German Federal Institute for Risk Assessment

Sulphur dioxide and sulphites: EFSA re-evaluation identifies health risks at high consumption; data situation still incomplete

Communication no. 039/2022 dated 20 December 2022, updated 11 January 2023

In the European Union, the use of sulphur dioxide (E 220) as well as salts containing sulphur dioxide (sulphites; E 221–228) as food additives is permitted in certain foodstuffs. Maximum level apply in each case. Sulphur dioxide and sulphites are added to foodstuffs as preservatives in order to inhibit the growth of fungi, bacteria, and yeasts. They are also added to certain fruit and vegetable products as an antioxidant in order to reduce or prevent browning. Sulphites also occur naturally in the body and in various foods. In the human body, sulphites are converted into the unproblematic sulphate with the help of the enzyme sulphite oxidase.

Sulphur dioxide acts as an irritant. In some people, contact with sulphur dioxide or sulphites can lead to reactions of the immune system – especially pseudoallergies. For example, individual studies show that a certain proportion of the asthma and/or rhinitis patients studied experience bronchial reactions and/or break out in hives after consuming foodstuffs containing sulphite. It is estimated that 5–10% of adult chronic asthmatics in Germany react to sulphites in varying degrees of severity. In contrast to allergic reactions, it is not proteins but rather small molecular substances such as sulphites or sulphur dioxide that cause the pseudoallergic reaction.

The European Food Safety Authority (EFSA) subjected the substances to a renewed risk assessment in 2016 as it routinely does for all food additives approved in the EU before 2009. The EFSA indicated that limited data are available. The validity of the previously derived acceptable daily intake (ADI) was thus limited in time *(temporary ADI*). In 2022, the EFSA carried out a new risk assessment. Animal studies showed indications of the potentially adverse health effects of sulphites on the central nervous system (e.g. a delayed response of nerve cells to stimuli, which is an early sign of nervous system dysfunction). Because no adequate new data have become available since the last assessment, the “temporary ADI” value was withdrawn.

Instead, the EFSA calculated a MoE *(Margin of Exposure)* value. This is the ratio between the dose that leads to a certain (small) adverse effect in animal studies and the amount of the substance to which one is estimated to be exposed (exposure). From the point of view of the EFSA, the MoE value in this case should be at least 80. In other words, if the MoE value is less than 80, there are health concerns. The exposure assessments of the EFSA have shown that the MoE is less than 80 for all age groups (except adolescents).

The EFSA points out that aspects such as immune system reactions to sulphites should be further investigated because of existing knowledge gaps. The Federal Institute for Risk Assessment (BfR) agrees with these conclusions and reiterates the need for an improved availability of data in order to be able to carry out a more robust risk assessment of sulphites.

In its risk assessment in 2016, the EFSA had changed the group ADI value of 0.7 milligrams of sulphur dioxide equivalents per kilogram of body weight (mg/kg BW) to a temporary group ADI value, stating that further data were needed for a more robust derivation of a group ADI value. The European Commission subsequently called on industry to provide further data. For its risk assessment in 2022, however, EFSA could not rely on adequate new data. Consequently, EFSA withdrew the temporary group ADI value and instead applied the MoE concept for its calculations. The EFSA uses the term “Margin of Exposure (MoE)” not only for the

risk characterisation of DNA-reactive genotoxic carcinogens for which no threshold for an effect can be assumed but also for substances such as sulphur dioxide and sulphites for which an effect threshold (a dose below which the effect does not take effect) can be assumed.

The BfR, on the other hand, uses the term “Margin of Safety (MoS)” for the risk characterisation of such substances. The MoE is the ratio between an experimentally determined reference point and the amount of the substance to which one is estimated to be exposed (exposure). For sulphur dioxide and sulphites, this reference point was determined as the “Benchmark Dose Lower Confidence Limit (BMDL)” based on the dose-effect relationship observed in animal experiments. From the point of view of the EFSA, the MoE value in this case should be at least 80. In other words, if the MoE value is less than 80, there are health concerns.

In addition to sulphur dioxide (E 220), the sulphites sodium sulphite (E 221), sodium hydrogen sulphite (E 222), sodium metabisulphite (E 223), potassium metabisulphite (E 224), calcium sulphite (E 226), calcium hydrogen sulphite (E 227), and potassium hydrogen sulphite (E 228) are currently permitted for use as food additives. As preservatives, they can extend the shelf life of certain foods and as antioxidants, slow the reaction of foods in contact with atmospheric oxygen (oxidation), and thus change their appearance. For example, dried apricots retain their orange colour when they have been “sulphurated”; they can otherwise turn dark without this treatment.

If they are added to foodstuffs, EU law requires this to be stated on the packaging. In accordance with Regulation (EU) No 1169/2011, if sulphur dioxide or sulphites are present in foodstuffs, regardless of the type of use, they must be labelled from a concentration of 10 milligrams per kilogram (mg/kg) (or 10 milligrams per litre (mg/L)) (as total sulphur dioxide present) because of a possible intolerance towards them. In the case of packaged foodstuffs, this is done in the list of ingredients by stating the class name (“preservative” or “antioxidant”) and the name of the substance or the E-number, e. g. with “Antioxidant: sodium metabisulphite”. In the case of wine, “*contains sulphites*” indicates that the wine has been treated accordingly. In the food service industry, the presence of sulphur/sulphites is indicated in the food or drink menu.

To the risk assessment of the EFSA: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7594

Further information on the subject of food additives on the BfR website

A–Z index: https://www.bfr.bund.de/en/a-z_index/food_additives-130074.html

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About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the German Federal Ministry of Food and Agriculture (BMEL).

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The BfR advises the Federal Government and the German federal 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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