EFSA explains risk assessment

Glyphosate

Glyphosate is an active substance that is widely used in pesticides. Glyphosate-based pesticides (i.e. formulations containing glyphosate and other chemicals) are used in agriculture and horticulture primarily to combat weeds that compete with cultivated crops. They are typically applied before crops are sown and as a pre-harvest desiccating treatment, accelerating and evening the ripening process.

What has EFSA done?

EFSA and EU Member States have carried out a risk assessment and peer review that updates our scientific knowledge of the toxicity of glyphosate. EFSA has published a Conclusion on glyphosate as part of this process. The conclusion will be used by the European Commission in deciding whether or not to keep glyphosate on the EU list of approved active substances, and to inform the subsequent evaluations by Member States on the use of glyphosate-based formulations in their territories. (See box: "How is the safety of glyphosate assessed in the EU?")

Main findings of the assessment

After considering the huge amount of relevant data, an EFSA peer review expert group made up of EFSA scientists and representatives nominated by EU Member States concluded that:

- The toxicity of glyphosate needs to be redefined. An acute reference dose (ARfD) of 0.5 mg/kg of body weight has therefore been proposed, the first time such a safety measure has been introduced for glyphosate. EFSA will use this ARfD during its review of the maximum residue levels for glyphosate, which will be carried out in cooperation with Member States in 2016. The acceptable operator exposure level (AOEL) has also been set at 0.1 mg/kg body weight per day and an acceptable daily intake (ADI) for consumers has been set in line with the ARfD at 0.5 mg/kg body weight per day.
- The substance is unlikely to be genotoxic (i.e. damaging to DNA) or to pose a carcinogenic threat to humans. Glyphosate is not proposed to be classified as carcinogenic under the EU regulation for classification, labelling and packaging of chemical substances. In particular, all the Member State experts but one agreed that neither the epidemiological data (i.e. on humans) nor the evidence from animal studies demonstrated causality between exposure to glyphosate and the development of cancer in humans.

How is the safety of pesticides assessed in the EU?

Under EU legislation, pesticide active substances in plant protection products are approved in the EU only if it may be expected that their use will not have any harmful effects on human and animal health or the environment.

The evaluation of both existing and new active substances follows a phased approach:

1. For each substance an initial draft assessment report (DAR) or renewal assessment report (RAR) is produced by a designated rapporteur Member State (RMS). Regarding applications for renewal of an approval, the Commission decides on the designation of a rapporteur Member State in consultation with all Member States and industry.
2. The RMS's risk assessment is peer reviewed by EFSA in cooperation with all Member States.
3. EFSA drafts a report ("Conclusion") on the active substance. The EFSA Conclusion informs the European Commission in the approval process, the subsequent assessments of plant protection products by the Member States, and the revision of maximum residue levels in food by EFSA.
4. The European Commission decides whether or not to include the substance in the EU's list of approved active substances. This determines whether the substance can be used in a plant protection product in the EU.
5. EU Member States assess or re-assess the safety of pesticides containing the active substance that are sold in their territory.

Why do some scientists say that glyphosate is carcinogenic?

The International Agency for Research on Cancer (IARC) said earlier this year that glyphosate was genotoxic and would "probably" cause cancer in humans.

However, the IARC report looked at both glyphosate – an active substance – and glyphosate-based formulations, grouping all formulations regardless of their composition. The EU assessment, on the other hand, considered only glyphosate. Member States are responsible for evaluating each plant protection product that is marketed in their territories.

This is because the EU and IARC take different approaches to the classification of chemicals. The EU scheme –assesses each individual chemical, and each marketed mixture separately. IARC assesses generic agents, including groups of related chemicals, as well as occupational or environmental exposure, and cultural or behavioural practices.

This is important because although some studies suggest that certain glyphosate-based formulations may be genotoxic (i.e. damaging to DNA), others that look solely at the active substance glyphosate do not show this effect. It is likely, therefore, that the genotoxic effects observed in some glyphosate-based formulations are related to the other constituents or "co-formulants". Similarly, certain glyphosate-based formulations display higher toxicity than that of the active ingredient, presumably because of the presence of co-formulants. In its assessment, EFSA proposes that the toxicity of each

pesticide formulation and in particular its genotoxic potential should be further considered and addressed by Member State authorities while they re-assess uses of glyphosate-based formulations in their own territories.

This distinction between active substance and pesticide formulation mainly explains the differences in how EFSA and IARC weighed the available data. For the EU assessment, studies conducted with glyphosate were more relevant than studies conducted with formulated products containing other constituents, particularly when the other constituents could not be clearly identified.

What data was used in this assessment?

The EFSA-led review considered a large body of evidence, including the IARC report. In addition to the original studies submitted by the applicants in line with the legal requirements, all available and published studies were considered.

IARC included a number of epidemiological studies in its monograph that were absent from the draft EU assessment; these studies were later added to the EU dossier.

In total EFSA assessed more evidence including additional key studies that were not considered by IARC.

How were the animal studies on carcinogenicity interpreted?

The EU peer review concluded that no significant increase in tumour incidence could be observed in any of the treated groups of animals in the nine long term rat studies considered. IARC, on the other hand, interpreted two studies as showing statistically significant carcinogenic effects. Similarly, with the mice studies, IARC identified positive carcinogenic trends in two studies that the EU peer reviewers assessed as insignificant.

The main differences between the EFSA and IARC evaluations are explained in detail in a special background document published by EFSA. As well as reviewing a larger number of studies, EFSA for example considered that carcinogenic effects observed at high doses were unreliable as they could be related to general toxicity.

What happens next?

The EFSA conclusion will inform the European Commission in deciding whether or not to retain the active substance glyphosate on the EU's list of approved active substances, in other words to authorise its continued use in pesticides in the EU.

Timeline

2012

May — Germany, as rapporteur member state (RMS), receives dossier in support of the possible renewal of the authorisation of glyphosate.

2013

December	RMS sends draft renewal assessment report (RAR) to EFSA.
2014	
January	Peer review begins. RAR sent to Member States and applicants for consultation and comments.
March	Public consultation launched, lasting 60 days.
July	RMS evaluates all comments.
August	Additional information requested from applicants.
2015	
Feb–March	EFSA organises expert consultations in the areas of mammalian toxicology, residues, environmental fate, and ecotoxicology
July	Member State consultation is launched on conclusions arising from peer review.
	IARC monograph published.
August	RMS prepares assessment of the monograph, which is circulated to Member States for comments.
September	Following receipt of comments, EFSA organises second expert consultation on carcinogenicity and mammalian toxicology.
October	Glyphosate authorisation provisionally extended until June 2016, pending finalisation of EU peer review
October	Peer review updated accordingly and final consultation takes place with Member States.

What do we mean by…

Active substance

An active substance is any chemical, plant extract, pheromone or micro-organism that acts against "pests" on plants, parts of plants or plant products.

Acute reference dose (ARfD)

An ARfD is an estimate of a chemical substance in food, expressed on a bodyweight basis, that can be ingested over a short period of time, usually during one meal or one day, without posing a health risk.

Co-formulant

Pesticides are marketed in different formulations that consist of the active substance and various co-formulants. Glyphosate can be used in combination with POE-tallowamine, a co-formulant that promotes the penetration of the active substance into plants.

Genotoxicity

Genotoxic chemicals damage the genetic information within a cell (DNA), causing mutations that may lead to cancer.

Maximum residue levels

A maximum residue level (MRL) is the highest concentration of an active substance that is legally permitted in food or feed when pesticides are applied correctly. EFSA is responsible for proposing MRLs in the EU.

Metabolite

Metabolites are breakdown products that form when a pesticide mixes with air, water, soil or living organisms. They are considered in EFSA's pesticide safety assessments

Weight of evidence

When there are many studies available on a subject, it is good practice to integrate all the available information and identify consistencies and inconsistencies in the results, then weigh the results according to their reliability and relevance.