CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - Fax: (+39) 06 5705 4593 - E-mail: codex@fao.org - www.codexalimentarius.net

Agenda Item 3(a)

CX/CF 12/6/5
January 2012

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON CONTAMINANTS IN FOODS

Sixth Session
Maastricht, The Netherlands, 26 – 30 March 2012

# MATTERS OF INTEREST ARISING FROM FAO AND WHO INCLUDING THE 74TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

1. This document provides information on FAO and WHO activities in the area of provision of scientific advice to Codex and Member countries, as well as other activities which are of interest for CCCF.

*Matters for information from the 74th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)*

2. The results of the 74th meeting of JECFA on food additives is now available[1]. The meeting report (WHO Technical Report Series No 966, 2011) is accessible through the WHO JECFA publications website: http://www.who.int/foodsafety/chem/jecfa/publications/en/index.html. The toxicological monographs (WHO FAS 65, 2012) will become available in due course.

The CCCF is invited to consider the scientific advice and the specific recommendations of JECFA regarding the re-evaluations requested for cyanogenic glycosides and fumonisins, the summaries of which are presented in Appendix 1.

*Publications and Other Provision of Scientific Advice from FAO and WHO*

3. Results of recent JECFA evaluations on food contaminants are include in the following publications:

- Report of the 72nd JECFA – Evaluation of certain contaminants in foods. WHO TRS 959, 2011.
- Report of the 73rd JECFA - Evaluation of certain food additives and contaminants. WHO TRS 960, 2011.
- Report of the 74th JECFA - Evaluation of certain food additives and contaminants. WHO TRS 966, 2011.
- Monographs of the 72nd JECFA - Safety evaluation of certain contaminants in food. WHO Food Additives Series No. 63, FAO JECFA Monographs 8, 2011.
- Monographs of the 73rd JECFA - Safety evaluation of certain food additives and contaminants. WHO Food Additives Series No. 64, 2011.
- Compendium of Food Additive Specifications, 74th JECFA meeting. FAO JECFA Monographs 11, 2011.

4. The 75th meeting of JECFA was held 7-17 November 2011 in Rome, Italy and was dedicated to residues of veterinary drugs in foods. The summary report is available at http://www.fao.org/fileadmin/user_upload/agns/pdf/jecfa/JECFA_75_summary_report.pdf and http://www.who.int/foodsafety/chem/jecfa/summaries/Summary75.pdf

[1] See the Report of the 74th Meeting of the Joint FAO/WHO Expert Committee on Food Additives can be found at: http://whqlibdoc.who.int/trs/WHO_TRS_966_eng.pdf

5. A joint FAO/WHO ad hoc expert meeting on dietary exposure assessment for veterinary drug residues in food was held in November 2011 in conjunction with the 75th JECFA meeting. The call for data was published at http://www.fao.org/ag/agn/agns/jecfa/JECFA_Call_for_data_food_consumption.pdf. The draft report is currently being reviewed by participants at the 75th JECFA meeting and will become available for public comment.

*Global Initiative for Food-related Scientific Advice (GIFSA)*

6. GIFSA is a mechanism established by FAO and WHO to facilitate the provision of extra-budgetary resources for scientific advice activities. For additional information and advice on the procedure for making a donation/contribution, contact Ms Dominique Di Biase, Policy Assistance and Resources Mobilization Division(Dominique.DiBiase@fao.org; Tel: + 39 06 57055391) at FAO; and Dr Angelika Tritscher, Department of Food Safety and Zoonoses, WHO (tritschera@who.int; Tel: + 41 22 7913569). In addition, FAO has developed a Strategy for the Provision of Scientific Advice for Food Safety (2010-2013). For more information, contact: Mary.Kenny@fao.org.

*FAO/WHO Guidance for application of Risk Analysis during food safety emergencies*

7. As part of the joint FAO/WHO publications series of tools (framework or guidance) during an emergency on food safety, FAO and WHO member states have expressed the need to generate guidance for application of risk analysis during food safety emergencies. It will contain the essential elements for establishing procedures for assessing and managing risks within the framework of the countries food safety emergency response plans. Even though the elements for conducting a risk analysis have been documented by Codex, the process of applying the risk analysis concept operationally during an emergency has not been sufficiently addressed. It is specially needed to take management decisions and communicating risk in the face of time constrains, lack of data and even knowledge gaps. A joint FAO/WHO Workshop to develop such guidance was held in Headquarters FAO Rome, 21-25 March 2011. The final document has been prepared and may be found at: http://www.fao.org/docrep/014/ba0092e/ba0092e00.pdf

*Requests for providing scientific advice*

8. Both organizations continue to jointly prioritise the requests for scientific advice taking into consideration the criteria proposed by Codex as well as the requests for advice from Member Countries and the availability of resources. A description of the current requests for scientific advice posed to FAO and WHO directly by Codex Alimentarius Commission and its subsidiary bodies as well as meetings being planned by FAO and WHO in response to requests from member countries has been prepared and will be presented at the next CAC.. In prioritizing the requests for scientific advice to be addressed, FAO and WHO continue considering the set of criteria for the prioritization proposed by Codex (ALINORM 05/28/3, para. 75) as well as the requests of advice from Member Countries and the availability of resources.

9. FAO and WHO would like to emphasize the severe financial problems faced by the Organizations for the scientific advice program. The current financial situation does not allow anymore to respond to all requests for scientific advice, including requests brought forth by the Codex Alimentarius Commission. It has to be emphasized that this scientific advice forms the basis for the respective Codex Standards. Efforts need to be undertaken by Members to provide support for scientific advice activities in order to be able to support the work of Codex.

Appendix 1

## Cyanogenic glycosides

1. The Third Session of the Codex Committee on Contaminants in Food (CCCF) in 2009 requested that JECFA reconsider the available data on cyanogenic glycosides, advise on the public health implications of cyanogenic glycosides and their derivatives in food and decide whether risk assessment is feasible and appropriate.

2. Reports of acute human poisoning associated with the consumption of foods containing cyanogenic glycosides were reviewed. The Committee therefore considered it appropriate to establish an acute reference dose (ARfD) for cyanogenic glycosides, expressed as cyanide equivalents. In addition, as there are a number of human diseases, specifically konzo, tropical ataxic neuropathy and iodine deficiency disorders, associated with the chronic consumption of underprocessed cassava as a staple food, it was recognized that the derivation of a chronic health-based guidance value would also be relevant.

### Derivation of the ARfD

3. Following review of a developmental toxicity study with linamarin, the Committee considered this study as suitable for establishing an ARfD. Benchmark dose (BMD) modelling of the data from this study provided a lower limit on the benchmark dose for a 10% response ($BMDL_{10}$) for linamarin of 85 mg/kg body weight for increased skeletal defects in developing hamster fetuses following acute exposure of maternal animals. While the study did not use dietary exposure, gavage dosing was considered relevant to establishing the ARfD.

4. Following application of a 100-fold uncertainty factor, the Committee established an ARfD for linamarin of 0.9 mg/kg body weight (equivalent to 0.09 mg/kg body weight as cyanide). This value was considered, when compared on a cyanide molar basis, to also be applicable to other cyanogenic glycosides. Therefore, the Committee recommended conversion of the ARfD for linamarin to a cyanide-equivalent dose of 0.09 mg/kg body weight. This cyanide-equivalent ARfD applies only to foods containing cyanogenic glycosides as the main source of cyanide.

### Derivation of the provisional maximum tolerable daily intake (PMTDI)

5. In a 13-week United States National Toxicology Program study not previously evaluated by the Committee, in which exposure to sodium cyanide was continuous via drinking-water, a variety of effects related to male reproductive organs were observed—namely, decreased cauda epididymis weights, decreased testis weights and decreased testicular spermatid concentration. Dose–response analysis of continuous data on absolute cauda epididymis weights generated the lowest BMDL for a one standard deviation response ($BMDL_{1SD}$) of 1.9 mg/kg body weight per day. On the basis of this $BMDL_{1SD}$, the Committee established a PMTDI of 0.02 mg/kg body weight by applying a 100-fold uncertainty factor. The Committee decided that it was not necessary to apply an additional uncertainty factor to account for the absence of a long-term study, considering the generally acute nature of cyanide toxicity and the sensitivity of the effect (i.e. the reduction of absolute cauda epididymis weight).

### Comparison of estimated dietary exposures with health-based guidance values and the impact of maximum limits (MLs) on dietary exposure

6. Estimated dietary exposures to total available hydrocyanic acid (HCN) were converted to cyanide equivalents and compared with the health-based guidance values established by the Committee at this meeting.

7. From the national acute dietary exposure estimates available to the Committee for review, the ARfD of 0.09 mg/kg body weight as cyanide equivalents was exceeded 3-fold for cassava for adults (based on raw samples), less than 2-fold for apple juice for children, between 2- and 5-fold for bitter apricot kernels and up to 10-fold for ready-to-eat cassava chips/crisps, depending on the population group. If ready-to-eat cassava chips contained a level equivalent to the recently established ML in Australia and New Zealand of 10 mg/kg as HCN, there was only a marginal exceedance of the ARfD for children. These results are based on dietary exposure to total HCN, which represents the maximum possible exposure for foods containing cyanogenic glycosides.

8. Based on national estimates of chronic dietary exposure to total HCN, there is also the potential to exceed the PMTDI of 0.02 mg/kg body weight as cyanide for populations reliant on cassava as a staple food: between 1- and 3-fold for children and between 1- and 2-fold for adults. There is also a potential for those populations not reliant on cassava to exceed the PMTDI: between 1- and 5-fold for children and between 1- and 3-fold for adults. For Australia and New Zealand, ready-to-eat cassava chips were the major contributor to dietary exposure to HCN (84–93%). When the cassava chips contain a level equivalent to the ML of 10 mg/kg as HCN, all mean dietary exposures were below the PMTDI. High-percentile exposures for children were between 1- and 2-fold above the PMTDI. All chronic dietary exposure estimates based on exposures from flavouring agents did not exceed the PMTDI. These results are based on dietary exposure to total HCN, which is a worst-case scenario.

9. Application of the ML of 50 mg/kg as HCN for sweet cassava could result in dietary exposures that exceed the ARfD by less than 2-fold for the general population and up to 4-fold for children and exceed the PMTDI by between 2- and 10-fold, depending on the population group assessed. These estimates do not take into consideration any reduction in concentration of total HCN as a result of food preparation or processing. For the ML of 10 mg/kg as HCN for cassava flour, there are no estimates of dietary exposure available that exceed the ARfD or PMTDI. This is supported by the maximum amount of food that can be consumed based on existing Codex MLs before the health-based guidance values would be exceeded, which is as low as 25 g/day for cassava for chronic exposure. More detailed estimates of cassava and cassava flour consumption and concentrations in food for cassava-eating communities would help in supporting the conclusion that dietary exposures to total HCN could exceed health-based guidance values.

10. The ML for sweet cassava is for the raw product. If the starting level of HCN in the raw sweet cassava were 50 mg/kg as HCN, the minimum effective processing would result in a concentration of 15 mg/kg as HCN, and the most effective processing would give a HCN concentration of 2 mg/kg.

ARfD: 0.09 mg/kg body weight as cyanide (applies only to foods containing cyanogenic glycosides as the main source of cyanide)

PMTDI: 0.02 mg/kg body weight as cyanide

Fumonisins

11. For the current evaluation of fumonisins, the Committee reviewed all relevant studies performed on fumonisins since 2001.

12. Exposure to fumonisins has been associated with a wide range of effects, which are often species and sex specific. Laboratory studies have identified the liver as the most sensitive organ in mice and the kidney as the most sensitive organ in rats.

13. Studies suitable for dose–response analysis have been conducted with rodents either employing purified fumonisin $B_1$ ($FB_1$) or using *Fusarium verticillioides* culture material containing $FB_1$. The latter studies typically use $FB_1$ as a marker for dietary exposure to the fumonisins and other metabolites of *Fusarium*. The studies employing purified $FB_1$ are generally better in experimental design for dose–response analysis. However, the Committee concluded that the studies with culture material were of sufficient quality to clearly indicate that other toxins produced by *F. verticillioides* either add to or potentiate the toxicity of $FB_1$. Although naturally contaminated corn would probably be more representative of actual human dietary exposure than either purified $FB_1$ or culture material, no suitable studies were identified that used naturally contaminated corn as a test material. As the implications are somewhat different, the Committee evaluated studies with purified $FB_1$ and *F. verticillioides* culture material separately.

14. For pure $FB_1$, the lowest identified $BMDL_{10}$ was 165 µg/kg body weight per day for megalocytic hepatocytes in male mice. Using a safety factor of 100 for intraspecies and interspecies variation, the Committee derived a PMTDI of 2 µg/kg body weight per day. As this was the same value as the previously established group PMTDI for $FB_1$, $FB_2$ and $FB_3$, alone or in combination, this group PMTDI was retained.

15. For culture material, the lowest identified $BMDL_{10}$ using $FB_1$ as a marker was 17 µg/kg body weight per day for renal toxicity in male rats. The Committee chose not to establish a health-based guidance value for culture material, because its composition was not well characterized and may not be representative of natural contamination.

16. The Committee concluded that, based on the national and international estimates, dietary exposure to $FB_1$ for the general population ranges from $0.12 \times 10^{-3}$ to 7.6 µg/kg body weight per day at the mean, whereas the 95th percentile exposure was estimated to be up to 33.3 µg/kg body weight per day. Dietary exposure to total fumonisins for the general population would range, for a consumer with average consumption, from $0.087 \times 10^{-3}$ to 10.6 µg/kg body weight per day, whereas for consumers with high consumption, exposure would be up to 44.8 µg/kg body weight per day. Maize is still the predominant source of exposure to $FB_1$ and total fumonisins.

17. Comparison of these estimates with the group PMTDI indicates that the group PMTDI is exceeded at the population level in some regions within some countries. The Committee concluded that adverse effects from fumonisin exposure may occur and that reduction of exposure to fumonisin and other toxins produced by *F. verticillioides* is highly desirable, particularly in areas of the world where maize is a major dietary staple food and where high contamination can occur.

18. As fumonisins do not carry over from feed to animal products in significant amounts, the occurrence of fumonisins in feed was considered not to be a human health concern.

19. The Committee concluded that implementation of the MLs proposed by CCCF could significantly reduce exposure (by more than 20%) to total fumonisins in six GEMS/Food consumption clusters (A, D, G, B, K, F). The main contribution to reduction was due to the proposed Codex ML for the category “Corn/maize grain, unprocessed”. The Committee noted that implementation of the proposed MLs would result in rejection of 2–88% of “Corn/maize grain, unprocessed” and 4–57% of “Corn/maize flour/meal” across the clusters. The Committee also noted that the national estimates of exposure to fumonisins show that the exceedance of the PMTDI occurs only in limited regions presenting high maize consumption levels and highly contaminated maize.

20. The Committee concluded that no or little effect was noticed on the international exposure estimates resulting from the implementation of MLs higher than those proposed by CCCF.

Group PMTDI for $FB_1$, $FB_2$ and $FB_3$, alone or in combination, of 2 µg/kg body weight was retained.