GM soya would have to be granted by the member states where cultivation was proposed under regulations enacting Directive 91/414 for pesticide use on Roundup.

The active ingredient in Roundup, glyphosate, has already been added to Annex 1 of this Directive and therefore has approval for use throughout EU. Member states then use domestic regulations to license the specific formulated products for specified uses, such as the use on RR GM soya crops.

Crucially, only if the "technical specification" of the glyphosate used in the product changes is its toxicity scrutinised again. Changes in "technical specification" relate to the purity of the glyphosate, increase in the maximum levels of other compounds or impurities and the presence of new chemicals. However if "the technical specification is considered to be sufficiently '**similar**' to the original specification...," there is no need to consider the changes further"[vi].

Under the GMO regulations, testing of GM crops is not even required on one laboratory mammal for a short period (14 weeks), but often performed. In contrast pesticides need to be tested on at least three mammals, one of which needs to be for a 24 month duration.

However, different formulations of Roundup are not tested in this way, as the regulators rely on safety data on the individual components, namely glyphosate and adjuvants, despite the fact that, "*Carrier solvents used in commercial formulations may change toxicological properties*[vii]." Thus only glyphosate is tested alone for two years[viii].

In the UK, adjuvants and other chemicals used in formulations of Roundup are tested separately and subject to a separate approval systems. If approved they are placed on the "Official List" and can be used in any

product thereafter. Adjuvant chemicals are either wetting, sticking, fogging or extending agents. They enable the active ingredient to work more effectively by allowing them to gain entry into plant cells, but also by side effects into human and animal cells. The combination of chemicals, the herbicide itself, are not tested.

Thus there is clear and potentially dangerous gap in the regulations of GM herbicide tolerant crops because residues arising from the use of Roundup on the crop will be present. The regulators relied only upon safety data for individual herbicide ingredients, when it is the combination of ingredients that makes them both effective and potentially toxic to non-target organisms. GMO authorisations cannot be relied on to detect problems arising from pesticide residues present because they are limited in duration and were not designed for that purpose.

Safety and efficacy data (known as "the data package") produced by another company can be submitted for applications for new products providing a "letter of access" from the company that "owns" the data is submitted. Thus, in theory, safety data can be traded between companies wishing to gain authorisation for the same active ingredient regardless of how reliable they are.

Lessons for Regulators and the Food Chain

The research findings outlined above suggest that the toxicity profile assumed for Roundup based on safety data for glyphosate and other components alone may underestimate the toxicity of the formulated products used on RR GM crops or other food/feed crops where it is authorised for use. The growing use of, and dependence on, Roundup by intensive arable systems using RR GM crops increases the likelihood of human exposure either in the field to workers or bystanders or via food residues. Farm animals and poultry can be exposed via residues in feed. The lack of long-term feeding studies of either RR crops or Roundup means potential health impacts have only recently begun to be studied. An Italian study comparing RR soya and its non GM parent fed to mice have highlighted impacts on liver aging, which could have long-term health implications for farm animals or people[ix].

Actions Required

The EU should carry out an immediate review of the safety of Roundup and other formulations of glyphosate. Licenses to use Roundup on food/feed crops should be suspended until data on the safety of all formulations to human and animal health has been established, including in the levels of residue likely to be found in food and animal feed.

UK Regulators should immediately lower the maximum residue level for glyphosate in imported RR GM soya beans to the previous level of 0.1mg/kg. This would greatly reduce the risk of further exposure while a full safety review of formulated glyphosate-based herbicides is undertaken

Food manufacturers, retailers and feed manufactures should undertake monitoring of all raw ingredients on which Roundup and other glyphosate-based herbicides have been used, including animal products fed on GM RR soya or maize, to ensure they are free of residues before entering the food chain until their safety can be established.

Farmers and growers should ensure that they, their farm workers and bystanders are not exposed to Roundup by only applying it using full protective clothing and preventing drift off-field onto people, livestock or other crops. Buffer zones must be established along roads, watercourses and around property to minimise bystander and whole population exposure.

Local authorities and other major users of Roundup and other glyphosate-based herbicides should adopt similar procedures to protect workers and bystanders.

Further Information

The research on the toxicity of Roundup formulations was carried out by Professor Gilles-Eric Séralini and Nora Benachour[1] of the Comité de Recherche et d'Information Indépendantes sur le génie Génétique (CRIIGEN), based at the University of Caen in France. For copies of the scientific paper and further information contact criigen@unicaen.fr.

Notes

[i] Benachour N and Séralini G-E, 2009. Glyphosate Formulations Induce Apoptosis and Necrosis in Human Umbilical, Embryonic, and Placental Cells, *Chemical Research in Toxicology* Vol22 No1 pp 97-105 available from http://pubs.acs.org/doi/pdf/10.1021/tx800218n
[ii] See http://www.publications.parliament.uk/pa/cm199899/cmhansrd/vo990714/text/90714w21.htm#90714w21.htm_sbhd4
[iii] See www.publications.parliament.uk/pa/cm199899/cmhansrd/vo990714/text/90714w21.htm#90714w21.htm_sbhd4
[iv] See www.reuters.com/article/pressRelease/idUS106176+03-Jan-2008+PRN20080103
[v] See www.isaaa.org/resources/publications/briefs/39/pptslides/default.html
[vi] See www.pesticides.gov.uk/applicant_guide.asp?id=1262
[vii] WHO/FAO Datesheet on Pesticides No 91 *Glyphosate* July 1996.
[viii] Williams, G. M., Kroes, R., and Munro, I. C. (2000) "Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for human". *Regul. Toxicol. Pharmacol. 31*, 117–65.
[ix] Malatesta M. et al. ,2008. "A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing". *Histochem Cell Biol.*, **130**: 967-977, 2008.