European Commission

Scientific Advice Mechanism (SAM)

EU authorisation processes of

Plant Protection Products

Group of Chief Scientific Advisors
Scientific Opinion 5/2018

Research and Innovation

EU Authorisation processes of plant protection products - from a scientific point of view

Group of Chief Scientific Advisors

European Commission
Directorate-General for Research and Innovation
Unit RTD.DDG1.02 - Scientific Advice Mechanism

E-mail EC-SAM@ec.europa.eu
RTD-PUBLICATIONS@ec.europa.eu

European Commission
B-1049 Brussels

Manuscript completed in June 2018.

Luxembourg: Publications Office of the European Union, 2018

Print	ISBN 978-92-79-67736-6	doi:10.2777/71851	KI-04-17-354-EN-C
PDF	ISBN 978-92-79-67735-9	doi:10.2777/238919	KI-04-17-354-EN-N

EUROPEAN COMMISSION

Scientific Advice Mechanism (SAM)
INDEPENDENT SCIENTIFIC ADVICE FOR POLICY MAKING

EU authorisation processes of **Plant Protection Products** from a scientific point of view

Group of Chief Scientific Advisors

Scientific Opinion 5,
(Supported by SAPEA Evidence Review Report No. 3)

Brussels, 4 June 2018

2018 Directorate-General for Research and Innovation

Table of Contents

List of Boxes

List of Tables

List of Figures

List of Annexes

Group of Chief Scientific Advisors

	**Janusz Bujnicki** Professor of Biology, International Institute of Molecular and Cell Biology, Warsaw
	**Pearl Dykstra** **Deputy Chair** Professor of Sociology, Erasmus University Rotterdam
	**Elvira Fortunato** Professor, Materials Science Department of the Faculty of Science and Technology, NOVA University, Lisbon
	**Rolf-Dieter Heuer** **Chair** Former Director-General of the European Organization for Nuclear Research (CERN), Geneva
	**Carina Keskitalo** Professor of Political Science, Department of Geography and Economic History, Umeå University
	**Paul Nurse** Director of the Francis Crick Institute, London

ACKNOWLEDGEMENTS

This Scientific Opinion on the authorisation processes of Plant Protection Products in Europe from a scientific point of view (hereafter 'the Opinion') was delivered to the European Commission by the Scientific Advice Mechanism (SAM) Group of Chief Scientific Advisors (hereafter 'the Scientific Advisors'). It responds to a request by the European Commission and in particular by Commissioner Vytenis Andriukaitis (Health & Food Safety), which the Scientific Advisors accepted on 23 March 2017 with the adoption of the corresponding Scoping Paper (Annex 1 on page 49). The Scientific Advisors in charge of developing this Opinion were Paul Nurse (lead), Rolf Heuer and Janusz Bujnicki. The Opinion has been endorsed by all members of the Group of Chief Scientific Advisors.

The Scientific Advisors wish to thank the many contributors for their support and input in the preparation of this Scientific Opinion:

- The Science Advice for Policy by European Academies (SAPEA) consortium[1] – a key component of the Scientific Advice Mechanism, which provided an Evidence Review Report (ERR) concentrating on risk assessment aspects for health. The ERR was prepared under the leadership of the SAPEA Working Group chair Evangelia Ntzani (University of Ioannina Medical School) and deputy chair David Coggon (University of Southampton); with Alan Boobis (Imperial College London), Jean Golding (University of Bristol), Susanne Hougaard Bennekou (Danish Environmental Protection Agency), Paul Miller (Cranfield University), Colin Ockleford (Lancaster University); aided by the SAPEA staff Nina Hobbhahn, Cosmas Lambini and Céline Tschirhart; and with the support of Ole Petersen, representative of the SAPEA Board for the topic.
- The European Commission's DG Joint Research Centre, in particular Alexandre Anger, Amalia Pineiro Munoz, Mauro Petrillo and Barbara Raffael who assisted with aspects of the literature review.
- All the scientific experts, expert practitioners and stakeholders from the science, policy, industry and civil society communities who contributed to the SAPEA ERR, expert workshops, stakeholder meeting and other *ad-hoc* meetings and consultations, and in particular, participants of the expert sounding board meeting: Thomas Backhaus, Hubert Deluyker, Daniel Dietrich, and Jørgen Schlundt – a comprehensive list can be found in Annex 3 (page 54).

[1] SAPEA brings together knowledge and expertise from over 100 academies and learned societies in over 40 countries across Europe. Funded through the EU's Horizon 2020 programme, the SAPEA consortium comprises Academia Europaea (AE), All European Academies (ALLEA), the European Academies Science Advisory Council (EASAC), the European Council of Academies of Applied Sciences, Technologies and Engineering (Euro-CASE) and the Federation of European Academies of Medicine (FEAM)

- The European Commission's DG Health and Food Safety; DG Agriculture and Rural Development; DG Internal Market, Industry, Entrepreneurship and SMEs; and DG Environment.
- Members of the European Commission's SAM Unit supporting the Group of Chief Scientific Advisors: Annabelle Ascher, Stuart Kirk, Gerjon Ikink, James Gavigan, Piotr Kwiecinski and Jeremy Bray; and other staff providing valuable administrative support.

EXECUTIVE SUMMARY

In this Scientific Opinion, we, the European Commission's Group of Chief Scientific Advisors, make recommendations to the European Commission in response to its request on whether *"the current EU dual system for approval and authorisation of plant protection products (PPP) can be rendered more effective, efficient and transparent, and if so, how?"*

Our recommendations address:

- Tensions between the regulatory goals of (a) the avoidance of harmful effects and (b) improvement of agricultural production as a result of PPP use; how these goals reflect societal views; how the tensions between them are resolved and how they are communicated
- Organisation and operation of the EU dual system for approval and authorisation of PPPs concerning: the role, mandate and the capacity of those involved; the extent to which data are effectively recorded and shared within and outside the system; and how divergent opinions are addressed
- The evolving nature of scientific hazard and risk assessment in terms of: the tools available for assessment; the types of PPPs submitted for approval; the assessment of risks associated with mixtures and aggregate exposure; and landscape-scale environmental effects, in part associated with over-use of PPPs

We note the plurality of strongly held views in different sections of society concerning perceived levels of risk and what constitutes acceptable risk in this and other health, environment and food safety related areas. We therefore make a general recommendation, beyond the specific recommendations below, that the European Commission:

Facilitate a broader discussion throughout society to establish an EU-wide, shared vision for food production, including the role of PPPs therein.

This would need to bring together all EU policies related to the food chain and the environment upon which it depends, and include broad consideration of costs and benefits to society, with due regard to trade-offs between ecosystem services.

We summarise our specific recommendations on the EU system for approval and authorisation of PPPs as follows:

1. Clarify the protection goals of the EU PPP approval and authorisation system and improve their communication – to ensure adequate functioning and to increase public trust

The objectives in the PPP Regulation are that *"substances (…) do not have any harmful effect on human or animal health, or any unacceptable effects on the environment (…) while improving agricultural production"*. However, these objectives may result in unachievable goals in practice. PPPs will almost always have biologically toxic effects, although the risks of actual harmful effects for health and the environment may be very small. For this reason, a literal interpretation of the objectives of the PPP Regulation with respect to protection of human health would thus not permit any PPP authorisation in the EU. This would impact agricultural production or practice.

Risk managers and legislators must therefore set clear criteria and levels for acceptable risk, taking into account that all choices, including the non-use of PPP, carry a component of risk. Risk managers must also define the minimum levels of certainty that they require from scientific assessments, and better communicate their final decisions, including justifications, with reference to these risks.

2. Improve the organisation and operation of the EU PPP system – to increase transparency, effectiveness and efficiency in scientific assessments and decision-making

There should be a functional separation between risk assessment and risk management – this is broadly the case in the EU, but it should be more rigorously applied, both at EU and Member State levels.

The division of responsibilities for risk assessments – of PPP active substances at EU-level and of PPP formulations at Member State level – may compromise consistency and efficiency, which can lead to public scepticism regarding their reliability. We therefore recommend that EU and Member State risk assessors collaboratively assess PPP formulations – as they currently do for active substances – with the support of a comprehensive IT platform for data sharing and to assist with collaborative working, analysis and quality control.

We also recommend that the current approach for the re-authorisation of each individual PPP be replaced by the assessment of groups of PPPs – grouped according to type of active substance, mode of action, and/or use. This will facilitate comparative assessments (see recommendation 6) and can also generate a positive list of safe PPP ingredients (active substances, co-formulants, safeners and synergists).

Furthermore, we question the added value and efficiency of the current two-step risk management process – approval of the active substance followed by authorisation of the PPP. We recommend moving to a single-step risk management decision on a PPP including all its ingredients. This risk management decision should be made either at EU or Member State level.

3. Implement systematic post-market vigilance – to ensure adequate protection is provided, and to increase trust

The current extent of monitoring concentrations of, and exposures to, approved PPPs to estimate their effects on health and the environment is inadequate. Improving this will enable better feedback into the approvals process and increased public trust.

We recommend the establishment of systematic post-market monitoring and periodic literature reviews to improve estimates of human exposure – through improved epidemiological studies and biomonitoring, as well as through observation of PPP applicator behaviour – and of concentrations and suspected ecological impacts in the environment. We recommend the registration of any acute illness following PPP exposure and landscape-scale monitoring of the environment. We finally recommend that the EC consider implementing a tiered PPP authorisation approach with integrated monitoring.

4. Secure and strengthen scientific knowledge and capacity in risk assessment – to enable excellence in protection methods

The PPP approval and authorisation process must better assess risks associated with PPP mixtures and long-term exposure, and keep pace with scientific and technological developments and the changing nature of PPPs, such as nano-pesticides and the increasing shift to biological control agents.

This requires the expansion of, and stable support for, a strong EU-wide expert network, establishing a 'virtual' European centre of excellence to advance scientific assessment methods and to provide adequate expertise and capacity in risk assessment.

5. Improve guidance, oversight and transparency of pre-market studies – to ensure the availability and quality of data to perform proper assessments

Comparable processes in other sectors, such as medicinal products, include dialogue between EU risk assessors and applicants prior to dossier submission, which can improve risk assessment quality and process transparency. We recommend that this also be implemented for PPPs.

We observe some scepticism at present regarding the independence and reliability of some pre-market studies. To improve openness and public confidence in the process, we recommend mandatory pre-registration of all such studies, including a description of what will be learnt from the test and the names of the test facilities where the tests will take place. In practical terms, this will permit inspection of test facilities when these studies are being performed and ensure that no relevant studies are omitted from the risk assessment.

We also recommend that the EC reflect on the current criteria for data confidentiality and for access to raw data, with a view to increasing the transparency of the process.

6. Re-examine the treatment of hazards, risks, costs and benefits – to provide reassurance that the system is fit-for-purpose

We recognise both merits and shortcomings of the hazard-based approach, and that it has some risk-based elements embedded in it.

We recommend that this approach be re-examined to determine whether it is delivering intended levels of protection and appropriate outcomes. We recommend undertaking comparative risk assessments for new candidate PPPs to ensure that those which are less safe than those already marketed are not authorised. Finally, we recommend that risk managers give careful consideration to making systematic use of risk-cost-benefit assessments, also aimed at preventing over-use of PPPs.

7. Augment mechanisms to resolve divergent scientific assessments – to safeguard public trust in scientific advice

Although divergences in scientific assessments of PPPs between professional risk assessors are rare, they do sometimes occur. Once in the public domain, science can be misused and politicised in debates, which can be detrimental to public trust. Whilst the above recommendations can reduce the likelihood of diverging conclusions arising between EU risk assessments, some further specific recommendations are made to help resolve divergent assessments between the EU and international bodies when they occur, and to safeguard public trust in scientific advice:

To pro-actively resolve, or at least adequately explain, divergence in an EU PPP risk assessment, we recommend that the EU Panel on Plant Protection Products and their Residues (PPR) be actively involved in early resolution, within the context of procedures that are already in place. For divergences in scientific assessments that might arise between EU risk assessors and international assessment bodies, we recommend expanding and strengthening international cooperation between the relevant scientific bodies. This should include liaison at the highest level and aligning communications. Should divergence in scientific assessments at EU or international level persist, we are ready to facilitate the provision of scientific advice in exceptional cases, including through expert examination by an *ad-hoc* scientific panel.

* * *

This Scientific Opinion is informed by scientific review reports, notably the Science Advice for Policy by European Academies (SAPEA) evidence review report (ERR), by reviews of primary scientific literature and by the outcomes of the various consultations undertaken with experts and stakeholders by SAPEA and ourselves. This Opinion is complementary to the EC's forthcoming review of PPP legislation under its Regulatory Fitness and Performance (REFIT) programme.

Introduction & Background

1. INTRODUCTION & BACKGROUND

This Scientific Opinion, hereafter 'the Opinion', has been produced by the Group of Chief Scientific Advisors of the European Commission's Scientific Advice Mechanism, hereafter 'the Scientific Advisors', in response to a request from the European Commission formulated by the Commissioner for Health and Food Safety, Vytenis Andriukaitis – see Scoping Paper (Annex 1 on page 49).

This Opinion takes a scientific point of view of the transparency, effectiveness and efficiency of the EU's authorisation processes for Plant Protection Products (PPPs), more commonly referred to as 'pesticides' (see glossary in Annex 6 on page 62), covering the scientific methods of assessment and procedures. It does not offer views on values or politics, except for a recommendation that the European Commission (EC) initiates a broad dialogue about a shared long-term EU vision for food production. It provides the EC with a series of recommendations aimed at improving the current dual approval and authorisation system for Plant Protection Products (PPPs) in the European Union (EU), hereafter 'the EU PPP system'.

Although this Opinion focuses primarily on agricultural use of PPPs, most of its findings are also relevant to non-agricultural use, for example in parks and gardens. An overview of the current EU PPP system is given in Box 1 (page 14) and in Table 2 & Table 3 (page 32).

The Scientific Advisors have responded closely to the questions and suggestions set out in the Scoping Paper, summarised as follows:

> *Can the current EU dual system for approval and authorisation of plant protection products be rendered more transparent, effective and efficient and if so, how could this be achieved? Pay particular attention to: possible methods of arbitration; alignment of risk assessment procedures; factors influencing risk acceptance; and similar authorisation systems used in non-EU OECD countries.*

A comparison with non-EU OECD countries is provided in Box 2 (page 15).

This Opinion is submitted to the EC in a context of broader policy and legislative reviews. These include the European Commission's ongoing REFIT[2] exercise "Evaluation of the EU legislation on plant protection products and pesticides residues", and the recently adopted proposal on the "Transparency and sustainability of the EU risk assessment model in the food chain" (COM(2018)179), which draws on the results of the fitness check of the General Food Law[3].

---

[2] Evaluation in the Regulatory Fitness and Performance programme: https://ec.europa.eu/food/plant/pesticides/refit_en

[3] https://ec.europa.eu/food/safety/general_food_law/transparency-and-sustainability-eu-risk-assessment-food-chain_en

Box 1 – Overview of the EU PPP dual system

The scientific assessment and the approval of active substances (and in principle also of safeners and synergists), as well as the setting of Maximum Residue Levels (MRLs), is carried out at EU-level. Approval of an active substance at EU-level qualifies it for subsequent assessment as part of the final formulation of a PPP, which commonly contains additional ingredients. Although the approval is only for the active substance, the process nevertheless requires that at least one representative use and formulation is assessed and deemed acceptable. The subsequent scientific assessment and the authorisation of PPPs containing an EU approved active substance are the exclusive responsibility of individual Member States.

EU-level: approval of active substance and setting of MRLs

Based on an applicant's (i.e. the manufacturer(s)) submitted dossier containing pre-market test results, one Member State risk assessor (the rapporteur Member State) prepares a draft risk assessment, which includes an assessment according to hazard-based exclusion criteria (see Box 6 on page 42). This assessment is peer-reviewed by EU and Member State risk assessors and finalised in the form of a 'conclusion' issued by EFSA. Based on the conclusion, the EC, as risk manager, prepares a proposal for approval or non-approval, on which Member State risk managers vote in a dedicated 'Standing Committee', referred to as a 'comitology' procedure (see also Table 2 on page 32). Approval is for a period up to 10 years, after which a renewal is required, which follows a very similar procedure, but also includes a review of relevant scientific literature (e.g. epidemiological studies on real-world usage). The procedure for MRL setting is also very similar.

Member State, including zonal, level: authorisation of PPPs

Applications, again in the form of a dossier, are typically assessed by one Member State risk assessor on behalf of their respective regulatory 'zone', which groups Member States with similar climatic conditions – North, Central or South. Subsequently, each Member State risk manager can individually decide on national authorisation of PPPs (see also Table 3 on page 32).

The risks and benefits associated with the use of PPPs have recently also been the subject of considerable public and political debate, which often features in the media, in particular linked to the process for the renewal of approval of the active substance glyphosate (see also Scientific Advisors' explanatory note[4]), illustrated by

[4] https://ec.europa.eu/research/sam/index.cfm?pg=glyphosate

the European Citizens' Initiative "Ban glyphosate and protect people and the environment from toxic pesticides" (submitted on 6 October 2017[5] and answered on 12 December 2017[6]) and the setting up of a European Parliament special committee (PEST) to look into the matter[7].

Box 2 – Comparison with non-EU OECD countries

When comparing the EU PPP system with similar systems employed in non-EU OECD countries, with a view to identifying possible improvements, the following major differences were identified:

- The EU PPP system has been described by some scholars as the 'strictest in the world' regarding the high level of consumer and environmental protection that is aimed for (Bozzini, 2017b). Indeed, the EU generally has the lowest MRLs and it is only in the EU that the 'precautionary principle' is codified as a specific objective in legislation (see also Box 3 on page 26).

- An almost unique feature of the EU PPP system is that substances which do not meet the EU's predetermined hazard-based criteria do not receive approval, or renewal of approval, or will have prior approval withdrawn. In this approach, the risk associated with actual exposure is typically not taken into account in decision-making (see also Box 6 on page 42).

- Non-EU OECD countries typically assess active substances and their final formulations (equivalent to PPPs) together and by the same entity, whilst in the EU these assessments are performed sequentially, with tasks and responsibilities split between EU-level and Member States (see also Box 1 on page 14).

- The EU is world-leading in its separation of the roles of risk assessor and risk manager, which is internationally-recognised best practice. Elsewhere, the risk assessment and risk management roles are often combined and/or carried out within the same entity.

- Unlike other responsible bodies, the EU risk assessor, EFSA, does not have its own laboratories, research staff, or inspection services, but relies on the EU Member States for these, nor does EFSA have a research budget.

5 http://ec.europa.eu/citizens-initiative/public/initiatives/successful/details/2017/000002
6 http://ec.europa.eu/citizens-initiative/public/initiatives/successful/details/follow-up/2017/000002/en
7 http://www.europarl.europa.eu/news/en/press-room/20180118IPR92014/pesticides-parliament-to-set-up-special-committee

The regulation most pertinent to this Opinion is Regulation (EC) No 1107/2009, concerning the placing of PPPs on the market. Its stated objectives are:

> *"to ensure a high level of protection of both human and animal health and the environment and at the same time to safeguard the competitiveness of Community agriculture. Particular attention should be paid to the protection of vulnerable groups of the population, including pregnant women, infants and children. The precautionary principle should be applied and this Regulation should ensure that industry demonstrates that substances or products produced or placed on the market do not have any harmful effect on human or animal health or any unacceptable effects on the environment"*

and:

> *"to improve the functioning of the internal market through the harmonisation of the rules on the placing on the market of plant protection products, while improving agricultural production."*

Also of relevance, albeit not the main focus of this Opinion, is Regulation (EC) No 396/2005 on Maximum Residue Levels (MRLs) of pesticides, that is: *"the upper legal level of a concentration for a pesticide residue in or on food or feed (…) based on good agricultural practice and the lowest consumer exposure necessary to protect vulnerable consumers"*, which is stated to be:

> *"in the interest of free movement of goods, equal competition conditions among the Member States, as well as a high level of consumer protection".*

Protection of animal health is afforded by the MRLs established for animal feed, whereas wild-life is considered as part of the environment. Human health relates both to dietary risks, covered by MRLs for food, and to non-dietary risks. Non-dietary risks relate to exposure through inhalation and skin contact by agricultural operators and workers, as well as by bystanders and residents. In this Opinion, we generally use the term 'health' to include both human health and health of animals other than wild-life.

The Scientific Advisors also take note of the importance of preventing the over-use of PPPs in general, as envisaged by Directive 2009/128/EC that aims to achieve the sustainable use of pesticides.

The Opinion draws upon evidence, knowledge and views gathered from a series of workshops, targeted consultations and evidence reviews. In response to a request from the Scientific Advisors, part of this was provided by SAPEA, including a SAPEA Evidence Review Report (ERR), drawing on the expertise of the natural and social science Academies throughout Europe. The SAPEA ERR focuses on methods and procedures for assessing potentially harmful effects on human health from the use of PPPs.

This was complemented by an expert meeting convened by the Scientific Advisors focusing on the environmental aspects of PPP use, and a SAPEA Social Science expert workshop focusing on risk perception relating to PPPs.

The Opinion also benefited from additional targeted consultations with experts and a stakeholder meeting. For more information on the methodologies and the sources of information and evidence used to develop this Opinion, see Annex 2 (page 52).

Recommendations

2. RECOMMENDATIONS

The debate around the authorisation and use of PPPs opens up the wider issue of desired models for food production. The Scientific Advisors observe a lack of a shared vision of the ways in which we, as EU society, want our food to be produced. Differing and often conflicting opinions are expressed by different groups, including food producers, NGOs, and the general public. These opinions correspond to different interests, understanding and views on food safety, food security, food affordability, environmental protection, and the industrialisation of food production, as well as different underlying values and ideologies. The absence of a shared vision hinders the development of a well-defined policy with clear objectives and views on risk acceptability. Therefore, the Scientific Advisors recommend that the EC initiate a broad dialogue with the aim to:

2.0 Establish a shared, comprehensive and long-term EU vision for food production, including the role of PPPs therein

Specific to the context of this Opinion are considerations for agriculture and the role of PPPs therein, which could build upon EU experience in the recent REFIT reviews of the Common Agricultural Policy (CAP)[8], including the deliberations on the Future of Food and Farming[9], as well as the policy to achieve the sustainable use of pesticides (Directive 2009/128/EC) and its implementation[10]. Specific elements of sustainable use that should be considered in such a future vision include more efficient and selective use of PPPs, such as precision farming and crop insurance schemes or mutual funds (Furlan et al., 2018), Integrated Pest Management, and the replacement of more hazardous PPPs with less hazardous ones. In addition to technical issues, this process would need to address matters of values and politics. The vision should be informed by broad considerations of the benefits of PPPs to farming and wider society, with due regard to trade-offs between ecosystem services (e.g. food, clean water)[11] and the mitigation of negative impacts that can arise from food production, such as water pollution. Such considerations should take into account, among others, affordability of food for consumers, income and long-term viability of food producers, as well as risks to health and the environment associated with different scenarios for the use of PPPs, including a zero use scenario.

Development of a shared, comprehensive and long-term vision would require a commitment by the EU to adopt an integrated perspective for EU policies on food production that includes, but is not limited to, agricultural production and the environment. Impacts on and effects of other food production chains, such as

8 https://ec.europa.eu/info/law/law-making-process/evaluating-and-improving-existing-laws/refit-making-eu-law-simpler-and-less-costly/refit-platform/refit-platform-recommendations-and-other-work_en#agriculture-and-rural-development
9 https://ec.europa.eu/agriculture/sites/agriculture/files/future-of-cap/future_of_food_and_farming_communication_en.pdf
10 https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_sup_report-overview_en.pdf
11 http://www.teebweb.org/

fisheries/aquaculture and new emerging food production methods, such as lab-grown food, would need to be taken into account. In addition, attention may need to be paid to aspects beyond primary food production, including food safety and other public health considerations, consumer choices, food security, food quality, cost of food, food waste, as well as the United Nations Sustainable Development Goals.

Furthermore, this vision would require a commitment to operationally 'join-up' relevant legislation to help ensure food security in terms of both quantity and quality, including nutritional value, and to achieve sustainable food production systems that protect health and the environment. For agriculture, this would concern legislation such as the placing of PPPs on the market (Regulation (EC) No 1107/2009), the Water Framework Directive (WFD; Directive 2000/60/EC), the Groundwater Directive (Directive 2006/118/EC), the Directive on sustainable use of pesticides (SUD; Directive 2009/128/EC), the Habitats Directive (Council Directive 92/43/EEC) and the General Food Law (GFL; Regulation (EC) No 178/2002). In addition, this would require attention to areas such as soil protection where no specific legislation exists. Substantial beneficial changes could result from such a shared vision, which could affect PPP authorisation and use in the future.

Meanwhile, prior to such a vision being in place, improvements to the current EU PPP system regarding its transparency, effectiveness and efficiency can be made now, and these make up the remaining recommendations of this Opinion.

In making recommendations for improvements, the Scientific Advisors recognised that the EU has made significant progress in the effectiveness of its PPP risk assessments in recent years, and has also established very low tolerance for MRLs in food and feed. It has authorised new acceptable PPPs, and has taken a stringent approach to renewals of approval, which has contributed to the withdrawal of hazardous substances from the market (Bozzini, 2017a, 2017c; Deluyker, 2017; EFSA, 2018). However, the EU PPP system must constantly adapt, both to embrace new scientific and technological developments (e.g. in toxicity testing) and to meet new challenges such as the changing nature of PPPs. Moreover, the Scientific Advisors are concerned by the widespread and prophylactic use of PPPs and the effects thereof on the environment, which require greater consideration in the EU PPP system, especially with regard to post-market vigilance.

As suggested in the Scoping Paper (Annex 1 on page 49), comparisons of the EU PPP system with similar authorisation systems used in non-EU OECD countries have been made and main differences are presented in Box 2 (page 15).

To further guide the process of developing the Opinion, the Scientific Advisors identified the following desirable features of a modern EU PPP system with respect to transparency, effectiveness and efficiency:

Transparency:

- A clear over-arching objective and explicit protection goals for human and animal health, and the environment, including wild-life
- The ability to engage and communicate effectively with stakeholders, including the public, concerning processes, decisions and their justifications

Effectiveness and efficiency:

- Risk assessment methods and risk management procedures that follow internationally-recognised best practice
- A system that integrates risk assessment with costs-benefit analyses, and includes consideration of the sustainable use of PPPs
- Effective and efficient post-market vigilance and enforcement
- Adequate capacity in skilled and impartial risk assessors, risk managers and risk communicators (see Annex 6 for definitions on page 62)
- An adaptable system that embraces continuous improvement to all aspects of its operations to meet changing demands

The improvements that were identified are presented as seven recommendations. The main contributions that each recommendation could make to transparency, effectiveness and/or efficiency are presented in Table 1 (page 24). None of the proposed recommendations is considered to significantly affect transparency, effectiveness or efficiency in a negative manner.

Table 1 – Overview of specific recommendations

	Recommendation	Transparency	Effectiveness	Efficiency	Sub-recommendations
1	Clarify the protection goals of the EU PPP system and improve their communication	●	●	●	▪ Set realistic, practical, unambiguous and quantifiable protection goals ▪ Systematically assess the level of certainty in risk assessments ▪ Agree on a transparent scheme for conveying uncertainty levels to the risk manager ▪ Clearly communicate the protection goals, decisions and justifications to the public
2	Improve the organisation and operation of the EU PPP system	●	●	●	▪ Give risk assessors the autonomy to determine all risk assessment elements ▪ Assess PPPs as rigorously as active substances, by EU risk assessors collaboratively ▪ Review PPPs grouped by ingredients, type and/or use in 'bulk evaluations' ▪ Establish a continuously updated, mandatory 'positive list' of safe PPP ingredients ▪ Establish an EU IT platform for risk assessment methods, data, analysis and results ▪ Move to a single-step risk management decisions on PPPs including all ingredients
3	Implement systematic post-market vigilance	●	●		▪ Systematically collect and share data on 'real life' behaviour and practices of operators ▪ Establish mandatory prospective cohort studies upon PPP authorisation ▪ Systematically collect, collate and assess PPP-related acute illness data ▪ Establish systematic landscape scale post-market environmental monitoring and analysis ▪ Consider moving to a tiered PPP authorisation approach with integrated monitoring ▪ Perform periodic literature review for health and environmental impacts of PPPs
4	Secure and strengthen EU's scientific knowledge and capacity in risk assessment		●	●	▪ Expand, strengthen and provide stable support for an adequate expert network in the EU to address the changing nature of PPPs, scientific and technological developments in risk assessment methods, the effects mixtures of substances and aggregate exposure
5	Improve guidance, oversight and transparency of pre-market studies	●	●	●	▪ Hold pre-submission meetings with the applicant to clarify data requirements ▪ Establish mandatory pre-registration of pre-market studies ▪ Re-examine the current criteria for data confidentiality
6	Re-examine the treatment of hazards, risks, costs and benefits	●	●		▪ Assess if the hazard based cut-off criteria approach is performing as intended ▪ Perform comparative risk assessments before PPP authorisations ▪ Use risk-cost-benefit analysis for transparent decision-making
7	Augment mechanisms to resolve divergent scientific assessments	●			▪ Involve EFSA's PPR panel to help resolve early divergences in scientific assessments ▪ Strengthen international scientific cooperation to help ensure consistent scientific advice ▪ Request SAM to provide advice in extraordinary cases of divergent scientific conclusions

2.1. Clarify the protection goals of the EU PPP system and improve their communication

Regulation (EC) No 1107/2009 is intended to ensure that marketed PPPs "do not have any harmful effect on human or animal health or any unacceptable effects on the environment" and that "the precautionary principle should be applied". These statements are not specified much further in the Regulation and it has been observed that the 'precautionary principle' suffers from a degree of 'vagueness' (Bozzini, 2017a) (see also Box 3 on page 26). Regulation (EC) No 1107/2009 is further intended to "safeguard the competitiveness of Community agriculture" and also states "improving agricultural production" as a purpose. These objectives are in addition to the protection of human or animal health and the environment, and the order of priority of these different, sometimes conflicting, objectives is not specified.

Because this ambiguity is not addressed, the risk manager effectively leaves the risk assessor to decide in practical terms what is acceptable and how the different objectives should be balanced. However, the responsibility and accountability for decisions on protection goals and risk acceptability should lie with legislators and risk managers, not with scientists. Without precisely described protection goals and risk acceptability criteria, it is also difficult for the risk assessor to evaluate if its methods are fit-for-purpose to achieve the legislative objectives, and to communicate properly if the legislative objectives are achieved. Furthermore, this ambiguity can lead to unnecessarily 'inconclusive' scientific advice by the risk assessor, whereas clarity on protection goals and risk acceptability criteria could have led to a clear advice on approval or non-approval (Expert Elicitation).

It is also important to recognise that it is not possible to ensure that products or substances of any sort placed on the market will not have any harmful effect on human or animal health under all circumstances. Agricultural crops to which no PPPs have been applied can also present risks, arising for example from naturally occurring toxins that can be present in food, such as mycotoxins, which may be increased if PPPs are not used. It also needs to be understood that all scientific assessments contain some degree of uncertainty, that the absence of an effect is scientifically impossible to prove, and that there is always the potential for unforeseen risks.

Thus, zero risk is impossible to ensure. In practice, the risk assessor aims to ensure a high level of certainty that harmful effects will not occur, whilst minor adverse effects are considered acceptable if the risk is deemed sufficiently small; this is expressed as an 'acceptable risk' by the risk assessor (SAPEA, 2018a).

Box 3 – The precautionary principle

The precautionary principle is detailed in Article 191 of the Treaty on the Functioning of the European Union, and guidelines on its use are presented in a Communication (COM(2000)1) as follows: "the principle may be invoked when a phenomenon, product or process may have a dangerous effect, identified by a scientific and objective evaluation, and if this evaluation does not allow the risk to be determined with sufficient certainty".

In its press release accompanying that Communication, the Commission clarifies that "where action is deemed necessary, measures should be proportionate to the chosen level of protection, non-discriminatory in their application and consistent with similar measures already taken. They should also be based on an examination of the potential benefits and costs of action or lack of action and subject to review in the light of new scientific data and should thus be maintained as long as the scientific data remain incomplete, imprecise or inconclusive, and as long as the risk is considered too high to be imposed on society. Finally, they may assign responsibility for the burden of proof - for producing the scientific evidence necessary for a comprehensive risk assessment. These guidelines guard against unwarranted recourse to the precautionary principle as a disguised form of protectionism".

Furthermore, "the Communication makes it clear that the precautionary principle is neither a politicisation of science nor the acceptance of zero-risk but that it provides a basis for action when science is unable to give a clear answer. The Communication also makes it clear that determining what is an acceptable level of risk for the EU is a political responsibility".

For example, temporary, mild skin sensitisation experienced by agricultural operators and workers due to PPPs is considered acceptable, given that some plants themselves cause stronger skin sensitisation, and so banning of the PPP would be disproportionate (Expert Elicitation). Therefore, this practice does not strictly respect the current protection goal in the Regulation of no harmful effect on health. In addition, PPPs will almost always have biologically toxic effects, although the risks may be very small for health and the environment. A literal interpretation of the objective of the PPP Regulation with respect to the protection of human health would thus not permit any PPP authorisation in the EU. This illustrates how, in practice, the risk assessors, i.e. scientists, are left to determine what is an 'acceptable risk'. This also applies to the environment, where "unacceptable effects" are not precisely defined by the legislation and/or the risk manager.

The Scientific Advisors therefore recommend that the EC ensure the setting of realistic, practical, unambiguous and quantifiable protection goals. These goals should cover human and animal health, and the environment, including wild-life. Related acceptability of risks and the required levels of certainty of the risk assessment must be clearly defined by the risk manager. These goals will need to reflect that some trade-offs between production and protection objectives are inevitable, and that trade-offs may also exist between the protection of health and the protection of the environment. In addition, 100% certainty can never be achieved and zero risk is impossible to ensure (see also SAPEA, 2018a).

At the same time, **the Scientific Advisors recommend that the risk assessors assess the level of certainty in their risk assessments.** It is understood that not all uncertainty can be quantified empirically, and so to an extent, will depend on the judgement of experts who may have different views on the certainty that particular test results provide. However, expert judgement on certainty can be captured in a semi-quantifiable manner (Benford et al., 2018). Furthermore, a systematic analysis of uncertainty will aid the consistency between different risk assessors and risk assessments, while improving the transparency of the scientific assessment (SAPEA, 2018a).

The Scientific Advisors also recommend that the risk assessor and risk manager agree on a simple and transparent scheme to translate the (semi-quantitative) assessment of uncertainty into the final conclusions of the risk assessment. This will help to ensure that expressions of certainty are not misinterpreted by the risk manager (see also SAPEA, 2018a). The Scientific Advisors are aware that EFSA has recently undertaken steps towards formal uncertainty analyses as part of risk assessments (Benford et al., 2018), and endorse such developments.

In order to improve and maintain public trust in the EU PPP system, **the Scientific Advisors recommend that the risk manager clearly communicate the protection goals and the decisions made following the risk assessment.** This should include their justifications and a description of factors considered beyond the risk assessment. Important aspects that need careful communication by both risk assessors and risk managers are uncertainty, the difference between hazard and risk, and what this means for achieving the protection goals. Uncertainty is often difficult to address and to convey in risk communication to the satisfaction of all sectors of society (SAPEA, 2018b), whilst the meanings (or even existence) of the terms 'hazard' and 'risk' are not the same in all languages. In all cases, communications need to be appropriate and accessible to the intended audience ranging from expert practitioners to the general public in all relevant countries and cultures. The risk manager and risk assessor should work in close collaboration towards this goal, drawing in particular on advice from EFSA's communications advisory panel.

2.2. Improve the organisation and operation of the EU PPP system

2.2.1. Separation between risk assessment and risk management

The strict separation between risk assessment and risk management is internationally recognised as best practice in the procedural manual of the Codex Alimentarius Commission (Joint FAO/WHO Food Standards Programme, 2016). This separation is important to avoid real or perceived political influence in scientific processes, to ensure independence and objectivity, and to provide clarity on accountability for decision-making (Bozzini, 2017a). Scientific independence should apply to the entire risk assessment process, including quality assurance. Whilst recognising that the division in roles is broadly adhered to in the EU PPP system, the Scientific Advisors recommend that the separation between risk assessor and risk manager be more rigorously applied in the EU PPP system, both at EU-level and in Member States. Beyond the risk manager setting clear protection goals and the required levels of certainty (see 2.1), the Scientific Advisors recommend that the risk manager should not be a part of or influence the scientific aspects of the risk assessment – compare Table 2 & Table 3 (page 32) with Table 4 (page 33). Specifically, the data requirements, methods and processes used in EU-level risk assessments applied by EFSA are currently determined by the EC and Member State risk managers through comitology (Regulation (EC) No 178/2002). Therefore, to ensure independence, **the Scientific Advisors recommend that the risk assessor be given autonomy to determine all working procedures, methods, data requirements, the selection and training of staff and experts, and the presentation and communication of the results.** This recommendation equally applies to risk assessment processes in the Member States.

2.2.2. Risk assessment

Currently, risk assessments for PPPs are split between active substance assessment performed at EU-level by EFSA, supported by Member States, and PPP assessment in its final formulation performed exclusively at Member State level (see Table 2 & Table 3 on page 32). This makes for a complicated picture of risk assessment tasks and responsibilities that is potentially confusing for stakeholders, including the public. From a scientific viewpoint, the primary concern is the potential impact of this complicated system on the robustness and efficiency of the risk assessments (see also SAPEA, 2018a). Moreover, concerns have been expressed by experts that some Member States lack up-to-date risk assessment methods and expertise capacity, resulting in over-reliance on EU-level risk assessments of active substances for their decisions on PPPs (Expert Elicitation). It is of concern that actual uses and formulations of authorised PPPs may not have been subjected to the same rigorous risk assessments as the representative uses and formulations proposed in the active substance application (see Box 1 on page 14).

Performing risk assessments distributed over EU and Member State level, as currently practiced, contributes to fragmentation of risk assessment data and

methods, as well as sub-optimal use of available expertise (Expert Elicitation). Correspondingly, it can give rise to duplication of work, incompatible data formats and databases, and variations in the quality and comprehensiveness of scientific assessment, all with the potential to produce conflicting results (see also Box 4 on page 33) (EFSA, 2018; SAPEA, 2018a; Expert Elicitation). Overall, EU data management relating to PPPs is of variable quality and is more fragmented than in similar systems within EFSA's remit (e.g. food additives under Regulation (EC) No 429/2008), in other domains in the EU (e.g. medicines under Regulation (EC) No 726/2004) and in non-EU OECD countries, such as in the USA[12] and Canada[13] (Handford, Elliott, & Campbell, 2015; Rotter et al., 2017; Expert Elicitation). This fragmentation is sub-optimal and needs to be rectified.

The Scientific Advisors therefore recommend that each PPP be assessed rigorously by EU risk assessors working collaboratively, as currently practiced for risk assessments of active substances, with due attention paid to: 1) all of its ingredients, i.e. active substances (and their metabolites), co-formulants, safeners and synergists; 2) their interactions; 3) all uses and formulations intended for marketing by the applicant; 4) aggregate exposure to substances from different sources; and 5) any resulting risks to both health and the environment. It is understood that such a systematic assessment of the full formulation of PPPs may be challenging due to their large number, but the Scientific Advisors recommend that it be carried out to ensure proper protection of health and of the environment. This would require an enhanced degree of coordination and data sharing, which should lead to a greater degree of harmonisation of risk assessment procedures performed across the EU. This is best achieved by a single EU-wide risk assessment of a PPP, including all its ingredients, and taking account of regional environmental conditions, for example, soil type and climate. This assessment should be expanded and updated over time, also making best use of Geographic Information Systems (GIS) data and tools to access and store data on the relevant environmental conditions used in the assessment of environmental vulnerability as part of a PPP risk assessment. A broadly similar model for the organisation of risk assessments in the EU is proposed in the ERR (SAPEA, 2018a). Such an EU-wide risk assessment would help to ensure that all Member States have access to, and can make efficient use of, the best available data, methods and expertise.

For PPPs that are soon to require market re-authorisation, **the Scientific Advisors recommend 'bulk evaluations' of PPPs grouped according to their active substance, mode of action and/or use, covering all their ingredients, formulations and uses** (see also EFSA, 2018; SAPEA, 2018a). This would replace the individual evaluations for renewals of approval and subsequent re-authorisation that are currently scattered over several years, bundling these in a more efficient,

---

12 https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/databases-related-pesticide-risk-assessment

13 http://pr-rp.hc-sc.gc.ca/pi-ip/index-eng.php

single, group evaluation. Alternatively, these bulk evaluations could be performed in order of priority relating to their risks and with reference to the defined protection goals. EFSA has previously demonstrated in other areas that it is able to coordinate and carry out similar bulk reviews (e.g. evaluations of "general function" health claims[14] or re-evaluations of permitted food additives[15]). This can be achieved efficiently by proper planning, scheduling and pooling of all the necessary resources in the EU into a collective EU-wide risk assessment system that makes use of the best risk assessment tools and expertise from across the EU, and integrates and uses all relevant data.

Such bulk evaluations would set useful benchmarks or 'frames' for all future risk assessments and would assist with comparative assessments, covering all formulations and uses intended for marketing (see also SAPEA, 2018a). It would additionally improve consistency of assessment, and help to address potential over-reliance on risk assessments based upon a few 'representative' uses and formulations (see Box 1 on page 14). Additionally, **the Scientific Advisors recommend that such bulk evaluations also establish a continuously updated, mandatory 'positive list' of demonstrably 'safe' ingredients** (i.e. active substances, co-formulants, safeners and synergists proven to be acceptable in specified combinations and/or conditions). This positive list would restrict which ingredients can be permitted in PPPs, which is effectively already in place for active substances and in principle also for safeners and synergists, hence would expand to co-formulants as well. This would thus replace the current 'negative list' for co-formulants (Regulation (EC) No 1107/2009, Annex III). Although established in 2009, this negative list has not been populated to-date, thus at present contains no prohibited co-formulants (see also SAPEA, 2018a).

The Scientific Advisors also recommend the development of a supporting common IT platform to store and support the analysis of all relevant data (see Box 4 on page 33). The IT platform could accommodate additional data from for example REACH, other relevant legislation, literature searches and non-EU sources. Data on Member State-specific risk elements, such as climates and soils contained in GIS, as mentioned above, but also cultural or historical differences in agricultural practices and risk mitigation measures could be taken into account in risk models. The IT platform would also better enable cooperation, and the analysis and exchange of information on mixtures and aggregate exposure, thus significantly improving the comprehensiveness of future PPP risk assessments. Additionally, the IT platform could also assist with semi-automated assessments and in the preparation of communication materials designed to enhance transparency and efficiency in the risk assessment process. In accordance with EFSA's policy on openness, this IT platform should be publically accessible, which may additionally

[14] https://www.efsa.europa.eu/en/topics/topic/article13
[15] https://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation_en

help farmers and other users to make better informed decisions when choosing between similar products (see also SAPEA, 2018a).

2.2.3. Risk management

Similar to the risk assessment, the risk management phase also presents a potentially complicated and confusing picture. Here the split of risk management decisions between active substance approval at EU-level, including the comitology procedure with Member States, and subsequent risk management decisions on PPP authorisation exclusively at Member State level (see Box 1 on page 14 and Table 2 & Table 3 on page 32) can lead to confusion and lack of transparency as to where responsibility and accountability ultimately lie. Moreover, the Scientific Advisors question the added value of a prior risk management decision on an active substance; given that the final risk management decision on the authorisation of the PPP must also take into account the active substance and its metabolites, as well as any effects of the other ingredients (co-formulants, safeners and/or synergists) in the PPP.

The Scientific Advisors therefore recommend that risk management decisions on the authorisation of PPPs and their ingredients be made in one and the same step and not in two subsequent steps, as is the current practice; hence dispensing with a prior risk management decision on active substances. To aid transparency on responsibility and accountability, this decision should be made either by Member States or centrally by the EC (see Table 4 on page 33), but not by a mixture of both as is the current practice (see Table 2 & Table 3 on page 32). The risk management decisions should in either case be fully informed by the scientific evidence provided in the single EU-wide risk assessment as described in 2.2.2. The Scientific Advisors recognise subsidiarity rights and the legitimacy of Member States considering variables other than science when deciding whether to authorise the use of PPPs on their territories. The above approach, combined with clarity about such variables, should reduce the chance that scientific risk assessments are questioned when Member States differ in decisions on PPPs for non-scientific reasons. It is understood that some decisions pertaining to trade and the single market, such as on permitted MRLs in food and feed, need to be centralised, as is currently the case.

Table 2 – Current approval process for active substances

Active substances[a]		EC	Rapporteur Member State	EFSA	Individual Member States
Risk Assessment	Method	●		●[b]	
	Draft Assessment		●		
	Peer-Review			●	●
	Opinion			●	
Risk Management	Protection Goal	●		●[c]	
	Proposal	●			
	Decision	●[d]			●[d]

See Box 1 on page 14 for details

[a] in principle also applies to safeners and synergists
[b] proposal
[c] practical interpretation
[d] through comitology

Table 3 – Current authorisation process for PPPs

Plant Protection Products		EC	Rapporteur Member State	EFSA	Individual Member States
Risk Assessment	Method		●	If mandated	
	Draft Assessment		●		
	Peer-Review				●[a]
	Opinion		●		
Risk Management	Protection Goal	●			●
	Proposal		●		●[a]
	Decision				●

See Box 1 on page 14 for details

[a] through zonal group

Table 4 – Proposed integrated process for active substances & PPPs

PPPs (all ingredients[a])		Collaboration of EU Risk Assessors[b]	Either EC or Member States
Risk Assessment	Method	•	
	Draft Assessment	•	
	Peer-Review	•	
	Opinion	•	
Risk Management	Protection Goal		•
	Proposal		•
	Decision		•[c]

[a] active substances, their metabolites, co-formulants, safeners and synergists
[b] EFSA & Member State experts
[c] no prior risk management decision is made on the active substance

Box 4 – Current information management issues

The Scientific Advisors have identified a number of concerns in the current EU PPP system regarding information management and data availability:

- There is no standardised EU-wide IT platform or database to support the PPP assessment process, including post-market monitoring. This results in the fragmentation of important information.
- Assessments of active substances, including 'representative' uses and formulations, are not systematically updated when new (or previously undisclosed) data become available in the subsequent assessments of PPPs containing these active substances. In such cases, no risk refinement takes place despite the potential availability of valuable data.
- There is currently no complete single overview of which PPPs are authorised, including where they are authorised in the EU and for which uses, as well as their market penetration and actual use.
- Information on non-dietary health risks (e.g. agricultural worker safety) and environmental risks of PPPs is commonly not fully available to all risk assessors and risk managers due to lack of systematic monitoring and data sharing.

2.3. Implement systematic post-market vigilance

Current post-market monitoring of concentrations and exposure to PPPs in the EU, with relevance to both health and the environment, is considered by many experts to be patchy and not sufficiently systematic. This is especially true for the environment and agricultural workers, for which monitoring data is generally inadequate (Expert Elicitation), making the already difficult task of attributing ecological damage and health effects more challenging. Indeed, it is typically only after many years of a PPP being on the market that unexpected environmental or health impacts are eventually recognised, which may be due to unforeseen risks, inadequate exposure models and/or incorrect use (Boyd, 2018; Schäffer et al., 2018; Storck, Karpouzas, & Martin-Laurent, 2016).

Improving data on 'real-life' application of PPPs would benefit both health and environmental risk assessments. For example, there is a need to improve data on the volumes and mixtures that are used – either applied simultaneously or consecutively – and their mode of application, to better assess cumulative and synergistic effects (Expert Elicitation). **The Scientific Advisors therefore recommend that Member States systematically collect and share data on 'real-life' behaviour and practices of operators with regard to use of equipment and application techniques**, and investigate the extent to which operator behaviour and practices can be improved (see also SAPEA, 2018a). At the same time, this could improve compliance checking and enforcement of correct PPP use.

There is also a significant need for more and better human biomonitoring and epidemiological data, and more consistent use of these in PPP risk assessments, as practiced in the USA (i.e. NIOSH and SENSOR-Pesticides program, and NHANES program) (Ockleford et al., 2017; SAPEA, 2018a; Expert Elicitation). **The Scientific Advisors recommend mandatory monitoring of exposure and health directly following the market authorisation of a PPP**. This monitoring should be based upon a prospective study in a representative sample of an appropriate cohort – e.g. agricultural operators applying the PPP and workers entering the fields following PPP treatment of the crops (Ockleford et al., 2017; SAPEA, 2018a). It is understood that this entails costs, but the Scientific Advisors consider this justified to ensure adequate protection and generate data to improve the models used in risk assessments. Furthermore, **the Scientific Advisors recommend that Member States put in place a scheme for the systematic collection, collation and assessment of acute illness which could possibly be attributed to PPPs** (see also SAPEA, 2018a). The data thus obtained should be collated and stored in a comprehensive EU IT platform for data sharing, cooperation and analysis (see 2.2).

The Scientific Advisors recommend that systematic landscape-scale post-market environmental monitoring and analysis be significantly improved in the EU PPP system. Such post-market vigilance should include monitoring of the concentration of and exposure to PPPs and their metabolites in soil, water, and target and non-target living organisms (Boyd, 2018; Milner & Boyd, 2017; Schäffer

et al., 2018). It should include an expansion of the scale at which environmental risk assessment is commonly carried out, taking a systems approach to include 'out of field' impacts. It should also take into consideration PPPs applied as mixtures or used sequentially. Systematic use should be made of environmental monitoring of PPPs already carried out as part of the Water Framework Directive (Directive 2000/60/EC) and the related Groundwater Directive (Directive 2006/118/EC).

Environmental monitoring to discern ecological impacts should be based upon appropriate biodiversity indicator species using existing data associated with the Habitats Directive (Council Directive 92/43/EEC) and Member State and EU biodiversity monitoring programmes, or from additional, specifically developed monitoring. Where feasible, mechanistic population models should be developed for specific non-target species, including pollinators, and ecological/environmental scenarios. This will allow for spatial-temporal extrapolation of risk to be estimated that can cover the ecological and environmental variability of the EU. These models and scenarios can also be used to evaluate the effectiveness of risk mitigation measures and policy goals.

In general, the environmental elements of post-market vigilance should be based upon a combination of monitoring, modelling and experimental activities. These results can be partly made available in EU and/or Member State Geographic Information Systems (GIS) and should be linked to or part of the IT platform envisaged in 2.2. The data and knowledge thus gained should be used to assess or reassess risks as part of the EU PPP system. In this way a 'reality check' feedback loop will be established for the impact of PPPs on the environment – an important component of adaptive management that can inform appropriate mitigation measures. A more detailed assessment of risk and impact should be carried out for land receiving high toxic loads and/or more persistent substances over prolonged periods.

Some experts propose a tiered authorisation approach, whereby PPPs could be initially authorised for only a limited time-period, cultivation area and use, which would be subject to intensive monitoring under real application conditions (Schäffer et al., 2018). Only if no negative effects were observed, could the authorisation and monitoring be extended to other areas and additional crops. In addition to post-market environmental vigilance, this approach could also be useful for the protection of health. Such an approach has similar merits to clinical trials in medicine (Milner & Boyd, 2017), effectively only allowing wide-scale use of a substance after an intensively monitored, small-scale, real-world application. Therefore, **the Scientific Advisors recommend that the EC consider moving to a tiered PPP authorisation approach with integrated monitoring, in particular for higher risk PPPs and more vulnerable environments.**

To make full use of research in the field, **the Scientific Advisors also recommend that a system be established to monitor the peer-reviewed literature at appropriate intervals for epidemiological papers and case reports concerning health effects of PPPs, and studies of the environmental**

impacts of PPPs (see also SAPEA, 2018a). It is important that this information be shared with all relevant risk assessors across the EU.

2.4. Secure and strengthen scientific knowledge and capacity in risk assessment

EFSA does not have its own laboratories, research staff or budget to commission research (see also Box 2 on page 15). As a result, scientific knowledge and expertise in the EU depends on the risk assessment bodies and universities in the Member States. However, these often do not receive stable funding. Therefore, expertise that is built up over several years can be lost and knowledge scattered over the EU, with some Member States losing relevant expertise capacity (Expert Elicitation). At the same time, the changing nature of PPPs and the complexity of their interactions, the emergence of new scientific and technological developments as well as increased public concern, add to the already high demands on the risk assessors to deliver high quality, state-of-art and timely risk assessments. Design and implementation of systematic post-market vigilance for health and the environment will additionally increase this burden (see 2.3).

Regarding **the changing nature of PPPs**, the data requirements for the approval of active substances (Commission Regulation (EU) No 283/2013) and authorisation of PPPs (Commission Regulation (EU) No 284/2013) are still mainly based on those for classic synthetic chemicals, although many of the current applications are for Biological Control Agents (BCAs) for which much of these data requirements may not always be appropriate (see also Box 5 on page 38) (SAPEA, 2018a). Similarly, the specific risks of another modern class of PPPs, 'nano-pesticides', may also not be appropriately covered by the current data requirements (SAPEA, 2018a). The expertise to address these issues requires dedicated development.

In addition, recent **scientific and technological developments in methods** aimed at making risk assessments more complete and representative may also entail a significant shift in the type of work and expertise required. Traditionally, toxicology testing of substances is performed by assessing dose responses and specific endpoints *in vivo* in experimental animals (e.g. tumour growth in mice). Although valuable, not all relevant adverse effects in humans are covered by these tests and, in general, there are limitations in translating the results in animal experiments to humans (SAPEA, 2018a). The developments include a shift in emphasis towards Mode of Action (MoA) and Adverse Outcome Pathway (AOP) assessments of substances, however they are produced, through the integration of modern *in vivo*, *in vitro* and *in silico* methodologies, including high-throughput screening (HTS) assays. Such approaches have been described, in detail, in the ERR and elsewhere (Deluyker, 2017; EFSA, 2014; SAPEA, 2018a). It is understood that these developments should in time reduce the need for laboratory animal testing (see also SAPEA, 2018a). However, these are at different stages of development and reliability, and while MoAs provide for quantitative relationships for a given

substance and thus form a good basis for risk assessment, there is debate on the usefulness of some of the developments, in particular AOPs, for regulatory risk assessments (Expert Elicitation). Expert capacity is needed within the EU expert network to monitor, co-develop and validate such methods for timely implementation when sufficiently well developed.

Furthermore, there is a demand that the EU PPP system better address **mixtures of substances**, as these may result in larger effects on health and the environment than separate exposure to each substance individually (Rotter et al., 2017; SAPEA, 2018a; Schäffer et al., 2018). Although most PPPs contain only one active substance, they can contain two or more, and commonly also contain multiple other ingredients: co-formulants, safeners and/or synergists. Additionally, multiple PPPs can be mixed before application as a 'tank mixture' or become mixed in the field or wider environment as a result of sequential application. Different substances can have similar negative effects on health or the environment, resulting in a cumulative increase of negative effects. In addition, some substances have the potential to interact with other substances, which can synergistically change their toxicity. Exposure to the same substance can occur via multiple routes, referred to as **'aggregate exposure'**, as some substances used in PPPs are also used in other products, resulting in a higher than expected exposure. The current EU PPP system does not provide specific procedures to address this, including for MRL setting (Rotter et al., 2017; SAPEA, 2018a; Schäffer et al., 2018; Expert Elicitation). Some EU research projects already seek to address this, such as the ACROPOLIS[16] and EUROMIX[17] projects.

There are other improvements to the risk assessment methods and/or processes that feature in the ERR, which also merit further consideration, for example improvements to methodologies for synthesising and analysing non-standardised studies (see also SAPEA, 2018a). These and all the above-mentioned developments and issues clearly require an adequate and stable body of expertise in risk assessment and associated training and research capacity to ensure that state-of-art and appropriate risk assessment methods and technologies be developed, evaluated and implemented in a timely manner. **The Scientific Advisors recommend that scientific knowledge and capacity be secured by supporting, expanding and strengthening the expert network of EU agencies, Member State bodies, institutes and university research groups involved in risk assessments,** thereby establishing a 'virtual' European centre of excellence, the work of which would be relevant beyond PPP assessments. As a pre-requisite to the above, a critical mass of expertise with a long-term stable funding structure needs to be in place.

[16] https://acropolis-eu.com/
[17] https://www.euromixproject.eu/

These actions, including EU-wide training of experts, would improve the effectiveness and efficiency of the EU PPP system, enabling the EU to maintain its position at the forefront of risk assessment science.

Box 5 – Biological Control Agents (BCAs)

Many of the current active substance and PPP applications are for Biological Control Agents (BCAs). These include living microorganisms, such as bacteria, fungi and viruses, and their products, but also chemicals of natural origin, such as plant extracts, also called 'botanicals', and bio-communication substances, known as semiochemicals, such as insect pheromones (Ehlers, 2011).

BCAs are regarded by some as more safe. Indeed, most BCAs currently on the market are likely 'low-risk' PPPs, as defined in the Regulation (Hauschild, Speiser, & Tamm, 2011). However, it should be understood that BCAs are or produce chemicals, which often occur in complex mixtures. Those BCAs therefore can carry risks similar to synthetic chemicals but may also have extra specific risks. Plants extracts and fungal metabolites can be more toxic than synthetic chemicals; replicating microorganisms have the increased danger of being potentially persistent in the environment; and BCAs can be less specific than classic PPPs, which increases their risk and potential harm to the environment. It should therefore be understood that BCAs should not automatically be classed as 'low-risk'.

2.5. Improve guidance, oversight and transparency of pre-market studies

In the EU, the applicant seeking market authorisation must prove that the PPP it intends to put on the market is safe, and assumes the associated costs. Such pre-market assessment studies must be performed in Good Laboratory Practice (GLP)-accredited test facilities, following GLP-principles that are audited by local regulatory bodies. A number of features of this application and testing process have however been criticised for not being transparent and cause suspicion amongst some stakeholders, including the public, regarding independence and objectivity (Storck et al., 2016). Specifically, the applicant typically directly funds the research, chooses the GLP test facility, which may be outside the EU, and has the option to flag results or other data of the tests as confidential, thus not made public (such as personal data, commercially sensitive or proprietary data).

The data requirements that have to be fulfilled by the pre-market assessment studies are set out in the relevant legislation (Commission Regulations (EU) No 546/2011, No 283/2013 and No 284/2013). Although this provides transparency and consistency, there are concerns that the inflexibility of these data requirements

can result in data gaps or the supply of data that are not relevant (SAPEA, 2018a; Expert Elicitation). This means there can be insufficient information for adequate decision-making, while at the same time resources, including experimental animals, are wasted on unnecessary tests. EFSA's assessments are often 'inconclusive'[18] due to data gaps, either because necessary data are not covered by the data requirements in the legislation, or because legal requirements were modified between submission and assessment (Bozzini, 2017a; Expert Elicitation). Importantly, some of these data gaps are already known to the risk assessor prior to or during submission and could be resolved by early intervention, if the procedures would allow for this flexibility (Expert Elicitation).

The Scientific Advisors therefore recommend that the risk assessor be empowered to hold PPP pre-submission meetings with the applicant, as is already an option at Member State and zonal levels for PPP authorisations[19], in other regulatory domains in the EU, such as for medicines by EMA[20], and for pesticides in non-EU countries, such as in the USA[21] and Canada[22]. During pre-submission meetings, information should be provided on application-specific scientific, legal and regulatory aspects, including which data must be provided and which tests should be used, to ensure that all necessary information will be available for proper risk assessment and that an acceptable level of scientific certainty is achieved. As the relevant regulations allow for the scientifically justified omission or replacement of certain data requirements, such pre-submission meetings should discuss which data should be provided to enable a proper risk assessment and the scientifically reasoned justifications to not supply any data deemed irrelevant or unnecessary. Such meetings are especially important when the application concerns a PPP of a novel nature, type and/or use, such as Biological Control Agents (see Box 5 on page 38) and 'nano-pesticides', as current data requirements are mainly based on those for classic synthetic chemical PPPs and may not be appropriate for these modern PPPs, as discussed in 2.4. However, a balance must be found between the need for flexibility and the need to achieve an appropriate level of comparability and consistency between risk assessments. To ensure consistency, the criteria and data requirements from previous similar PPP assessments can be used as a 'blueprint', updated to the latest scientific understanding and legal requirements, including insights from the 'bulk assessments' as described in 2.2. Pre-submission meetings would also allow for clarification of the demands on the test facilities where the tests are performed, that is: to ensure that the tests are performed where competence and transparency can be assured and can be demonstrated to the public. The content of such pre-submission meetings should be made available to the public. To

[18] https://ec.europa.eu/food/sites/food/files/gfl_fitc_comm_staff_work_doc_2018_part1_en. pdf
[19] https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_mut-rec_en.pdf
[20] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000167.jsp&mid=WC0b01ac0580b18196
[21] https://www.epa.gov/pesticide-registration/guidance-pre-application-meetings-new-active-ingredients-major-new-uses-and
[22] https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/registrants-applicants/submission-consultations.html

improve efficiency of the EU PPP system, applications should be evaluated with due consideration of the information on data requirements provided in the pre-submission meeting, unless new concerns arise from the safety studies or overriding safety concerns dictate otherwise.

The Scientific Advisors recommend the mandatory pre-registration of GLP-studies, including the lab that will perform the tests, the tests that are planned and what will be learnt from the tests, as is standard practice for clinical trials in medicine. Although these tests must be funded by the applicant, concerns about independence and objectivity of these 'industry-sponsored' studies can in part be addressed by such pre-registration, which will increase transparency of where studies are carried out and will allow the auditing of the GLP-labs while the tests are performed. Moreover, pre-registration will ensure that all relevant studies performed on a particular substance are known and are thus not omitted from the risk assessment (Deluyker, 2017). Considering that these tests may be performed outside the EU, international collaboration towards this goal is essential, especially via the OECD.

To further address concerns about a lack of transparency, **the Scientific Advisors recommend that the EC reflect on the current criteria for data confidentiality and on who has access to the original (raw) data in the dossier**, with a view to make as much information available to the public as reasonably and legally permissible.

2.6. Re-examine the treatment of hazards, risks, costs and benefits

2.6.1. The role of hazard-based cut-off criteria

Regulation (EC) No 1107/2009 , Annex II, states that an active substance, safener or synergist cannot be approved if it is carcinogenic; mutagenic; toxic for reproduction; persistent, bio-accumulative and toxic for the environment (PBT); a persistent organic pollutant (POP); very persistent and very bio-accumulative (vPvB); or endocrine disruptive. This hazard cut-off criteria approach thus means that an active substance, safener or synergist is not approved for use in the EU if it has any of these hazardous properties, regardless of the likelihood of the hazard causing actual harm (i.e. the risk), with some derogations permitted (see Box 6 on page 42). Outside of the EU, only one country was identified that employs similar hazard cut-off criteria, Brazil, which adopted it in 1989, though without derogations (Paumgartten, 2012; Pelaez, da Silva, & Araújo, 2013). All other countries consider the likelihood of the hazard causing harm as part of a risk assessment, based upon one or more use scenarios that might include risk mitigation measures that render the risk acceptable.

It is noted that two other major EU regulatory frameworks also employ hazard cut-off criteria, specifically for Biocides (Regulation (EU) No 528/2012), in a similar

manner to the PPP Regulation, and REACH, which identifies substances of very high concern as 'candidates for substitution' (Regulation (EC) No 1907/2006), although the regulatory actions that follow the hazard identification are different. Other major regulatory frameworks, including the assessment of medicines, do not employ hazard-based cut-offs.

Stakeholders and experts alike were found to be divided in their views on the wisdom and practical effectiveness of the hazard-cut-off criteria approach as currently employed in the EU PPP system. Perceived advantages of the hazard cut-off criteria approach are that it should be faster and less expensive (Bozzini, 2017a), and some argue it is more protective (Expert Elicitation). Supporters also argue that it is valuable to exclude substances with the potential for most harm, which is especially important given that existing exposure models may underestimate risks, especially for new substances where no empirical real-world exposure data are available (Ockleford et al., 2017; SAPEA, 2018a; Schäffer et al., 2018; Expert Elicitation). The potential shortcomings of these models are evidenced by the typical PPP 'authorisation and withdrawal cycles', whereby unacceptable health or environmental impacts of a PPP become apparent only after several years of use (Boyd, 2018; Schäffer et al., 2018; Storck et al., 2016). Furthermore, the hazard cut-off criteria allow the regulator to send a clear message to the market that intrinsically less hazardous substances will be favoured over ones that may be more hazardous.

Opponents argue that the hazard cut-off criteria approach is fundamentally unscientific and may needlessly exclude much needed PPPs from the market despite the unlikelihood that their inherent hazard will translate into a significant risk (Expert Elicitation). Specifically, excluding useful substances from the market that in reality, once subject to appropriate mitigation measures, such as strict conditions of use, may be less or no more dangerous or damaging than alternatives already on the market. Although the current regulatory system allows for some derogations by such mitigation measures, these only apply where contact between the substance and humans can be strictly excluded. At the same time, the alternative approach to the hazard-based cut-off is to proceed to a full risk assessment, which could provide additional valuable information to decision-makers and would not otherwise be available to them (Bozzini, 2017a; Lofstedt, 2011). It should be noted that hazard identification and characterisation are always done as the first steps in risk assessments, so in a well-informed and well-regulated authorisation system, proceeding to risk assessment need not necessarily be less protective (Expert Elicitation). It is also necessary to recognise that there are risk-based elements that are integral to the EU's hazard-based cut-off criteria (see also Box 6 on page 42).

The debate would clearly benefit from a critical scientific assessment of how well the hazard cut-off criteria approach is working in practice, including evidence from post-market monitoring, and from regions outside the EU. Therefore, **the Scientific Advisors recommend that the EC re-examine the hazard-based cut-off criteria approach as applied in the EU PPP system, to critically assess**

whether it is performing well against its intended objectives and what improvements, if any, it could benefit from. This could be achieved, for example, by running comparative assessments of hazard-based exclusion criteria vs. full risk assessment, which includes hazard characterisation, and analysing the results to ascertain the resulting levels of protection and precaution. This should help in answering if hazard-based exclusion should be used, what the criteria should be and how these are set and assessed.

Box 6 – Hazard cut-off determination

Regulation 1107/2009 specifies several hazardous properties which serve as rejection criteria: if a substance is deemed to have any one of these properties it cannot be approved. The hazardous properties in question are:

- carcinogenic;
- mutagenic;
- toxic for reproduction;
- persistent, bio-accumulative and toxic for the environment (PBT);
- persistent organic pollutant (POP);
- very persistent and very bio-accumulative (vPvB); or
- endocrine disruptive

Some facets of these properties have clear 'yes/no' thresholds and indicators (e.g. for persistence: "the half-life in soil is more than 120 days"), but most properties are not well defined in the regulation, and must be attributed on the basis of expert judgement and a 'weight of evidence determination' from a range of data sources, including laboratory animal experiments, epidemiological studies, clinical case-reports, occupational accident data, etc. Therefore there is an element of risk-based assessment integral to the EU's hazard-based criteria.

In addition, only the mutagenic, PTB, POP and vPvB criteria are strictly excluded on the basis of the hazard, whereas substances that are carcinogenic, toxic for reproduction and/or endocrine disruptive can be approved, as a derogation, if human exposure is negligible under realistic proposed conditions of use, hence requiring consideration of risk.

In conclusion, the setting of the thresholds, the determination of the hazards and the use of derogations, in fact, require a combination of hazard and risk-based decisions.

2.6.2. The role of comparative risk and risk-cost-benefit analyses

To aid the replacing of higher-risk PPPs by sufficiently effective lower-risk PPPs, **the Scientific Advisors recommend that the EC consider making comparative**

assessments mandatory in the authorisation process of PPPs. The principle objective for this should be that newly authorised PPPs should not entail higher risks and/or lower benefits than already existing products, while recognising trade-offs may exist between the protection of health and of the environment. In order not to overload the system, one approach could be to run a comparative assessment for a new PPP against the market leader, with its active substance(s), as similar to comparative assessments performed for new medicines (i.e. superiority/non-inferiority tests) (CPMP, 2000). Also similar to medicines, it is nonetheless important to have some redundancy in available PPPs to use as back-ups in case of resistance. Data analysed and automated processes made available as a result of the recommendations in 2.2 would substantially assist with this process.

With respect to risk management decisions, cost-benefit analyses, sometimes as part of an Integrated Impact Assessment (IIA), are routinely used in several OECD countries, including some EU Member States, but are currently not normally part of the EU PPP system (Bozzini, 2017a). However, if performed well and objectively, such tools can contribute to a more comprehensive and transparent decision-making process at the risk management stage. **The Scientific Advisors recommend that risk managers give careful consideration to making more systematic use of high quality and broad risk-cost-benefit assessments as a transparent means of decision-making**. In doing so, due consideration should be given to unnecessary risks to health and the environment as well as other unnecessary costs relating to over-use of PPPs, such as increased costs for water treatment and ecological restoration measures. Over-use may also lead to pest resistance to a PPP with additional costs to farmers.

Guidance on best methods and standards for risk-cost-benefit analysis should be produced specifically for the EU PPP system. A standard approach should be developed with the aim of producing an agreed fit-for-purpose method, which would also prevent analyses becoming overly onerous, or biased. It is recommended that institutions with the most expertise in risk-cost-benefit analyses contribute most to the development of these methods and offer support by training and peer-review to help ensure efficiency and objectivity of such analyses. The use of such high-quality methods will further enhance the predictability and transparency of the risk assessment and risk management processes.

2.7. Augment mechanisms to resolve divergent scientific assessments

In addition to considering how to improve the transparency, effectiveness and efficiency of the EU PPP system, the Scientific Advisors were requested to look at possible "*methods of arbitration (…) to solve issues arising from diverging assessments*" (see Scoping Paper in Annex 1 on page 49).

It should be stressed that divergent scientific assessments between professional risk assessors are rare (Expert Elicitation). Procedures and fora are already in place that

resolve most differences, both in the EU, such as the EFSA Advisory Forum, and internationally, in particular the joint FAO/WHO expert meetings. Nevertheless, some divergences can persist for reasons described earlier in this Opinion and elsewhere[23]. Divergences can occur when the scientific evidence is limited and interpretation of data is inconsistent. They may also occur where different scientific bodies with different remits can be tasked to answer different scientific questions relating to the same or similar substances, or may be asked to classify substances according to different criteria – which can result in real or perceived differences in scientific assessments.

Where scientific assessments produce divergent or perceived divergent conclusions, either within the EU or between EU and non-EU bodies, the absence of a reconciliation and/or a sufficiently clear explanation of why divergence exists (or existed) can be problematic. Conclusions about risks announced in the absence of such clarity can undermine trust in the EU PPP system and even in scientific advice more generally.

The Scientific Advisors are concerned that this can lead to stakeholders, including the public and politicians, making selective use of incomplete scientific evidence to match their value-based views or to discredit the scientific methodology of the risk assessor. This is particularly problematic as scientific assessment procedures and risk are commonly not well understood by the general public, and scientific assessments can be easily misrepresented. Even without misrepresentation of assessments, the failure to transparently resolve or explain divergence can have equally damaging consequences for public trust. A particular level of uncertainty is also inherent to all risk assessments, and divergent conclusions might consequently arise between EU risk assessors and between those of the EU and international bodies.

Acting on the previous recommendations in this Opinion would help to prevent such diverging assessments arising, at least within the EU: notably the systematic analyses of uncertainty (2.1); enhanced collaboration between risk assessors, sharing of information and harmonisation of methods (2.2); adequate capacity of well-trained expertise (2.4); and avoiding important data gaps (2.5). Nevertheless, additional, more specific recommendations are required to ensure that divergent assessments are adequately and efficiently addressed and communicated to safeguard public trust in scientific assessments and advice, both within the EU and beyond.

Within the EU, the Scientific Advisors recommend that EFSA's independent Scientific Panel on Plant Protection Products and their Residues (PPR) further help to resolve, at an early stage, diverging views arising in scientific assessments. This would be done as an extension of existing procedures that relate to expert inputs, and in the context of Regulation 1107/2009, which

[23] https://ec.europa.eu/research/sam/index.cfm?pg=glyphosate

contains a provision (Article 30) for resolving divergences in scientific opinions. Furthermore, it is vital that these procedures be rigorously followed and that explanations be provided of the divergence and/or how divergent assessments have been reconciled. This information should be clearly communicated to stakeholders, including the public, to improve transparency and to reduce the potential for misuse of scientific assessments.

Beyond the EU, the Scientific Advisors recommend that EU and non-EU scientific bodies strengthen their cooperation to pro-actively avoid contradictory scientific conclusions and/or advice. Where real or apparent divergence in scientific assessments occur, these should be swiftly and jointly addressed by the responsible scientific bodies to determine if the divergent assessments can be reconciled. Justifications for remaining divergences or apparent divergences, for example due to differing scientific methodologies or aims, should be clearly and carefully communicated to prevent the erosion of trust in science. This should also be done pro-actively in close collaboration within and between the relevant scientific bodies, including at the highest levels, and in which EFSA's communications advisory panel could also provide advice.

If, despite these procedures, real or apparent differences remain, **the Scientific Advisors are, in exceptional cases, ready to be called upon by the EC to provide scientific advice on the matter**. This would require scrutiny of the relevant scientific assessments and would explain the differences between them. Such scrutiny may also include analysis of whether proper scientific processes have been respected and of the robustness of scientific assumptions made. In that case, such advice would extend beyond that which was prepared previously by the Scientific Advisors in relation to glyphosate[24], so that in addition to describing the reasons for perceived divergence (for example, different mandates, scope and classification schemes), it would also analyse the experiments, methods and data analyses upon which actual differences in conclusions were based (for example, the appropriateness of the use of different statistical methods to analyse experimental data). An *ad-hoc* expert panel could be established to assist with these analyses. The Scientific Advisors underline the importance of making use of such expertise while appropriately managing any interests they may have. This panel would report to the Scientific Advisors, who would then issue a Scientific Opinion on the matter. The Scientific Advisors may not only be called upon to provide such scientific advice on issues specific to PPP authorisation processes, but also to address similar issues in other areas and matters that fall between regulatory regimes. In no circumstances, however, should their involvement be viewed as that of an appeal body within any such regulatory processes. The Scientific Advisors' involvement, including any expert panel, their advice and its use should be clearly communicated to stakeholders, including the public.

[24] https://ec.europa.eu/research/sam/index.cfm?pg=glyphosate

Annexes

Annex 1 – Scoping Paper

This scoping paper was adopted at the 7th HLG meeting (23-24 March 2017). However, it was agreed by the Commission and High Level Group of Scientific Advisors* that question (b) "Methods of arbitration" would be addressed only if time, and an appropriate form of evidence interrogation and consultation permits.

Authorisation processes of plant protection products in Europe from a scientific point of view

1. ISSUE AT STAKE

Plant protection products are indispensable in agriculture but their use may involve risks to human and animal health and to the environment. In order to ensure the safety and efficacy of plant protection products, the EU legal system concerning the placing on the market of such products provides for a double authorisation procedure before they can be placed on the market[1].

The Commission approves active substances (i.e. the agent used to achieve the protective effect) for the use in plant protection products (i.e. the end product) following a comprehensive assessment by experts of Member States and of the European Food Safety Authority (EFSA). The EU decisions define the content of the national measures authorising products containing those substances in terms of specification of the technical material, conditions of use, risk mitigation measures, and others. Only when a substance is approved, Member States can authorise plant protection products containing that substance. The national authorisation defines the source (production site) of active substance to be used in the products, the precise formulation of the products, its hazard classification and conditions of use. Issues that may arise from the co-existence of an active substances and for instance one or more co-formulants used in the plant protection product are currently considered at product authorisation stage at Member State level, but not at the stage of approval of an active substance. The applicable rules divide the EU in three zones with similar conditions as concerns e.g. climate, soils, or agricultural production. Authorisations by Member States belonging to a specific geographical zone are subject to mutual recognition unless a Member State considers that the risk associated to the use of the product is unacceptable.

---

* The "High Level Group of Scientific Advisors" ('HLG') was renamed to "Group of Chief Scientific Advisors" during the development of this Opinion (Commission Decision C(2018)1919 of 5 April 2018).

1 Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC, OJ L 309, 24.11.2009, p. 1. MRLs for pesticides to protect all consumer groups are set in accordance with Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC, OJ L 70, 16.3.2005, p. 1.

2. EU POLICY BACKGROUND

Each of the steps of the EU procedure (approvals at EU level and authorisation at national level) is based on a scientific risk assessment. The two risk assessments follow harmonised data requirements and decision-making principles. The data requirements establish a catalogue of tests and studies that must be provided by any applicant for the approval of an active substance and the authorisation of a sproduct as a basic minimum dossier as well as any necessary supplement in order to address possible requirements for a refined assessment. The Uniform Principles laid down in Commission Regulation (EU) No 546/2011[2] establish a harmonised methodology for the assessment and harmonised thresholds to decide whether an identified risk is acceptable or not. However, there is some flexibility within the risk assessment methodology. Risk assessments are carried out by different authorities, by EFSA for the active substance, by the different national competent Authorities for products) and not in all cases according to the same guidance documents. Consequently, different conclusions can be drawn from the same study even though the risk is supposed to be the same. Or one national guidance document might require additional studies which are not required by another country, increasing the burden on applicants in the absence of a clear scientific motivation for the difference between the two guidelines. In contrast to this EU system, not all third countries have dual authorisation systems despite the fact that many also have different agronomic zones.

Authorisation systems used in non-EU OECD countries might be a useful source of inspiration helping to formulate suggestions how current processes could be improved. When looking at possible improvements of such processes attention should be also given to the issue of scientific divergences, for instance divergences that may arise when different authorities assess the risk with a different result despite of the same science as a basis. The SAM HLG is asked to elaborate on possible methods of arbitration that could be used to solve such scientific divergences, taking into account not only technical and scientific considerations (e.g. full alignment of risk assessment procedures, scientific assessment of uncertainties, etc.) but also societal aspects such as for instance the underlying mechanisms of risk acceptance (incl. the way public opinions are formed, role of media and interest groups and the role of transparency in this process). The work on the scientific question addressed to the SAM HLG will therefore run in parallel with and complement the information that will be gathered in the context of the Refit Evaluation of Pesticides Legislation[3], but should not overlap with it. The objective of the Refit evaluation is to perform an evidence-based assessment of the implementation of the current regulations on plant protection products and pesticides residues.

---

[2] Commission Regulation (EU) No 546/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles of evaluation

[3] Roadmap is published at: http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_197_ealuation_plant_protection_products_en.pdf.

3. REQUEST TO THE SCIENTIFIC ADVICE MECHANISM

The SAM HLG is asked to provide a scientific opinion on the authorisation processes for plant protection products in Europe from a scientific point of view by 30 November 2017 in line with the request of Commissioners Moedas and Andriukaitis of July 2016[4].

This date will allow the Commission to look at conclusions from the SAM High Level Group and those from the Refit evaluation in parallel before the Refit evaluation study is finalised. The opinion shall assess the current risk assessment and risk acceptance procedures underlying the decision making processes which determine the placing on the market of plant protection products and on how to make these processes more efficient, effective and transparent.

The questions to be answered by the Scientific Advice Mechanism are the following:

a) EU dual system for approval and authorisation of plant protection products

Could the current EU dual system for approval and authorisation of plant protection products rendered more effective, efficient and transparent, and if so, how could this be achieved? To this end, the SAM HLG may wish to consider comparing the situation in the EU with non-EU OECD countries and to discuss the advantages and disadvantages of different systems. The assessment should be in scientific terms and not examine legal and policy issues.

b) Methods of arbitration

While replying to the question under point (a), the SAM HLG is requested to focus particular attention on the following aspects:

Which methodology of arbitration could be used to solve issues arising from diverging assessments by different competent authorities based on the same science, or on a different assessment of uncertainties?

To which extent would full alignment of risk assessment procedures solve the problem of different risk acceptance by different authorities? Which other factors and mechanisms are influencing risk acceptance by authorities and by the public? Could they be used to develop arbitration methods, and if so, how?

Apart from arbitration methods based on purely natural science or procedural aspects, societal aspects should also be considered. Among other factors and mechanisms that influence risk acceptance, it may be helpful to consider for instance the role of media and interest groups, transparency aspects, etc.

[4] Letter ARES (2016) 4126688 of 20 July 2016

Annex 2 – Methodology

Following adoption of the Scoping Paper by the SAM Group of Chief Scientific Advisors[*] on 24 March 2017 (Annex 1 on page 49), three members of the group, Paul Nurse, Rolf-Dieter Heuer and Janusz Bujnicki, led the development of the Scientific Opinion on behalf of the Group of Chief Scientific Advisors, with a final publication date 4 June 2018. In this task, the Scientific Advisors were aided by SAPEA[†], which agreed to produce part of the underlying supporting evidence for the Opinion in the form of an Evidence Review Report (ERR) on the health aspects of the Opinion, and an expert workshop on risk perception and risk acceptance relating to the authorisation and use of PPPs. The Scientific Advisors were also aided by staff of the SAM Secretariat who provided supplementary, targeted literature searches of scientific and 'grey' literature on items ranging from the EU regulatory landscape to pesticide authorisation systems in other, non-EU OECD countries. For this, the SAM Secretariat was supported by knowledge management experts of the Joint Research Centre (JRC).

Although the technical aspects of risk assessments of PPPs are well covered by scientific literature, the organisation and performance of EU authorisation processes of PPPs are generally not the subject of academic research. SAPEA's ERR, focussing predominantly on such technical aspects, should therefore be regarded as a complementary document to this Opinion. Knowledge and evidence gaps in broader aspects of the EU authorisation processes of PPPs were addressed primarily with expert elicitation, which covered both academic experts and expert practitioners. To this end, the SAM Secretariat assisted the Scientific Advisors in organising an expert workshop relating to environmental impacts of PPPs, an expert 'sounding board meeting' on the draft themes of Opinion, and ad-hoc expert consultations and requests for information. Finally, the SAM Secretariat aided the Scientific Advisors in convening a stakeholder meeting at which the draft outputs of the SAPEA ERR and the draft themes of the Opinion were presented by SAPEA experts and the Scientific Advisors respectively (23 February 2018, Brussels, Belgium).

Thus, both expert elicitation and literature reviews were used in the development of the Opinion. The main lines of evidence used can be summarised as follows (see also Figure 1 below):

---

[*] Prior to Commission Decision C(2018)1919 named the SAM 'High Level Group' or 'HLG'.

[†] SAPEA (Science Advice for Policy by European Academies) operates under the framework of the Scientific Advice Mechanism (SAM). SAM consists of the Group of Chief Scientific Advisors and their supporting team, the SAM Secretariat, and the SAPEA Consortium. SAPEA brings together knowledge and expertise from over 100 academies and learned societies in over 40 countries across Europe. Funded through the EU's Horizon 2020 programme, the SAPEA consortium comprises Academia Europaea (AE), All European Academies (ALLEA), the European Academies Science Advisory Council (EASAC), the European Council of Academies of Applied Sciences, Technologies and Engineering (Euro-CASE) and the Federation of European Academies of Medicine (FEAM)

a) Coordination Group Meeting – Evidence exploration with presence of SAPEA and selected experts, as well as observers from relevant DGs, 30-31 August 2017, Brussels, Belgium (SAM Secretariat)

b) Expert Workshop A – "Authorisation processes of Plant Protection Products (PPP) in Europe from a scientific point of view", 26 October 2017, Brussels, Belgium (SAPEA)

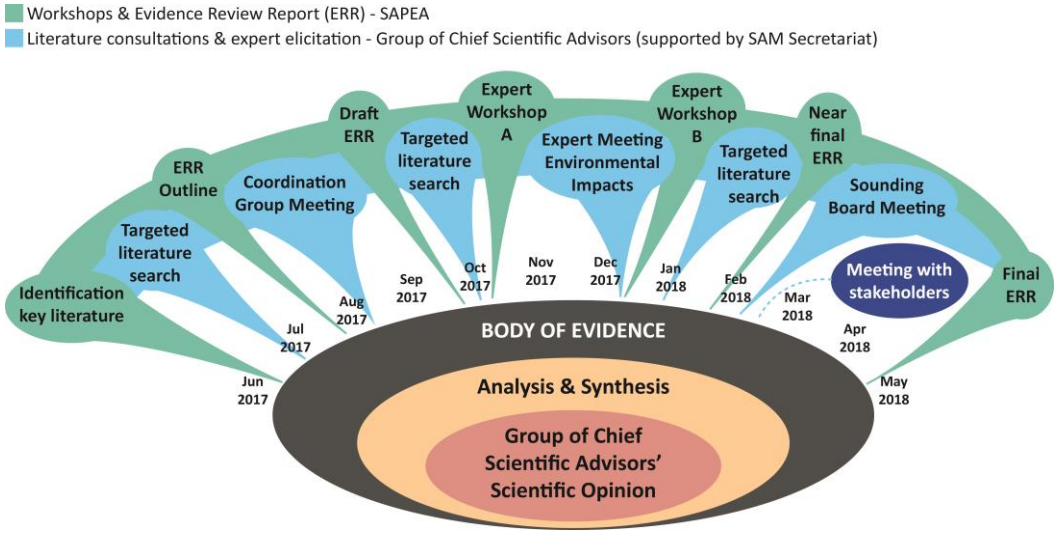
c) Expert Meeting – "Environmental impacts of Plant Protection Products", 19 December 2017, Berlin, Germany (SAM Secretariat)

d) Expert Workshop B – "Risk Perception and the Acceptability of Human Exposure to Pesticides", 20 December 2017, Berlin, Germany (SAPEA)

e) Sounding Board Meeting – Discussion with selected experts on the draft themes of the PPP SAM Scientific Opinion, 16 February 2018, Geneva, Switzerland (SAM Secretariat)

f) Evidence Review Report (ERR) – "Improving authorisation processes for plant protection products in Europe: a scientific perspective on the potential risks to human health" (incorporating the findings from the SAPEA literature review, aided by JRC knowledge management experts, and the expert workshop of 26 October 2017). Final report publication in June 2018 (SAPEA)

Figure 1 – Lines of evidence used in this Scientific Opinion



Annex 3 – List of experts and stakeholder representatives consulted

Achterberg	Franziska	Greenpeace	*
Alonso Prados	José Luis	Spanish Institute for Agricultural and Food Research and Technology (INIA)	*
Backhaus	Thomas	University of Gothenburg	
Berggren	Elisabet	EC DG - Joint Research Centre (JRC)	
Bitterhof	Almut	EC DG - Health and Food Safety (SANTE)	
Boivin	Arnaud	French Agency for Food, Environmental and Occupational Health & Safety (ANSES)	
Bonduelle	Jean-Bernard	European Association of Fruit and Vegetable Processing Industries (PROFEEL)	*
Boobis	Alan	Imperial College London	
Bopp	Stephanie	EC DG - Joint Research Centre (JRC)	
Bosc	Kevin	Comité du Commerce des céréales, aliments du bétail, oléagineux, huile d'olive, huiles et graisses et agrofournitures (COCERAL)	*
Botham	Phil	European Crop Protection Agency (ECPA)	*
Boulova	Anna	FRUCOM (FRuits, Conserves, Miel)	*
Brock	Theodorus	Wageningen Environmental Research (Alterra), Wageningen University and Research Centre	
Burioni	Massimo	EC DG - Research and Innovation (RTD)	*
Busquet	Francois	Center for Alternatives to Animal Testing (CAAT-EUROPE)	*
Capri	Ettore	Faculty of Agriculture, Food and Environmental Sciences, Università Cattolica del Sacro Cuore	
Cary	David	International Biocontrol Manufacturers' Association (IBMA)	*
Coggon	David	University of Southampton	
Corvi	Raffaella	EC DG - Joint Research Centre (JRC)	
D'Avino	Alberto	EC DG - Agriculture and Rural Development (AGRI)	
de Graeff	Robert	European Landowners Association (ELO)	*
de Seze	Guilhelm	European Food Safety Authority (EFSA)	
Deluyker	Hubert	Retired from European Food Safety Authority (EFSA)	
Dermine	Martin	Pesticide Action Network (PAN)-EUROPE	*
Dietrich	Daniel	Human and Environmental Toxicology Department, University of Konstanz	
Drobne	Damjana	University of Ljubljana	
Duquesne	Sabine	German Federal Environment Agency (Umweltbundesamt, UBA)	

Eklo	Ole Martin	Department of Plant and Environmental Sciences, Norwegian University of Life Sciences (NMBU)	
Evelin	Loit	Estonian University of Life Sciences	
Galay Burgos	Malyka	Independent scientist at Galay Biosciences	
Ganci	Patrizia	EC DG - Agriculture and Rural Development (AGRI)	
Glukhof	Pavel	European Plant Protection Association (EPPA)	*
Golding	Jean	University of Bristol	
González	César	European Farmers and their Cooperatives (COPA-COGECA)	*
Hamey	Paul	Chemicals Regulation Division, Health & Safety Executive (HSE)	
Hart	Andy	Visiting Professor at Newcastle University	
Heimbach	Udo	Julius Kühn-Institut, Federal Research Centre for Cultivated Plants	
Helbig	Jürgen	EC DG - Environment (ENV)	
Hernandez Jerez	Antonio	University of Granada	
Hougaard Bennekou	Susanne	Danish Environmental Protection Agency	
Hugas	Marta	European Food Safety Authority (EFSA)	
Inese	Martinsone	Laboratory of Hygiene and Occupational Diseases (LV)	
Innamorati	Angelo	EC DG - Agriculture and Rural Development (AGRI)	
Izquierdo	Raquel	European Potato Trade Association (Europatat)	*
Jamers	An	EC DG - Internal Market, Industry, Entrepreneurship and SMEs (GROW)	
Joschka	Jahn	Institute for Advanced Sustainability Studies (IASS)	
Kaiser	Matthias	University of Bergen	
Karjalainen	Tuomo	EC DG - Research and Innovation (RTD)	*
Kettlitz	Beate	European food and drink industry (Fooddrink Europe)	*
Koof	Peter	International Plant Protection Association (WIP)	*
Krick	Alexander	International Confederation of European Beet Growers (CIBE)	*
Laura	Maxim	Institut des Sciences de la Communication du CNRS	
Liégeois	Eric	EC DG - Internal Market, Industry, Entrepreneurship and SMEs (GROW)	*
Löfstedt	Ragnar	Kings College London	

Lohmann	Mark	German Federal Institute for Risk Assessment (BfR)	
Lucyna	Kapka-Skrzypczak	UK Institute of Rural Health	
Marini	Marina	EC DG - Health and Food Safety (SANTE)	
Mattaar	Johannes	European Crop Care Association (ECCA)	*
McComas	Katherine	Cornell University Ithaca	
Mihnea	Preotesi	Romanian Academy	
Miller	Paul	Cranfield University	
Nienstedt	Karin	EC DG - Health and Food Safety (SANTE)	
Ntzani	Evangelia	University of Ioannina Medical School	
Ockleford	Colin	Lancaster University	
Pagani	Stephen	European Food Safety Authority (EFSA)	*
Parent-Massin	Dominique	University of Brest	
Pedross	Pia	European Technology Platform for organic food and farming and for low input agriculture (TP Organics)	*
Petrillo	Mauro	EC DG - Joint Research Centre (JRC)	
Pineiro Munoz	Amalia	EC DG - Joint Research Centre (JRC)	
Raffael	Barbara	EC DG - Joint Research Centre (JRC)	
Rambourg	Marie-Odile	French Agency for Food, Environmental and Occupational Health and Safety (ANSES)	
Reinert	Wolfgang	EC DG - Health and Food Safety (SANTE)	
Renn	Otwin	Institute for Advanced Sustainability Studies (IASS)	
Riemer	Hilke	EC DG - Agriculture and Rural Development (AGRI)	
Saner	Marc	University of Ottawa - Institute for Science, Society and Policy	
Schlundt	Joergen	Nanyang Technological University Food Technology Centre (NAFTEC)	
Shpend	Shahini	Agricultural University of Tirana	
Simon	Noa	European Beekeeping Coordination (BEE-LIFE)	*
Skinner	Michael	Washington State University	
Smith	Anthony	European Food Safety Authority (EFSA)	
Solecki	Roland	German Federal Institute for Risk Assessment	
Stab Bryndum	Louise	Danish Environmental Protection Agency (DEPA)	*
Straif	Kurt	International Agency for Research on Cancer (IARC)	

Streloke	Martin	German Federal Office for Consumer Protection and Food Safety	
Tarazona	Jose	European Food Safety Authority (EFSA)	
Uteß	Matias	German Federal Office of Consumer Protection and Food Safety (BVL)	*
Vagenende	Benedicte	European Food Safety Authority (EFSA)	
Van de Plassche	Erik	European Chemicals Agency (ECHA)	
Van Den Eede	Guy	EC DG - Joint Research Centre (JRC)	
Van Gelder	Janine	Board for the Authorisation of Plant Protection Products and Biocides (CTGB)	*
Virone	Alessia	Eurogroup for Animals	*
Waldhardt	Rainer	University of Giessen	
Webb	Morag	Comité de Liaison Europe-Afrique- Caraïbes-Pacifique (COLEACP)	*
Whelan	Maurice	EC DG - Joint Research Centre (JRC)	
Wiedermann	Peter	Australian Centre for Electromagnetic Bioeffects Research	

* only involved in Stakeholder Meeting

Annex 4 – References

This Opinion is strongly informed by expert elicitation (see Annex 2 on page 52). Statements and evidence directly attributed to expert elicitation are highlighted with an **'Expert Elicitation'** reference in the text. Other references are listed below:

Barr, D. B. (2008). Biomonitoring of exposure to pesticides. *Journal of Chemical Health and Safety*, *15*(6), 20–29. https://doi.org/https://doi.org/10.1016/j.jchas.2008.07.001

Benford, D., Halldorsson, T., Jeger, M. J., Knutsen, H. K., More, S., Naegeli, H., … Hardy, A. (2018). Guidance on Uncertainty Analysis in Scientific Assessments. *EFSA Journal*, *16*(1), e05123. https://doi.org/10.2903/j.efsa.2018.5123

Boyd, I. L. (2018). An inside view on pesticide policy. *Nature Ecology & Evolution*. https://doi.org/10.1038/s41559-018-0557-8

Bozzini, E. (2017a). EU Pesticide Regulation: Principles and Procedures BT - Pesticide Policy and Politics in the European Union: Regulatory Assessment, Implementation and Enforcement. In E. Bozzini (Ed.) (pp. 27–56). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-52736-9_2

Bozzini, E. (2017b). Policy Changes in EU's Regulation of Pesticides BT - Pesticide Policy and Politics in the European Union: Regulatory Assessment, Implementation and Enforcement. In E. Bozzini (Ed.) (pp. 57–75). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-52736-9_3

Bozzini, E. (2017c). Setting the Context: A Short History of Technology, Toxicology and Global Politics of Pesticides BT - Pesticide Policy and Politics in the European Union: Regulatory Assessment, Implementation and Enforcement. In E. Bozzini (Ed.) (pp. 1–25). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-52736-9_1

Buzea, C., Pacheco, I. I., & Robbie, K. (2007). Nanomaterials and nanoparticles: Sources and toxicity. *Biointerphases*, *2*(4), MR17-MR71. https://doi.org/10.1116/1.2815690

CPMP (Committee for Propriety Medicinal Products). (2000). Points to consider on switching between superiority and non-inferiority. *EMEA*, *CPMP/EW P/*.

Deluyker, H. (2017). Is scientific assessment a scientific discipline? *EFSA Journal*, *15*(11), e15111–n/a. https://doi.org/10.2903/j.efsa.2017.e15111

EFSA (European Food Safety Authority). (2014). Modern methodologies and tools for human hazard assessment of chemicals. *EFSA Journal*, *12*(4), 1–88. https://doi.org/10.2903/j.efsa.2014.3638

EFSA (European Food Safety Authority). (2018). Scientific risk assessment of pesticides in the European Union (EU): EFSA contribution to on-going reflections by the EC. *EFSA Supporting Publications*, *15*(1), 1367E. https://doi.org/10.2903/sp.efsa.2018.EN-1367

Ehlers, R.-U. (2011). Regulation of Biological Control Agents and the EU Policy Support Action REBECA BT - Regulation of Biological Control Agents. In R.-U. Ehlers (Ed.) (pp. 3–23). Dordrecht: Springer Netherlands. https://doi.org/10.1007/978-90-481-3664-3_1

EPRS (European Parliamentary Research Service). (2017). Plant protection products and biocides : in-depth analysis (EU policy, Vol. PE 599.428). https://doi.org/10.2861/39154

Fischhoff, B. (2015). The realities of risk-cost-benefit analysis. *Science*, *350*(6260). https://doi.org/10.1126/science.aaa6516

Furlan, L., Pozzebon, A., Duso, C., Simon-Delso, N., Sánchez-Bayo, F., Marchand, P. A., … Bonmatin, J.-M. (2018). An update of the Worldwide Integrated Assessment (WIA) on systemic insecticides. Part 3: alternatives to systemic insecticides. *Environmental Science and Pollution Research*. https://doi.org/10.1007/s11356-017-1052-5

Handford, C. E., Elliott, C. T., & Campbell, K. (2015). A review of the global pesticide legislation and the scale of challenge in reaching the global harmonization of food safety standards. *Integrated Environmental Assessment and Management*, *11*(4), 525–536. https://doi.org/10.1002/ieam.1635

Hauschild, R., Speiser, B., & Tamm, L. (2011). Regulation According to EU Directive 91/414: Data Requirements and Procedure Compared with Regulation Practice in Other OECD Countries BT - Regulation of Biological Control Agents. In R.-U. Ehlers (Ed.) (pp. 25–77). Dordrecht: Springer Netherlands. https://doi.org/10.1007/978-90-481-3664-3_2

Joint FAO/WHO Food Standards Programme. (2016). *Codex Alimentarius Commission: Procedural Manual* (25th ed.). Food and Agriculture Organization of the United Nations & World Health Organisation.

Lofstedt, R. E. (2011). Risk versus Hazard – How to Regulate in the 21st Century. *European Journal of Risk Regulation*, *2*(2), 149–168. https://doi.org/DOI: 10.1017/S1867299X00001033

Milner, A. M., & Boyd, I. L. (2017). Toward pesticidovigilance. *Science*, *357*(6357), 1232 LP-1234. https://doi.org/10.1126/science.aan2683

Ockleford, C., Adriaanse, P., Berny, P., Brock, T., Duquesne, S., Grilli, S., … Hernandez-Jerez, A. F. (2017). Scientific Opinion of the PPR Panel on the follow-up of the findings of the External Scientific Report "Literature review of epidemiological studies linking exposure to pesticides and health effects." *EFSA Journal*, *15*(10), e05007. https://doi.org/10.2903/j.efsa.2017.5007

Paumgartten, F. J. R. (2012). The Brazilian hazard-based cut-off criteria for pesticide registration: a critical appraisal. *Vigilância Sanitária Em Debate: Sociedade, Ciência & Tecnologia*, *1*(1), 03–11. https://doi.org/10.3395.v1i1.6

Pelaez, V., da Silva, L. R., & Araújo, E. B. (2013). Regulation of pesticides: A comparative analysis. *Science and Public Policy*, *40*(5), 644–656. Retrieved from http://dx.doi.org/10.1093/scipol/sct020

Rotter, S., Beronius, A., Hanberg, A., Zilliacus, J., Nikolopoulou, D., Machera, K., & Solecki, R. (2017). Report on mixtures and implementation strategy in Europe – Assessment of chemical mixtures under consideration of current and future regulatory requirements and scientific approaches. *EuroMix - European Test and Risk Assessment Strategies for Mixtures - Deliverable 9.1 - Report*. https://doi.org/doi:10.5281/zenodo.1067586

SAPEA (Science Advice for Policy by European Academies). (2018a). Improving authorisation processes for plant protection products in Europe: a scientific perspective on the potential risks to human health. *Berlin: SAPEA*. https://doi.org/https://doi.org/10.26356/plantprotectionproducts

SAPEA (Science Advice for Policy by European Academies). (2018b). Workshop Report: Risk Perception and the Acceptability of Human Exposure to Pesticides. *Berlin: SAPEA*. Retrieved from www.sapea.info/workshopriskperceptionacceptability

Schäffer, A., Filser, J., Frische, T., Gessner, M., Köck, W., Kratz, W., … Scheringer, M. (2018). The silent spring – On the need for sustainable plant protection. *Leopoldina Discussions No. 16; 61*.

Storck, V., Karpouzas, D. G., & Martin-Laurent, F. (2016). Towards a better pesticide policy for the European Union. https://doi.org/10.1016/j.scitotenv.2016.09.167

Annex 5 – List of Abbreviations

AOP	Adverse Outcome Pathway
BCA	Biological Control Agent
CAP	Common Agricultural Policy
EC	European Commission
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EMA	European Medicines Agency
ERR	Evidence Review Report
EU	European Union
FAO	Food and Agriculture Organisation
GFL	General Food Law: Regulation (EC) No 178/2002
GIS	Geographic Information Systems
GLP	Good Laboratory Practice
HTS	High-throughput screening
IIA	Integrated Impact Assessment
MoA	Mode of Action
MRL	Maximum Residue Level
NGO	Non-Governmental Organisation
OECD	Organisation for Economic Co-operation and Development
PBT	Persistent, bio-accumulative and toxic for the environment
POP	Persistent organic pollutant
PPP	Plant Protection Product
PPR	Panel on Plant Protection Products and their Residues
REACH	Regulation (EC) No 1907/2006 on Registration, Evaluation, Authorisation and Restriction of Chemicals
REFIT	Regulatory Fitness and Performance programme
SAM	Scientific Advice Mechanism
SAPEA	Scientific Advice for Policy by European Academies
SUD	Sustainable Use of Pesticides Directive: Directive 2009/128/EC
vPvB	Very persistent and very bio-accumulative
WFD	Water Framework Directive: Directive 2000/60/EC
WHO	World Health Organisation

Annex 6 – Glossary

Active substance: The essential ingredient(s) in a Plant Protection Product (PPP) that enable(s) the PPP to have its intended effect, which can be a chemical and/or a Biological Control Agent, e.g. a microorganism or chemicals of natural origin.

Adverse effect: A change in the health, growth, behaviour or development of an organism that impairs its ability to develop or survive, in other words: harm.

Adverse outcome pathway (AOP): The description of a chain of biochemical events linked by causality that may lead to a harmful outcome for living organisms. An AOP covers the events between a 'molecular initiation event' (i.e. the cause) and an adverse effect.

Aggregate exposure: The exposure to the same substance via all exposure routes (i.e. ingestion, inhalation and dermal contact) and from different sources (e.g. different consumer products and/or in combination with food).

Applicant: A person/organisation, typically the manufacturer, that submits an application for the approval or renewal of approval of an active substance, or for the authorisation or re-authorisation of a PPP.

Approval: In the context of this Opinion, the process by which an active substance is currently approved by the EU risk managers for authorisation to be used in PPPs in the EU. First approval is for a period not exceeding 10 years, after which renewal of approval is required.

Authorisation: In the contexts of this Opinion, the administrative act by which the risk managers of a competent authority of a Member State authorises the placing on the market of a PPP with specific use recommendations and/or restrictions.

Bio-accumulation: The accumulation (i.e. build up) of substances in a living organism. Bio-accumulation occurs when an organism absorbs a substance at a rate faster than that at which the substance is broken down and/or lost by excretion.

Biocide: A product used to eradicate or control unwanted living organisms that are harmful to human or animal health, or that cause damage to human activities. Examples are rat-poison, mosquito repellents, disinfectants and wood preservatives. A biocide can be called a pesticide if it targets pests. In EU legislation, a biocide designed to protect plants (in agriculture, parks and gardens) falls under the Plant Protection Product Regulation (Regulation (EC) No 1107/2009), and not under the Biocide Regulation (Regulation (EU) No 528/2012). The Biocides Regulation thus applies to products that protect other materials than plants (e.g. plastics, paints, textiles, timber) from harmful living organisms, or protect health, for example against vector-borne diseases (like malaria), food-borne diseases (like salmonella) and hospital-acquired infections (like MRSA).

Biodiversity: A term used to describe the variety of living organisms existing in a specific environment. Biodiversity is important for ecosystem robustness and is

considered to provide many key ecosystem services, including nutrient cycling for soil fertility, pest regulation and pollination.

Biological Control Agents (BCA): Living organisms or substances and mixtures from natural sources that are used (mainly) to eradicate or control pests, including weeds. As PPPs, these include microorganisms, such as bacteria, fungi and viruses, plant extract (or 'botanicals'), fungal metabolites, and pheromones, repellents and attractants of natural origin. BCAs in the form of macroorganisms, such as insects, mites and nematodes, do not fall under the EU Regulation on Plant Protection Products. See also Box 5 on page 38.

Biomonitoring: The measurement of concentrations of a substance, its metabolite or reaction product in biological media, typically blood or urine, to determine if an exposure has occurred and the extent of that exposure.

Carcinogenicity: Cancer-causing property of a substance when an animal or human is exposed to it.

Co-formulant: Any inactive or inert substance added to the active substance in the final formulation of a PPP, except for safeners and synergists.

Comitology: A set of procedures through which EU Member States control how the European Commission implements EU law. 'Comitology committees' assist the Commission in executing its implementing powers by giving an opinion on draft implementing measures before they are adopted. They include representatives from all EU Member States and are chaired by a Commission official.

Comparative risk assessment: In the context of this Opinion, the systematic evaluation of the differences in risks associated with the potential use of different PPPs or different uses, or restrictions on the use, of a particular PPP. Sometimes used synonymously to the term 'risk-risk analysis'.

Cumulative effect: A term used to describe how exposure to different substances with similar modes of action, or repeated exposure of the same substance, affect a living organism. The resulting adverse effects may be more pronounced than those of a single exposure.

Dose response: The relationship between the amount of a substance to which an individual organism, population or ecosystem is exposed and the way in which it responds (e.g. in terms of toxicity).

Ecosystem: A system involving the interactions between a community of living organisms in a particular area and its non-living environment (e.g. air, water and soil).

Ecosystem services: Benefits to humans provided by an ecosystem, such as food or fuel provision, water purification, medicinal ingredients, pollination and maintenance of soil fertility. Ecosystems may also be considered as providing education, recreation and cultural heritage services.

Endocrine disruptor: A substance that adversely affects the endocrine (hormone) system leading to negative effects for organisms and/or their offspring.

Endpoint: In toxicological studies, a physical or chemical outcome that can be assessed by a test; for example, a change in body weight or levels of a potential toxin in the body.

Environmental Risk Assessment (ERA): The process of assessing potential harm to the environment caused by a substance, activity or natural occurrence. This may pertain to the use of PPPs, but also the spread of plant pests.

Epidemiology: The study of how diseases and other health conditions occur in different groups of people and why. It includes the study of health-related measurements (e.g. PPP exposure or vitamin deficiency) in a population and how they may influence the risk of ill health.

European Food Safety Authority (EFSA): EU's independent scientific agency, established by the General Food Law (Regulation (EC) No 178/2002), carrying out risk assessments and providing scientific advice to the European Commission, Member States and the European Parliament on all issues impacting directly or indirectly on food and feed safety, animal health and animal welfare, plant health, human nutrition, and Genetically Modified Organisms.

Exposure: Concentration or amount of a particular substance that is taken in by an individual, population or ecosystem in a specific frequency over a certain amount of time. Exposure can occur via ingestion via the diet, but also through inhalation or dermal contact.

Geographic Information Systems (GIS): A system designed to capture, store, manipulate, analyse, manage, and present spatial or geographic data.

Good laboratory practice (GLP): A standardised way of planning, performing and reporting studies to ensure an accredited high standard of quality, reliability and reproducibility.

Hazard: In the context of this Opinion, the intrinsic potential of a substance to cause harm to living organisms. It is important to understand that a hazard does not necessarily imply the harm will occur: this depends on the risk, which is a product of both hazard and exposure.

Hazard identification and characterisation: Hazard identification is the first step in risk assessment and involves the identification of the capability of biological, chemical, and physical agents to cause harm to living organisms or the environment. Hazard characterisation is second step in risk assessment and involves defining the nature of the harm associated with these agents. The process should, if possible, involve an understanding of the dose response.

High-Throughput Screening (HTS): The quick and typically automated assaying of the biological or biochemical activity of a large number of substances. This is widely used by the pharmaceutical industry in drug discovery processes.

***In silico*:** Virtual research method, which involves computer simulations and computational modelling, e.g. to predict the likely toxicological effects of substances.

***In vitro*:** Laboratory research method, which involves testing cells or tissues extracted from living organisms, e.g. to assess the cellular toxicity of substances.

***In vivo*:** Laboratory research method, which involves testing individual living animals or populations of living animals, e.g. to assess the toxicity of substances on living organisms.

Integrated Pest Management (IPM): The integrated application of biological, biotechnological, chemical, physical or agricultural measures, with only heavily restricted use of synthetic Plant Protection Products. Also known as 'integrated plant protection'.

Landscape-scale: The physical/geographic scale at which a study is performed, based on the ecosystem being studied; greater than field-scale and normally smaller than the scale of a country.

Low-risk active substance: According to Regulation (EC) No 1107/2009, an active substance that does not have any of the following characteristics: carcinogenic, mutagenic, toxic to reproduction, sensitising chemicals, very toxic or toxic, explosive, corrosive, persistent (half-life in soil is more than 60 days), bio-accumulative (bioconcentration factor is higher than 100), endocrine disruptive, neurotoxic or has immunotoxic effects.

Maximum Residue Level (MRL): The highest concentration of a substance that is allowed to be present in or on food or animal feed during consumption, expressed as milligrams per kilogram.

Metabolite: A substance that has formed as a product of metabolism, i.e. the conversion of a substance into another within a living organism. Breakdown products, or 'degradates', are sometimes also included in the term 'metabolites'.

Mixture: A combination of substances that have been deliberately (e.g. in the sprayer tank as 'tank mixture') or unintentionally mixed. In a mixture, each substance may have a separate identifiable adverse effect on living organisms and the environment and/or a combined effect with the other substances.

Mode of Action (MoA): A sequence of events which explains an observed effect. In the context of this Opinion: the way in which a PPP or its active substance physiologically affects a living organism following treatment/exposure. This typically includes the mechanism of action, if known, which can be defined as the molecular/biochemical process by which the effect in produced.

Mutagenicity: The capacity to cause permanent, typically negative, changes to an organism and any offspring by altering its genetic code.

Nanomaterial: A natural, incidental or manufactured material containing 'nanoscale' structural components or particles. In principle, the 'nanoscale' is 1-1000 nanometer (nm; 1 nm is a billionth of a meter), but it is more commonly defined as 1-100 nm. This is because most particles tend to physically behave like 'normal' particles above 100 nm, although this does depend on the material type. Nanomaterials can behave significantly differently from 'normal' materials due to surface and quantum effects that affect their chemical reactivity of materials as well as their mechanical, optical, electric, and magnetic properties. This may alter the risks they pose to health and the environment.

Non-target organism: Any living organism other than the one that is intended to be eradicated or controlled.

Panel on Plant Protection Products and their Residues (PPR): Comprised of independent expert scientists, the panel provides EFSA with scientific advice and guidance on the risk assessment of pesticides for operators, agricultural workers, consumers and the environment.

Persistence: The resistance (to a certain degree) to environmental degradation through chemical, biological, and photolytic (light/radiation-induced molecular breakdown) processes.

Pest: A living organism (e.g. an insect, rodent, weed, fungus or virus) that is detrimental to humans and human interests. In the context of this Opinion, the term mainly refers to a living organism that is harmful to cultivated plants and/or their products (e.g. seeds, fruits).

Pesticide: Substance used to eradicate or control pests, including disease-carrying living organisms and undesirable plants, insects and other animals. Pesticides include some Plant Protection Products (PPPs) and biocides.

Plant Protection Product (PPP): Products used to protect, preserve or influence the growth of desirable plants or to eradicate or control the growth of unwanted plants (or parts of plants). Examples are herbicides, fungicides and insecticides, but also plant growth regulators and rooting hormones. A PPP can be called a pesticide if it targets pests. The PPP is the final formulation in which the product is placed on the market. Apart from one or more active substances, a PPP usually contains other ingredients (safeners, synergists and/or co-formulants), that help to increase its efficacy and better protect the plant on which it is applied.

Post-market vigilance: Post-market monitoring of the effects of pesticides (or PPPs) on both the environment and health, understanding the impacts related to their (widespread) use, as well as alertness for and adequate response to any unforeseen consequences.

Precautionary principle: A principle/approach mainly based on the United Nations 1992 Rio Declaration on Environment and Development stating that "Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent

environmental degradation", which is applied beyond the protection of the environment in the EU (see also Box 3 on page 26).

Precision farming: A process which aims at managing variations in the field accurately to grow more food using fewer resources, including PPPs, thus reducing production costs.

Prophylactic use: In the context of this Opinion, the preventative use of PPPs, i.e. application to crops without any sign of pests, infection, etc. or when these are not a threat. This is in contrast to responsive use (i.e. 'curative'/'therapeutic'), where a PPP is used only when crops are actually threatened.

Protection goals: In the context of this Opinion, the objectives specified in legislation with respect to the protection of humans and other living organisms, also in context of the environment, from possible adverse effects of (substances in) PPPs.

Re-authorisation: The renewal assessment of PPPs following the renewal of approval of one of their active substances, aimed to ensure that the PPPs comply with the updated assessment of the active substance and with new scientific and technical knowledge. Such renewals, or re-authorisations, are carried out on a zonal level.

Renewal of approval: The re-evaluation of an active substance when its approval period expires. The renewal of the approval is for a period not exceeding 15 years.

Representative formulation/use: A specified formulation containing an active substance and its use, as proposed by the applicant, which is used to assess if the active substance could (hypothetically) be used in a safe way for humans and the environment, in order to be approved. Representative formulations/uses for active substances do not necessarily correspond with the formulations/uses of the PPPs containing this active substance subsequently submitted for market authorisation.

Risk: The chance or probability that harm or the experience of an adverse effect will occur if exposed to a hazard.

Risk acceptability: The level of risk that is tolerated by a person or entity, such as a risk manager or legislator.

Risk assessment: A scientifically-based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment and risk characterisation.

Risk assessor: The entity responsible for carrying out the risk assessment and subsequently provide scientific advice to the risk manager. In the current EU PPP system, the risk assessor at EU-level is the European Food Safety Authority (EFSA). Member States have various (scientific) bodies, councils or authorities (or parts thereof) that perform the role of risk assessor.

Risk characterisation: The final stage of risk assessment, in which the likelihood that a particular substance will cause harm is calculated in the light of the nature of the hazard and the extent to which people, animals, plants and/or the environment is exposed to it.

Risk communication: The interactive exchange of information and opinions throughout and subsequent to the risk analysis process as regards hazards and risks, risk-related factors and risk perceptions amongst risk assessors, risk managers, consumers, food and feed businesses and the academic community, including the explanation of risk assessment findings and the basis of risk management decisions.

Risk management: The process of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options to protect consumers, animals and the environment.

Risk manager: The entity responsible for taking risk management decisions. In the current EU PPP system, the risk manager for active substance is the European Commission together with Member State representatives through a comitology procedure. For PPPs, the risk managers are currently the dedicated authorities in the individual Member States, typically ministries.

Risk-cost-benefit analysis: An analytical-deliberative process involving the systematic evaluation of risks, costs and benefits in a manner that allows comparisons to be made between options. In the context of this Opinion, this relates to the potential use of different PPPs or different uses, or restrictions on the use, of a particular PPP. Benefits may range from the effectiveness of a PPP on a target organism to the estimation of broader socio-economic aspects. Benefits may or may not be monetised, for example, relating to an anticipated decrease in crop yield loss.

Safener: A substance that suppresses or reduces the effects of a PPP on the crop it is applied to.

Synergist: A substance that is formally inactive or weakly active (at the applied concentration), but can significantly enhance the activity of an active substance or another ingredient in a PPP.

Synergistic effect: An interaction (e.g. between different substances) that multiplies outcomes. The outcome in question may be beneficial or adverse.

Toxicity: The state and degree to which a substance can damage a living organism, dependent on its dose.

Uncertainty: In the context of this Opinion, a lack of full knowledge about a situation or possible outcome, which is an important component of a risk assessment.

Uncertainty analysis: A method of identifying the sources of uncertainty in a risk assessment calculation and estimating their size and impact so that potential errors in the results of an assessment can be taken into account.

Vulnerable group: Persons needing special consideration when assessing the acute and chronic health effects of PPPs. These include pregnant and nursing women, the unborn, infants and children, the elderly and workers and residents subject to high pesticide exposure over the long term.

Weight of evidence determination: A process in which all of the available evidence relating to a decision is simultaneously evaluated by experts to come to a single conclusion, assessing in particular the robustness, quality and statistical power of the various tests, the consistency of results between different tests, and the relevance of the tests to the decision (e.g. relating to health).

Sources: relevant regulations; SAPEA ERR; EC DG SANTE; EFSA; EPRS; HSE; IPCC; RIVM; WHO; Collins English Dictionary; Barr, 2008; Buzea, Pacheco, & Robbie, 2007; Ehlers, 2011; EPRS, 2017; Fischhoff, 2015

Reader's Notes

Getting in touch with the EU

IN PERSON

All over the European Union there are hundreds of Europe Direct Information Centres. You can find the address of the centre nearest you at: **http://europa.eu/contact**

ON THE PHONE OR BY E-MAIL

Europe Direct is a service that answers your questions about the European Union. You can contact this service

– by freephone: **00 800 6 7 8 9 10 11** (certain operators may charge for these calls),

– at the following standard number: **+32 22999696** or

– by electronic mail via: **http://europa.eu/contact**

Finding information about the EU

ONLINE

Information about the European Union in all the official languages of the EU is available on the Europa website at: **http://europa.eu**

EU PUBLICATIONS

You can download or order free and priced EU publications from EU Bookshop at: **http://bookshop.europa.eu.** Multiple copies of free publications may be obtained by contacting Europe Direct or your local information centre (see http://europa.eu/contact)

EU LAW AND RELATED DOCUMENTS

For access to legal information from the EU, including all EU law since 1951 in all the official language versions, go to EUR-Lex at: **http://eur-lex.europa.eu**

OPEN DATA FROM THE EU

The EU Open Data Portal (**http://data.europa.eu/euodp/en/data**) provides access to datasets from the EU. Data can be downloaded and reused for free, both for commercial and non-commercial purposes.

This Scientific Opinion responds to a request from the European Commission formulated by Commissioner Vytenis Andriukaitis (Health and Food Safety) for scientific advice on how to render the current EU dual system for approval and authorisation of Plant Protection Products (PPPs), more transparent, effective and efficient. PPPs are more commonly referred to as 'pesticides'.

The advice takes the form of several recommendations. Although recognising that the EU has made significant progress in the effectiveness of its authorisation system for PPPs, the Group of Chief Scientific Advisors feels there is room for improvement regarding: clarity on protection goals and their communication; structural aspects of the system concerning who does what and when; impacts of widespread and prophylactic use of PPPs on the environment; post-market vigilance; sharing of knowledge and the capacity of expertise; availability and quality of pre-market studies; ways to address hazards, risks, costs and benefits; and preventing the misuse of science in value-based disagreements.

The advice also extends to a call for a dialogue to develop an EU-wide shared vision of how citizens want their food to be produced, including the role of PPPs therein, whilst endorsing the EU's efforts to achieve a more sustainable use of pesticides.

This Scientific Opinion is based on an analysis of publicly available scientific and technical literature as well as close consultation with the scientific community and expert practitioners. In particular, it is informed by outcomes of various expert workshops and by an Evidence Review Report produced by SAPEA, an independent Horizon 2020-funded consortium of European scientific academy networks, which constitutes a key component of the European Commission's Scientific Advice Mechanism (SAM).

The advice will inform preparatory work for the revision of the EU legislation on PPPs, which will also be informed by the outcomes of the European Commission's review of the PPP legislation under its Regulatory Fitness and Performance (REFIT) programme; and also by the European Parliament's recently established special committee on authorisation procedures for pesticides in the European Union.

This Scientific Opinion is published at a time when public and media interest in PPP are high and it is hoped that its recommendations will be a valuable contribution both to the debate and to the EU's continued efforts to improve its policy and practice in this and related areas.

Studies and reports

Publications Office