

## FAQ

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# What are mixtures of chemicals and what do they mean for health?

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In our complex and industrialised world, people are exposed to a wide range of substances, many of which are man-made, i.e., not of natural origin. Articles of daily use and everyday products usually consist of several substances. If you come into contact with several substances at the same time, you are said to be exposed to mixtures. The German Federal Institute for Risk Assessment (BfR) has compiled selected questions and answers on this topic.

## What is meant by mixtures?

Mixtures are combinations of two or more substances.

## Where do mixtures occur and how do you come into contact with them?

People come into contact with a large number of different substances and mixtures every day in a wide variety of situations through everyday products, residues of plant protection products, disinfectants or undesirable substances in food (so-called contaminants) as well as through contact with the air.

## What are intentional mixtures?

If different substances are deliberately combined in a product, this is referred to as an intentional mixture. They are also often referred to as "formulations". In this case, the composition and concentration of the substances contained are known and have been deliberately chosen so that the product has certain properties (e.g. so that paints or varnishes can be spread easily, cosmetics are waterproof or detergents have a certain fragrance). By using a product, people come into contact with a known and therefore intended mixture of different substances.

## Do intended mixtures pose any health risks?

The manufacturer or distributor of a product in the European Union must ensure that a product is safe for the consumer when used as intended. Otherwise it can not be placed on the market. If we use a single product with an intended - i.e. known - mixture at a given time and use it as intended (i.e. follow its instructions for use or recommended dosage,

depending on the species of the product), no health risks are to be expected. However, manufacturers must also take into account the case of "foreseeable misuse" (e.g. if you also wash your hands with dishwashing detergent contrary to its actual purpose). In the case of toys (e.g. finger paints, play slime), not only the intended use but also the foreseeable use must be safe, taking into account the behaviour of children. This is also the case for biocidal products. Here, foreseeable use is taken into account in the assessment of wood preservatives, for example, if small children chew on treated pieces of wood. In the area of cosmetic products, responsibility for the safety of the cosmetic product lies with the manufacturer, who declares in a so-called "product information file" that the product is safe.

### **What is known about the risk of poisoning from mixtures?**

The vast majority of enquiries received by the German poison centres concern the improper use of products with intended mixtures. For example, accidents involving small children with dishwashing detergents or dishwasher cleaners, descaling agents or laundry detergents are particularly common in the home.

### **Does a mixture of substances have a stronger effect than a single substance?**

Not in principle. Mixtures can have different effects/impact depending on the mechanism of action of the individual substances. There are basically four ways in which substances can interact in a mixture:

- They can have different, independent effects.
- Their effects can add up (additive effect).
- Together they can have a stronger effect than the sum of the individual effects (synergistic effect).
- They can weaken each other's effect (antagonistic effect).

In the case of identical/similar effects, it is currently assumed that the effects generally add up. The prerequisite for this is that the substances ingested have the same mechanism of action and were absorbed by the organism at a relevant time.

### **In which areas is the risk assessment of mixtures already routinely carried out?**

**Plant protection products:** Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market requires that cumulative and synergistic effects must be taken into account. A guideline on the cumulative assessment of plant protection products was developed at the BfR, based on international discussions at the European Food Safety Authority (EFSA) and the European Chemicals Agency (ECHA), and published in 2014. The procedure has been used at the BfR in authorisation procedures for plant protection products since 2017. Essentially, the aim is to cumulatively assess various active substances in a plant protection product or in an authorized tank mixture in a multi-stage procedure. To this end, both the exposure of users (such as farmers who apply the product in the field) and the acute exposure of consumers (who ingest the residues via food) are considered, so that the groups most exposed to these mixtures are taken into account. Since 1 September 2020, workers and uninvolved third parties (residents and bystanders) have also been included in these considerations.

From the BfR's point of view, there is already a large body of scientific knowledge on the effects of multiple residues of plant protection products. There is no reason to assume that the assessments currently carried out are not sufficiently conservative (i.e. they tend to overestimate the risk). Nevertheless, these testing and assessment strategies are constantly being developed and are the subject of research projects.

**Biocidal products:** Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products requires cumulative and synergistic effects to be taken into account in the health risk assessment. A procedure for assessing such effects is described in the European Chemicals Agency (ECHA) [guidance document](#) on the assessment of biocides and is applied in the authorisation procedure for biocidal products. The aim is to consider the active substances and toxicologically relevant co-formulants / contained in a biocidal product together in order to cover possible additive or synergistic effects. The procedure considers both short-term and long-term exposure and is used at the BfR for the assessment of non-professional users and uninvolved third parties. The assessment for occupational users is carried out by the Federal Institute for Occupational Safety and Health (BAuA).

**Food contact materials:** The Framework Regulation (EC) No. 1935/2004 regulates for all items and materials in contact with food that, when used as intended or in a foreseeable manner, they must not release substances into food in amounts that could endanger the health of consumers. This therefore also applies to mixtures of substances. In addition, in particular for plastic food contact materials (FCMs) European Regulation (EU) No. 10/2011 applies. It contains a list of substances that may be used in the manufacture of plastic FCMs and defines conditions of use and, where applicable, migration (i.e. release) limits (i.e. the maximum amount of a substance that may migrate into food). Before substances are included in this list, the European Food Safety Authority (EFSA) carries out a risk assessment. If data is available, this assessment also takes into account the toxicity of the mixture.

In its assessment of substances for inclusion into the [BfR recommendations on food contact materials](#), the BfR also takes into account data on the mixture toxicity of substances - where available - and sets corresponding summation guide values for the tolerable transition into food or use of substances.

**Cosmetic products:** According to the definition in Cosmetics Regulation (EC) No. 1223/2009, cosmetic products are "substances or mixtures intended to come into external contact with parts of the human body (skin, hair system, nails, lips and external intimate regions) or with the teeth and mucous membranes of the oral cavity for the sole or vast purpose of cleansing, perfuming, altering the appearance, protecting, maintaining in good condition or correcting body odour."

Mixtures within the meaning of the Regulation are "mixtures or solutions consisting of two or more substances." According to Article 3 of the Regulation, cosmetic products made available on the market must be safe for human health under normal or reasonably foreseeable conditions of use. The regulation ensures this by requiring that the cosmetic product has undergone a safety assessment before being placed on the market and that a safety report for the cosmetic product has been drawn up in accordance with Annex I. The safety assessment must be carried out both for the individual ingredients and for the final product, so mixture toxicity is also taken into account in the safety assessment.

## What research projects are there on the subject of mixing effects?

International research projects have been working intensively on this topic for years. By actively participating in research projects on the risk assessment of mixtures, the BfR supports the further development of concepts and the necessary tools.

In the past, the BfR has participated in the following projects, among others:

- EuroMix: (EU H2020) Development and implementation of an internationally harmonised approach for the risk assessment of chemical mixtures through an integrated testing strategy (<https://www.euromixproject.eu/>)
- Combiomics 1 & 2: Combiomics (BMBF/eTOP) Development and application of multilevel omics methods to analyse the toxicity of mixtures ([more info](#))

The BfR is currently involved in the following projects:

- PANORAMIX (since 2021): An international research project funded by the European research framework programme "Horizon 2020", which investigates whether real-world random mixtures of various substances in umbilical cord blood, drinking water or food can impair the child's nervous system development or reproductive capacity. Within the project, the BfR is leading work package 7, which is specifically concerned with the question of whether the existing assessment system, which is based on the testing of individual substances, adequately covers health risks due to potential combination effects (<https://panoramix-h2020.eu>).
- RaceMic (EFSA Tender) Development of a roadmap for action on risk assessment of combined exposure to multiple chemicals
- Since 2022: "Partnership for the Assessment of Risks from Chemicals"; PARC is the largest EU research and innovation programme to date for the refinement of toxicological consumer protection and addressing new challenges in chemical safety. Together with ANSES as the French partner authority, the BfR is leading the work package for toxicology and is also involved in several other work packages. Possible mixing effects are a key component of this.

In addition, the BfR has established a junior research group on the topic of mixture toxicity.

## About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. The BfR advises the Federal Government and the States ('Laender') on questions of food, chemicals and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.

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