

# EFSA-SANTE Action Plan on Cumulative Risk Assessment for pesticides residues

## Summary

The EU Chemicals Strategy for Sustainability<sup>1</sup> (EU CSS) sets the framework for assessing the impact of chemical mixtures on human health and the environment. Pesticides form an integral part of this Strategy, as *"for pesticides, progress has been made in developing a targeted methodology, and work will be accelerated so that existing provisions can be fully implemented"*. Furthermore, in the context of the regulatory fitness and performance programme<sup>2</sup> (REFIT) for the pesticide legislation, the European Commission and EFSA committed to speed up the development of methods for the cumulative risk assessment (CRA) of pesticides and to develop an action plan by the end of 2020.

The present document provides this action plan and describes priorities for the ongoing work on method development and subsequent implementation. This action plan is divided in four areas requiring further progress.

In terms of dietary risk assessment, the establishment of new cumulative assessment groups (CAGs) will be based on a prioritisation method that will take into account dietary risks of the individual pesticides (substance and organ screening based on actual exposure). This will include i) the validation of the prioritisation method (Q1 2021), ii) the elaboration of a priority list of pesticides and organ systems to be considered for CAG development (Q1 2022) and iii) the subsequent elaboration of new CAGs for around 8 to 15 organ systems (2022-2030). The prioritisation will be repeated every three years and CAGs will be updated accordingly.

The elaboration of new dietary CRAs will be carried out for pesticides that have i) chronic effects on the nervous system (Q1 2021), ii) acute effects on craniofacial malformations (Q1 2022) and iii) effects on other organ systems in conjunction with the establishment of new CAGs as detailed above (2022-2030). These dietary CRAs are proposed to be repeated every three years, unless yearly changes in exposure patterns of single pesticides will indicate the need for an earlier re-evaluation.

CRAs will also need to be carried out in view of new active substance approvals and new product authorisations, for which specific scenarios will be developed (Q2 2021). In a subsequent step, a thorough assessment of its consequences and discussions with risk managers will be needed to enable a future implementation in regulatory decision-making. In this context, to ensure an efficient and transparent implementation, further improvement of an open source software with access to relevant input data will be explored.

The possible integration of non-dietary exposure into CRA will be investigated, starting from the tools currently used for the assessment of exposure of operators, workers, residents and bystanders to single pesticides. From 2022 onwards, EFSA will i) evaluate the applicability of CAGs established for dietary CRA to non-dietary CRA, ii) identify available data sources and priorities for data generation/collection, and iii) integrate models for combining dietary and non-dietary exposure into the available open source CRA software.

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<sup>1</sup> [COM\(2020\) 667 final](#)

<sup>2</sup> [https://ec.europa.eu/food/plant/pesticides/refit\\_en](https://ec.europa.eu/food/plant/pesticides/refit_en)

## Background

Cumulative risk assessment (CRA) has been defined as the analysis, characterisation and possible quantification of the combined risks to health or the environment from multiple agents or stressors<sup>3</sup>. It differs from most current assessments which consider the effects of one agent or stressor in isolation.

Regulation (EC) No 396/2005<sup>4</sup> on Maximum Residue Levels (MRLs) of pesticides in or on food and feed requires cumulative and synergistic effects of pesticide residues to be taken into account for dietary risk assessment, when appropriate methodologies are available. Regulation (EC) No 1107/2009<sup>5</sup> concerning the placing of plant protection products on the market also requires that the residues of plant protection products shall not have any harmful effects on human health, taking into account known cumulative and synergistic effects where the scientific methods accepted by EFSA to assess such effects are available. For this reason, EFSA and the Panel on plant protection products and their residues (PPR panel) started in 2007 the development of the necessary methodologies to carry out CRA of pesticide residues. This methodological development included a tiered approach for the assessment of cumulative risks of pesticides residues<sup>6</sup>, a guidance on the use of probabilistic methodology for modelling dietary exposure to pesticide residues<sup>7</sup> and a procedure to establish cumulative assessment groups (CAGs) of pesticides on the basis of their toxicological profile<sup>8</sup>.

After development of the methodologies by the PPR Panel, EFSA initiated in 2014 a pilot programme aiming at implementing the CRA of pesticides. The objectives of this pilot programme were to evaluate the cumulative effects of pesticide residues on two organs which are known to be sensitive to pesticides (the nervous system and the thyroid), and to test the methodologies over the entire risk assessment process (hazard identification and characterisation, exposure assessment and risk characterisation) for acute and chronic effects. During this pilot phase, EFSA worked in close cooperation with the Dutch National Institute for Public Health and the Environment (RIVM), who had previously released the Monte Carlo Risk Assessment (MCRA) software, a web-based software that allows higher tier exposure assessment to multiple pesticides to be performed. The cooperation with RIVM was consolidated by means of a Framework Partnership Agreement, which mainly aimed at testing and improving the MCRA software in view of its implementation in CRA to pesticide residues. Concurrent with EFSA's pilot programme, the European Commission also established a Working Group with Member States on the Cumulative Risk Assessment of Pesticide Residues, under the umbrella of the Standing Committee on Plants, Animals, Food and Feed (SCoPAFF). The main objective of this Working Group was to discuss risk management aspects with Member States and EFSA, and to agree on several parameters and assumptions that should be applied when assessing cumulative exposure to pesticide residues.

In 2020, as a result of the pilot programme, EFSA issued two CRAs for the dietary exposure to pesticides that have chronic effects on the thyroid and pesticides that have acute effects on the nervous system<sup>9,10</sup>. These retrospective assessments (i.e. using monitoring data collected by Member States under their official pesticide monitoring programmes) were conducted for ten population groups from different countries and different age classes in the reference period 2014-2016. It was concluded,

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<sup>3</sup> U.S. EPA, 2003. *Framework for Cumulative Risk Assessment*. U.S. Environmental Protection Agency, Office of Research and Development, Center for Public Health and Environmental Assessment (CPHEA), formerly known as the National Center for Environmental Assessment (NCEA), Washington Office, Washington, DC, EPA/600/P-02/001F. Available at: [https://www.epa.gov/sites/production/files/2014-11/documents/frmrwrk\\_cum\\_risk\\_assmnt.pdf](https://www.epa.gov/sites/production/files/2014-11/documents/frmrwrk_cum_risk_assmnt.pdf)

<sup>4</sup> [OJ L 70, 16.3.2005, p. 1-16](#)

<sup>5</sup> [OJ L 309, 24.11.2009, p. 1-50](#)

<sup>6</sup> EFSA PPR Panel, 2008. *Scientific Opinion of the Panel on Plant Protection Products and their Residues (PPR Panel) on a request from the EFSA evaluate the suitability of existing methodologies and, if appropriate, the identification of new approaches to assess cumulative and synergistic risks from pesticides to human health with a view to set MRLs for those pesticides in the frame of Regulation (EC) 396/2005*. The EFSA Journal 2008;704. DOI: [10.2903/j.efsa.2008.705](#)

<sup>7</sup> EFSA PPR Panel, 2012. *Guidance on the Use of Probabilistic Methodology for Modelling Dietary Exposure to Pesticide Residues*. EFSA Journal 2012;10(10):2839. DOI: [10.2903/j.efsa.2012.2839](#)

<sup>8</sup> EFSA PPR Panel, 2013. *Scientific Opinion on the identification of pesticides to be included in cumulative assessment groups on the basis of their toxicological profile (2014 update)*. EFSA Journal 2013;11(7):3293. DOI: [10.2903/j.efsa.2013.3293](#)

<sup>9</sup> EFSA, 2020. *Scientific report on cumulative dietary risk characterisation of pesticides that have acute effects on the nervous system*. EFSA Journal 2020;18(4):6087. DOI: [10.2903/j.efsa.2020.6087](#)

<sup>10</sup> EFSA, 2020. *Scientific report on the cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid*. EFSA Journal 2020;18(4):6088. DOI: [10.2903/j.efsa.2020.6088](#)

with varying degrees of certainty, that cumulative exposure to these pesticides did not exceed the threshold for regulatory consideration. Hence, immediate action was not considered necessary by risk managers.

Despite the progress made, developing the methodology for CRA of pesticides turned out to be much more complex than initially expected. Only two organ systems have been addressed so far and CAGs need to be established for the remaining key organ systems (approx. 15). Furthermore, current methodologies only refer to retrospective assessments and further progress is needed on the elaboration of prospective methods for regulatory decision-making (i.e. in view of the approval of substances, authorisation of products or setting of MRLs).

In the context of the regulatory fitness and performance programme (REFIT) for the pesticide legislation, the Commission and EFSA committed to speed up cumulative risk assessment and to develop an action plan by the end of 2020 that would set out priorities for the ongoing work on method development and the subsequent implementation of the methodology<sup>11</sup>. The plan, which is presented in this document, will focus on the cumulative assessment of human health risks from dietary and non-dietary exposure to pesticides. It will be based on existing knowledge and will be flexible to respond to changing scientific developments and experiences gained.

Although legal requirements for the use of CRA currently only exist in the areas of pesticides and biocides<sup>12</sup>, the European Commission and EFSA share the common objective that these methodologies could be expanded also to other areas in the future based on the experiences gained. The development of harmonised methodologies for assessing the risk of combined exposure to multiple chemicals has been identified as a key priority. EFSA therefore organised a Scientific Colloquium on the harmonisation of human and ecological risk assessment of combined exposure to multiple chemicals in 2014<sup>13</sup> and, in March 2019, the Scientific Committee of EFSA published a guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals<sup>14</sup>.

Furthermore, while the EU CSS underlines that the effect of chemical mixtures needs to be taken into account and integrated more generally into chemical risk assessments, it provides for "*targeted methodologies to be further developed and explored for specific policy areas*". Hence, while the Chemicals Strategy acknowledges the establishment of a Mixture Assessment Factor as a pragmatic tool when a detailed risk assessment methodology for CRA is not available, the targeted methodology under development in the specific policy area of pesticides is considered a more refined and accurate way to estimate cumulative risk. EFSA also identified the risk assessment of combined exposure to multiple chemicals (RACEMiC) as one of the scientific themes to be prioritised for the outsourcing of scientific studies and research projects that would be of direct use in regulatory science. The vision, scope and opportunities of this scientific theme have been explained further in so-called 'theme papers' which underwent a phased consultation with the European Commission (DG SANTE, DG Joint Research Centre), EU Agencies, EFSA's Scientific Committee, Member States at EFSA's Advisory Forum, international partners and stakeholders. Feedback received from this consultation will be considered for the development of a roadmap, which will provide a full understanding on ongoing activities, knowledge gaps, societal interests and concerns as well as collaboration opportunities and potential partners. The final roadmap is expected to be delivered in Q4 2021 and will be the basis for prioritisation and decision making for project calls to be launched between 2022-2027.

This action plan on the implementation of CRA of pesticides and their residues will be part of the RACEMiC project and will be integrated in the associated roadmap. Within this context, EFSA will further explore collaborations and synergies will within the Partnership for the Assessment of Risks

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<sup>11</sup> Evaluation of Regulation (EC) No 1107/2009 on the placing of plant protection products on the market and of Regulation (EC) No 396/2005 on maximum residue levels of pesticides. [SANTE/11596/2019 Rev. 1](#)

<sup>12</sup> Regulation (EC) 528/2012 also requires cumulative and synergistic effects to be considered when granting authorisation of a biocidal product, [OJ L 167, 27.6.2012, p. 1-123](#)

<sup>13</sup> EFSA, 2015. *EFSA's 21<sup>st</sup> Scientific Colloquium on Harmonisation of human and ecological risk assessment of combined exposure to multiple chemicals*. EFSA supporting publication 2015:EN-784. DOI:[10.2903/sp.efsa.2015.EN-784](#)

<sup>14</sup> EFSA Scientific Committee, 2019. *Guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals*. EFSA Journal 2019;17(3):5634. DOI:[10.2903/j.efsa.2019.5634](#)

from Chemicals<sup>15</sup> (PARC), while linking it, where applicable, with the work done under the EU's Health Biomonitoring Programme<sup>16</sup> (HBM4EU)

## Prioritisation and elaboration of new cumulative assessment groups

Cumulative assessment groups (CAGs) were derived for two organ systems so far (i.e. the nervous system and the thyroid) and CAGs will be established for the remaining key organ systems, estimated to be around 15. To ensure an optimal use of resources, EFSA developed a prioritisation method which will allow identification of pesticides and organ systems that may present the highest risk in terms of dietary exposure. Hence, the elaboration of new CAGs will be based on the following milestones and deliverables:

- EFSA, in close cooperation with RIVM, will issue by mid-2021 an external scientific report on the validation of the prioritisation method by applying it to the CAGs previously established (i.e. the nervous system and the thyroid). This validation will support EFSA in the identification of the most appropriate parameter settings for the prioritisation method.
- The first implementation of the prioritisation method is scheduled for 2021, which will include a probabilistic exposure assessment for around 500 pesticides, both chronic and acute.
- In the first quarter of 2022, EFSA will then issue a scientific report identifying the pesticides and organ systems that do not require a refined cumulative risk assessment.
- From 2022 onwards, based on this prioritisation, EFSA will proceed with the elaboration of new CAGs for organ systems that require a refined cumulative risk assessment, starting with the most critical ones. In view of strengthening the assessment capacity and expanding the knowledge community, EFSA will explore possibilities for cooperation with Member States' competent organisations in 2021. This capacity building will allow EFSA to gradually increase the number of organ systems to be addressed from 2022 onwards, i.e. one organ system per year for the years 2022 and 2023, and two organ systems per year from 2024 onwards.
- The total number of organ systems to be addressed will depend on the outcome of the prioritisation, but it is expected that the elaboration of new CAGs will be required for between 8 and 15 organ systems. As a minimum estimation, CAGs will be required for 8 organ systems (i.e. only for half of the 15 remaining organ systems estimated). In this case CAGs are expected to be established for all relevant organ systems by 2026. As a maximum estimation, CAGs will need to be established for 15 organ systems. In this case, all CAGs are expected to be available by 2030.
- The prioritisation will be repeated every three years which will result in an evolutive list of pesticides and organ systems to be (re-)considered for cumulative risk assessment. CAGs will then also be updated in order to include new substances emerging from the prioritisation exercise, and to update the toxicological characterisation of pesticides when new information is available to EFSA.

## Retrospective cumulative risk assessment

Retrospective cumulative risk assessments generally aim at assessing risks resulting from the actual exposure to pesticides (i.e. using monitoring data) and provides a baseline for the subsequent elaboration of prospective risk assessment (i.e. in view of regulatory decisions, e.g. on the approval of substances, authorisation of products or setting of MRLs). Retrospective CRAs will therefore need to be carried out in conjunction with the prioritisation and elaboration of new CAGs described above.

Pending the implementation of the prioritisation method, the plan for retrospective CRAs is described as follows:

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<sup>15</sup> [https://ec.europa.eu/info/files/european-partnership-chemicals-risk-assessment\\_en](https://ec.europa.eu/info/files/european-partnership-chemicals-risk-assessment_en)

<sup>16</sup> <https://www.hbm4eu.eu/about-hbm4eu/>

- In the first quarter of 2021 EFSA issued a retrospective CRA report for pesticides that have chronic effects on the nervous system<sup>17</sup>. Previous CRA for acute effects on the nervous system revealed that organophosphorus insecticides are the main risk drivers of acute brain and/or erythrocyte AChE inhibition. Considering that binding of these compounds to AChE is irreversible, it was recommended to perform a chronic retrospective CRA for the same CAG.
- In the first quarter of 2022 EFSA will issue a retrospective CRA report for pesticides that have acute effects on craniofacial malformations. Preliminary work of the EFSA PPR Panel revealed that seven triazole pesticides shared this specific effect<sup>18</sup>. Building on this work and recommendations, EFSA will propose a more appropriate CAG and the retrospective CRA for this specific effect will be further refined.
- From 2022 onwards, EFSA will proceed with the retrospective CRA for the remaining organ systems described above. As for the elaboration of new CAGs, EFSA will explore possibilities for capacity building with Member States' competent organisations and gradually increase the number of organ systems assessed. Depending on the outcome of the prioritisation exercise, it is expected that a first retrospective CRA will have been delivered for all relevant organ systems by 2026 at earliest, and by 2030 at latest.
- Retrospective assessments will need to be repeated on a regular basis to account for changes in the exposure patterns and possible updates of the CAGs. It is therefore proposed to repeat retrospective CRAs every three years, which is consistent with the 3-year cycle of the EU Multi-Annual Control Programme (MACP) and with the update of CAGs described above. It cannot be excluded, however, that exposure patterns will change yearly. EFSA therefore issued a statement in the first quarter of 2021, comparing cumulative exposure to pesticides for the reference periods 2014-2016 and 2016-2018<sup>19</sup>. Furthermore, experience has demonstrated that the outcome of CRA of pesticides is driven by a small number of pesticides. EFSA will therefore move towards a gradual integration of probabilistic risk assessment into the annual report on pesticide residues, which will allow EFSA to better identify possible changes in exposure patterns of single pesticides. When such changes are observed, a possible deviation from the 3-year cycle will be considered.

## Prospective cumulative risk assessment

Only retrospective CRAs have been performed so far and the development of prospective scenarios is required in order to understand how new authorisations may impact on cumulative risks estimated under the retrospective assessments. Such prospective scenarios will be applicable, for example, to the assessment of new MRLs (e.g. those under Article 10 of Regulation (EC) No 396/2005), to the approval processes for new active substances under Regulation (EC) No 1107/2009 and, possibly, to the authorisation decisions for plant production products at Member States level.

The implementation of prospective CRA will proceed as follows:

- EFSA and RIVM, in close cooperation with the Commission and Member States, are currently investigating the appropriateness of different prospective scenarios by means of case studies. A scientific report is expected to be published by mid-2021 and will serve as a basis for the subsequent implementation of prospective CRA.
- Implementation of prospective CRA in regulatory decision-making will need thorough discussions with risk managers and assessment of its possible consequences in the decision-making processes. To this end, a specific experts' group comprising experts from EFSA, the Commission and Member States will meet at least once per year, followed up by the regular meetings of the Standing Committee for Plants, Animal, Food and Feed. This working group

<sup>17</sup> EFSA, 2021. *Scientific report on the cumulative dietary risk assessment of chronic acetylcholinesterase inhibition by residues of pesticides*. EFSA Journal 2021;19(2):6392, 151 pp. <https://doi.org/10.2903/j.efsa.2021.6392>

<sup>18</sup> EFSA PPR Panel, 2009. *Scientific Opinion on risk assessment for a selected group of pesticides from the triazole group to test possible methodologies to assess cumulative effects from exposure throughout food from these pesticides on human health on request of EFSA*. EFSA Journal 2009;7(9):1167. DOI:[10.2903/j.efsa.2009.1167](https://doi.org/10.2903/j.efsa.2009.1167)

<sup>19</sup> EFSA, 2021. *Statement on the comparison of cumulative dietary exposure to pesticide residues for the reference periods 2014–2016 and 2016–2018*. EFSA Journal 2021;19(2):6394, 28 pp. <https://doi.org/10.2903/j.efsa.2021.6394>

will define the necessary technical parameters (work ongoing, expected finalisation by end of 2021/begin 2022) that will serve risk managers to take decisions and evaluate possible risk management options, e.g. actions to be taken when the risk cup is full, but where applications for new MRLs are received. However, before such a methodology can be implemented in practice, all options must be carefully assessed. To gain such experience with practical implementation, a “mock” assessment based on a real application for a substance (e.g. through article 6 of Regulation (EC) 396/2005) will be selected as an example during 2022 and carried through the risk assessment and risk management process following the established parameters to mimic and evaluate the process and to define possible further needs for data and/or procedures. Once the above decisions have been taken, a gradual implementation in risk management practice will be envisaged for existing CAGs first and later be extended to additional GAGs.

- To ensure an efficient and transparent implementation of the agreed scenarios in a regulatory environment, EFSA will explore the possibility of a renewal of its partnership with RIVM, possibly involving other Member States’ competent organisations. This partnership will be dedicated to the development and maintenance of an open source MCRA software with connection to the most relevant input data (where possible). Simplified interfaces for standard regulatory users will also be developed.

## Integration of non-dietary exposure

Non-dietary exposure of operators, workers, residents and bystanders to pesticides is currently calculated by means of the OPEX tool<sup>20</sup>. The tool draws on data from 34 validated exposure studies to provide deterministic estimates of non-dietary exposure under specific conditions of use. This tool is currently under revision to include the additional scenario of exposure from use of plant protection products in greenhouses and is expected to be delivered by end 2021.

Although this tool will be used as a starting point, further methodological developments will be required for the integration of non-dietary exposure into the CRA of pesticides. Like the approach followed for the dietary risk assessment, EFSA will first focus on the integration of non-dietary exposure into retrospective CRAs, which will provide a clearer view on the risks associated to pesticides in use. This will provide a solid basis for the subsequent development of prospective scenarios aiming at predicting cumulative risks within regulatory decision-making on e.g. new approvals of active substances and product authorisations.

To facilitate the integration of non-dietary exposure into retrospective CRA, EFSA will initiate the following development activities from 2022 onwards:

- EFSA will assess whether the CAGs established for dietary CRA can be applied to non-dietary CRA and whether synergistic effects can be excluded based on low exposure levels (like for the dietary exposure). This activity may be undertaken by the EFSA PPR Panel.
- EFSA will identify available sources of data to calculate non-dietary exposure (e.g. surveys on the use of pesticides at operator/worker level<sup>21</sup>, ESTAT data, information gathered by Member States and published literature) and priorities for the generation/collection of additional data. This will be part of a research project, for instance under RACEMiC, aiming at inventorying data sources for the estimation of non-dietary exposure to multiple chemicals in general. Possible exchange of data with PARC will also be considered.
- EFSA will explore the availability of a model for combining dietary and non-dietary exposure and possible integration of that model, together with the OPEX calculator, into the MCRA software. This activity may be carried out using the partnership dedicated to the development and maintenance of an open source MCRA software (see above)

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<sup>20</sup> EFSA, 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874. DOI:[10.2903/j.efsa.2014.3874](https://doi.org/10.2903/j.efsa.2014.3874)

<sup>21</sup> EFSA External Scientific Report, 2012. *Collection and assessment of data relevant for non-dietary cumulative exposure to pesticides and proposal for conceptual approaches for non-dietary cumulative exposure assessment*. EFSA Supporting Publications 2012:EN-346. DOI:[10.2903/sp.efsa.2012.EN-346](https://doi.org/10.2903/sp.efsa.2012.EN-346)

## Annex – Questions & Answers

### **1. Will EFSA conduct a cumulative risk assessment for all organ systems?**

Yes. In the first quarter of 2022, as part of the prioritisation method, EFSA will deliver a cumulative risk assessment for all organ systems. Yet, this assessment will rely on a conservative approach, also referred to as the Hazard Index (HI), which is expected to overestimate risks of combined toxicity. This first-tier assessment will therefore allow EFSA to differentiate organ systems that do not require a refined cumulative risk assessment, from organ systems that require the establishment of specific cumulative assessment groups (CAGs).

### **2. Will EFSA establish one cumulative assessment group per organ system?**

No. As explained above in question 1, CAGs will be established only for organ systems requiring a more refined cumulative risk assessment. In such case, CAGs will be established for each toxicological effect of relevance for combined toxicity. The number of CAGs per organ will depend on the number of relevant effects that may be observed within that organ. Whereas five effects were previously found to be relevant for the nervous system, only two effects were considered relevant for the thyroid.

### **3. How did or will EFSA decide on the organ systems to be addressed first?**

The organ systems to be assessed for cumulative risks are currently selected based on previous experiences and assessments, where potential risks for a certain organ or effect had been reported (e.g. risks for acute craniofacial malformations associated with the use of triazole pesticide).

In 2021, EFSA will implement a prioritisation method (see also questions 1 and 5) that will allow the selection of organ systems in a more systematic way. For each organ system, both the chronic and acute HI will be calculated. The organ system with the highest HI, regardless whether this is a chronic or an acute HI, will be selected with the highest priority for further refinement.

### **4. Why does it take so much time to perform cumulative risk assessments?**

The establishment of CAGs for specific effects is a laborious process. In a first step, a mapping of all relevant target organs and associated effects needs to be performed for each pesticide. In a second step, experts need to select effects that are relevant for cumulative risk assessment and define indicators for characterising the toxicological potency of pesticides causing those effects. To complete the process, study results are collected in accordance with the agreed indicators and the potency of each pesticide is characterised. This last step does not only require extensive expert judgement, it also requires manual data extraction and frequent consultation of original study reports.

Once the CAGs are established, combined exposure to the relevant pesticides is calculated and associated risks are estimated. These calculations make use of complex modelling techniques. To provide risk managers with the most complete picture possible, an analysis is also conducted to identify limitations in scientific knowledge and evaluate implications for scientific conclusions. This uncertainty analysis is carried out by means of a rigorous elicitation of expert knowledge.

### **5. How will the prioritisation method help to speed up the process?**

The prioritisation method, which will be deployed in 2021, will consist of two parts.

A probabilistic risk assessment will be carried out for each pesticide individually (around 500 in total). In accordance with the recommendations of the World Health Organisation (WHO), only the pesticides

that exceed a certain threshold of risk, will be considered for cumulative risk assessment.<sup>22</sup> To ensure that the selected threshold will provide adequate protection to the most vulnerable consumers (i.e. in terms of age and consumption habits), a validation of this approach is currently ongoing. Nevertheless, preliminary estimations have indicated that this screening may reduce the number of pesticides to be assessed by 50 to 70%.

Pesticides that exceed the above threshold, will be grouped on the basis of the target organ and a cumulative risk assessment will be carried out for each target organ. As explained above in question 1, assessments for the target organs may be used as a first-tier assessment to identify organs that do not need to be refined for toxicological effects.

Hence, the prioritisation method is expected to reduce the number of CAGs that need to be established and the number of pesticides for which toxicological data need to be collected.

## **6. Are there other ways to speed up the process?**

Yes. The toxicological data required for the establishment of CAGs are currently not available in a structured and searchable data format. This requires a manual extraction of the data from available assessment and study reports. In the framework of the Transparency Regulation,<sup>23</sup> EFSA will implement the electronic submission of applications and, for pesticide applications, the IUCLID software will be used. This will allow EFSA to automate extraction of the relevant data and to concentrate its resources on the appraisal of the data. A new release of IUCLID, scheduled for October 2021, will include further format alignments with the pesticides area. It is expected that in 2023 a sufficient number of admissible dossiers will be available in EFSA to put automated data extraction procedures into production. This will allow EFSA to concentrate resources on the appraisal of the data.

## **7. Can the work be shared with other organisations?**

Yes. One of the main objectives in 2021 will be to set up partnerships with Member States' competent authorities, who will support EFSA in establishing CAGs and conducting cumulative risk assessments. Nevertheless, conducting cumulative risk assessment covers a wide range of niche areas where expertise throughout the EU is still limited. The partnership will therefore primarily focus on knowledge transfer in 2022 with the aim of a gradual increase of the assessment capacity from 2024 onwards.

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<sup>22</sup> WHO (World Health Organisation), 2019. Expert Consultation on Dietary risk assessment of chemical mixtures. Risk assessment of combined exposure to multiple chemicals. WHO, Geneva, 16-18 April 2019. [https://www.who.int/foodsafety/ar-eas\\_work/chemical-risks/Euromix\\_Report.pdf?ua=1](https://www.who.int/foodsafety/ar-eas_work/chemical-risks/Euromix_Report.pdf?ua=1)

<sup>23</sup> [OJ L 231, 6.9.2019, p. 1-28](#)