COM Evaluations - 2022

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EFSA assessment of the genotoxicity of acrylamide

2.9 Following a request by the European Commission (EC), the European Food Safety Authority (EFSA) published a statement on the assessment of recent publications on the genotoxicity of acrylamide (EFSA, 2022).

2.10 The request by the EC followed the publication of a review article by Eisenbrand (2020a) and its erratum (Eisenbrand, 2020b). However, as EFSA did not consider the review and erratum to be comprehensive, a literature search of the recent data on the genotoxicity and mode of action of acrylamide was also undertaken.

2.11 EFSA concluded that the majority of the new studies published since 2015 confirmed and extended the clastogenic properties of acrylamide/glycidamide. In addition to genotoxicity, non-genotoxic effects may contribute to the carcinogenicity of acrylamide. There was further substantial evidence for the genotoxicity of acrylamide mediated by the formation of its metabolite glycidamide. Overall, the new studies evaluated extend the information assessed previously and support EFSA's conclusion on the risks to human health related to the presence of acrylamide in food. EFSA further considered the Margin of Exposure (MOE) approach to still be appropriate and concluded that an update of its 2015 opinion is currently not required.

2.12 The COM considered the recent EFSA assessment and agreed that the information/data considered in the assessment confirmed and strengthened most aspects of EFSA's previous opinion.

2.13 The review paper by Eisenbrand 2020 argued against a genotoxic mode of action for the carcinogenicity of acrylamide and that genotoxic effects were only seen above normal physiological levels of exposure. Members had reservations about the paper by Eisenbrand and considered that it had limitations. The COM agreed that exposure to acrylamide induced gene mutation and was clastogenic in mammalian cells. The genotoxic mode of action appeared to occur via CYP2E1 metabolism to the mutagenic and clastogenic metabolite glycidamide. The role of acrylamide itself was unclear. Members considered that the genotoxicity arising from acrylamide exposure may also involve the

generation of reactive oxygen species (ROS) and oxidative damage.

2.14 Overall, the COM agreed with EFSA's conclusion that the MOE approach would still be appropriate.

Discussion paper on a coating in canned food packaging materials

2.15 This item was presented as a reserved item.

2.16 Members discussed the information provided to the Committee on a can coating as well as the assessment and discussions of the Joint Expert Group on Food Contact Materials (FCM JEG). Following the COMs assessment, the discussion paper was presented to the Committee on Toxicity, together with the discussions of the FCM JEG and COM. The work is ongoing, but a final assessment is expected in 2023.

Draft statement on the genotoxicity of hydroxyanthracene derivatives in food

2.17 The genotoxicity of hydroxyanthracene derivatives (HADs) used in foods had been discussed at the COM meeting in October 2021. Following a request from UK-wide Nutrition Labelling Composition and Standards (NLCS) policy group, the UK Food Standards Agency (FSA) commissioned an independent view from the COM on the mutagenicity of HADs based on consideration of the European Food Safety Authority (EFSA) 2018 opinion on HADs and any additional new data that have become available.

2.18 This discussion of the COM was held in March 2022. At this meeting, COM Members were asked by the FSA Secretariat to consider whether they agree with the following overall conclusions of the EFSA ANS Panel, i.e. i) emodin, aloe-emodin, and dantron are genotoxic *in vitro*; ii) HADs should be considered as genotoxic *in vivo* unless there are specific data to the contrary (such as for rhein); iii) there is a safety concern for plant extracts containing HADs (although there is some uncertainty); and iv) it is not possible to provide advice on a daily intake of HADs that does not give rise to health concerns (for both the general population, and vulnerable subgroups of the population). Furthermore, the COM was asked to consider whether any of these conclusions would be affected by the results of the studies published since the 2018 EFSA opinion.

2.19 Overall, the COM agreed that that the available evidence indicates that emodin, aloe-emodin, and dantron are genotoxic *in vitro*, namely from Ames

tests.

2.20 The COM agreed that the negative results from the *in vivo* bone marrow micronucleus assay are valid and concluded that there is reasonable evidence that there is no genotoxic effect or mechanism *in vivo*. Subsequently, a new *in vivo* genotoxicity study would not be helpful. The COM considered that the reported carcinogenic effects of HADs, including those seen in the comet assay of colon cells, are caused by the high levels of irritation, inflammation, and diarrhoea.

2.21 The Committee agreed that it should in theory be possible to establish a daily intake of HADs that does not give rise to health concerns using carcinogenicity data. However, more *in vivo* carcinogenicity data are needed to carry out dose response modelling and to identify a point of departure. The Committee agreed that a specification for supplements regarding HADS contents would be useful for comparison against this potential ADI.

2.22 The Committee agreed that the studies published after 2018 are mostly negative *in vivo* data, which weaken the evidence that there is a genotoxic effect *in vivo*.

2.23 Following the COM consideration and conclusions, a draft statement was produced (MUT/2022/01) and Committee Members were asked to provide any comments on the structure and content of the draft statement. The COM were content with the draft statement, and this was agreed with no significant amendments.

Review of titanium dioxide genotoxicity

2.24 Following the publication of the European Food Safety Authority (EFSA) opinion on titanium dioxide in 2021, which concluded that titanium dioxide could no longer be considered to be ‘safe’ for use in food, the Food Standards Agency (FSA) initiated a review of the EFSA opinion.

2.25 The EFSA opinion was presented to the COM in June 2021 (MUT/2021/03) and to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) in July 2021 (TOX/2021/36). The COM had a number of concerns over the EFSA opinion on the genotoxicity of titanium dioxide. Due to this and following the advice of the COT the FSA initiated an independent evaluation of the safety of the use of titanium dioxide as a food additive.

2.26 In October 2021, paper MUT/2021/08 was presented to the COM, which summarised the available genotoxicity on titanium dioxide. Members considered that it was not possible to evaluate the genotoxicity of titanium dioxide at that stage. The COM suggested a sifting approach to the available genotoxicity should be adopted as a first step before evaluation. The Chair of the COM, a subgroup of the COM and the secretariat subsequently attended meetings to discuss and agree the criteria and methodology for sifting to identify suitable papers for the evaluation of titanium dioxide.

2.27 At the COM June 2022 meeting, paper MUT/2022/05 provided information and papers on approaches relating to the sifting and evaluation of the quality genotoxicity studies and evaluating data on nanomaterials. As an update since that meeting, members were informed that a sub-group of the COM had met to discuss the process to select relevant and appropriate studies to be reviewed by the committee. A proforma had been produced, which would be shared with members. This considered two levels, namely, whether the characteristics of the test material had been sufficiently described (e.g., micro or nano sized particles) and the quality and reliability of how the genotoxicity studies had been conducted.

Update on the COM review of the EFSA evaluation of bisphenol-a

2.28 The Food Standards Agency (FSA) provided an update on the EFSA consultation on its draft opinion proposing a lowering of the Tolerable Daily Intake (TDI) for bisphenol A.

2.29 EFSA published a consultation on its draft opinion, which closed on the 22nd February 2022. In response to this consultation the FSA requested that the Committee on toxicity of chemicals in food consumer products and the environment (COT) provide a view to EFSA. The COT had a number of concerns over the approach used by EFSA in its evaluation, which the COT considered made it difficult to assess the toxicity database as a whole and had a number of concerns relating to the studies used to derive the new EFSA proposed TDI. The COT had requested the opinion of COM members on the EFSA evaluation of the genotoxicity data on bisphenol A and thanked the COM for its contribution. COM members were generally content with the EFSA review of the genotoxicity data and agreed with the overall EFSA conclusion that DNA strand breaks, clastogenic and aneugenic effects seen in mammalian cells *in vitro* following exposure to bisphenol A were very likely due to oxidative stress related mode of genotoxicity and that bisphenol A was not mutagenic *in vivo*. The combined COT and COM

comments had been submitted to EFSA.

2.30 Following the publication of the finalised EFSA opinion the FSA would need to consider whether it needed to be referred to the UK expert advisory committees again. It was considered unlikely that there would be a need to consult the COM further on the genotoxicity aspect and would more likely be referred to one of the other expert committees, such as the Committee on the carcinogenicity of chemicals in food consumer products and the environment (COC).