

New concept for identifying chemical combinations with potential health effects

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About 350,000 chemicals are registered worldwide. Some of these can contribute to human exposure to substances and mixtures via products, applications or food. In order to protect people in everyday life and at

work from potentially dangerous chemicals, the legislature has established a comprehensive legal framework. Notably the corresponding acts and regulations mainly cover the evaluation of individual substances and defined mixtures within their respective regulatory silos.

Effects that may result from possible co-exposures, e.g. the simultaneous use of substances across different regulations or due to background exposures from the environment, on the other hand, are more difficult and usually only accessible in retrospect. For the majority of these scenarios, neither an increased toxicity of the relevant substance combinations nor an insufficient protection by the existing regulatory framework can be assumed. In a recently published article, the German Federal Institute for Risk Assessment (BfR) now proposes for the first time a research-based concept for the generic identification of [chemical](#) combinations with potential health relevance. The concept addresses the following questions: 1) Which chemicals actually do realistically occur together and 2) Which of these combinations pose potential health-relevant effects not adequately covered by existing assessment concepts? The aim of the new approach is to provide a feasible approach of identifying potentially health relevant mixtures and background exposures.

The legislator has established a comprehensive legal framework to provide protection from potentially dangerous chemicals and mixtures. Currently, existing legislation provides extensive information on the respective substances within their respective scope of application. However, the corresponding assessments are mostly regulation-specific and deal predominantly with the evaluation of individual substances and defined mixtures as well as possible effects of foreseeable co-exposures within their respective legal scope or clearly defined areas of application only. The assessment of effects that may result from potential co-exposure, such as for example simultaneous use of substances subject to

multiple areas of regulation or environmental background exposure, is more difficult and usually addressed at best retrospectively. However, for most scenarios such co-exposure will not necessarily result in increased toxicity to such an extent that it would not be sufficiently covered by the existing regulatory framework.

Yet, in the interest of continuously improving consumer health protection, there is a need to identify possible substance combinations and unpredictable co-exposures that are potentially relevant to health. The BfR now proposes for the first time a concept for the prospective identification and assessment of such combinations of chemicals. In a first step the concept requires the development of a comprehensive exposure and use matrix across regulatory silos. This matrix can then be examined for possible instances of co-exposure. The substances and mixtures identified therein will subsequently be examined with regard to their toxicological properties and potential for effect-enhancement. The respective hazard ranking and [assessment](#) is performed on the basis of existing data, as well as on the basis of data generated with so-called New Approach Methods and suitable high-throughput bioassays.

By integrating the newly generated data with the verified classic toxicological information, it is possible to identify those [substances](#) and mixtures for which unexpected effects may occur and which are potentially relevant for human health. The proposed concept enables a research- and data-base identification of [health](#)-relevant mixed substance exposures across regulatory silos. Put to practice the [concept](#) would thus help to evaluate existing protection levels as well as to identify potential additional regulatory needs.

The article was published in *Nature Food*.

More information: T. Tralau et al, A prospective whole-mixture

approach to assess risk of the food and chemical exposome, *Nature Food* (2021). [DOI: 10.1038/s43016-021-00316-7](https://doi.org/10.1038/s43016-021-00316-7)

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