German Federal Institute for Risk Assessment

Draft Opinion on Bisphenol A: The BfR Comments on the Reassessment by the European Food Safety Authority

Updated BfR Communication No. 020/2022 of 26 July, 2022[1]

Bisphenol A is a chemical compound used as a raw material for the manufacture of polycarbonate plastics and epoxy resins. The European Food Safety Authority (EFSA) has reassessed possible health risks associated with Bisphenol A and published the result for public comment on December 15, 2021.[2] All comments received can be viewed on EFSA's website.[3]
The tolerable daily intake (TDI) newly derived by EFSA is 0.04 nanograms of Bisphenol A per kilogram of bodyweight per day. The TDI value describes the amount of a substance that can be ingested daily over a lifetime without any recognisable health risk. The new value is around 100,000 times lower than the temporary health based guidance value previously given by EFSA. Although the total intake of Bisphenol A in the population has been declining for years, it exceeds the new TDI for people of all ages by several orders of magnitude.
Numerous new studies have been published since EFSA set the temporary TDI in 2015. EFSA lowered the TDI primarily based on evidence from studies in mice. According to these, the offspring of dams that had ingested Bisphenol A during and after pregnancy showed an altered proportion of certain immune cells. The BfR has reviewed the EFSA draft opinion and identified points of criticism which, in the opinion of the BfR, call into question the risk assessment carried out by EFSA. The following are particularly noteworthy:
With the exception of those on genotoxicity, the studies considered in the EFSA assessment are exclusively from the years 2013 to 2018. Older and more recent studies – including some of higher quality and with significantly different results than the studies considered in the EFSA assessment – were not included. The decision as to whether or not a study was taken into account for the risk assessment as well as the weighting of the studies based on qualitative requirements were not done consistently.
EFSA has identified the increase in the proportion of so-called Th17 cells as the critical toxicological effect. However, there is currently no evidence that the observed increase has any adverse effects on the mice studied. Moreover, the relevance of the results to human health is questionable.
Due to these and other points of criticism, it is the opinion of the BfR that the central points of EFSA's opinion need to be revised. All available studies should be included according to their quality and an up-to-date exposure estimate should be carried out.

The risk assessment of Bisphenol A has been the subject of scientific and public discussions worldwide for years. In January 2015, EFSA published an expert opinion on the assessment of the health risks from Bisphenol A in food. Therein, the use of Bisphenol A in food contact materials and articles, such as polycarbonate containers and food cans with inner coatings made of synthetic resins, was identified as an important source of exposure. In July 2016, Bisphenol A was classified as toxic to reproduction (category 1B "May impair fertility") according to the CLP Regulation. As a result, Bisphenol A was identified as a substance of very high concern (SVHC) under the REACH Regulation in January 2017. The REACH Regulation is the European chemicals regulation for the registration, evaluation, authorisation and

[1] Replaces BfR Communication No. 041/2021 of December 15, 2021.

[2] https://www.efsa.europa.eu/en/news/Bisphenol-efsa-draft-opinion-proposes-lowering-tolerable-daily-intake.

[3] https://open.efsa.europa.eu/consultations/a0c1v00000JA9rGAAT, BfR comments from page 66.

restriction of chemical substances. In 2017 and 2018, the substance was additionally identified as an SVHC due to its properties as an endocrine disruptor (exogenous substance that interferes with the hormonal system thereby impairing health of the organism or its progeny) for human health and the environment, respectively.

The TDI of 4 micrograms (equivalent to 4,000 nanograms) per kilogram bodyweight per day published by EFSA in 2015 was considered temporary. The subsequently updated assessment results in a significant reduction in the TDI to 0.04 nanograms per kilogram of bodyweight per day. However, the BfR sees significant deficiencies in relation to the procedure for deriving this new TDI.

- The exclusion of studies published before 2013 or after 2018 from the assessment is contrary to internationally accepted principles of risk assessment (which EFSA also relies on itself). Accordingly, all relevant studies must be used for a scientifically sound assessment. A selection may only be made on the basis of the quality of the respective studies.

- The assessment of the quality and validity of the studies, on the basis of which these were or were not taken into account in the risk assessment, does not appear appropriate in some cases. The usual assessment criteria (also used by EFSA) were not applied consistently. For example, there are methodological deficiencies in some of the key studies, which – in the opinion of the BfR – do not allow the studies to be used for a quantitative risk assessment. In contrast, several studies of higher quality (e.g. in terms of methodology, documentation, and number of animals) were excluded from the assessment for formal reasons. The results of these often contradict the studies used by EFSA as key studies for the assessment.

- The critical toxicological effect on which the TDI was based consists of an increase in the proportion of certain cells in the immune system of the mice; so-called Th17 cells. For this and for several other reported effects, the EFSA statement does not provide evidence that these changes result in any adverse effect in the mice. Current data speaks against this. For example, the CLARITY-BPA research program initiated by the U.S. Food and Drug Administration (FDA) concluded in 2021 that the symptoms associated with Bisphenol A administration on the immune system occurred mostly sporadically, were moderate and not dose-dependent, and over the investigated period of one year did not exhibit an ongoing trend. As a result, the authors concluded that BPA-mediated changes observed are unlikely to compromise immune competence in adult rats.[4]

- It is yet to be clarified whether the effects observed in mice are also relevant for humans. Thus (also in EFSA's opinion), a causal link between Bisphenol A intake and immunological effects in humans has not been proven by any of the studies available to date.

- The estimate of the daily intake of the European population has not been updated by EFSA in its new draft opinion. The exposure estimate is based on data that is now, in most cases, more than ten years old. However, it is known that the intake of BPA in Europe has decreased significantly in recent years.

The BfR expressed these and other points of criticism after examining the EFSA draft as part of the public consultation phase. All comments received are available on EFSA's website.[3]

[4] https://ntp.niehs.nih.gov/ntp/results/pubs/rr/reports/rr18_508.pdf.

Many of the points raised by the BfR have also been addressed by other international risk assessment agencies such as the American Food and Drug Administration (FDA), the Dutch National Institute for Public Health and the Environment (RIVM) or the British Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). For its part, EFSA intends to examine the comments received by the end of 2022 and to revise its opinion as it sees fit.

The use of Bisphenol A for the production of baby bottles made of polycarbonate has already been banned across the EU since 2011. In 2018, the ban was extended to generally include drinking vessels and bottles made of polycarbonate for infants and young children. For all other plastic food contact materials, as well as epoxy resin inner coatings for canned food, a threshold for the transfer of Bisphenol A into food was set on the basis of EFSA's provisional TDI from 2015.

The use of Bisphenol A in thermal paper (e.g. receipts, parking tickets, parcel labels) in concentrations of more than 0.02% has been banned since 2020. In principle, this corresponds to a ban on use, as contents below 0.02 % do not facilitate the desired colour development.

The German authorities are currently preparing a draft proposal that is intended to largely restrict the use of Bisphenol A and other Bisphenols. The draft proposal is to be submitted to the expert committees of the European Chemicals Agency ECHA for examination in 2022.

Further information on the subject on the BfR website:

A-Z Index for Bisphenol A:
https://www.bfr.bund.de/de/a-z_index/bisphenol_a-4745.html

Bisphenol A in everyday products: Answers to frequently asked questions:
https://www.bfr.bund.de/en/a-z_index/bisphenol_a-129760.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 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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