CC/2014/10

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COC)

Consultation of the European Food Safety Authority on a Draft Scientific Opinion on Acrylamide in Food

Issue

1. The European Food Safety Authority (EFSA) issued a Draft Scientific Opinion on Acrylamide in Food for public consultation on 1 July 2014. The Food Standards Agency (FSA) is inviting the COC and COT to submit a response to the consultation. It is hoped that views from COC on the carcinogenicity, in the form of draft minutes of the discussion, can be provided to COT for discussion of other aspects of the draft opinion on 2 September, in order for a consolidated response to be submitted before the consultation closes on 15 September 2014.

Background

2. The COT and COC have not previously performed a risk assessment on acrylamide. In 2009, the COM issued a statement on the genotoxicity of acrylamide, which provided a comprehensive update of the mutagenicity review in an earlier EU risk assessment report[1]. The overall COM conclusions were:

- The EU risk assessment report concluded that acrylamide is an *in vitro* mutagen, and *in vivo* somatic cell and germ cell mutagen. The predominant effect was clastogenicity with some evidence for aneugenicity. The published evidence available since 1995 extends the effects of acrylamide to include identifiable glycidamide DNA adducts and gene mutations, detectable in cultured mammalian cells and somatic cells *in vivo,* and with mutation spectra which are consistent with those adducts. An element of the mutagenic effect of acrylamide, therefore, appears to be due to the formation of DNA adducts following metabolism to glycidamide.

- Assessment of the genotoxic potential of acrylamide is complicated by multiple potential mechanisms, which include extensive protein binding/enzyme inhibition, oxidative stress and DNA adduct formation. It is plausible that each of these mechanisms may contribute to the genotoxicity of acrylamide. These mechanisms are not mutually exclusive.

[1] http://www.iacom.org.uk/statements/documents/COM09S1Acrylamide_000.pdf

- Acrylamide is an *in vivo* mutagen. In experiments reviewed in this statement, genotoxic effects are generally only seen at relatively high acute doses (ca 50 mg/kg bw i.p. in mice). However genotoxic effects are also reported at much lower dose levels in repeat dose studies (ca 4 mg/kg bw, i.p. for 28 days in mice).

- The default assumption is that there is no level of exposure to this genotoxic carcinogen that is without some risk. In order to move away from this assumption, it will be necessary to identify evidence of a threshold with supporting mechanistic data for all of the potential genotoxic mechanisms of acrylamide in somatic cells and germ cells. Based on the currently available evidence, it should be considered that there is no level of exposure to acrylamide that is without some risk, although we acknowledge that the genotoxic effects of exposure to very low levels of acrylamide are likely to be pragmatically indistinguishable from background.

3. The draft EFSA opinion addresses the risk to human health related to the presence of acrylamide in food and can be found at http://www.efsa.europa.eu/en/consultations/call/140701.htm [2]. It incorporates data on acrylamide levels in different foods, estimation of dietary exposure, and review of toxicokinetic, toxicological and epidemiological data. The approach to risk characterisation for carcinogenicity is based up on the Margin of Exposure approach, consistent with the COC strategy for risk assessment of chemical carcinogens[3]. The epidemiological data are tabulated in Appendix J of the draft opinion. Details of the benchmark dose modelling are in Appendix K.

4. With respect to genotoxicity, the draft EFSA conclusions are:

- In vitro genotoxicity studies indicate that acrylamide is a weak mutagen in mammalian cells but an effective clastogen.

- Glycidamide is a strong mutagen and a clastogen. It induces mutations via a DNA adduct mechanism.

- In vivo, acrylamide is clearly genotoxic in somatic and germ cells.

- Acrylamide exerts its mutagenicity via metabolism by CYP2E1 to GA. Acrylamide can also induce gene mutations by a pathway involving the generation of reactive oxygen species (ROS) and oxidative DNA damage.

5. Since these are consistent with the earlier COM conclusions, it is not proposed to seek COM views on the EFSA draft opinion.

---

[2] A printed version can be obtained, if required, from diane.benford@foodstandards.gsi.gov.uk
[3] http://www.iacoc.org.uk/guidancestatements/documents/G01overarchingstatementVersion4.pdf

Questions for the COC

6. COC members are invited to comment on any aspect of the draft opinion, but may wish to focus on the following sections:

i. Section 7.2: biomarkers of exposure/effects

ii. Section 7.3.4: Long term toxicity/carcinogenicity

iii. Section 7.3.6.4: Modes of action of carcinogenicity

iv. Section 7.4.1: Epidemiological studies: cancer, and the key conclusion that “the overall evidence is limited and inconsistent”.

v. Section 7.5: Consideration of critical effects and possibilities for derivation of a health-based guidance value, and the selection of the Harderian gland as the most sensitive endpoint to be used in the Margin of Exposure calculation

vi. Section 8: Risk characterisation and the key conclusion that “the MOEs across surveys and age groups indicate a concern with respect to neoplastic effects”

vii. Conclusions, recommendations and summary

Secretariat
June 2014