SUMMARY

FRENCH REPUBLIC

ASSESSMENT OF HEALTH AND ENVIRONMENTAL RISKS BY AGENCIES: FINDING WAYS TO BUILD CONFIDENCE

Parliamentary Office for Scientific and Technological Assessment

Information report by Mr Philippe BOLO, Mrs Anne GENETET, Members of the National Assembly, Mr Pierre MÉDEVIELLE and Mr Pierre OUZOULIAS, Senators

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Assessment against standards entrusted to specialised agencies

Over the past twenty years, agencies specialising in evaluating health and environmental risks have been set up in France and throughout the European Union. Their experts produce **scientific opinions to inform political decision-making** in the sensitive fields of medicines and health products, but also on chemicals and food.

How do these agencies work? Can we have confidence in the quality of the expert evaluations produced? Who are the experts? These questions arose during the dispute over the renewal of glyphosate approval in 2017. The OPECST was asked by the National Assembly's Economic Affairs and European Affairs Committees to investigate the independence and impartiality of these agencies.

The focus was placed on the European Food Safety Authority (EFSA) and the European Chemicals Agency (ECHA) at the European level, and on the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) at the national level.

These agencies conduct assessments which have become mandatory under increasingly stringent regulations (REACH Regulation, Pesticides Regulation, Biocides Regulation, etc.), in order to make knowledge of the risks associated with chemicals a **prerequisite for market access** ("no data, no market" principle).

The manufacturers are responsible for producing and financing the series of toxicological and ecotoxicological tests included in the documentation submitted to the agencies. In the context of the globalisation of science, these tests meet international standards established under the aegis of organisations such as the OECD, including compliance with Good Laboratory Practice (GLP) and Good Evaluation Practice (GEP). Consequently, the agencies **tend to use similar assessment methodologies**, based on the requirement for collective expert evaluations carried out by competent independent experts who make their conclusions public.

Risk assessment frameworks are not set in stone and are constantly evolving: *in vivo* tests carried out on laboratory animals may be supplemented and sometimes replaced by *in vitro* or even *in silico* tests, and the regulatory requirements are regularly updated, especially by updating the guidelines that provide the reference framework, in order to adapt to developments in science and analytical techniques.

Risk assessments are produced in the form of written assessment reports which are used as the basis of risk management measures implemented by the political authorities (approval, prohibition or restriction), according to the principle of the separation of risk assessment and management functions.

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Difficulties and blind spots in expert evaluations

The need for competent and independent experts: conflicts of interest the focus of debate

The experts who participate in the groups established by the agencies must be available, competent and independent. The existence of conflicts of interest is liable to cast doubt upon the impartiality of expert evaluations. There is now a generalised obligation for experts to **provide public declarations of interest (PDIs)**, which are regularly updated. However, there is a **fine line between interests and conflicts of interest**. Each agency possesses its own code of ethics. The European agencies consider that if a firm contributes less than 25% of the funding to a research project, this will not create a conflict of interest with an expert who benefits from it. Declared interests are not monitored systematically, but the disclosure requirement encourages people to provide accurate declarations. **Maintaining a robust public research sector is essential to maintaining a pool of experts who are unaffected by conflicts of interest**, in a context of more stringent independence requirements.

Transparent and multifaceted expert evaluations

Expert evaluations are **invariably collective**, to guard against excessive subjectivity. Agencies always seek to ensure diversity in their groups of experts, particularly with regard to the disciplines they cover.

The agencies' activities are published and this publication now includes their preparatory work.

Stakeholders are asked to give their observations in the framework of assessment activities, providing an opportunity for evaluations by citizens.

Expert evaluations are strongly reliant on manufacturers' data

The majority of the data required by the agencies for the assessment of chemicals, biocides and other substances are **provided by the firms**. These data are not always accessible to the public, even though greater openness has been promised by industrialists since 2018 and is required by the European Union justice system.

The agencies can also base their findings on academic studies, although the latter do not always meet the methodological requirements set down by the regulations and are therefore sometimes excluded on grounds of their lack of relevance in light of the regulatory criteria.

Expert assessments hindered by insufficient knowledge

Although there are many regulatory tests, they do not always provide a complete picture of the effects of a substance or product. For example, ecotoxicity tests are relatively incomplete (insufficient data on effects on soils in particular). The majority of the EFSA and ANSES opinions require more data.

Long-term and combined effects are still poorly understood: the search for **endocrine-disrupting effects** has recently been incorporated and criteria were defined in 2017 (for biocides) and 2018 (for agricultural pesticides). **Cumulative and cocktail effects** are still difficult to identify.

However, these uncertainties do not necessarily imply a failure of assessments. The agencies do mention the limitations of their work in their assessments and have developed methods for dealing with uncertainties.

Key issues concerning the regulations on risk assessments

The European regulations governing risk assessments are highly technical and complex. **The content of the assessments depends on the regulatory methods used**. The time frames required for the recognition of new tests, such as those on pollinating insects, are sometimes long because they must be subject to an international scientific consensus.

The regulations require the organisation of assessments in order to produce risk management decisions: criticisms of approvals are often criticisms of the assessments carried out by agencies.

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The central challenge: improving confidence in the work of experts

Fears of biased expert evaluations fuel persistent mistrust of the agencies

As public decision-making relies on scientific evaluations, firms have implemented **strategies to influence expert evaluations**.
The practices revealed by the "Monsanto Papers" have troubled the public, who are calling for higher ethical standards to be imposed upon agencies and their experts.
Agencies face the challenge of increasing the transparency of their processes and the need to **improve their communication** about their work, which is sometimes misunderstood.

Improving the monitoring of exposures and their effects

The **vigilance schemes** (biovigilance, phytopharmacovigilance etc.) that have been introduced are more focused on detecting acute rather than chronic effects.
Epidemiological studies are expensive and can be difficult to interpret, but they must be developed to improve our understanding of the health impacts of products present in our environment.
Biomonitoring of populations and the environment must also foster a better understanding of the **exposome** (exposure to different substances throughout an entire human life span).
Periodic re-assessments of substances and products are an opportunity to increase our knowledge of the risks by conducting new tests and taking account of data derived from experience of their use.

Why is glyphosate classified as a probable carcinogen by the International Agency for Research on Cancer (IARC) but not by the health and environmental agencies?

In March 2015, the IARC classified glyphosate as a probable carcinogen (monograph no. 112). However, in November 2015, EFSA, in line with almost all other official national assessment agencies (US-EPA in the United States, FSC in Japan, APVMA in Australia, etc.), considered that "*glyphosate is unlikely to pose a carcinogenic hazard to humans*".

This divergence is troubling for the general public and is explained by the use of different sources:
- The **IARC considers all formulations containing glyphosate**, while the EFSA studies the pure form of glyphosate.
- The IARC and EFSA refer to almost identical sources for the **epidemiological studies**, including the US Agricultural Health Study (AHS) and conclude that there is limited (IARC) or very limited (EFSA) evidence of the carcinogenicity of glyphosate to humans.
- The IARC identifies two **animal studies** that reveal a significant link between exposure to glyphosate and cancer, which were rejected by EFSA on grounds of non-compliance with OECD criteria. Conversely, EFSA had access to unpublished manufacturers' studies, unlike the IARC (which analysed only 3 studies on mice out of the 5 used by EFSA, and the IARC analysed only 3 studies on rats out of the 9 used by the EFSA).
- The **IARC also considers there to be strong mechanistic evidence** that exposure to glyphosate causes genotoxic effects or induces oxidative stress, whereas EFSA considers that glyphosate is unlikely to be genotoxic.

These divergent assessments can also be explained by **differences in the interpretation of the available data**, especially regarding the biological relevance of animal testing data and EFSA's failure to take account of secondary cytotoxicity.

Finally, the **scope of the work carried out by the IARC and EFSA differs**. The IARC focuses on assessing whether glyphosate poses a hazard (irrespective of the exposure level), whereas EFSA analyses the risks to human health or the environment (combining hazards and exposure). The minimum intakes at which the studies start to identify carcinogenic effects in animals (above the absorption of 1,000 mg/kg of bodyweight) are very high and therefore unlikely to be attained, with an acceptable daily intake (ADI) set at 0.5 mg/kg of bodyweight, corresponding to a "no observable adverse effect level" (NOAEL) of 50 mg/kg, to which a safety factor of 100 is applied. To date, the agencies have therefore ruled out the carcinogenic risk of exposure to glyphosate, under normal conditions of use of this substance.

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The rapporteurs' proposals

Increase the agencies' capacities to assess regulated risks

1. Enable agencies to initiate studies to improve knowledge of hazards and exposures via an inter-agency research fund.

2. Pool all studies and data available on all regulated products within shared information systems.

3. Improve the identification of endocrine-disrupting, carcinogenic, mutagenic and genotoxic effects by quantifying them precisely and developing tools to understand the cumulative risks.

4. Develop alternative methods to animal experimentation for the identification of health and environmental risks.

5. Encourage regular updates of guidelines to prevent delays to the adoption of new methods or sensitive and reliable tests.

6. Develop instruments for monitoring the effects of regulated products in actual situations: vigilance, biomonitoring and epidemiological studies.

Improve the transparency of assessment activities

7. Make all data contained in files submitted to the assessment agencies available to the public in order to enable citizens to perform an independent assessment.

8. Ensure transparency vis-à-vis personal interests and monitor declared personal interests in the context of stringent ethical obligations imposed upon the agencies' staff and experts.

Reinforce the agencies' ability to perform their risk-assessment role

9. Make it more attractive for scientists to participate in the expert evaluation activities performed by the agencies.

10. Structure the dialogue between assessment bodies to prevent differences in risk assessment that could hamper decision-making.

11. Give agencies broader powers to identify emerging risks.

Make risk assessment accessible and understandable.

12. Improve the organisation of public debate about risks, before decisions are made.

13. Explain and clarify the results of risk assessments carried out by the agencies.

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