



European
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JRC SCIENCE FOR POLICY BRIEF

Supporting EU policies with independent evidence throughout the whole policy cycle

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Something from nothing? Ensuring the safety of chemical mixtures

Headlines

- Humans and the environment are exposed to a cocktail of chemicals from different sources.
- Combined exposure to multiple chemicals can lead to health/environmental effects even if single substances in the mixture do not exceed safe levels.
- The assessment and management of mixtures is only partly covered by current legislation, which focuses on single substances in isolated sectors.
- Methodology to address mixture risks is available, yet many knowledge gaps need to be filled. In particular, real co-exposure patterns are mostly unknown.
- JRC is performing research on new strategies to assess the combination effects of chemicals.

The problem

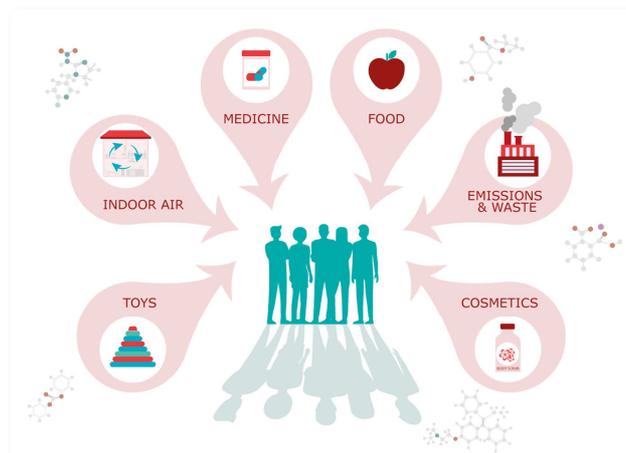
Humans and wildlife are exposed to an infinite number of different combinations of chemicals, via food, consumer products and the environment.

Combined exposure to multiple chemicals can lead to unacceptable effects, even if single substances in the mixtures are below their individual safety thresholds.

The assessment and management of chemical mixtures is only partly covered by current legislation, which focuses on single substances in isolated sectors.

In particular, while formulated products are covered, unintentional mixtures are not

consistently addressed. Their composition is often unknown and changes over time, making them difficult to regulate. The assessment of unintentional mixtures is therefore usually limited to specific legislative sectors, such as pesticide residues in food.



How to assess mixtures?

Mixture risks are assessed either by testing the whole mixture (e.g. in effect-based monitoring of surface water) or by predicting the combined risk based on concentration and effect information of the individual components in the mixture (e.g. in the assessment of dioxins and dioxin-like compounds in food and feed).

Several international frameworks are available for the assessment of chemical mixtures, e.g. from [WHO/IPCS](#).

However, there are major knowledge gaps hampering their application. The [EC Communication on "Combined effects of chemicals – chemical mixtures" \(2012\)](#)

This brief is based on the JRC report: Cross-sector EU approach to combined exposures and effects. JRC110683, 2018.

Chemical Mixtures: Terminology

Combined exposure: Exposure to multiple chemicals via one or several sources and routes, also called exposure to **chemical mixtures**.

Aggregate exposure: Sum of exposures to one chemical via several sources and routes.

Intentional mixtures: Manufactured products, e.g. pesticide/biocide formulations, cosmetic products, laundry detergents.

Unintentional mixtures: Coincidentally formed and variable mixtures originating from one or several sources, such as surface water contaminations or pesticide residues in food.

called for an improved understanding of the exposure to chemical mixtures, the toxic effects, modes of action and potential interactions of chemicals, as well as the identification of specific mixtures to be addressed with priority.

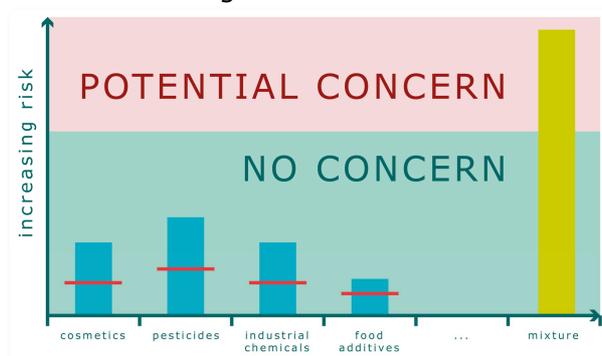
Specific challenges

Combined exposure: Unravelling the composition of unintentional mixtures remains difficult. Neglecting relevant mixture constituents can lead to an underestimation of risks. However, chemical monitoring data are scarce, although becoming more consistently available via the EC platform [IPCHEM](#). Moreover, chemical analyses only measure the chemicals expected to be present. Another challenge is to take into account sequential exposures at different moments in time. Biomonitoring chemical concentrations in wildlife or humans is a means to identify realistic co-exposure. Modelling tools for exposure assessment need to be further developed.

Combined effects: It is not feasible to test all possible mixtures experimentally, considering the large number of potential chemical combinations. On the other hand, prediction of mixture effects based on the individual chemicals is often limited by lack of knowledge of their toxicity and toxic modes of action. Therefore, smart strategies and more efficient tools are needed, relying less on *in vivo* testing and instead on alternative experimental and computational tools.

Combined risks: Managing the risks from exposure to chemical mixtures presents a policy challenge. Each individual chemical might be at a safe level of exposure, but the combination of chemicals may pose a risk. Even if chemicals within a legislative sector are addressed as mixtures, combined effects from chemicals regulated under different sectors might occur. Thus, risk

management decisions may need to be taken on which chemicals or sources should be subject to restrictions. To cope with the large number of possible mixtures, priority mixtures of particular concern should be identified, as well as the individual chemicals driving their risk.



JRC activities on mixtures

JRC is performing research on the use of alternative (non-animal) methods and new strategies to assess the combination effects of chemicals. Having reviewed current EU regulatory requirements and mixture assessment practices, JRC is currently exploring links between mixtures and diseases, interaction effects of chemicals, as well as the use of biomonitoring data in exposure assessment.

JRC collaborates with five EU funded research consortia focusing on chemical mixture assessment for the environment (SOLUTIONS), human health (EuroMix, HBM4EU), endocrine disruption (EDC-MixRisk) and alternatives to animal testing (EUToxRisk).

JRC also facilitates and provides scientific input to discussions with EU regulators from European Commission DGs and agencies. Furthermore, JRC is actively involved in international initiatives under the auspices of the OECD and the WHO.

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Related JRC reports

Review of case studies on the human and environmental risk assessment of chemical mixtures. [EUR27968](#), 2016.

Scientific methodologies for the assessment of combined effects of chemicals – a survey and literature review. [EUR 27471](#), 2015.

Assessment of mixtures – review of regulatory requirements and guidance. [EUR 26675](#), 2014.