COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COT)

PAPER FOR INFORMATION

COT response to the EFSA Consultation on a draft scientific opinion on the risks to public health related to the presence of acrylamide in food

Secretariat
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COT and COC Response to the EFSA Consultation on a draft scientific opinion on the risks to public health related to the presence of acrylamide in foodstuffs

General Comments

This response combines the views of the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) and Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC). Both COT and COC commented on the high quality and comprehensive nature of the scientific opinion and were broadly in agreement with the evaluation and conclusions reached. They made recommendations for improvements in a number of areas, particularly relating to other potentially significant exposure sources.

As a minor point, the use of AA as an abbreviation for acrylamide seems unnecessary and makes the document harder to read.

Abstract

It would be helpful to add to the end of the last sentence ending '...with respect to neoplastic effects', the phrase 'based on evidence from animal studies.' As currently written, and for the reader unfamiliar with toxicological evidence who may only read the abstract, the current wording could be confusing as it discusses no evidence of carcinogenicity from human studies but then raises concern about neoplastic effects.

Section 6: Human Exposure Assessment

Section 6.1.1.

The use of the scenario modelling is appropriate but the base-line scenario is not sufficiently explained.

Section 6.2.1.

The exposure estimates in Table 8 appear very similar and it is not possible to determine if the levels are really different. Members asked if it was possible to comment on the uncertainties around the means.

Section 6.4: Potential non-dietary sources of exposure

This section could be expanded, and should include quantitative data on other sources wherever possible (or note when this is not possible) which would allow for a better understanding of the contribution of dietary exposure and would aid in interpreting the epidemiological studies and risk characterisation. This particularly relates to quantification of acrylamide exposures in smokers and also from environmental tobacco smoke.

Data from studies that have measured haemoglobin adducts as an index of internal dose may be particularly helpful in this regard, but other analytical approaches could also be useful (e.g. estimation of inhaled doses, given measured concentrations in the air of workplaces).

Section 7: Hazard Characterisations and Assessment

Section 7.1: Toxicokinetics

Greater consideration could be given to potential impact of CYP2E1 being polymorphic in humans, highly inducible by alcohol, and expressed in Clara cells.
It is recommended that a detailed analysis be made of kinetic differences between the inhalation and oral routes in humans, and also between human and animal exposures to investigate further the differences in susceptibility to tumours between species and following different routes of exposure.

Section 7.3: Toxicity in Experimental Animals
Section 7.3.4.1.
The COC agreed that the Harderian gland was an appropriate tumour to use for the BMDL derivations. Whilst not present in humans, it was well established that tumours in this gland were typically associated with genotoxic carcinogens and therefore it was difficult to exclude them from an assessment of carcinogenic potential. However, it was not clear from Appendix K why the Harderian gland had been selected, as lower BMDL values were obtained for mammary gland fibroadenomas in rats, which appeared to be equally appropriate to use. It was recommended that more clarification should be given about the choice of BMDL.

Section 7.4: Observations in Humans
The focus is largely on the marginal impact of relatively small and imperfectly measured variations in dietary intake, with smoking (including the additional exposure to acrylamide that it entails) treated as a potential confounding variable. However, such marginal effects are not directly relevant to the assessment of exposure-response, especially if smoking contributes more than diet to internal dose. While presentation of results stratified by smoking is helpful in this regard, it would be valuable also to consider the human evidence on risks in relation to total exposure to acrylamide from all sources. The studies that have examined risk of cancer in relation to haemoglobin adducts do this. However, the adduct levels are not necessarily representative of long term exposure.
When evaluating the studies of occupational exposures, results should be set in the context of estimated internal doses as compared with those from dietary sources in the general population. It would be helpful to know whether they are likely to have been similar in magnitude or orders of magnitude higher.
Another consideration should be the risk of relevant health outcomes in relation to smoking – about which there will often be quite a lot of information. Tobacco smoke contains many other toxic substances as well as acrylamide, but it seems unlikely that its other constituents would importantly protect against adverse effects of acrylamide. Thus, if smoking has a major impact on personal exposures to acrylamide, and there is good evidence that a health outcome is not importantly related to smoking, then it is reasonable to suggest that outcome is probably not caused by acrylamide. Such consideration might be relevant, for example, to colon and thyroid cancer.
The review carefully presents information about stratification by smoking and results on non-smokers – it may help to state that conclusions would be similar if considering results in non-smokers or results from (the small number of studies) with information on adducts.

Similarly, when reviewing reproductive and developmental outcomes, background data on associations of relevant outcomes with smoking might provide an upper estimate of risk for effects from dietary exposures to acrylamide.
At several points in the section on human studies, there is reference to "subsequent quintiles". "Subsequent" means occurring after in time, and is not the right word here. "Increasingly higher quintiles" would be better.

Section 7.4.1.1.
It was noted that EFSA had concluded that epidemiological studies of occupational exposure to acrylamide did not indicate an increased risk of cancer whereas earlier authors had judged that the evidence was suggestive of a risk[1].
Section 7.4.1.2.
The epidemiological studies are predominantly based on Food Frequency Questionnaire (FFQ) data. Such data are not very reliable, and the limitations should be explained better in the relevant discussion section, line 6621 onwards. In particular, a number of studies provided some validation information and this could be discussed further e.g. correlation coefficients comparing FFQ estimated intakes with those from food diaries and with measured adducts in Hb.
In relation to the case-control studies, some discussion around possible biases should be included.
Lines 6147-8 refer to assessment of habitual diet 20 years before interview by a validated food frequency questionnaire. A comment about the reliability of such data should be incorporated.
The major limitation of the evidence above anything else is exposure misclassification and this should be mentioned at the start of the limitations (line 6608) due to limitations in estimation of both dietary and non-dietary exposure sources. Exposure misclassification is likely to have resulted in bias towards the null and it would be helpful to discuss if this is the key factor in why epidemiological studies in the general population have not found cancer risks (in contrast to animal studies), or whether this is a question of dose.
Section 7.4.2
It should be considered whether caffeine could have been the cause of the effects observed in the Norwegian Mother and Child Cohort.
Section 7.4.3
Data on exposures resulting in neurotoxicity, or discussion of why such exposures cannot be meaningfully characterised, would be helpful.

Section 7.5: Considerations of the Critical Effects and Possibilities for Derivation of a Health Based Guidance Value
Section 7.5.2
Is the proposed critical BMDL for neurological effects in rats likely to be lower than the exposures that have given rise to human neurotoxicity.

Section 8: Risk Characterisation

[1] Siemiatycki et al (2004) Environmental Health Perspectives 112 (15) pp 1447-1459. The Burden of Occupational Cancer in the UK. Technical report: Pancreatic Cancer. Bagga et al.

The Risk Characterisation should be expanded to consider the context of other sources of exposure.

Section 9: Uncertainties

It would be useful to summarise the most important sources of uncertainty.
Section 9.5.
It is unclear why the entry relating to occupational studies in Table 31 indicates underestimation of exposure/risk.

Conclusions and Recommendations

Given the effects on the rodent testis, a comment on the possibility of transgenerational effects, would be useful together with a recommendation for research.
In relation to the third recommendation, it was noted that correlation of urinary metabolites to dietary exposure needs to take into account other possible sources of exposure, such as smoking or exposure to environmental tobacco smoke.