codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 15 (i) **CX/FAC 04/36/34-Add. 1**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES AND CONTAMINANTS

Thirty-sixth Session

Rotterdam, The Netherlands, 22 -26 March 2004

DISCUSSION PAPER ON ACRYLAMIDE

- COMMENTS

The following comments have been received from: Canada, Denmark, and Sweden

CANADA:

Canadian Position

Canada would like to recognise the accomplishments of the Drafting Group, led by the United Kingdom and the United States, in preparing this draft Discussion Paper.

Canada fully supports the recommendations made in this draft paper, and the impending work of JECFA, the results of which will provide the scientific foundation for the development of appropriate and effective approaches to risk management.

General Comments

Canada would like to suggest that the document undergo an in-depth review, as there are a number of inaccuracies, due either to the writing style or to misquoting or misinterpretation of the primary data. Some examples are as follows:

Para 9: "Acrylamide induces genetic mutations .... in cultured cells in vitro". As far as we are aware, acrylamide has NOT shown genotoxicity in bacterial or mammalian cells in vitro, although its metabolite, glycidamide, has done so.

Para 10: second-to-last sentence "Studies in rats and mice have shown that acrylamide impairs male fertility, although it is not clear whether this effect was secondary to neurotoxicity". While effects on male fertility may be a less sensitive endpoint for acrylamide toxicity, direct effects of acrylamide on sperm formation and germ cell toxicity affecting male fertility have been noted.

Para 46: "Acrylamide causes cancer in laboratory animals in high doses .... However, it is not clear whether acrylamide causes cancer in humans, at the much lower levels of exposure from its presence in food". While carcinogenic doses of acrylamide in rodents are somewhere in the area of 1000 times higher than dietary levels (excluding additional exposure from smoking), carcinogenic doses in rodents in the range of 0.5 to 2 mg/kg bw/day would not be considered high, and a 1000 times margin of safety for a genotoxic carcinogen would be considered only just acceptable as opposed to "much lower."

Para 52: "Acrylamide and its epoxide metabolite, glycidamide, are widely distributed in all tissues of the body, including milk." Milk is not a tissue and therefore acrylamide and glycidamide would be excreted in milk, not distributed in it. "Acrylamide probably accounts for neurotoxicity while glycidamide may be more critical for the carcinogenic and genotoxic properties in animals" would be more meaningful if worded as "Acrylamide is likely directly involved in the induction of neurotoxicity while its metabolism to glycidamide may be more critical for the carcinogenic and genotoxic activity observed in animals."

Para 56: "Less is known about the effects of acrylamide on the developing nervous system..." We believe that this should be "Nothing is known ..."

Para 57: "The molecular mechanisms of acrylamide neuropathy, ... is unknown". It might, however, be worth mentioning here that in the early stages anyway, the neuropathy is reversible. This contributes useful information about the molecular mechanisms (i.e. some regeneration of affected targets of acrylamide toxicity is possible).

DENMARK:

Denmark welcomes the positive initiative and the paper drafted by the United Kingdom and its co-workers.

We find that the paper gives a useful background knowledge to be used as basis for the understanding of the issue and for further discussion in Codex. Furthermore, we find it important to have this food safety issue on the agenda for a discussion of the risk management (and assessment). Knowledge on formation of acrylamide, prevention etc. is increasing these years and the work in Codex can be very useful, and will have to follow the increasing knowledge.

Concerning the text, we only have minor comments:

The title after paragraph 11 should read: “Exposure”, as this chapter does not address risk for humans. Risk assessments made in Sweden, Norway and USA should be referenced in the chapter.

Paragraph 13: we think that the units used should be micrograms instead of milligrams

Paragraph16: Swedish exposure data should be referenced here, see e.g.

We agree with the recommendation number 50 to ask JECFA for a risk assessment. We have the following proposals for an additional question to the suggested request:

JECFA should include the uncertainties clearly in the opinion, highlighting data which might be mission, and

Include considerations on the connection between productions conditions and formation of acrylamide and its degradations products

We propose to add a recommendation more, as follows:

Anticipating that JECFA classify acrylamide in food as a safety problem, CCFAC should start to elaborate a Code of Practice for prevention and reduction of acrylamide during processing.

SWEDEN:

Sweden welcomes this discussion paper as a good starting point for future work within the CCFAC. Some comments are given below.

Paragraph 13, 6th and 7th line: probably an editing error: mg should be µg

Paragraph 34: Add web-site reference:

HEATOX (Heat-generated food toxicants: identification, characterisation and risk minimisation). EC project FOOD-CT-2003-506820-STREP. http://www.heatox.org.

Paragraph 47, 1st sentence: needs to be further developed. It could at present be interpreted as if the exposure is acceptable. However, a previously unknown health risk is not automatically an acceptable risk.

Paragraph 58: Based on acrylamide adduct levels, less margins between exposure and the NOAEL have been observed in studies of acrylamide exposed Chinese workers (Calleman et al, 1994) and Swedish tunnel workers (Hagmar et al, 2001), than the 500-fold margin referred to in the text. Data from these studies indicate a 10-300 fold margin between exposure and NOAEL.

Paragraph 65: In the micronucleus test in vivo it has been shown that the metabolite of acrylamide, i.e. glycidamide, is the predominant genotoxic factor (Paulsson et al 2003). Furthermore, in the flow cytometer-based micronucleus test in vivo, a chromosome breaking mechanism (no aneuploidy) after acrylamide exposure has been clearly demonstrated, i.e. a linear dose-response relationship. (Abramsson Zetterberg, 2003).

References

Calleman et al. 1994. Toxicol Appl Pharmacol 126, 361-371.

Hagmar et al. 2001. Scand J Work Environ Health 27, 219-226.

Paulsson et al. 2003. Mutation Res 535, 15-24.

Abramsson-Zetterberg. 2003. Mutation Res 535, 215-222.