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## ANNEX 5

### Theme (concept) paper on Risk Assessment of Combined Exposure to Multiple Chemicals (RACEMiC)

**Revised theme paper in light of the comments received from the European Commission (DG SANTE, JRC), ENVI Agencies, EU Member States and EFSA's Scientific Committee members in the phases 1 & 2 of EFSA's consultation process**

#### ***Vision:***

- By 2030, EFSA and partners will be equipped for the routine implementation of human health risk assessment to multiple chemicals, across EFSA's domains of activity. Harmonised tools and consolidated data will be available for a structured and efficient assessment of both dietary and non-dietary exposure to multiple chemicals. Available methods will be fit-for-purpose and address requirements from the sectoral legislations.

#### ***Scope and objectives:***

- The main objective is to develop and implement a harmonised approach for the assessment of human health risks resulting from both dietary and non-dietary exposure to multiple chemicals. The proposed theme will therefore be divided in four work packages: methods development, tools harmonisation, data consolidation and implementation.
- In a first instance, EFSA will screen the deliverable of previous projects to identify relevant methodological developments in this area. These methods will then be translated into practical and harmonised tools that can be applied across all domains of EFSA, and necessary input data will be consolidated into structured formats. In a second instance, EFSA will continue to monitor other ongoing projects and identify possible needs for further innovation and methodological development in both hazard and exposure assessment.
- In order to ensure a steady and manageable progress, risk assessment to multiple chemicals will be implemented with a stepwise approach. EFSA will first prioritise the routine risk assessment of dietary exposure to multiple pesticides, with a subsequent integration of non-dietary exposure to pesticides. Methods to prioritise other chemicals will also be developed and, building on the experience gained in the area of pesticides, the scope of the implementation plan will be extended to other chemicals.
- In view of increasing the outreach towards national competent authorities, EFSA will promote the implementation of the methods and tools developed and provide adequate training, where necessary.



### **Opportunities:**

- Available methods are already well described in the guidance of EFSA Scientific Committee (2019<sup>1</sup>), which includes several recommendations for future methodological developments. Together with the recent pilot assessments in the area of pesticides and the practical experience gained by other European and international partners, EFSA will have a strong basis to identify all requirements for further guidance and methodological development. All proposals for methodological developments will be collected, prioritised and potential partners for innovative research projects will be identified.
- The HORIZON 2020 Framework Programme for research has delivered several projects which may be relevant for the risk assessment of combined exposure to multiple chemicals (e.g. EuroMix, Human Exposome Project, HBM4EU and FOODSAFETY4EU). These projects provide a good opportunity to identify most recent methodological developments in this area and will also support EFSA in the identification of possible future developments and innovation projects.
- Software tools for the assessment of multiple chemicals have been developed in different frameworks and are now available on different platforms (e.g. MCRA Software, EuroMix Toolbox, Danish Mixture Calculator, MYCHIF, BIKE etc). To ensure proper use of the different calculators, all tools will be brought together into a harmonised, well-structured (i.e. modular) and fully transparent (i.e. open source) platform. After deployment of the common platform, new additional modules will be added to address new methodological developments.
- Over the recent years, EFSA made progress on the harmonised collection of food consumption data and chemical occurrence data in food. These data are adequate for assessing dietary exposure to multiple chemicals because they allow identification of co-occurring chemicals and foods that are consumed simultaneously. Regarding the combined toxicity of multiple chemicals, however, structured data are still limited. To ensure a better access to the relevant toxicological data, EFSA will further expand its [OpenFoodTox Database](#)<sup>2</sup>, which is currently at EU level the most comprehensive open-access repository of toxicity information.
- Several national competent authorities have reported the availability of chemical occurrence data in (drinking) water and other data that may be useful for the assessment of non-dietary exposure. This will support EFSA in reviewing availability of relevant occurrence data and identifying needs for further monitoring data in this area. This will need to be considered together with activities planned under the umbrella of environmental risk assessment.
- The recent pilot assessments on cumulative risk assessment for pesticides (EFSA, 2020a<sup>3</sup>; EFSA, 2020b<sup>4</sup>) are a solid basis for the future implementation in this area. Based on this experience EFSA is developing a screening method for a leaner approach in elaborating cumulative assessment groups. The Commission and EFSA will develop an action plan by

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<sup>1</sup> EFSA Scientific Committee, More SJ, Bampidis V, Benford D, Bennekou SH, Bragard C, Halldorsson TI, Hernandez-Jerez AF, Koutsoumanis K, Naegeli H, Schlatter JR, Silano V, Nielsen SS, Schrenk D, Turck D, Younes M, Benfenati E, Castle L, Cedergreen N, Hardy A, Laskowski R, Leblanc JC, Kortenkamp A, Ragas A, Posthuma L, Svendsen C, Solecki R, Testai E, Dujardin B, Kass GEN, Manini P, Jeddi MZ, Dorne J-LCM and Hogstrand C, 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, 77 pp. <https://doi.org/10.2903/j.efsa.2019.5634>

<sup>2</sup> <http://www.efsa.europa.eu/en/press/news/180719>

<sup>3</sup> EFSA (European Food Safety Authority), 2020a. Scientific report on cumulative dietary risk characterisation of pesticides that have acute effects on the nervous system. EFSA Journal 2020;18(4):6087, 79 pp. <https://doi.org/10.2903/j.efsa.2020.6087>

<sup>4</sup> EFSA (European Food Safety Authority), 2020b. Scientific report on the cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid. EFSA Journal 2020;18(4):6088, 71 pp. <https://doi.org/10.2903/j.efsa.2020.6088>



the end of 2020 that would set out priorities for the ongoing work on method development and the subsequent implementation of the methodology for the assessment of combined exposure to pesticides.

- A draft roadmap on the assessment of human health risks from combined exposure to multiple chemicals was already elaborated by EFSA and discussed with Member States under the umbrella of EFSA's Advisory Forum. This draft document already provides a solid basis for the development of a more comprehensive roadmap within the current framework.

### **Cooperation:**

- A [European Partnership for the Assessment of Risk from Chemicals \(PARC\)](#)<sup>5</sup> and the additional calls for proposals under the [Green Deal](#)<sup>6</sup> priorities in 2020 (e.g. call 8 topic 2 "Fostering regulatory science to address chemical and pharmaceutical mixtures: from science to evidence-based policies") is currently under preparation with Horizon Europe aiming to start in 2022 and 2021, respectively. This partnership may be considered for funding innovative research projects which may support the development of new methods in the area of multiple chemicals.
- Several national competent organisations have acquired valuable experience in the development of tools and calculators, specifically designed for the assessment of multiple chemicals (i.e. RIVM, DTU, ANSES, Finnish Food Authority). Harmonisation efforts were also undertaken in the framework of the EU-funded project EuroMix, which involved additional organisations such as BfR, BPI, FERA, HSE, etc. These organisations may be considered by EFSA to set up a wider partnership specifically dedicated to the elaboration of a collaborative platform for harmonised tools on multiple chemicals risk assessment.
- EFSA already has a framework contract with Istituto Mario Negri for the enhancement of the OpenFoodTox Database and EFSA previously cooperated with DTU for the collection of toxicological data in the area of pesticides. These successful experiences are a solid basis for EFSA to build another partnership on the consolidation of toxicological data required for multiple chemicals risk assessment. This partnership could include other Member States organisations that may be specialised/interested in certain effects or organ systems
- The European Green Deal announces the development of a chemical strategy for sustainability in 2020, which will require the EU agencies and scientific bodies to move towards a process of one assessment for one substance (avoiding contradicting assessment outcomes from the different agencies). ECHA, EMA and EFSA will therefore need to strengthen their cooperation in view of developing risk assessment approaches that address combined exposure via multiple routes. The capacity to assess risks for combined dietary and non-dietary exposure will be the first step towards a more holistic approach addressing combined exposure to multiple chemicals. Activities of JRC and EEA, which mainly addresses non-dietary exposure to chemicals, will need to be monitored as well.
- EFSA will cooperate with international partners WHO and OECD to ensure harmonisation with their assessment frameworks for multiple chemicals. Furthermore, EFSA will explore possibilities to re-use work from non-EU partners. This includes the US EPA's Adverse Outcome Pathways Database (which may serve as a basis for future enhancement of OpenFoodTox) and Health Canada's cumulative risk assessment of triazole pesticides (which may be of relevance for EFSA's assessment of cranio-facial malformations scheduled in

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<sup>5</sup>[https://ec.europa.eu/info/sites/info/files/research\\_and\\_innovation/funding/documents/ec\\_rtd\\_he-partnerships-chemical-risk-assessment.pdf](https://ec.europa.eu/info/sites/info/files/research_and_innovation/funding/documents/ec_rtd_he-partnerships-chemical-risk-assessment.pdf)

<sup>6</sup>[https://ec.europa.eu/info/research-and-innovation/strategy/european-green-deal/call\\_en](https://ec.europa.eu/info/research-and-innovation/strategy/european-green-deal/call_en)



2021). EFSA's cooperation with international partners will be fostered through the International Liaison Group on Methods for Risk Assessment of Chemicals in food (ILMERAC).

***Impact for EFSA and partners:***

- Enhanced capability to produce fit-for-purpose risk assessments of combined exposure to multiple chemicals to better safeguard public health, especially in the area of pesticides as recently emphasized in the [Report from the Commission to the European Parliament and the Council on the Evaluation of Regulation \(EC\) No 1107/2009 and Regulation \(EC\) No 396/2005](#)<sup>7</sup>.
- Preparedness for future requirements on the assessment of multiple chemicals, which may arise within or across food sector areas.
- Co-ownership of tools, data and processes used by partners will help avoid duplication of assessments by Member States and better accept the outcome of EFSA's assessments.
- Coherent and harmonised approaches for the assessment of multiple chemicals, both at European level and internationally.

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<sup>7</sup> [https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides\\_ppp\\_report\\_2020\\_sw\\_d\\_en.pdf](https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_report_2020_sw_d_en.pdf)