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Concerns about glyphosate's approval

Friends of the Earth Europe, June, 2013

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Introduction

Glyphosate is the world's best-selling chemical herbicide. Glyphosate-containing herbicides, such as Monsanto's Roundup, are the most widely used herbicides in Europe and are applied in farming, forestry, parks, public spaces and gardens. Glyphosate-containing herbicides are also crucial to the production of genetically modified herbicide resistant crops. In recent years a number of scientific studies have raised concerns about glyphosate's safety and there have been calls for glyphosate-containing herbicides to be banned. New research by Friends of the Earth has detected glyphosate residues in the urine of 44 percent of people tested, from 18 different European countries.

Glyphosate was patented by Monsanto in the 1970s, and the first herbicide (Roundup) was approved in the USA in 1974 and shortly afterwards in European countries. In 1991, legislation was brought in by the European Commission to harmonize pesticides approvals (Directive 91/414), and glyphosate was granted an EU-wide approval in 2002. On the basis of these approvals, the pesticides industry claim glyphosate is safe. For example, in advice to users Monsanto claims glyphosate is "*practically non-toxic*" [1].

But glyphosate's approvals do not mean its safety has been independently tested. In fact, regulatory agencies don't carry out any testing of pesticides. Instead, if a company wants to get a pesticide approved it conducts the required safety tests itself, or pays for them to be done, and the regulators examine the results. This process was used for glyphosate's original 1974 approval in the USA [2] and for its 2002 European Union approval [3]. New EU pesticides legislation came into force in 2011 (Regulation 1107/2009), adding some extra requirements such as a review of scientific literature, and consideration of whether the pesticide causes endocrine disrupting effects. However, approvals continue to follow the same general procedure as before - there is still no independent testing, and many of the test requirements remain unchanged.

Glyphosate's approval in the European Union

Glyphosate's 2002 approval was based on a dossier of evidence supplied by Monsanto and a number of other pesticide companies. This dossier was first examined by the predecessor agency of the German Federal Office for Consumer Protection and Food Safety (BVL), which had been appointed as the 'rapporteur' for glyphosate, liaising between the industry and EU authorities. In 1999, the German rapporteur produced a report favourable to glyphosate and this paved the way for full approval in 2002. Since then, many hundreds of glyphosate-containing herbicides have been licensed by countries across the EU, with uses ranging from agriculture, forestry, parks and urban spaces to gardens, railway lines and even use in lakes and rivers [4].

Glyphosate's ten year approval should have ended in 2012. In 2010, Monsanto asked for a renewal [5] and following the application, the Commission extended glyphosate's approval until 2015 [6]. The reason given was to "*enable the applicants to prepare their applications*" [7], but it seems the explanation may actually lie inside the European Commission. In 2008, following threats of legal action from pesticide companies, the Commission allowed a large number of pesticides that had failed to get EU approval to be re-evaluated under a less demanding procedure known as 'resubmission' [8]. This created a huge backlog of work for the Commission, member states and the European Food Safety Authority, causing a three year delay in all other work, including the re-evaluation of glyphosate [9].

'Acceptable Daily Intake' of glyphosate

One of the core purposes of pesticide safety assessment is to set the 'acceptable daily intake' (ADI) for people's everyday exposure to the chemical, for example through residues in food. In its 1999 evaluation of glyphosate, the German authorities proposed a high ADI for glyphosate of 0.3 mg per kilogram of body weight. They calculated this figure by reviewing the industry feeding trials using glyphosate and choosing the one they felt to be most sensitive to the effects of the chemical. In this case, the German authorities considered the most sensitive test to be a rat feeding trial. From this they calculated the 'no observed adverse effect level' (NOAEL). The ADI was then set at 100 times lower than this [10]. This ADI of 0.3 mg/kg was agreed by the European Commission, and is now law. But even four of the companies applying for approval of glyphosate differed in their interpretations of the

industry feeding trials – based on the same studies; they suggested the ADI should be lower, ranging from 0.05mg/kg to 0.15 mg/kg [11].

In 2012, the ADI for glyphosate was re-examined by a group of scientists (including four professors) from universities in the UK and Brazil [12]. When they looked at the industry-funded feeding trials assessed by the German authorities, they noted some studies showed adverse effects at lower doses than in the rat feeding trial, but these findings had been ruled out for various reasons. They claim this led to "*significant bias*" in the data used. They commented that, if all the industry-funded studies had been included, a "*more objectively accurate*" ADI would be 0.1 mg/kg bodyweight per day. The group then examined the findings of independent trials of glyphosate published in scientific journals since 2002. Based on these, they concluded the ADI should correctly be 0.025mg/kg bodyweight per day, or "*12 times lower than the ADI… currently in force in the EU*".
The ADI for glyphosate is not monitored.

Narrow focus

Because of the way Directive 91/414 was written, glyphosate's EU approval focussed largely on the pure chemical. But the hundreds of different glyphosate-containing herbicides in which it is actually sold contain other ingredients, and these can affect the toxicity of glyphosate [13]. In fact, the toxicities of different glyphosate-containing herbicides have been found to vary by as much as 150 times [14]. Such chemical interactions were not addressed in the European Commission's 2002 report into the safety of glyphosate [15], and only the acute toxic effects of each glyphosate-containing herbicide need to be tested, such as might be caused by a user accidentally spilling the product on themselves [16].

From 2014, the other ingredients used in herbicide formulations will also have to be assessed [17]. However, the chemicals will be examined separately, not as the mixtures in which they are sold. There are also provisions in the new legislation for more thorough examinations of glyphosate-containing herbicides, but it remains to be seen what will be required by regulators.

Until recently, the approvals process ignored whether a pesticide would cause disruption of hormone and reproductive systems at low doses, called endocrine disruption. The new

pesticides regulation 1107/2009 does address this, stating that a pesticide can only be approved if "*it is not considered to have endocrine disrupting properties that may cause adverse effect*" [18]. However, the European Food Safety Authority has set a high level for proof of endocrine disruption. In 2013 it stated there will have to be evidence of an effect on endocrine systems, evidence of harm from animal studies and a "*plausible link*" between the endocrine disrupting effect and the findings of the animal studies [19]. But the Endocrine Society, which represents specialist scientists from around the world, has already criticised this approach. They argue the EU's definition of endocrine disruption is "*complicated and problematic*" and that "*the ability of a chemical to interfere with hormone action is a clear predictor of adverse outcome*" [20].

Lack of transparency

In all of glyphosate's approvals so far, the evidence presented to regulators did not have to come from independent studies published in scientific journals. Instead, the studies were largely conducted by private laboratories and paid for by the pesticides industry. They were rarely peer reviewed, and the findings were often classed as commercial secrets, meaning they were never published. During glyphosate's EU approval, pesticide companies asked for more than 130 safety studies to be kept secret [21], covering everything from its toxicity, to how it behaved in soil, to how it affected beneficial insects such as ladybirds. When the World Health Organisation evaluated glyphosate's safety in 2004, only 29 out of the 134 studies presented by industry had been published [22].

Much of the data on pesticides is only available to regulators. As a result, the public and wider science community have little opportunity to examine a pesticide's safety during the approvals process, and little hope of challenging decisions made by government authorities. Pesticide approvals end up being based on the opinions of a small, relatively anonymous circle of officials, who face little accountability for their decisions. For this reason, farming, consumer health and environmental organisations from across the European Union have called for the pesticides approvals system to be made more independent, open and accountable [23].

Independent science is ignored

Since 2002, studies published in scientific journals have raised a number of concerns about the safety of glyphosate and glyphosate-containing herbicides. They have found indications of damage to DNA, endocrine disruption, birth defects, developmental and neurological toxicity (For further information see [Briefing 3]). There is also growing evidence of harm to the environment (For further information see [Briefing 5]).

Yet even as the evidence grows, the EU authorities have refused to revise their opinion of glyphosate. The European Food Safety Authority has dismissed two studies published in scientific journals which showed adverse effects from the herbicide Roundup. In each case they criticised the methods used [24] [25]. In 2011, a report by independent scientists concluded that both industry-funded and published studies show evidence glyphosate may cause birth defects [26]. The European Commission's response was that the report provided "*little new evidence*" [27]. The German rapporteur has been particularly resistant to reviewing the evidence about glyphosate. In 2010, the German authorities stated there is a "*huge and reliable database*" on the safety of glyphosate [28].

Good Laboratory Practice

Guidelines for 'Good Laboratory Practice' (GLP) were first developed by the US Food and Drug Administration in the 1970s, after the discovery of widespread malpractice by pharmaceutical testing laboratories [29]. In 1981, the OECD agreed international GLP regulations, partly so that companies could use the same data for approvals in different countries [30]. The regulations set out systems for quality control, including record-keeping and presentation of results. They are important for preventing poor practice by private laboratories, but in a recent article written by 30 public health scientists from around the world, it was pointed out that Good Laboratory Practice "specifies nothing about the quality of the research design, the skills of the technicians, the sensitivity of the assays or whether the methods employed are current or out of date." [31]

Peer review

Before being published in a scientific journal, academic studies are subjected to a process called peer review, in which other scientists examine the methods, results, analysis and conclusions in order to check for mistakes or problems. Following publication, the wider scientific community can comment, repeat the study or attempt to disprove the results. Not only is peer review a more rigorous examination than required by 'good laboratory practice' [32], but because the results of industry studies often remain unpublished, they cannot be subjected to scientific follow-up.

The EU authorities appear to rely almost exclusively on industry toxicological studies. The German BVL has even commented that "*for regulatory decisions published studies are only of limited use"* [33]. But industry studies have been criticised for their focus on short-term, high dose animal trials [34]. In contrast, real-life exposure occurs over the long term, at low or fluctuating doses. Anyone born since the 1970s may have been exposed to glyphosate throughout their entire life. And the industry's reliance on animal feeding studies has been criticised for not reflecting developments in academic research, including the use of more sensitive techniques such as human cell cultures [35].

Different standards

So why do the EU authorities dismiss the findings of independent science? The German BVL has stated that *"studies are more reliable and reproducible when performed under GLP conditions and according to an internationally agreed design*" [36]. But the international OECD standards are focussed on the requirements of the approvals system, and if meeting these standards is used as the main criterion for judging the value of independent scientific studies, then much published research will be ruled out of consideration.

Differences between industry and academic studies

Industry studies on pesticides	Academic studies on pesticides
Funded by companies manufacturing or selling pesticides	Funded by governments, national research organisations, charitable trusts etc.
Produced to meet regulatory requirements	Produced to investigate issues of concern or develop new research techniques
Largely unpublished	Largely published
Main focus is high dose animal testing of the pesticide 'active ingredient'	Use a range of different techniques, also examining herbicide formulations and their ingredients.
OECD regulations and Good Laboratory Practice	Peer review and scientific follow up

The German government statement implies that science done outside the approvals process is considered to be of lesser value. But independent studies are likely to have been conducted by researchers who are unconnected to industry, and who work in state institutions such as universities. They are likely to be specialists in their field, involved in advancing understanding of the issues involved. It seems strange that this is the work sitting outside the regulatory system. In any case, internal documents released by the German authorities show that for glyphosate's 2002 approval, many industry-funded studies did not meet GLP standards either. The government documents include a list of toxicology and metabolism studies submitted by the pesticide companies [37], and less than half (48%) are recorded as meeting GLP standards.

Under the new pesticides regulation, published scientific studies will have to be considered during approvals of pesticides. But it is the pesticide companies who will conduct the search and review of scientific literature [38], and it remains to be seen how will they treat independent research that finds adverse effects from their product.

Fundamental changes required in the pesticide approval process

The problems with glyphosate's approval are in large part due to fundamental problems with procedures for the approvals of pesticides. Friends of the Earth Europe believes the

following changes are essential to ensure that protection of citizens and the environment is at the heart of the pesticides approval process.

In the short term:

- Member states should not be allowed to continue indefinitely in the role of rapporteur for any one pesticide, allowing a fresh view of historic approvals. In the case of glyphosate, the German BVL should not be the rapporteur for glyphosate's reapproval.
- all the data provided by pesticide companies, and the assessment of this data by the authorities, must be publicly accessible. For example, it should be published online and in a form that can be easily statistically analysed. The protection of trade secrets should not be allowed as a reason for companies to withhold information.
- independent researchers should evaluate the data provided by companies and approved by the authorities.
- all independent scientific studies should be adequately considered in the approval process for pesticides.
- it should no longer be possible to reject results of independent studies on the grounds that they do not comply with Good Laboratory Practice and OECD international standards
- the minutes of all meetings between companies and the regulatory authorities should be promptly published on the EFSA website, as well as on the websites of national regulatory bodies.
- all formulated products as used by farmers, growers, railway companies etc. should be subject to full testing, taking into account effects of other ingredients.
- no authorization of a pesticide should be given if there is no validated testing system available for residues in food (including animal products) and feed and water

In the medium term:

- companies should only be required to provide a sample of their pesticide for testing. All testing and evaluation should be done by independent researchers and commissioned by EU public authorities. Industry would bear the costs of producing the studies needed for the approval process.
- the international OECD protocols should be overhauled to make the tests capable of assessing health risks in a more realistic manner. Test protocols should be

established that are sufficiently sensitive to detect adverse effects including: endocrine disruption, immunotoxicity, chronic toxicity, carcinogenicity, and reproductive effects (multigenerational studies). Realistic doses (low to medium doses and mixtures) should be tested over the long term, rather than the current practice of testing very high doses over short time scales.

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Friends of the Earth Europe campaigns for sustainable and just societies and for the protection of the environment, unites more than 30 national organisations with thousands of local groups and is part of the world's largest grassroots environmental network, Friends of the Earth International.

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