

# CODEX ALIMENTARIUS COMMISSION



Food and Agriculture  
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Organization

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**JOINT FAO/WHO FOOD STANDARDS PROGRAMME  
CODEX COMMITTEE ON CONTAMINANTS IN FOODS  
13<sup>th</sup> Session  
Yogyakarta, Indonesia, 29 April – 3 May 2019**

**WORKING DOCUMENT FOR INFORMATION AND USE IN DISCUSSIONS RELATED TO  
CONTAMINANTS AND TOXINS IN THE GSCTFF  
(Prepared by Japan and the Netherlands)**

## Background

1. This document has been prepared by Japan and the Netherlands in accordance with the recommendation endorsed by CCFAC38 (ALINORM 06/29/12, para. 116) and on the basis of the document CX/CF 07/1/6 published for the first Session of the Codex Committee on Contaminants in Foods (CCCF1) held in 2007. It incorporates all the decisions made at CCCF12 (REP18/CF) and subsequently adopted by CAC41 (REP18/CAC).
2. As CCCF3 agreed to discontinue work on the food categorization system to be used for the purpose of the General Standard for Contaminants and Toxins in Food and Feed (GSCTFF) (ALINORM 09/31/41, para. 37), the following changes are made in the list of MLs:
  - Where an ML was adopted at Step 8 or 5/8 by the Commission with the Codex Code for the commodity, the Codex Code was retained in the List; and
  - Where an ML was adopted at Step 8 or 5/8 by the Commission without the Codex Code for the commodity, the Codex Code was not included.Some texts were added in the Explanatory Notes to indicate whether and where commodity descriptions are found.
3. In order to assist consideration of maximum levels in various steps, issues arising from previous Codex discussions of maximum levels for a contaminant/toxin and JECFA recommendations to CCCF are surrounded by broken lines while information on the nature and toxicity is surrounded by solid lines in the list.
4. The list of maximum levels for contaminants and toxins in foods is attached to this document (starting from page 2). Schedule I (renamed "Schedule" in 2014) is no longer included in this Information Document as agreed by CCCF4 but is available in the GSCTFF (CXS 193-1995) (REP14/CF, Appendix VII).

## Working Document for Information and Use in Discussions on the GSCTFF

This working document presents contaminants and toxins that are or have been dealt with in the CCFAC and CCCF. It does not only encompass the contaminants and toxins for which Codex standards exist or are being developed, but also those for which further information is sought or about which a Codex decision has been taken.

The Working Document has the purpose of providing an overview of the situation regarding Codex decisions about this subject and guidance about further actions required. Therefore, also relevant information and references are added to the list.

The list of maximum levels / guideline levels is thus active, which needs regular update.

The situation regarding contaminants and toxins is very complex and many substances are or have been the subject of scientific research and discussion regarding their occurrence in foods and their significance for human and animal health. On a national level, there are many activities, sometimes implying legal measures which may affect international trade in foods and feeds. It is obviously important for CCCF to take note of the developments in this field and to consider the necessity of actions. In order to obtain an overview of the situation, CCCF shall develop and maintain a working document in which more comprehensive information regarding contaminants and toxins in foods is presented in a summary form.

The Working Document has two parts: *Part 1* containing maximum and guideline levels developed by CCFAC/CCCF and contaminant provisions included in commodity standards; and *Part 2* containing maximum levels developed for copper, iron and zinc which are regarded as quality factors as opposed to safety factors. *Part 1* also contains those levels still at various steps of the Codex elaboration procedure for the facilitation of consideration of proposed maximum levels by CCCF.

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## Background of the Working Document

The Working Document was established in its current form when the CCFAC36 agreed to integrate the Annotated List of Contaminants and Toxins in Foods (Annex IV then to the Preamble of the General Standard for Contaminants and Toxins in Foods [GSCTF], Part 1 and Part 2) into a separate document "Working document for information and use in discussions on the GSCTF" (ALINORM 04/27/12, para. 119). Annex IV had the purpose of providing an overview of the situation regarding Codex decisions about contaminants and toxins and guidance about further actions required. It was originally included in the GSCTF as an introduction text without the lists of contaminants and toxins (ALINORM 97/12, para. 68). All is now included in the Working Document.

It was agreed that the Working Document (ANNEX IV at the time) would:

- contain information not only for contaminants and toxins for which Codex standards exist or are being developed, but also those for which further information is sought or about which a Codex decision has been taken, and that relevant information and references are added in order to give guidance about further actions required (ALINORM 04/27/12, para. 116 and Appendix XIII);
- include references to validated methods of analysis as well as references to information on toxicological guidance, if available (ALINORM 95/12A, para. 99);
- exclude references to revoked standards (ALINORM 04/27/12, para. 116); and
- include maximum levels for quality-related parameters such as copper, zinc, iron, etc. as a record of the complete range of contaminants in the Codex system (ALINORM 04/27/12, para. 120).

The format of the Working Document is that of Schedule I. This results from the agreement of the CCFAC32 to create a new Schedule I to the GSCTF, for which a working document was created in its format, and under the name of Schedule I. It was noted that Schedule I would not be added to the GSCTF until the relevant levels were adopted by the Commission (ALINORM 01/12, para. 79).

At the following Sessions of the Committee, it was agreed that this Schedule I:

- should include all current maximum and guideline levels for contaminants in food and those under elaboration by the Committee, as well as current maximum and guideline levels contained in Codex commodity standards, with an indication of their step status (ALINORM 01/12, para. 118);
- would contain two lists, i.e., List 1 with MLs for contaminants and toxins already adopted as final texts and List 2 with MLs for contaminants and toxins under discussion at different steps of the Codex procedure (ALINORM 03/12, para. 104); and
- would be used as a working document during the Working Group and the plenary sessions (ALINORM 03/12, para. 104).

In this Schedule I as prepared for the CCFAC36, it was identified that List 2 was in fact ANNEX IV, and was renamed accordingly to distinguish it clearly from Schedule I, the list of adopted Standards (CX/FAC 04/36/16). The Committee endorsed the recommendation to include Schedule I (List 1) in the GSCTF (ALINORM 04/27/12, para. 117). The Committee noted that ANNEX IV was useful in providing an overview of the situation regarding Codex decisions about contaminants and toxins, and to give guidance about further actions required by CCFAC. The Committee agreed with the recommendation that such information should be part of a working document to be updated yearly and presented at each session of the Committee, and requested the Netherlands and Japan to perform this task (ALINORM 04/27/12, paras. 118 and 119).

During the work of the editorial amendments to GSCTFF, which was adopted at CAC37, CCCF8 agreed to delete (i) short information notes on the substance at the end of the provisions on contaminants in Schedule I, (ii) scientific references and (iii) operating characteristic curves (OC curves) in the sampling plans from Schedule I in the GSCTFF. The Committee agreed that all information that is deleted would be transferred to this Working Document (INF 1)(REP14/CF, paras. 87-89). Therefore, this document is keeping such information which is not included in the current GSCTFF.

The current Working Document is the subsequent result.

**EXPLANATORY NOTES**

Reference to JECFA:	References to the JECFA meeting in which the contaminant was evaluated and the year of that meeting.
Toxicological guidance value:	Toxicological advice about the tolerable intake level of the contaminant for humans, expressed in milligrams (mg) per kg body weight (bw). The year of recommendations and additional explanation are included.
Contaminant definition:	Definition of the contaminant in the form of which the ML or GL applies or which may or should be analyzed in commodities/products.
Synonyms:	Symbols, synonyms abbreviations, scientific descriptions and identification codes used to define the contaminant.
Related code of practice:	Name of any code(s) of practice related to the contaminant and its (their) reference number(s).
Commodity/ product name:	<p>The commodities or products, to which the ML or GL applies, other than the terms feed or food, are those that are intended for human consumption, unless otherwise specified.</p> <p>The ML or GL contained in Codex commodity standards apply to the commodities within the scope of the Codex commodity standard. Reference to the Codex Standard is provided and the definition of the commodity/product is the definition as provided in the Codex commodity standard.</p> <p>When the ML or GL applies only to the commodity within the scope of the Codex commodity standard then the reference is mentioned as “Relevant Codex commodity standard(s) is (are) ...”. In case the reference to Codex commodity standards is provided as example for commodities to which the ML or GL applies then the reference is mentioned as “Relevant Codex Commodity standards include ...”</p> <p>For the other commodities or products not contained in Codex commodity standards the definition of the commodity or product is provided in the Classification of Foods and Animal Feeds (CXM 4-1989), unless otherwise specified.</p> <p>In case a ML or GL applies to a product group (e.g. legume vegetables), the ML or GL applies to all individual products belonging to the group as defined in CXM 4-1989.</p> <p>For any other commodities or products other than those described above, where necessary, the definition of the commodity/product is provided in “Notes/Remarks”.</p>
Step:	Step of the Codex Elaboration Procedure at which each maximum level is (at the time of the publication of this paper). See the Codex Procedural Manual. The term “Adopted” is used for an adopted MLs and Codex Standards.
Reference or adoption year:	Reference number of the commodity standard in which the maximum level is established or the year of adoption of the maximum level following the recommendation of the Codex Committee on Food Additives and Contaminants (up to 2006) and the Codex Committee on Contaminants in Food (after 2007).
Portion of the Commodity/Product to which the maximum level (ML) or guideline level (GL) applies	The portion of the feed or food to which the ML or GL applies, is the portion defined in the Codex commodity standard or CXM 4 or defined at the establishment of the ML or GL, unless otherwise specified.

**Definitions of some toxicological terms**

PMTDI:	<p><i>(Provisional Maximum Tolerable Daily Intake).</i></p> <p>The use of the term “provisional” expresses the tentative nature of the evaluation, in view of the paucity of reliable data on the consequences of human exposure at levels approaching those with which JECFA is concerned.</p> <p>The endpoint used for contaminants with no cumulative properties. Its value represents permissible human exposure as a result of the natural occurrence of the substance in food and in drinking-water. In the case of trace elements that are both essential nutrients and unavoidable constituents of food, a range is expressed, the lower value representing the level of essentiality and the upper value the PMTDI.</p>
PTWI:	<p><i>(Provisional Tolerable Weekly Intake)</i></p> <p>For contaminants that may accumulate within the body over a period of time, JECFA has used the PTWI and PTMI. On any particular day, consumption of food containing above-average levels of the contaminant may exceed the proportionate share of its weekly or monthly tolerable intake (TI). JECFA’s assessment takes into account such daily variations, its real concern being prolonged exposure to the contaminant, because of its ability to accumulate within the body over a period of time.</p> <p>An endpoint used for food contaminants such as heavy metals with cumulative properties. Its value represents permissible human weekly exposure to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods.</p>
PTMI:	<p><i>(Provisional Tolerable Monthly Intake)</i></p> <p>An endpoint used for a food contaminant with cumulative properties that has a very long half-life in the human body. Its value represents permissible human monthly exposure to a contaminant unavoidably associated with otherwise wholesome and nutritious foods.</p>
ADI:	<p><i>(Acceptable Daily Intake)</i></p> <p>The estimate of the amount of a chemical in food or drinking-water, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk to the consumer. It is derived on the basis of all the known facts at the time of the evaluation. The ADI is expressed in milligrams of the chemical per kilogram of body weight (a standard adult person weighs 60 kg). It is applied to food additives, residues of pesticides and residues of veterinary drugs in food.</p>
ARfD	<p><i>(Acute Reference Dose)</i></p> <p>The estimate of the amount of a substance in food or drinking-water, expressed on a body weight basis, that can be ingested in a period of 24 h or less without appreciable health risk to the consumer. It is derived on the basis of all the known facts at the time of evaluation. The ARfD is expressed in milligrams of the chemical per kilogram of body weight.</p>
BMDL:	<p><i>(Benchmark Dose Lower Limit)</i></p> <p>The lower one-sided confidence limit of the benchmark dose (BMD) for a predetermined level of response, called the benchmark response (BMR), such as a 5 or 10% incidence of an effect. It is determined by dose-response modeling of toxicological data.</p>
MOE	<p><i>(Margin of Exposure)</i></p> <p>The ratio between the BMDL and the estimated intake in humans. It can be used to prioritize different contaminants, providing that a consistent approach has been adopted. Its acceptability depends on its magnitude and is ultimately a risk management decision.</p>

A full list of toxicological terms and explanations can be found in Environmental Health Criteria 240: Principles and methods for the risk assessment of chemicals in food.

<http://www.who.int/foodsafety/publications/chemical-food/en/>

**Metals****Aluminium**

Reference to JECFA:	67 (2006), 74 (2011)
Toxicological guidance value:	PTWI 2 mg/kg bw (2011, for all aluminium compounds in food, including additives)
Synonyms:	Al
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/ Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

The WHO Representative clarified that exposure through food contact utensils and containers had been considered during the evaluation by JECFA and that it was concluded that they were not main contributors for human exposure to aluminium (ALINORM 07/30/41, para. 31).

JECFA67 (2006) established a PTWI for Al of 1 mg/kg bw for all aluminium compounds in food, including additives; previously established ADIs and PTWI for aluminium compounds were withdrawn. The Committee concluded that aluminium compounds have the potential to affect the reproductive system and developing nervous system at doses lower than those used in establishing the previous PTWI.

The evaluation of the PTWI was based on the combined evidence from several studies: the studies conducted with dietary administration of aluminium compounds were considered most appropriate. The lowest LOELs for Al of different studies in mice, rats and dogs were in the range of 50-75 mg/kg bw per day. An uncertainty factor of 100 was applied (to 50 mg/kg bw per day) to allow for inter- and intraspecies differences. An additional uncertainty factor of 3 was applied to cover deficiencies in the database (absence of NOELs in majority of studies and absence of long-term studies on relevant toxicological endpoints). Also, deficiencies are counterbalanced by the probable lower bioavailability of the less soluble aluminium compounds present in food. Because of the potential for bioaccumulation JECFA confirmed that the resulting health-based guidance value should be expressed as a PTWI.

The Committee noted that the PTWI is likely to be exceeded to a large extent by some population groups, particularly children, who regularly consume foods that include aluminium-containing additives. JECFA also noted that dietary exposure to Al is expected to be very high for infants fed on soya-based formula.

The Committee recommended: Further data on the bioavailability of different aluminium-containing food additives are required; There is a need for an appropriate study of developmental toxicity and a multigeneration study incorporating neurobehavioral end-points, to be conducted on a relevant aluminium compound(s); Studies to identify the forms of aluminium present in soya formulae, and their bioavailability, are needed before an evaluation of the potential risk for infants fed on soya formulae can be considered.

At JECFA74 (2011) evaluated aluminium-containing food additives (including new food additives potassium aluminium silicate and potassium aluminium silicate-based pearlescent pigments). New data was submitted including studies of bioavailability and reproductive, developmental and neurobehavioral effects. The absorption of aluminium compounds is found to be generally in the region of 0.01-0.3% with soluble compounds appearing to be more bioavailable. It was not possible though to draw conclusions on quantitative differences in the overall toxicokinetics of different aluminium-containing food additives or between experimental animals and humans. Recent evidence did not show effects of aluminium on reproductive outcomes. The Committee concluded that there continues to be a lack of consistency regarding the reported neurodevelopmental effects in animals and most studies involved administration of aluminium compounds in drinking-water rather than in the diet.

The Committee noted that a study, in which aluminium citrate was administered in drinking-water, provided a NOAEL of 30 mg/kg bw per day. Based on the higher solubility of aluminium citrate compared to many other aluminium compounds and the fact that it is likely to be more bioavailable from drinking-water than from food, The Committee concluded that the NOAEL of 30 mg/kg bw per day was an appropriate basis for establishing a PTWI for aluminium compounds. Because long-term studies on the relevant toxicological endpoints had become available since the 67th meeting, an additional uncertainty factor for deficiencies in the database was considered to be no longer necessary. A PTWI of 2 mg/kg bw was established by applying an uncertainty factor of 100 for interspecies and intraspecies differences.

The PTWI applies to all aluminium compounds in food, including food additives. The Committee noted that dietary exposure of children to aluminium-containing food additives, including high-level dietary exposure, can exceed the PTWI by up to 2-fold. For potassium aluminium silicate-based pearlescent pigments at the maximum proposed use levels and

**Metals****Aluminium**

using conservative estimates, JECFA noted that dietary exposure at the highest range of estimates is 200 times higher than the PTWI.

The Committee recommended: Provisions for food additives containing aluminium included in the GFSA should be compatible with the revised PTWI for aluminium compounds of 2 mg/kg bw as aluminium from all sources. Furthermore, there is a need for convincing data to demonstrate that Al is not bioavailable from potassium aluminium silicate-based pearlescent pigments. Studies to identify the forms of Al present in soya-based formula and their bioavailability are still required.

Aluminium occurs in the environment in the form of silicates, oxides and hydroxides, combined with other elements, such as sodium and fluorine, and as complexes with organic matter. Aluminium is a major component of the earth's crust. It is released to the environment both by natural processes and from anthropogenic sources, whereby natural processes far outweigh the contribution of anthropogenic sources. Mobilization of aluminium through human actions is mostly indirect and occurs as a result of emission of acidifying substances to the atmosphere. Aluminium is highly concentrated in soil-derived dusts from natural processes, coal combustion, and activities as mining and agriculture. In addition, aluminium finds use in a wide variety of applications including structural materials in construction, automobiles and aircraft, packaging materials, various containers and kitchen utensils and pharmaceuticals (Environmental health criteria for aluminium; International Programme on Chemical Safety (IPCS); 1997).

Non-occupational human exposure to aluminium is primarily through ingestion of food and water. Food being the principal contributor, as aluminium is naturally present in varying amounts in most foodstuffs consumed. The intake of aluminium can be increased greatly through the use of aluminium-containing pharmaceutical products (especially antacids) (Environmental health criteria for aluminium; International Programme on Chemical Safety (IPCS); 1997).

Aluminium and its compounds appear to be poorly absorbed in humans; the mechanism of gastrointestinal absorption has not yet been fully elucidated. Variability results from the chemical properties of the element and the formation of various chemical species, which is dependent upon the pH, ionic strength, presence of competing elements and complexing agents within the gastrointestinal tract. The urine is the most important route of aluminium excretion. Aluminium has a long half-life (Environmental health criteria for aluminium; International Programme on Chemical Safety (IPCS); 1997).

**Metals****Arsenic**

Reference to JECFA: 5 (1960), 10 (1967), 27 (1983), 33 (1988), 72 (2010)

Toxicological guidance value: BMDL<sub>0.5</sub>: 3.0 µg/kg bw per day (2.0-7.0 µg/kg bw per day based on the range of estimated total dietary exposure) (2010, for inorganic arsenic)

Contaminant definition: Arsenic: total (As-tot) when not otherwise mentioned; inorganic arsenic (As-in); or other specification

Synonyms: As

Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)  
Code of Practice for the Prevention and Reduction of Arsenic Contamination in Rice (CXC 77-2017)

Commodity / Product Name	Maximum Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity to which the ML applies	Notes/Remarks	Notes for CCCF
Edible fats and oils	0.1	Adopted	CXS 19-1981, CXS 33-1981, CXS 210-1999, CXS 211-1999, 2017	FO, CF	Whole commodity	Relevant Codex commodity standards are CXS 19-1981, CXS 33-1981, CXS 210-1999, CXS 211-1999 and CXS 329-2017. For fish oils covered by CXS 329-2017, the ML is for (As-in). Countries or importers may decide to use their own screening when applying the ML for As-in in fish oils by analysing total arsenic (As-tot) in fish oils. If the As-tot concentration is below the ML for As-in, no further testing is required and the sample is determined to be compliant with the ML. If the As-tot concentration is above the ML for As-in, follow-up testing shall be conducted to determine if the As-in concentration is above the ML.	Fish oils were included in 2017.
Fat spreads and blended spreads	0.1	Adopted	CXS 256-2007	FO		Relevant Codex commodity standard is CXS 256-2007.	1)
Natural mineral waters	0.01	Adopted	CXS 108-1981	NMW, CF		Relevant Codex commodity standard is CXS 108-1981. Calculated as total As mg/l.	Changed from 0.05 mg/l in 2001. 2)
Salt, food grade	0.5	Adopted	CXS 150-1985	NFSDU, FA		Relevant Codex commodity standard is CXS 150-1985.	
Rice, polished	0.2	Adopted	2014	CF	Whole commodity	The ML is for inorganic arsenic (As-in). Countries or importers may decide to use their own screening when applying the ML for As-in in rice by analysing total arsenic (As-tot) in rice. If the As-tot concentration is below or equal to the ML for As-in, no further testing is required and the sample is determined to be compliant with the ML. If the As-tot concentration is above the ML for As-in, follow-up testing shall be conducted to determine if the As-in concentration is above the ML.	4)



**Metals****Arsenic**

Commodity / Product Name	Maximum Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity to which the ML applies	Notes/Remarks	Notes for CCCF
Rice, husked	0.35	Adopted	2016	CF	Whole commodity	The ML is for inorganic arsenic (As-in). Countries or importers may decide to use their own screening when applying the ML for As-in in rice by analysing total arsenic (As-tot) in rice. If the As-tot concentration is below or equal to the ML for As-in, no further testing is required and the sample is determined to be compliant with the ML. If the As-tot concentration is above the ML for As-in, followup testing shall be conducted to determine if the As-in concentration is above the ML.	3), 4)

- 1) The Standard for fat spreads and blended spreads contain the following wording for the mentioned contaminant MLs: "The products covered by the provisions of this Standard shall comply with MLs being established by CAC but in the meantime the following limits will apply". (only applying to Pb and As)
- 2) The Standard for Natural Mineral Waters contains the level in the Section 3.2 "Health-related limits for certain substances". The CCCF2 (2008) temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41 para. 23-27). After establishment of an EWG by CCCF4 (2010), CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90)
- 3) CAC39 (2016) adopted the ML on the understanding that the ML would be reviewed three years after the implementation of the Code of practice for the prevention and reduction of arsenic contamination in rice taking into account all available data from all regions (REP16/CAC, para. 65).
- 4) CCCF12 (2018) agreed to similarly amend the note on screening for arsenic in rice with mercury in fish (REP18/CF, para. 84).

A position document CX/FAC 99/22 on arsenic discussed in CCFAC31 (1999) noted that several countries have established MLs for arsenic in food commodities and some of these were stringent regarding seafoods, so trade problems might occur. The present range of Codex MLs for arsenic in some commodities do not cover all national MLs. The document concluded however that in general there are no indications that specific Codex MLs for arsenic in food commodities would be necessary. Also, at present there is no sufficient basis to decide about the establishment of Codex MLs for arsenic, due to the uncertainties mentioned about the levels of naturally occurring arsenic species in foods, about their toxicity and about the availability of suitable analytical methods. It was acknowledged that at present especially the ML for arsenic in drinking water and in mineral water is relevant. The Committee agreed that a finalized position paper would form the basis for future work until such time as routine methodology became available to determine toxic arsenic compounds in food (ALINORM 99/12A, para. 137).

JECFA72 (2010) derived an inorganic arsenic BMDL for a 0.5% increased incidence of lung cancer (BMDL<sub>0.5</sub>) by using a range of assumptions to estimate exposure from drinking-water and food, with differing concentrations of inorganic arsenic. The BMDL<sub>0.5</sub> was computed to be 3.0 µg/kg bw per day (2–7 µg/kg bw per day based on the range of estimated total dietary exposure). The uncertainties in this BMDL relate to the assumptions regarding total exposure and to extrapolation of the BMDL<sub>0.5</sub> to other populations due to the influence of nutritional status, such as low protein intake, and other lifestyle factors on the effects observed in the studied population. The Committee noted that the PTWI of 15 µg/kg bw (2.1 µg/kg bw per day) is in the region of the BMDL<sub>0.5</sub> and therefore was no longer appropriate, and the Committee withdrew the previous PTWI.

Reported mean dietary exposure to inorganic arsenic in the United States of America (USA) and various European and Asian countries ranged from 0.1 to 3.0 µg/kg bw per day. The

**Metals****Arsenic**

Committee noted that drinking-water was a major contributor to total inorganic arsenic dietary exposures and, depending on the concentration, can also be an important source of arsenic in food through food preparation and possibly irrigation of crops, particularly rice. For certain regions of the world where concentrations of inorganic arsenic in drinking-water are elevated (e.g. above the WHO guideline value of 10 µg/L), the Committee noted that there is a possibility that adverse effects could occur as a result of exposure to inorganic arsenic from water and food.

The Committee also noted that more accurate information on the inorganic arsenic content of foods as they are consumed is needed to improve assessments of dietary exposures of inorganic arsenic species. Analytical constraints to achieving this goal include the lack of validated methods for selective determination of inorganic arsenic species in food matrices and the lack of certified reference materials for inorganic arsenic in foods. The proportion of inorganic arsenic in some foods was found to vary widely, indicating that dietary exposures to inorganic arsenic should be based on actual data rather than using generalized conversion factors from total arsenic measurements.

CCCF5 (2011) agreed to initiate new work on maximum levels for arsenic in rice subject to approval by CAC34 and also agreed to re-convene the EWG, led by China, would prepare a working paper considering MLs for arsenic in rice based on the considerations made at plenary for deliberation at the next session of the Committee.

CAC34 (2011) approved the new work (REP11/CAC, para.142).

CCCF6 (2012) agreed that an EWG chaired by China and co-chaired by Japan would prepare a discussion paper on the possibility to develop a COP. In addition, China would prepare proposals for maximum levels for inorganic arsenic in rice (raw and processed) for consideration by CCCF8 based on additional data provided by that time to GEMS Food. The committee also agreed to retain at Step 4 the proposed draft maximum levels for inorganic or total arsenic in rice (raw) at 0.3 mg/kg and inorganic arsenic in rice (polished) at 0.2 mg/kg until the Committee resumed the consideration of this matter at its 8th Session based on the outcome of proposals to be prepared by China and to inform the Executive Committee accordingly (REP12/CF, paras. 63-65).

CCCF7 (2013) agreed to re-establish the EWG led by China and co-chaired by Japan to further develop the discussion paper, and to look into management practices to determine which risk management measures were readily available to the extent that could provide the basis for the preliminary development of a COP and, if so, to attach a proposed draft COP for consideration by CCCF8 (REP13/CF, para. 107).

CCCF7 also agreed that the above-mentioned EWG would also prepare a discussion paper on proposals for maximum levels for inorganic arsenic in rice and rice products for consideration at the 8th session. The Committee encouraged members to submit relevant data to the EWG, especially those from rice-producing countries, and data on indica rice, to reflect them into the discussion paper (REP13/CF, para. 110).

CCCF8 (2014) noted extensive support for an ML of 0.2 mg/kg of inorganic arsenic for polished rice and analysis for total arsenic as screening method. However, divergent views were expressed as to what the ML for husked rice should be in terms of protection of human health while not having a negative impact on international trade, in particular as rice was a major staple-food in Asian countries and the ML established may affect availability of rice. Possible levels discussed were 0.25 mg/kg, 0.3 mg/kg and the proposed ML of 0.4 mg/kg.

The Committee could not reach agreement on an ML for husked rice. However, in view of the relevance of this matter for many Codex members, the Committee encouraged countries, especially rice-producing countries to submit data to GEMS/Food. Data submitted could then be considered in the EWG in order to facilitate the discussion of this matter at CCCF9 before taking a final decision on the feasibility to establish an ML for this product. In view of this, the remaining recommendations on the development of a "polishing procedure" and the establishment of a worldwide "conversion factor" were not considered (REP14/CF, paras. 37, 42-43).

The Committee agreed to forward the proposed draft ML of 0.2 mg/kg for inorganic arsenic in polished rice to Step 5/8 (with omission of Steps 6/7) for adoption by CAC37 (REP14/CF, para. 46 and Appendix III).

The Committee agreed to return the proposed draft ML for inorganic arsenic in husked rice to Step 2/3 for further elaboration in the EWG, circulation for comments at Step 3 and consideration at the next session of the Committee and further agreed to re-establish the EWG led by China and co-chaired by Japan to prepare a proposed draft ML for husked rice (REP14/CF, para. 45 and 47).

**Metals****Arsenic**

The Committee noted wide support for the development of a Code of practice for the prevention and reduction of arsenic contamination in rice as supportive for the implementation of the MLs. A proposal however was made that current available management practices for containing arsenic contamination in rice mainly relate to source directed measures and whether it would be more appropriate to revise the Code of practice for source directed measures (CXC 49-2001) to address measures to reduce arsenic contamination rather than proceeding with the development of a separate COP at this point in time. In this regard, it was noted that although most of the management measures readily available at present mainly refer to source directed measures, other management measures were also available and relevant and should be included in the COP (REP14/CF, para. 94).

The Committee agreed to initiate new work on a Code of practice for the prevention and reduction of arsenic contamination in Rice for approval by CAC37 (Appendix VIII). The Committee agreed to establish an EWG, led by Japan and co-chaired by China to develop the COP for comments at Step 3 and consideration at the next session of the Committee (REP14/CF, paras. 95-96, Appendix VIII).

CAC37 adopted the proposed draft ML of 0.2 mg/kg for inorganic arsenic in polished rice at Step 5/8. Egypt and Sri Lanka expressed reservation about the ML (REP14/CAC, paras. 79-82, Appendix III).

CCCF9 (2015) noted general support for the establishment of an ML for inorganic arsenic in husked rice and proceeded with the discussion of the possible levels. However controversial discussion was made on the proposed ML between 0.25, 0.3, 0.35 and 0.4 mg/kg. As a compromise solution, the Committee agreed on an ML for husked rice at 0.35 mg/kg and to send this proposal to the Commission for adoption at Step 5. EU, Japan and Norway expressed their reservation to this decision. The Committee agreed that the ML for inorganic arsenic in husked rice should be accompanied by a note on analysis of total arsenic as a screening method. However, in view of the opinions expressed in relation to the need for more geographically representative data, the Committee agreed to re-establish the EWG, chaired by Japan and co-chaired by China, to further consider new/additional data provided by countries especially main rice-producing countries and countries where husked rice was a major staple food. The Committee should then consider the outcome of the analysis performed by the EWG based on the current and new/additional data to confirm or change the ML of 0.35 mg/kg at its next session. The Committee encouraged countries concerned to submit data to GEMS/Food so that the ML could be finalised at the next session of CCCF (REP15/CF, paras. 56-69).

The Committee agreed to return the COP for the prevention and reduction of arsenic contamination in rice to Step 2/3 for further development, comments and consideration by CCCF10. The Committee also agreed to re-establish the EWG, led by Japan and co-chaired by China to further develop the COP in light of comments submitted and decisions taken at this session (REP15/CF, paras. 73-74).

The Committee discussed the report of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for evaluation by JECFA and agreed to include inorganic arsenic for evaluation of non-cancer effects (neurodevelopmental, immunological and cardiovascular) (REP15/CF, para. 147).

CAC38 (2015) adopted the proposed draft ML for inorganic arsenic in husked rice at Step 5 as proposed by the Committee and advanced the draft ML to Step 6 for comments.

CCCF10 (2016) discussed whether to retain the draft ML of 0.35 mg/kg. There was support for the draft ML of 0.35 mg/kg, but also support for the proposal for an ML of 0.25 mg/kg. Noting the lack of consensus, the Committee considered a proposal by the Chair to discontinue the work on the ML for inorganic arsenic in husked rice. There was limited support to discontinue the work as views were expressed that an ML would assist in reducing exposure to inorganic arsenic and that there was a possibility that countries would apply the ML for polished rice to husked rice or that there would be different MLs applied by countries, which could impact negatively on the trade of husked rice. As a compromise, and noting the ongoing work on the COP for the prevention and reduction of arsenic in rice, the Chair proposed that the level of 0.35 mg/kg be accepted on the understanding that following the implementation of the COP (of which one of the aims is to assist in the meeting of the ML for polished rice and husked rice) the Committee would consider all available data with the intention to lower the ML.

As the result of the discussion, the Committee agreed to advance the ML of 0.35 mg/kg for husked rice for adoption at Step 8 by CAC39 on the understanding that the ML would be reviewed three years after the implementation of the COP for prevention and reduction of arsenic in rice, and would take into account all available data to clearly lower the ML of 0.35 mg/kg. The Committee noted the reservations of EU and Norway, and India. The Observer of Consumers International reiterated its concern with this decision. (REP16/CF, paras. 30-45)

**Metals****Arsenic**

CAC39 (2016) adopted the proposed ML of 0.35 mg/kg for inorganic arsenic in husked rice on the understanding that the ML would be reviewed three years after the implementation of the COP, as agreed by CCCF, and would take into account all available data from all regions. Reservations to this decision were expressed by Egypt, EU and Norway, India, Philippines and Sri Lanka. Consumers International and the National Health Federation expressed their strong concern on this decision (REP16/CAC, paras. 58-66).

The Committee discussed that the work on COP for the prevention and reduction of arsenic in rice either be postponed (pending the results of the studies being undertaken) or that work should continue on finalizing the COP (with the currently available information) on the understanding that the COP could be revised when information from such studies became available. There was general agreement on the need for work to continue on the COP, but varying views on how to proceed.

As the result, the Committee agreed to continue work on the finalisation of the COP through an EWG to be chaired by Japan and co-chaired by Spain, taking into account all decisions previously taken by the Committee, the adequacy of all current and new information submitted in response to the aforementioned CL as well as written comments submitted at this session, for consideration by the next Session of the Committee with the understanding that the COP could be reviewed in future when more information and data became available. (REP16/CF, paras. 91-100).

The Committee listed inorganic arsenic in the priority list of contaminants and naturally occurring toxins for evaluation by JECFA (REP 16/CF, appendix VI).

CCCF11 (2017) noted the request of CCFO25 (2017) to establish ML for arsenic, in particular inorganic arsenic, and ML for lead in fish oil (REP17/FO, paras. 22, 23 and 28) and noted that in seafood, arsenic is mainly found in its less toxic organic form. Similarly, while oils derived from fish can contain elevated levels of total arsenic, the majority is in the form of arsenosugars and arsenolipids. The Committee therefore agreed that the ML for arsenic in fish oils can be the same as the current ML for arsenic in edible fats and oils. However, the Committee considered it appropriate to indicate the ML for fish oils to be specific to inorganic arsenic and to apply a note that total arsenic could be used for screening purposes (REP17/CF paras. 17 and 18 and Appendix II).

The Committee revised the COP based on the revised version and agreed on several amendments to improve the clarity and accuracy of the text. The Committee agreed that complementary information for further consideration of measures would be better placed in the report as a guide for the further development of the COP when new data and information on mitigation measures become available as follows:

The results of ongoing or planned research studies on the effectiveness of measures to prevent and reduce arsenic concentration in rice should be considered in future revisions to this COP. Research on the following topics may help in further developing this COP:

- Effects of soil amendments and fertilizers (e.g. silicates, phosphates and organic materials) on arsenic concentrations in rice including considering the effects of applying different amounts of the materials or applying the materials with different timing and frequency (e.g. one-off or repeated use in each season);
- Indirect effects (e.g. change of yield, cadmium concentration in rice) of implementing measures to reduce arsenic concentrations in rice;
- Effects of varying the timing and duration of flooded/aerobic conditions during the rice growth period;
- Understanding factors affecting arsenic concentrations in rice, including from the arsenic concentrations in soil and/or other factors (e.g. iron, silicates, phosphates concentrations etc.) before cultivation; and
- Efficiency and cost of removing arsenic in soil using agricultural crops that absorb and accumulate arsenic from the soil or using chemical compounds that adsorb arsenic and are easily separated from the soil.

The Committee agreed to send the proposed draft COP to CAC40 for adoption at Step 5/8 (REP17/CF, paras. 100-103).

CAC40 (2017) adopted the proposed draft COP at Step 5/8 (REP17/CAC Appendix III).

CCCF12 (2018) agreed to similarly amend the note on screening for arsenic in rice with that of methylmercury in fish (REP 18/CF, para. 84).

**Metals****Arsenic**

CAC41 (2018) adopted the amendment to the note for the ML on inorganic arsenic in rice (REP 18/CAC, Appendix VIII).

Arsenic is a metalloid element which is normally occurring in mineral bound form in the earth's crust and which can become more easily available by natural sources such as volcanic activity and weathering of minerals, and by anthropogenic activity causing emissions in the environment, such as ore smelting, burning of coal and specific uses, such as arsenic-based wood preservatives, pesticides or veterinary or human medicinal drugs. As a result of naturally occurring metabolic processes in the biosphere arsenic occurs as a large number of organic or inorganic chemical forms in food (species). Especially in the marine environment arsenic is often found in high concentrations of organic forms, up to 50 mg/kg of arsenic on a wet weight basis in some seafood including seaweed, fish, shellfish and crustaceans. In fresh water and in the terrestrial environments arsenic is normally found in much lower levels (typically 0-20 µg/kg) in crop plants and in livestock. Higher levels may be found in rice, mushrooms and sometimes in poultry which is fed fish meal containing arsenic. Levels of arsenic in drinking water are of concern in many countries; levels exceeding 200 mg/l have been reported, which can adversely affect the health of consumers.

The most toxic forms of arsenic are the inorganic arsenic (III) and (V) compounds; the inorganic arsenic trioxide is well known as a rat poison, which was also sometimes used for homicide. Methylated forms of arsenic have a low acute toxicity; arsenobetaine which is the principal arsenic form in fish and crustaceans is considered non-toxic. In shellfish, molluscs and seaweed dimethylarsinylriboside derivatives occur ("arsenosugars"), the possible toxicity of which is not known in detail. Only a few percent of the total arsenic in fish is present in inorganic form, which is the only form about which a PTWI has been developed by JECFA.

The human epidemiological data used for this risk assessment is based on exposure to inorganic arsenic in drinking water. IARC has classified inorganic arsenic as a human carcinogen, and the estimated lifetime risk for arsenic-induced skin cancer which may be caused by drinking water at or in excess of the WHO guideline for arsenic in drinking water is estimated at  $6 \times 10^{-4}$ .

The analysis of total arsenic in food has up to date suffered from difficulties with respect to accuracy and precision. Furthermore, specified data for arsenic are strongly needed because of the large differences in toxicity to humans of the various forms of arsenic.

The intake of total arsenic in the human diet is usually dominated by organic arsenic derived from seafood. The available data about the possible human exposure to inorganic arsenic (often using the assumption that non-seafood commodities contain only inorganic arsenic) suggest that the PTWI will normally not be exceeded, unless there is a large contribution from drinking water. Further research is needed about the fate of organic arsenicals and the possibility that they might be converted to more toxic inorganic forms of arsenic, whether by processing or by metabolism in animals or humans.

**Metals****Cadmium**

Reference to JECFA: 16 (1972), 33 (1988), 41 (1993), 55 (2000), 61 (2003), 64 (2005), 73 (2010), 77 (2013)

Toxicological guidance value: PTMI 25 µg/kg bw (2010)

Contaminant definition: Cadmium, total

Synonyms: Cd

Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Brassica vegetables	0.05	Adopted	2005	FAC	Head cabbages and kohlrabi: whole commodity as marketed, after removal of obviously decomposed or withered leaves. Cauliflower and broccoli: flower heads (immature inflorescence only). Brussels sprouts: "buttons" only.	The ML does not apply to Brassica leafy vegetables.	VB 0040
Bulb vegetables	0.05	Adopted	2005	FAC	Bulb/dry onions and garlic: whole commodity after removal of roots and adhering soil and whatever parchment skin is easily detached.		VA 0035
Fruiting vegetables	0.05	Adopted	2005	FAC	Whole commodity after removal of stems. Sweet corn and fresh corn: kernels plus cob without husk.	The ML does not apply to tomatoes and edible fungi.	VC 0045 VO 0050
Leafy vegetables	0.2	Adopted	2005	FAC	Whole commodity as usually marketed, after removal of obviously decomposed or withered leaves.	The ML also applies to Brassica leafy vegetables.	VL 0053
Legume vegetables	0.1	Adopted	2001	FAC	Whole commodity as consumed. The succulent forms may be consumed as whole pods or as the shelled product.		VP 0060
Pulses	0.1	Adopted	2001	FAC	Whole commodity	The ML does not apply to soya bean (dry).	VD 0070
Root and tuber vegetables	0.1	Adopted	2005	FAC	Whole commodity after removing tops. Remove adhering soil (e.g. by rinsing in running water or by gentle brushing of the dry commodity). Potato: peeled potato.	The ML does not apply to celeriac.	VR 0075 VR 0589

**Metals****Cadmium**

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Stalk and stem vegetables	0.1	Adopted	2005	FAC	Whole commodity as marketed after removal of obviously decomposed or withered leaves. Rhubarb: leaf stems only. Globe artichoke: flower head only. Celery and asparagus: remove adhering soil.		VS 0078
Cereal grains	0.1	Adopted	2001	FAC	Whole commodity	The ML does not apply to buckwheat, cañihua, quinoa, wheat and rice.	GC 0081
Rice, polished	0.4	Adopted	2006	FAC	Whole commodity		CM 1205
Wheat	0.2	Adopted	2005	FAC	Whole commodity	The ML applies to common wheat, durum wheat, spelt and emmer.	GC 0654
Cephalopods	2	Adopted	2006	FAC	Whole commodity after removal of shell.	The ML applies to cuttlefishes, octopuses and squids without viscera.	IM 0152
Marine bivalve molluscs	2	Adopted	2006	FAC	Whole commodity after removal of shell.	The ML applies to clams, cockles and mussels but not to oysters and scallops.	IM 0151
Natural mineral waters	0.003	Adopted	CXS 108-1981	NMW, CF		Relevant Codex commodity standard is CXS 108-1981. The ML is expressed in mg/l.	1)
Salt, food grade	0.5	Adopted	CXS 150-1985	NFSDU, FA		Relevant Codex commodity standard is CXS 150-1985.	
Chocolate products containing or declaring < 30% total cocoa solids on a dry matter basis	0.3-0.4	4		CF		Including milk chocolate, family milk chocolate, milk chocolate couverture, Gianduja milk chocolate, table chocolate, milk chocolate Vermicelli/milk chocolate flakes	CL 2019/08-CF CX/CF 19/13/6
Chocolate and chocolate products containing or declaring ≥ 30% to < 50% total cocoa solids on a dry	0.9	4		CF		Including sweet chocolate, Gianduja chocolate, semi – bitter table chocolate, Vermicelli chocolate / chocolate flakes, bitter table chocolate, couverture	CL 2019/08-CF CX/CF 19/13/6

**Metals****Cadmium**

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
matter basis						chocolate.	
Chocolate containing or declaring $\geq 50\%$ to $< 70\%$ total cocoa solids on a dry matter basis	0.8	Adopted	2018	CF	Whole commodity as prepared for wholesale or retail distribution	Including sweet chocolate, Gianduja chocolate, semi – bitter table chocolate, Vermicelli chocolate / chocolate flakes, and bitter table chocolate.	
Chocolate containing or declaring $\geq 70\%$ total cocoa solids on a dry matter basis	0.9	Adopted	2018	CF	Whole commodity as prepared for wholesale or retail distribution	Including sweet chocolate, Gianduja chocolate, semi – bitter table chocolate, Vermicelli chocolate / chocolate flakes, and bitter table chocolate.	
Cocoa powder (100% total cocoa solids on a dry matter basis).	3.0-4.0	4		CF		Product sold for final consumption.	CL 2019/08-CF CX/CF 19/13/6

- 1) The Standard for Natural Mineral Waters contains the level in the Section 3.2 "Health-related limits for certain substances". CCCF2 (2008) temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41 para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).

**MLs**

At JECFA61 (2003) it was estimated that the total intake of cadmium ranged from 2.8 to 4.2  $\mu\text{g}/\text{kg}$  bw per week. This was calculated from available data on concentrations and food consumption taken from the GEMS/Food regional diets and corresponds to approximately 40-60% of the current PTWI of 7  $\mu\text{g}/\text{kg}$  bw/week. Regarding major dietary sources of cadmium, the following foods contributed 10% or more to PTWI in at least one of the GEMS/Food regions: rice, wheat, starchy roots/tubers, and molluscs. Vegetable (excluding leafy vegetables) contribute  $>5\%$  to the PTWI in two regions.

CCFAC36 (2004) decided to discontinue the work on developing MLs for cadmium in fruits, meat of cattle, pigs, sheep and poultry; horse meat; herbs, fresh; fungi (edible); celeriac; soya beans (dry); and peanuts as no levels were necessary because these foods were no major contributors to cadmium intake (ALINORM 04/27/12, para. 176).

JECFA64 (2005) conducted intake and impact assessment requested by CCFAC36 for the seven commodity groups; rice, wheat, potatoes, stem and root vegetables, leafy vegetables, other vegetables and molluscs taking into account different MLs. The Committee concluded that the effect of different MLs on the overall intake of cadmium would be very small.

JECFA73 (2010) re-evaluated cadmium as there had been a number of new epidemiological studies that had reported cadmium-related biomarkers in urine following environmental exposure. Urinary  $\beta_2$ -microglobulin level was chosen as the most suitable biomarker for cadmium toxicity because it was widely recognized as a marker for renal pathology and



**Metals****Cadmium**

consequently had the largest number of available data. Because of the long half-life of cadmium in human kidneys (15 years), it was concluded that determination of a critical concentration of cadmium in the urine was most reliable using data from individuals of 50 years of age and older. Using the dose-response relationship of  $\beta_2$ -microglobulin excretion in urine to cadmium excretion in urine for this population group, a critical concentration of 5.24 (confidence interval 4.94–5.57)  $\mu\text{g}$  of cadmium per gram creatinine was estimated. Using a one-compartment toxicokinetic model, a corresponding dietary cadmium exposure of 0.8  $\mu\text{g}/\text{kg}$  body weight per day or 25  $\mu\text{g}/\text{kg}$  body weight per month was estimated based on the lower bound of the 5th percentile dietary cadmium exposure (on a population level). Considering the exceptionally long half-life of cadmium and the fact that daily or weekly daily ingestion in food would have a small or even negligible effect on overall exposure, the Committee decided to express the tolerable intake as a monthly value in the form of a provisional tolerable monthly intake (PTMI). The Committee withdrew the PTWI of 7  $\mu\text{g}/\text{kg}$  body weight and established a PTMI of 25  $\mu\text{g}/\text{kg}$  body weight.

CCCF5 (2011) agreed that no follow-up was necessary since the estimates of exposure to cadmium through the diet for all age groups, including consumers with high exposure and subgroups with special dietary habits (e.g. vegetarians), examined by JECFA72 were below this PTMI.

JECFA77 (2013) conducted an assessment of exposure from cocoa and cocoa products at the request of CCCF6 (2012). The estimates of mean population dietary exposure to cadmium from products containing cocoa and its derivatives for the 17 new GEMS/Food Cluster Diets ranged from 0.005 to 0.39  $\mu\text{g}/\text{kg}$  bw per month, which equated to 0.02–1.6% of the PTMI of 25  $\mu\text{g}/\text{kg}$  bw. The potential dietary exposures to cadmium for high consumers of products containing cocoa and its derivatives in addition to cadmium derived from other foods were estimated to be 30–69% of the PTMI for adults and 96% of the PTMI for children 0.5–12 years of age. The Committee noted that this total cadmium dietary exposure for high consumers of cocoa and cocoa products was likely to be overestimated and did not consider it to be of concern.

CCCF8 (2014) agreed to initiate new work on MLs for cadmium in chocolate and cocoa-derived products for approval by CAC37. The Committee agreed to establish an EWG led by Ecuador, co-chaired by Ghana and Brazil to prepare proposals for MLs for comments at Step 3 and consideration at the next session of the Committee, subject to approval by CAC. (REP14/CF, paras. 141-142, Appendix XI)

CAC37 (2014) approved the new work (REP14/CAC, para. 96, Appendix VI).

CCCF9 (2015) agreed to re-establish the EWG, chaired by Ecuador and co-chaired by Brazil and Ghana to reconsider the proposed draft MLs taking into account the comments submitted to this session. The Committee noted the EWG should clearly identify the products for which the MLs were being established and provide the rationale for the MLs. The Committee agreed to return the proposed draft MLs to Step 2/3 for further consideration by the EWG, circulation for comments and further consideration by the next session of CCCF (REP15/CF, paras. 52-55).

CCCF10 (2016) agreed to establish an in-session WG chaired by Ecuador and co-chaired by Brazil and Ghana to discuss an agreement on the food categories to work on for the establishment of MLs for cadmium due to the difficulty to agree on the food categories to which the MLs should apply. The Committee considered the recommendations of the in-session WG and agreed on the recommended food categories on which MLs for cadmium would be set.

The Committee agreed to return the work on MLs for chocolate and cocoa-derived products to Step 2/3 for further elaboration, comments and consideration by CCCF11, and to re-establish the EWG, chaired by Ecuador and co-chaired by Brazil and Ghana to continue work on the development of MLs for cadmium in the intermediate products (i.e. cocoa liquor and cocoa powder) and finished products based on total cocoa solids content (%) (i.e. chocolate and cocoa powder ready for consumption) (REP16/CF, paras. 101-119).

CCCF11 (2017) agreed to establish an in-session WG to propose recommendations for the categorization of chocolates and cocoa derived products and dry mixtures of cocoa and sugars. The Committee agreed:

- to endorse the proposed categories for “chocolates” and for “cocoa powder and dry mixtures of cocoa and sugars”;
- to establish an EWG, chaired by Ecuador and co-chaired by Brazil and Ghana to prepare proposals for MLs for the identified categories for “chocolates” and “cocoa-powder and dry mixtures of cocoa and sugars” sold for final consumption;
- to discontinue work on intermediate products. Future new work could be proposed on these products in future;
- that the Codex Secretariat would issue a request for data through a CL;
- to revise the deadline for completion by two years to 2019 and to inform the CCEXEC accordingly (REP17, paras. 90-99 and Appendix XIII).

**Metals****Cadmium**

In the Committee, Peru introduced a new work on COP for the prevention and reduction of cadmium contamination in cocoa and explained that the proposed COP aimed to guide Member States and the cocoa production industry in preventing and reducing cadmium contamination in cocoa beans during the production and processing phases. The Committee agreed to establish an EWG, led by Peru to prepare a discussion paper and project document for discussion on the opportunity to develop such COP and the risk mitigation measures available to that would support the development of a COP (REP17/CF, paras. 154-155).

CCCF12 (2018) agreed:

- i. to advance the ML of 0.8 mg/kg for adoption at Step 5/8 by CAC41 for chocolate containing or declaring  $\geq 50\%$  to  $< 70\%$  total cocoa solids on a dry matter basis;
- ii. to advance the ML of 0.9 mg/kg for adoption at Step 5/8 by CAC41 for chocolate containing or declaring  $\geq 70\%$  total cocoa solids on a dry matter basis;
- iii. to continue work on the category of chocolate and chocolate products containing or declaring (1)  $< 30\%$  and (2)  $\geq 30\%$  to  $< 50\%$  total cocoa solids on a dry matter basis and to assess if it is feasible to merge these two categories to derive one ML for chocolate containing or declaring  $< 50\%$  total cocoa solids on a dry matter basis;
- iv. to discontinue work on dry mixtures of cocoa and sugars sold for final consumption; and
- v. to continue work on cocoa powder (100% total cocoa solids on a dry matter basis) taking into consideration MLs established for other product categories.

The CCCF further agreed to re-establish an EWG chaired by Ecuador, co-chaired by Brazil and Ghana reporting to CCCF13, to work on points above iii) and v) (REP18/CF, paras. 67-68).

The Committee noted the request from CAC40 that CCCF consider including quinoa in the MLs for lead and cadmium in cereals in the General Standard for Contaminants and Toxins in Food and Feed (CX/CF 18/12/02, para. 7). The Committee agreed to discuss the MLs for lead and cadmium in quinoa at CCCF13 based on the paper from the Codex and JECFA Secretariats (REP 18/CF, para. 14). CAC41 (2018) adopted the proposed MLs, noting the reservation expressed by Peru and that they applied to the final product (chocolate) as opposed to the raw material (cocoa beans) since the name of the product was "chocolate" and the relevant note stated that the MLs applied to the whole commodity as prepared for wholesale or retail distribution (REP 18/CAC, para. 32).

**Code of practice**

CCCF12 (2018) noted the recommendation of the EWG to administer a survey to gather information on validated practices throughout the food chain for the prevention and reduction of cadmium contamination in cocoa prior to starting new work on the development of a COP. To gather this information, the Committee agreed that a circle letter would be prepared for the survey and distributed by the Codex Secretariat. The JECFA Secretariat requested CCCF to pay a particular attention to mitigation measures that would be feasible even for small-scale farmers to apply since they were the ones affected most by this issue (REP 18/CF, para.141 and 143).

The Committee agreed to re-establish an EWG chaired by Peru, co-chaired by Ghana and Ecuador to further elaborate the discussion paper to:

- i. determine whether mitigation measures available at present would support the development of the COP; and
- ii. identify the scope of the COP (e.g. whether the COP will cover the whole production chain or only primary production) based on the replies provided to the survey.

If the conditions under i) and ii) above are met, then the EWG should provide a project document and a first draft of a COP (REP 18/CF, paras. 144-146).

Cadmium is a relatively rare element, released to the air, land, and water by human activities. In general, the two major sources of contamination are the production and utilization of cadmium and the disposal of wastes containing cadmium. Increases in soil cadmium content will result in an increase in the uptake of cadmium by plants; the pathway of human exposure from agricultural crops is thus susceptible to increases in soil cadmium. The cadmium uptake by plants from soil is greater at low soil pH. Edible free-living food organisms such as shellfish, crustaceans, and fungi are natural accumulators of cadmium. Similar to humans, there are increased levels of cadmium in the liver and kidney of horses and some feral terrestrial animals. Regular consumption of these items can result in increased exposure. Tobacco is an important source of cadmium uptake in smokers (Environmental health criteria for cadmium; International Programme on Chemical Safety (IPCS); 1992)

Data from experimental animals and humans show that pulmonary absorption is higher than gastrointestinal absorption. The gastrointestinal absorption of cadmium is influenced by

**Metals**

**Cadmium**

the type of diet and nutritional status. Cadmium absorbed from the lungs or the gastrointestinal tract mainly accumulates in the liver and kidneys. Although cadmium accumulates in the placenta, transfer to the fetus is low. Excretion is normally slow, and the biological half-time is very long (decades). The binding of intracellular cadmium to metallothionein in tissues protects against the toxicity of cadmium. Excretion occurs mainly via urine (Environmental health criteria for cadmium; IPCS; 1992)

The kidney is considered the critical target organ for the general population as well as for occupationally exposed populations. The accumulation of cadmium in the kidney leads to renal dysfunction. Chronic obstructive airway disease is associated with long-term high-level occupational exposure by inhalation (Environmental health criteria for cadmium; IPCS; 1992).

The IARC classified cadmium and cadmium compounds in group 1, carcinogenic to humans (1993).

**Metals****Lead**

Reference to JECFA: 10 (1966), 16 (1972), 22 (1978), 30 (1986), 41 (1993), 53 (1999), 73 (2010)  
 Toxicological guidance value: - (PTWI withdrawn in 2010)  
 Contaminant definition: Lead, total  
 Synonyms: Pb  
 Related code of practice: Code of Practice for the Prevention and Reduction of Lead Contamination in Foods (CXC 56-2004)  
 Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Cranberry	0.2	Adopted	2015	CF	Whole commodity after removal of caps and stems.		
Currants	0.2	Adopted	2015	CF	Fruit with stem.		
Elderberry	0.2	Adopted	2015	CF	Whole commodity after removal of caps and stems.		
Fruits	0.1	Adopted	2001, 2016	FAC, CF	Whole commodity. Berries and other small fruits: whole commodity after removal of caps and stems. Pome fruits: whole commodity after removal of stems. Stone fruits, dates and olives: whole commodity after removal of stems and stones, but the level calculated and expressed on the whole commodity without stem. Pineapple: whole commodity after removal of crown. Avocado, mangos and similar fruit with hard seeds: whole commodity after removal of stone but calculated on whole fruit.	The ML does not apply to cranberry, current and elderberry.	4) CCCF10 included berries and other small fruits (except cranberry, currants, elderberry) in this category (REP16/CF, para 83 and 84)
Brassica vegetables	0.1	Adopted	2015	CF	Head cabbages and kohlrabi: whole commodity as marketed, after removal of obviously decomposed or withered leaves. Cauliflower and broccoli: flower heads (immature inflorescence only). Brussels sprouts: "buttons" only.	The ML does not apply to kale and leafy Brassica vegetables.	
Bulb vegetables	0.1	Adopted	2001	FAC	Bulb/dry onions and garlic: whole commodity after removal of roots and adhering soil and whatever parchment skin		VA 0035

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Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Fruiting vegetables	0.05	Adopted	2015	CF	is easily detached. Whole commodity after removal of stems. Sweet corn and fresh corn: kernels plus cob without husk.	The ML does not apply to fungi and mushrooms.	
Leafy vegetables	0.3	Adopted	2001	FAC	Whole commodity as usually marketed, after removal of obviously decomposed or withered leaves.	The ML applies to leafy Brassica vegetables but does not apply to spinach.	VL 0053
Legume vegetables	0.1	Adopted	2015	CF	Whole commodity as consumed. The succulent forms may be consumed as whole pods or as the shelled product.		
Fresh farmed mushrooms (common mushrooms ( <i>Agaricus bisporous</i> ), shiitake mushrooms ( <i>Lentinula edodes</i> ), and oyster mushrooms ( <i>Pleurotus ostereatus</i> ))	0.3	Adopted	2018	CF	Whole commodity	Relevant Codex commodity standard is CXS 38-1981.	
Pulses	0.1	Adopted	2017	CF	Whole commodity		VD 0070
Root and tuber vegetables	0.1	Adopted	2001	FAC	Whole commodity after removing tops. Remove adhering soil (e.g. by rinsing in running water or by gentle brushing of the dry commodity). Potato: peeled potato.		VR 0075
Canned fruits	0.1	Adopted	2015 2016	CF	The ML applies to the products as consumed.	Relevant Codex commodity standards are CXS 242-2003, CXS 254-2007, CXS 78-1981, CXS 159-1987, CXS 42-1981, CXS 99-1981, CXS 60-1981, CXS 62-1981, CXS 319-2015.	CCCF9 noted that the ML also applied to canned mixed fruits (REP15/CF, para. 39). Canned berries and other small fruits were included by CCCF10 (REP16/CF, para. 58).
Jams, jellies and marmalades	0.4	Adopted	2017	CF		Relevant Codex commodity standard is CXS 296-2009	
Mango chutney	0.4	Adopted	2018	CF		Relevant Codex commodity	

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Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
						standard is CXS 160-1987.	
Canned vegetables	0.1	Adopted	2015 2016 2018	CF	The ML applies to the products as consumed.	Relevant Codex commodity standard is CXS 297-2009	CCCF9 noted that the ML also applied to canned mixed vegetables. (REP15/CF, para. 42)
Preserved tomatoes	0.05	Adopted	2017	CF		Relevant Codex commodity standard is CXS 13-1981.	
Table olives	0.4	Adopted	2016	CF		Relevant Codex commodity standard is CXS 66-1981.	CCCF10 agreed to re-evaluate in future when more data became available (REPCF/16, para. 77).
Pickled cucumbers (cucumber pickles)	0.1	Adopted	2016	CF		Relevant Codex commodity standard is CXS 115-1981.	
Canned chestnuts and canned chestnuts puree	0.05	Adopted	2017	CF		Relevant Codex commodity standard is CXS 145-1985.	
Fruit juices	0.03	Adopted	2015 2016	CF	Whole commodity (not concentrated) or commodity reconstituted to the original juice concentration, ready to drink. The ML applies also to nectars, ready to drink.	The ML does not apply to juices exclusively from berries and other small fruit. Relevant Codex commodity standard is CXS 247-2005.	CCCF10 included passion fruit juice in this category (REP16/CF, para. 56).
Fruit juices exclusively from berries and other small fruits	0.05	Adopted	2015 2018	CF	Whole commodity (not concentrated) or commodity reconstituted to the original juice concentration, ready to drink. The ML applies also to nectars, ready to drink.	The ML does not apply to grape juice. Relevant Codex commodity standard is CXS 247-2005.	CCCF12 added the exception note for grape juice (REP18/CF, Appendix II)
Grape juice	0.04	Adopted	2018	CF	Whole commodity (not concentrated) or commodity reconstituted to the original juice concentration, ready to drink. The ML applies also to nectars, ready to drink.	Relevant Codex commodity standard is CXS 247-2005.	
Cereal grains	0.2	Adopted	2001	FAC	Whole commodity	The ML does not apply to buckwheat cañihua and	GC 0081

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Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Infant formula, Formula for special medical purposes intended for infants and Follow-up formula	0.01	Adopted	2014	CF	Whole commodity	quinoa. Relevant Codex commodity standards are CXS 72-1981 and CXS 156-1987. The ML applies to formula as consumed.	
Fish	0.3	Adopted	2006	FAC	Whole commodity (in general after removing the digestive tract)		
Meat of cattle, pigs and sheep	0.1	Adopted	2001	FAC	Whole commodity (without bones)	The ML also applies to the fat from meat.	MM 0097
Meat and fat of poultry	0.1	Adopted	2001	FAC	Whole commodity (without bones)		PM 0110 PF 0111
Cattle, Edible offal of	0.5	Adopted	2001	FAC	Whole commodity.		MO 0812
Cattle, Edible offal of	0.15	4		CF	Whole commodity.		CL 2019/07-CF CX/CF 19/13/5
Pig, Edible offal of	0.5	Adopted	2001	FAC	Whole commodity.		MO 0818
Pig, Edible offal of	0.15	4		CF	Whole commodity.		CL 2019/07-CF CX/CF 19/13/5
Poultry, Edible offal of	0.5	Adopted	2001	FAC	Whole commodity.		PO 0111
Poultry, Edible offal of	0.1	4		CF	Whole commodity		CL 2019/07-CF CX/CF 19/13/5
Edible fats and oils	0.08	Adopted	2018	CF	Whole commodity as prepared for wholesale or retail distribution.	Relevant Codex commodity standards are CXS 19-1981, CXS 33-1981, CXS 210-1999, CXS 211-1999 and CXS 329-2017.	
Fat spreads and blended spreads	0.04	Adopted	2018	CF	Whole commodity as prepared for wholesale or retail distribution.	Relevant Codex commodity standard is CXS 256-2007.	1)
Milk	0.02	Adopted	2001	FAC	Whole commodity	Milk is the normal mammary secretion of milking animals obtained from one or more milkings without either addition to it	ML 0106 The previous footnote "For dairy products, an appropriate concentration factor

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Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
						or extraction from it, intended for consumption as liquid milk or for further processing. A concentration factor applies to partially or wholly dehydrated milks.	should apply” was changed by CAC26.
Secondary milk products	0.02	Adopted	2001	FAC	Whole commodity <sup>f</sup>	The ML applies to the food as consumed.	
Natural mineral waters	0.01	Adopted	CS 108-1981	NMW, CF		Relevant Codex commodity standard is CXS 108-1981. The ML is expressed in mg/l.	2)
Salt, food grade	1	Adopted	2018	CF	Whole commodity as prepared for wholesale or retail distribution.	Relevant Codex commodity standard is CXS 150-1985. Excluding salt from marshes.	
Wine	0.2	Adopted	2001	FAC			3)
Wine	0.05 or 0.1	4		CF		The ML applies to wine made from grape harvested after the date of the established of the ML	CL 2019/07-CF CX/CF 19/13/5
Fortified or liqueur wines	0.15	4		CF		The ML applies to products made from grape harvested after the date of the established of the ML	CL 2019/07-CF CX/CF 19/13/5

- 1) The Standard for fat spreads and blended spreads contain the following wording for the mentioned contaminant MLs: “The products covered by the provisions of this Standard shall comply with MLs being established by CAC but in the meantime the following limits will apply.” (only applying to Pb and As).
- 2) The Standard for Natural Mineral Waters contains the level in the Section 3.2 “Health-related limits for certain substances”. CCCF2 (2008) temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41, para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).
- 3) The OIV requested special consideration to be given to levels of lead in wines that had been stored for long periods of time (ALINORM 01/41, para.123).



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- 4) The category of “Berries and other small fruits” is still retained in the current version of the GSCTFF (amended in 2018) though CCCF10 agreed to combine the category of fruits with the category of berries and other small fruits (MLs = 0.1 mg/kg) and make the necessary adjustments to the ML for fruits so that it accommodate berries and other small fruits.

CAC32 (2001) requested reevaluation of the lead MLs in milk and milk fat (ALINORM 01/41, para. 121); see also ALINORM 03/12 paras. 135-137. CCFAC35 (2004) discussed the issue of the necessity of an ML for milk, as milk was not a major contributor to the intake of lead. However, in view of opinions that milk is a major contributor to the exposure of infants and young children, the ML for milk was maintained. The Committee decided to inform CAC that the current level for lead in milk fat (0.1 mg/kg) should be revoked (no documentation of such a decision is found in the CAC 2003 report however). CCFAC35 (2005) agreed to retain the current ML for milk.

In the informal ad hoc Working Group on priorities for evaluation by JECFA held at CCCF3 (2009), the USA proposed including lead in the priority list of JECFA evaluation, since new epidemiological data indicated that effects were seen below the practical threshold of blood lead levels of 10 µg/dl. The request was made to particularly evaluate the dose- response effects of lead below this ‘threshold’. Since there was data readily available and because of possible public health implications, the WG decided to include lead in the priority list for evaluation by JECFA with high priority. The Committee endorsed the priority list of contaminants and naturally occurring toxicants for JECFA evaluation as proposed by the Working Group. (ALINORM 09/32/41, para 120 and CRD 2)

CCCF4 (2010) noted that CCPFV had elaborated several general standards for groups of canned fruits and vegetables thereby replacing individual standards for canned fruits and vegetable which were revoked by the Commission on adoption of the general standards. It was further noted that the scope of these general standards had also been expanded to include other commodities for which individual standards had not previously existed. These general standards contained the general statement on contaminants from the Procedural Manual. At the same time, several MLs for lead for canned fruits and vegetables from the revoked standards were listed in the GSCTFF. The Committee therefore considered whether the levels for lead applied to the more general standards with particular regard to whether these levels could also be extended to those commodities now included in these general standards for which levels had not previously been established. The Committee agreed to not take action until JECFA73 (2010) had completed its evaluation (ALINORM 10/33/41, paras. 18-22).

JECFA73 (2010) re-evaluated lead and concluded that the effects on neurodevelopment and systolic blood pressure provided the appropriate bases for dose–response analyses. Based on the dose–response analyses, the Committee estimated that the previously established PTWI of 25 µg/kg bw was associated with a decrease of at least 3 IQ points in children and an increase in systolic blood pressure of approximately 3 mmHg (0.4 kPa) in adults, which were considered important effects when viewed on a population level. The Committee therefore withdrew the PTWI as it could no longer be considered health protective. Because the dose–response analyses did not provide any indication of a threshold for the key effects of lead, the Committee concluded that it was not possible to establish a new PTWI that would be considered to be health protective.

The Committee concluded that the conducted dose–response Analyses should be used to identify the magnitude of effect associated with identified levels of dietary lead exposure in different populations. The mean dietary exposure estimates for children aged about 1–4 years ranged from 0.03 to 9 µg/kg bw per day and for adults from 0.02 to 3 µg/kg bw per day. The higher end of the exposure range for children was deemed by the Committee to be a concern, as it was higher than the level of 1.9 µg/kg bw per day calculated by the Committee to be associated with a population decrease of 3 IQ points. For adults, the higher end of the exposure range, a population increase of approximately 2 mmHg (0.3 kPa) in systolic blood pressure would be expected to occur. An increase of this magnitude had been associated, in a large meta-analysis, with modest increases in the risks of ischaemic heart disease and cerebrovascular stroke. The Committee considered the expected effects in children of more concern than the effects in adults.

The Committee stressed that other (than dietary) sources of exposure to lead needed also to be considered. Also, The Committee concluded that, in populations with prolonged dietary exposures to lead that are at the higher end of the ranges identified above, measures should be taken to identify major contributing sources and foods and, if appropriate, to identify methods of reducing dietary exposure that are commensurate with the level of risk reduction.

CCCF5 (2011) agreed to establish an EWG, led by USA, to: (i) reconsider the existing MLs with a focus on foods important for infants and children and also on the canned fruits and vegetables and (ii) reconsider if other existing maximum levels should be addressed.

CCCF6 (2012) agreed to start new work on the revision of the MLs for lead in fruit juices, milk and secondary milk products, infant formula, canned fruits and vegetables, fruits and cereal grains (except buckwheat, cañihua and quinoa). It was noted that where possible follow-up formula could be taken into account during this work because the data that was

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used for infant formula could also apply to this product. The Committee also agreed to establish an EWG lead by the United States of America to revise the MLs for lead for comments at Step 3 and consideration at the 7th session (REP12/CF, paras. 126-127 and Appendix VIII). CAC35 (2012) approved the new work (REP12/CAC, Appendix VI).

CCCF7 (2013) agreed to retain the current MLs of 0.02 mg/kg for milks and 0.2 mg/kg for cereals. The Committee noted that the ML for milk might be reviewed in future when new data became available and might be revised in light of the review of the MLs for milk products and also noted that if different MLs would be considered for cereal grains in future, stricter MLs could be applied to certain cereal grains in light of available data (REP13/CF, paras. 28-29). The Committee agreed to retain the ML of 0.05 mg/kg for juices and nectars from berries and other small fruits, ready-to-drink, and noted that in future, there might be a need for different MLs for fruit juices depending on the outcome of discussions on the ML for lead in fruit (REP13/CF, paras. 31-32).

The Committee agreed to advance the proposed draft ML of 0.03 mg/kg for fruit juices and nectars, ready-to-drink (excluding juices from berries and other small fruits); the proposed draft ML of 0.1 mg/kg for canned fruits, including canned mixed fruits (excluding canned berry and other small fruits); and the proposed draft ML of 0.1 mg/kg for canned vegetables, including canned mixed vegetables (excluding canned brassica vegetables, canned leafy vegetables and canned legume vegetables) to CAC36 for adoption at Step 5/8. Following this decision, the Committee agreed to request the Commission to revoke the MLs for lead for the individual standards for canned fruits (i.e. canned fruit cocktail, canned tropical fruit salad, canned grapefruit, canned mandarin oranges, canned mangoes, canned pineapples, canned raspberries and canned strawberries) and to revoke the MLs for lead for the individual standards for canned vegetables (i.e. canned asparagus, canned carrots, canned green beans and canned wax beans, canned green peas, canned mature processed peas, canned mushrooms, canned palmito (palm hearts), canned sweet corn, canned tomatoes and table olives) (REP13/CF, para.41-43 and APPENDIX II).

The Committee agreed to continue with the review of MLs for lead in fruits, vegetables, milk products and infant formula, follow-up formula and formula for special medical purposes for infants. The Committee therefore agreed to re-establish the EWG led by the USA to continue with the review of the MLs for lead for the above-mentioned commodities in the GSCTFF (REP13/CF, para. 39-40).

CAC36 (2013) agreed to adopt the MLs at Step 5 with the understanding that countries that had intervened commit to submit data to GEMS/Food database within a year, to allow CCCF to further consider the revision of the MLs in 2015 for submission to CAC38. Following this decision, the Commission did not revoke MLs for the individual standards for canned fruits and vegetables (REP13/CAC, para. 79 and 102).

CCCF8 (2014) noted wide support for the retention of the current MLs in the GSCTFF for “assorted (sub)tropical fruits, edible peel”, “assorted(sub)tropical fruits, inedible peel”, “citrus fruits”, “pome fruits”, “stone fruits”, “bulb vegetables”, “leafy vegetables”, “root and tuber vegetables” and “secondary milk products” and therefore no further action needed to be taken in regard to these MLs. The Committee noted that retention of these MLs implied that the relevant accompanying explanatory notes should be retained (REP14/CF, para. 21).

The Committee noted that for the commodity group “berries and other small fruits” the proposed lower ML may be acceptable when applied to the occurrence data of this group as a whole. However, when the data are split into the individual species or varieties of berries and small fruits, the proposed reduction may be problematic for some berries such as cranberries, currants, elderberries and strawberry tree. Therefore, it was advisable to postpone the discussion of this ML until CCCF9 to allow interested countries to submit new or additional data to GEMS/Food for analysis on the understanding that if no data were made available, the Committee would accept the proposed lower ML for adoption at its 9th session. The Committee recalled that this approach was similar to the one taken on infant formula at its 7th Session (REP14/CF, para. 22).

The Committee agreed to request the EWG to also undertake the review of the data submitted on lead contamination in fruit juices and nectars, canned fruits and canned vegetables in reply to CL 2013/23-CF, with a view to facilitating their discussion and finalization at CCCF9. The Committee further agreed that the EWG would be led by the USA (REP14/CF, paras. 26-27).

The Committee agreed to forward the proposed draft ML of 0.01 mg/kg for lead in infant formula and formula for special medical purposes intended for infants and follow up formula (as consumed) to Step 5/8 (with omission of Steps 6/7) for adoption by CAC37. EU and Norway expressed their reservation to this decision.

In taking this decision, the Committee further agreed to request the Commission to revoke the current ML of 0.02 mg/kg for lead in infant formula in the GSCTFF and to request the Committee on Nutrition and Foods for Special Dietary Uses to remove this ML from the section on contaminants in the Standard for Infant Formula and Formulas for Special Medical

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Purposes Intended for Infants (CXS 72-1981) and instead to make reference to the GSCTFF(CXS 193-1995, REP14/CF, paras. 32-34. Appendix II).

CAC37 (2014) adopted the revised ML of 0.01 mg/kg for lead in Infant Formula and Formula for Special Medical Purposes and for Follow-Up Formula as proposed by CCCF8. The EU, Egypt, Malaysia and Norway expressed their reservation (REP14/CAC, para. 74, Appendix III). The Commission agreed to revoke the Maximum Level for Lead in Infant Formula in the GSCTFF (REP14/CAC, para. 94, Appendix V).

CCCF9 (2015) agreed to reduce the ML for lead in fruit juices and nectars, ready-to-drink from 0.05 to 0.03 mg/kg. The Committee also agreed to retain the ML of 0.05 mg/kg for juices and nectars from berries and other small fruit at 0.05 mg/kg, and agreed that exclusion for juices from berries and other small fruits should be limited to juices that were “exclusively” prepared from berries and other small fruits. The Committee also agreed to exclude passion fruit juice from the ML for fruit juices and nectars and wait until CCCF10 to make a final decision on this matter based on the recommendation of the EWG (REP15/CF, paras. 36-38).

The Committee agreed to reduce the ML for canned fruits (excluding berries and other small fruits) from 1 mg/kg to 0.1 mg/kg. The Committee noted that the ML also applied to canned mixed fruits. Following this decision, the Committee agreed to make consequential amendments to the MLs for lead in the GSCTFF by revocation of MLs of corresponding fruits. The Committee agreed to retain the MLs for canned raspberries and canned strawberries at 1 mg/kg for consideration at CCCF10 based on the recommendation of the EWG (REP15/CF, paras. 39-40).

The Committee agreed to reduce the ML for berries and other small fruits from 0.2 mg/kg to 0.1 mg/kg and to exclude certain types of berries i.e. cranberry, currant, elderberry and to retain the existing ML of 0.2 mg/kg for these fruits (REP15/CF, para. 41).

The Committee agreed to reduce the ML for canned vegetables (excluding canned brassica, leafy and legume vegetables) from 1 mg/kg to 0.1 mg/kg. The Committee noted that the ML also applied to canned mixed vegetables. The Committee agreed to make consequential amendments to the MLs for lead in the GSCTFF by revocation of MLs of corresponding vegetables and noted that MLs for canned brassica vegetables, canned leafy vegetables and canned legume vegetables would be considered by the EWG (REP15/CF, paras. 42-44).

The Committee agreed with the following: (i) reduce the ML for brassica vegetables from 0.3 mg/kg to 0.1 mg/kg; (ii) reduce the ML for legume vegetables from 0.2 mg/kg to 0.1 mg/kg; (iii) reduce the ML for fruiting vegetables, cucurbits from 0.1 mg/kg to 0.05 mg/kg; and (iv) reduce the ML for fruiting vegetables, other than cucurbits from 0.1 mg/kg to 0.05 mg/kg (excluding fungi and mushrooms). The Committee noted a proposal to exclude sweet corn from the ML for fruiting vegetables, other than cucurbits, however data in support of this reduction came mainly from one region while global GEMS/Food data supported inclusion of canned sweet corn under the ML for fruiting vegetables, other than cucurbits. The Committee also noted that in view of the exclusion of fungi and mushrooms from the ML for fruiting vegetables, other than cucurbits, MLs for these commodities would be considered by the EWG (REP15/CF, paras. 45-47).

Consequently, the Committee agreed to forward draft MLs for fruit juices and nectars (excluding juices exclusively from berries and other small fruits and passion fruit), ready-to-drink at 0.03 mg/kg, canned fruits (excluding berries and other small fruits) at 0.1 mg/kg and canned vegetables (excluding canned brassica, leafy and legume vegetables) at 0.1mg/kg to CAC38 for adoption at Step 8, and proposed draft MLs for berries and other small fruits (excluding cranberry, currant and elderberry) at 0.1 mg/kg; cranberries at 0.2 mg/kg; currant at 0.2 mg/kg; elderberry at 0.2 mg/kg; brassica vegetables at 0.1 mg/kg; legume vegetables at 0.1 mg/kg; fruiting vegetables, cucurbits at 0.05 mg/kg; and fruiting vegetables, other than cucurbits at 0.05 mg/kg (excluding fungi and mushrooms) to CAC38 for adoption at Step 5/8.

The Committee also agreed to recommend revocation of the following MLs by CAC38: canned grapefruit, canned mandarin oranges, canned mangoes, canned pineapples, canned fruit cocktail, canned tropical fruit salad, canned asparagus, canned carrots, canned mature processed peas, canned mushrooms, canned palmito (palm hearts) and canned sweet corn. (REP15/CF, paras. 49-51)

The Committee also agreed to re-establish the EWG, chaired by USA to continue to work on outstanding issues related to the review of MLs for lead in fruits and vegetables in the GSCTFF namely review of MLs for passion fruit juice; juices and nectars from berries and other small fruits; canned berries and other small fruits; jams (fruit preserves) and jellies; mango chutney; canned chestnuts and canned chestnuts puree; canned brassica vegetables; canned leafy vegetables; canned legume vegetables; pickled cucumbers (cucumber

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pickles); preserved tomatoes; processed tomato concentrates; table olives; fungi and mushrooms (REP15/CF, para. 48).

CAC38 (2015) adopted the draft and proposed draft MLs for lead at Step 8 and 5/8 (REP15/CAC, para. 13, Appendix III).

CCCF10 (2016) agreed to forward to CAC39 the proposed draft revised MLs for fruit juices and nectars, ready-to-drink (inclusion of passion fruit) (ML = 0.03 mg/kg); canned fruits (inclusion of canned berries and other small fruits) (ML = 0.1 mg/kg); canned vegetables (inclusion of canned leafy vegetables and canned legume vegetables) (ML = 0.1 mg/kg); jams, jellies and marmalades (revised ML = 0.1 mg/kg and inclusion of marmalades); pickled cucumbers (revised ML = 0.1 mg/kg); preserved tomatoes (revised ML = 0.05 mg/kg and deletion of the note on the adjustment of the ML to take into account the concentration of the product); table olives (revised ML = 0.4 mg/kg) for adoption at Step 5/8. The Committee also agreed to request CAC39 to revoke the MLs for lead in the GSCTFF for the following food categories: canned raspberries (ML = 1 mg/kg), canned strawberries (ML = 1 mg/kg), canned green beans and canned wax beans (ML = 1 mg/kg); canned green peas (ML = 1 mg/kg); jams (fruit preserves) and jellies (ML = 1 mg/kg); pickled cucumbers (1 mg/kg); preserved tomatoes (ML = 1 mg/kg); and table olives (ML = 1 mg/kg). The Committee agreed to re-establish the EWG chaired by USA to continue work on the review of the MLs for lead on the following food categories: fruit juices and nectars that are obtained exclusively from berries and other small fruits; canned brassica vegetables; canned chestnuts and chestnut puree; fungi and mushrooms; mango chutney; processed tomato concentrates and to add two new food categories i.e. fish and pulses for consideration by CCCF11 (REP16/CF paras. 46-90).

CAC39 (2016) discussed MLs for lead. The Commission noted the concern of several delegations in relation to the adoption of MLs for preserved tomatoes and jams, jellies and marmalades. These delegations pointed out that there were not sufficient data available to be able to examine the proposed level for these products. These delegations requested more time to gather data to review the existing MLs in order to ensure both consumer health protection and fair trade practices and proposed to adopt these MLs at Step 5 only. The Chairperson therefore proposed to adopt the MLs as proposed by CCCF; to note the concerns of those Members in relation to the MLs for preserved tomatoes and jams, jellies and marmalades; to request CCCF to consider their revision in future should new/additional data become available; and to encourage Members to urgently work on the generation and submission of data so that the MLs could be revisited based on all the data and information available. The Commission agreed with the proposal of the Chairperson to adopt the MLs at Step 5/8 as proposed by CCCF with the exception of the MLs for preserved tomatoes and jams, jellies and marmalades which would be adopted at Step 5 only, on the understanding that countries concerned would submit relevant data in reply to a call for data to be issued shortly in order to finalize these MLs at CCCF11 (REP16/CAC, paras. 67- 74). The Commission did not revoke the MLs for lead in preserved tomatoes and in jams (fruit preserves) and jellies, for which revisions were only adopted at Step 5 (REP16/CAC, para. 94).

CCCF11 (2017) noted the request of CCFO25 (2017) to establish ML for arsenic, in particular inorganic arsenic, and ML for lead in fish oil (REP17/FO, paras. 22, 23 and 28) and noted that the ML for lead in fish oils can be the same as the current ML for lead in edible fats and oils. The Committee therefore agreed to add a reference to the Standard for Fish Oils to the remarks column of the ML for lead in edible fats and oils once the standard is adopted (REP17/CF para. 16 and Appendix II).

The Committee agreed to advance the MLs for preserved tomatoes (ML = 0.05 mg/kg), jams, jellies and marmalades (ML = 0.4 mg/kg), canned chestnuts (ML = 0.05 mg/kg) and pulses (ML = 0.1 mg/kg) to Steps 8 and 5/8. The Committee agreed to delete the note for preserved tomatoes in the GSCTFF on the adjustment of the ML to take into account the concentration of the product, and to re-evaluate jams, jellies and marmalades in future when more data became available. India expressed its reservation to the decision on the jams, jellies and marmalades and Thailand expressed its reservation to the decision on the pulses.

The Committee agreed to advance the ML for processed tomato concentrate (ML = 0.05 mg/kg) and canned brassica vegetables (ML = 0.1 mg/kg) to Step 5. The Committee also agreed to delete the note for tomato concentrate in the GSCTFF (on the adjustment of the ML to take into account the concentration of the product). In addition, the Committee also encouraged countries and observer organizations to submit data to GEMS/Food and any additional information e.g. type of product (tomato paste, tomato puree), concentration factors etc. as remarks to the GEMS/Food database in order to better identify the product when deriving proposed lower MLs for this food category.

The Committee also agreed to propose that CAC revoke the existing MLs for the categories proposed for adoption at Steps 8 and 5/8, to establish an EWG chaired by the United States of America to work on the following food categories: grape juices (to determine if a lower ML could be established as part of the positive list to apply to juices obtained exclusively from berries and other small fruits); processed tomato concentrates; mango chutney; canned brassica vegetables; fungi and mushrooms; salt; wine; edible fats and oils, and, fats spreads and blended spreads. For the fats, oils and spread categories, the Committee agreed that a simplified approach should be preferable rather than having a detailed breakdown

**Metals****Lead**

of these categories in order to facilitate the establishment of MLs and their enforcement.

The Committee agreed to retain the ML of 0.05 mg/kg for juices obtained exclusively from berries and small fruits and to work on a positive list of these fruits that could achieve lower levels (e.g. 0.03 or 0.04 mg/kg) as more data became available, and to retain the current ML of 1 mg/kg for mango chutney as a stand-alone category and to encourage member countries concerned to submit data to GEMS/Food in order to make a final decision at its next session. The Committee agreed to maintain the ML for fish at 0.3 mg/kg. The Committee agreed to further consider an ML for farmed fungi and mushrooms (i.e. common mushroom, shiitake and oyster) at its next session and encouraged member countries to submit data to GEMS/Food in order to finalize the ML(s) at its next session.

The Committee agreed that work on new MLs for lead in food categories, which are currently not listed in the GSCTFF, would need further analysis based on their public health concern and their relevance to international trade and request the EWG led by Brazil to prepare a discussion paper on a structured approach to prioritize commodities not in the GSCTFF taking into account public health for which new MLs for lead could be established (REP17/CF, paras. 41-89).

CAC40 adopted the MLs for lead in selected processed fruits and vegetables and noted the reservations of Uganda on the ML for preserved tomato and of Cuba on the ML for jams, jellies and marmalades (REP17/CAC, paras. 55-57).

CCCF12 (2018) agreed:

- to advance the MLs for grape juice (0.04 mg/kg), mango chutney (0.4 mg/kg), canned brassica vegetables (include in the canned vegetable category with an ML of 0.1 mg/kg), fresh farmed mushrooms (0.3 mg/kg), salt (excluding salt from marshes) (1 mg/kg), fat spreads and blended spreads (0.04 mg/kg), edible fats and oils (0.08 mg/kg) to CAC41 for adoption at Step 5/8 (with omission of Steps 6/7);
- to propose that CAC41 revoke the existing MLs for the mango chutney, salt, fat spreads and blended spreads, edible fats and oils in view of the adoption of revised MLs, and the ML for processed tomato concentrates categories noting that the current ML for fruiting vegetables (which includes fresh tomatoes) of 0.05 mg/kg could be used to derive, with concentration factors, an ML for tomato concentrates, and that such an approach would be in line with the desire of CCCF to consolidate MLs where possible, and would provide for flexibility in the application of MLs for this food category (REP18/CF, paras. 45);
- to establish an EWG chaired by the United States of America, to continue work on MLs for wine made from grapes and for fortified wines, made from grapes harvested after the date of the established of the ML and on edible offals as previously agreed; and
- to communicate to CCEXEC that the work could be expected to be concluded at CCCF13 (REP18/CF, paras. 38, 46).

CCCF12 agreed to discuss the MLs for lead and cadmium in quinoa at CCCF13 based on the paper from the Codex and JECFA Secretariats (REP18/CF, para. 14).

CAC41 (2018) adopted the MLs for lead in selected commodities and revoked corresponding MLs. (REP18/CAC, Appendix III and V).

Exposure to lead can occur from many sources but usually arises from industrial use. Lead and its compounds can enter the environment during mining, smelting, processing, use, recycling, or disposal. The main uses of lead are in batteries, cables, pigments, plumbing, gasoline, solder and steel products, food packaging, glassware, ceramic products, and pesticides. The main exposure of the general non-smoking adult population is from food and water. Airborne lead may contribute significantly to exposure, depending on such factors as use of tobacco, occupation, and proximity to sources such as motorways and lead smelters. Food, air, water, and dust or soil are the main potential sources of exposure of infants and young children.

The rate of absorption of lead after ingestion can range from 3% to 80%. It is heavily influenced by food intake, much higher rates of absorption occurring after fasting than when lead is ingested with a meal. Absorption is also affected by age, the typical absorption rates in adults and infants being 10% and 50%, respectively. Up to 50% of the inhaled lead compound may be absorbed. After its absorption and distribution in blood, lead is initially distributed to soft tissues throughout the body. Eventually, bone accumulates lead over much of the human life span and may serve as an endogenous source of lead. The half-life for lead in blood and other soft tissues is about 28-36 days, but it is much longer in the various bone

**Metals**

**Lead**

compartments. The percentage retention of lead in body stores is higher in children than adults. Inorganic lead is not metabolized. Lead that is not distributed is mainly excreted through the kidney.

Lead is a classical chronic or cumulative poison. In humans, lead can result in a wide range of biological effects depending upon the level and duration of exposure. Health effects are generally not observed after a single exposure. Many of the effects that have been observed in laboratory animals have also been observed in humans, including hematological effects, neurological and behavioral effects, renal effects, cardiovascular effects, and effects on the reproductive system. In addition, lead has been shown to have effects on bone and on the immune system in laboratory animals. Children are more vulnerable to the effects of lead than adults. Lead has been shown to be associated with impaired neurobehavioral functioning in children. Impaired neurobehavioral development and increase in systolic blood pressure were considered to be the most critical effect (JECFA73, 2010).

Inorganic lead compounds are classified by the IARC as probably carcinogenic to humans (Group 2A; Vol. 87, 2006)

**Metals****Mercury**

Reference to JECFA:	10 (1966), 14 (1970), 16 (1972), 22 (1978), 72 (2010)
Toxicological guidance value:	PTWI 4 µg/kg bw for inorganic mercury (2010)
Contaminant definition:	Mercury, Total
Synonyms:	Hg
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Natural mineral waters	0.001	Adopted	CXS 108-1981	NMW, CF		Relevant Codex commodity standard is CXS 108-1981. The ML is Expressed in mg/l	1)
Salt, food grade	0.1	Adopted	CXS 150-1985	NFSDU, FA		Relevant Codex commodity standard is CXS 150-1985.	

- 1) The Standard for Natural Mineral Waters contains the level in the Section 3.2 "Health-related limits for certain substances". CCCF2 (2008) temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41 para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).

No CCFAC/CCCF position document was available about mercury.

JECFA72 (2010) considered that, based on the toxicological database for mercury (II) chloride, that there was limited evidence for carcinogenicity of inorganic mercury, but that direct DNA damage was not demonstrated, and that therefore setting a health-based guidance value was appropriate. The lowest BMDL<sub>10</sub> for relative kidney weight increase in male rats was calculated to be 0.11 mg/kg bw per day as mercury (II) chloride. This corresponds to 0.06 mg/kg bw per day as mercury, adjusted from a 5 day per week dosing schedule to an average daily dose and for the percent contribution of inorganic mercury to dose. After application of a 100-fold uncertainty factor, the Committee established a PTWI for inorganic mercury of 4 µg/kg bw. The previous PTWI of 5 µg/kg bw for total mercury, established at the sixteenth meeting, was withdrawn.

The new PTWI for inorganic mercury was considered applicable to dietary exposure to total mercury from foods other than fish and shellfish. For dietary exposure to mercury from these foods the previously established PTWI for methyl mercury should be applied. The upper limits of estimates of average dietary exposure to total mercury from foods other than fish and shellfish for adults (1 µg/kg bw per week) and for children (4 µg/kg bw per week) were at or below the PTWI for inorganic mercury.

The Committee noted that there was a lack of quantitative data on methylmercury in non-fish products and on inorganic mercury in foods in general.

Mercury is a naturally occurring metallic element which can be present in foodstuffs by natural causes; elevated levels can also occur due to e.g. environmental contamination by industrial or other uses of mercury. Methylmercury and also total mercury levels in terrestrial animals and plants are usually very low; the use of fish meal as animal feed can however also lead to higher methyl mercury levels in other animal products.

**Metals****Methylmercury**

Reference to JECFA: 22 (1978), 33 (1988), 53 (1999), 61 (2003), 67 (2006)  
 Toxicological guidance value: PTWI 0.0016 mg/kg bw (2003; confirmed in 2006)  
 Contaminant definition: Methylmercury  
 Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Tuna	1.2	Adopted	2018	CF	Whole commodity fresh or frozen (in general after removing the digestive tract)	Countries or importers may decide to use their own screening when applying the ML for methylmercury in fish by analysing total mercury in fish. If the total mercury concentration is below or equal to the ML for methylmercury, no further testing is required and the sample is determined to be compliant with the ML. If the total mercury concentration is above the ML for methylmercury, follow-up testing shall be conducted to determine if the methylmercury concentration is above the ML.  The ML also applies to fresh or frozen fish intended for further processing.  Countries should consider developing nationally relevant consumer advice for women of childbearing age and young children to supplement the ML.	CAC41 agreed that CCCF could consider revising the ML in the light of additional data after three years. (REP 18/CAC, para. 39)
Alfonsino	1.5	Adopted	2018	CF	Whole commodity fresh or frozen (in general after removing the digestive tract)	See notes for tuna	
Marlin	1.7	Adopted	2018	CF	Whole commodity fresh or frozen (in general after removing the digestive tract)	See notes for tuna	
Shark	1.6	Adopted	2018	CF	Whole commodity fresh or frozen (in general after removing the digestive tract)	See notes for tuna	

CCFAC24 (1992) informed CAC and CCFFP that the recommended GLs for mercury in fish referred to total mercury rather than methylmercury. CAC20 (1993) decided to maintain the GLs for methylmercury in fish as previously adopted, while recommending that the establishment of corresponding GLs for total mercury in fish be considered by CCFAC at its next meeting. CCFAC26 (1994) noted that analysis of total mercury was generally adequate to ensure that GLs for methylmercury were not exceeded and decided that the establishment of GLs for total mercury in fish was not necessary. CCFAC29 (1997) noted that CCEXEC43 (1996) had recommended that CCFAC initiate a new risk analysis on methylmercury. It was decided to defer any decision on the question of GLs based on methylmercury or total mercury until JECFA had performed the risk assessment.

JECFA53 (1999) calculated the human exposure to methylmercury in regional diets to range from 0.3-1.5 µg/kg bw/week. Nationally reported dietary exposures are in the range 0.1-



**Metals****Methylmercury**

2.0 µg/kg bw/week. The Committee maintained the PTWI of 3.3 µg bw for methylmercury set in the previous meetings of JECFA and recommended that methylmercury be re-evaluated in 2002 when new information on the cohort in one of the studies could be assessed and possibly other new relevant data could be available. The Committee also recommended that the nutritional benefits of fish consumption are weighted against the possibility of harm when limits on methylmercury concentrations in fish or on fish consumption are being considered.

CCFAC32 (2000) took note of these recommendations made by JECFA53.

CCFAC37 (2005) agreed that the revision of the GLs requires more comprehensive consideration by CCFAC in order to take into account all factors related to the consumption of fish, in particular, risks and benefits. In the meantime, the existing GLs can be retained with the understanding that enforcement can be performed by determination of total mercury as a screening method (for facilitating control/monitoring). Methylmercury needs only be determined for verification purposes (ALINORM 05/28/12, para. 202).

CCFAC38 (2006) agreed: to forward a request to CAC for an FAO/WHO expert consultation on health risks associated with methylmercury and dioxins and dioxin-like PCBs in fish and health benefits of fish consumption; to postpone consideration on the need to revise the guideline levels for methylmercury in fish pending the outcome of the requested FAO/WHO consultation and to retain the current Codex guideline levels; not to start compiling data on the ratio of methylmercury to total mercury in different fish species; and to postpone discussion on the risk communication aspects of methylmercury in fish (ALINORM 06/29/12, paras. 191-194).

JECFA67 (2006) confirmed the PTWI of 1.6 µg/kg bw, set in 2003, based on the most sensitive toxicological end-point (developmental neurotoxicity) in the most susceptible species (humans). However, the Committee noted that life-stages other than the embryo and fetus may be less sensitive to the adverse effects of methylmercury.

The Committee considered that intakes of up to about two times higher than the existing PTWI would not pose any risk of neurotoxicity in adults, except for women of childbearing age in order to protect the embryo and fetus. Concerning infant and children up to about 17 years no firm conclusions could be drawn; it is clear that they are not more sensitive than the embryo or fetus, but may be more sensitive than adults because significant development of the brain continues in infancy and childhood. Therefore, no level of intake higher than the existing PTWI could be identified of infants and children.

The Committee recommended that:

- Known benefits of fish consumption need to be taken in consideration in any advice aimed at different populations, since fish make an important contribution to nutrition, especially in certain regional and ethnic diets. Risk managers may wish to consider whether specific advice should be given concerning children and adults after weighing the potential risks and benefits.
- Setting of guideline levels for methyl mercury in fish may not be an effective way of reducing exposure for the general population, however advice to population subgroups that may be at risk may provide an effective method for lowering the number of individuals with exposures greater than the PTWI.

CCCF1 (2007) was informed by the WHO Representative that JECFA's conclusion with respect to guideline levels must be considered in relation to the fact that guidelines already in place in some national jurisdictions had already influenced the range of observed mercury concentrations by eliminating fish containing high concentrations of mercury from the market. The Committee reaffirmed the decision made by CCFAC38 to postpone consideration of the need to revise the guideline levels for methylmercury in fish pending the outcomes of a joint FAO/WHO expert consultation on health risks associated with methylmercury and dioxins and dioxin-like PCBs in fish and the health benefits of fish consumption and to retain the current Codex guideline levels for the time being (ALINORM 07/30/41, paras. 34-35).

CAC30 (2007) recalled that CAC29 had requested FAO and WHO for scientific advice on the health risks associated with methylmercury and dioxins and dioxin-like PCBs in fish and the health benefits of fish consumption. The Representative of FAO, speaking on behalf of FAO and WHO, informed the Commission that a step-wise preparatory process was being taken, given the complex nature of the issue and the need for innovative principles and methodology. The Representative indicated that, possibly at a first stage, FAO and WHO would consider conducting qualitative risk-benefit assessment of fish consumption, specifically addressing issues related to the impact of methylmercury exposure on women of child-bearing age and at a later stage, conducting quantitative assessment including the intake of dioxin and dioxin-like PCBs, taking into account consumption of fatty fish, considered as a significant source of beneficial fatty acids (ALINORM 07/30/REP, para. 192).

FAO and WHO organized an expert consultation on the risks and benefits of fish consumption, taking into consideration the health risks associated with methylmercury (MeHg), dioxin

**Metals****Methylmercury**

and dioxin-like PCBs (DLC) and the nutritive and health benefits of eating fish, in response to the request of CAC29 (ALINORM 09/32/41, para. 24). The Expert Consultation was held in January 2010. It was concluded that consumption of fish provides energy, protein, and a range of other important nutrients, including the long-chain n-3 poly unsaturated fatty acids (LC n-3 PUFA), that eating fish was part of the cultural traditions of many peoples and that in some populations fish was a major source of food and essential nutrients.

The Consultation concluded that among the general adult population, consumption of fish, particularly oily fish, lowers the risk of coronary heart disease (CHD) mortality and that probable or convincing evidence of CHD risks of MeHg was absent. When considering benefits of LC n-3 PUFA vs. risks of MeHg among women of childbearing age: maternal fish consumption lowered the risk of suboptimal neurodevelopment in their offspring compared to women not eating fish in most circumstances evaluated. Among infants, young children, and adolescents, the available data were insufficient to derive a quantitative framework of health risks and benefits of eating fish. However, the Consultation stated that healthy dietary patterns that include fish and are established early in life influence dietary habits and health during adult life. To minimize risks in target populations, the Consultation recommended a series of steps that member states should take to better assess and manage the risks and benefits of fish consumption and more effectively communicate with their citizens.

CCCF5 (2011) agreed to consider the need to review the existing GLs for methylmercury in fish and predatory fish when the full report of the Joint FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption becomes available.

CCCF6 (2012) agreed to the development of a discussion paper on the review of the guideline level for methylmercury in fish and predatory fish through an EWG led by Norway and co-chaired by Japan for consideration and discussion at the 7th session with the view of identification of possible actions or new work on this issue (REP12/CF, para. 174).

CCCF7 (2013) agreed that consumer advice should not be developed at the international level and that such guidance was more appropriate at the national level. It was agreed to review the GLs with a view to their revision or conversion to MLs. The Committee therefore re-established the EWG, led by Japan and co-chaired by Norway, to prepare a discussion paper; collect data on total mercury and methylmercury in fish species important in international trade in order to review the current GLs; and explore the possibility of revising the GLs or their conversion to MLs and to identify the fish for which the level or levels could apply (REP13/CF, paras. 125,126).

CCCF8 (2014) noted that there was wide support for establishment of an ML for methylmercury, and agreed that this would be the approach with the use of total mercury for screening purposes, but that further consideration was needed on an appropriate level or levels; and the fish classification would have to be further developed as proposed by the chair of the EWG. The Committee further noted that this decision did not preclude the usefulness of consumer advice and confirmed the decision of the last session of the Committee that consumer advice should be developed at the national or regional level as the advice would vary between countries because of the risk of mercury exposure from the diet would depend on, amongst others, the patterns of consumption of fish and the types of fish consumed; and that no further work would be done at the international level. The Committee agreed to re-establish the EWG, led by Japan and co-chaired Norway to develop a discussion paper to provide proposals for ML(s) for methylmercury, to express to which fish species these should apply, and to include a project document for a new work proposal for consideration by the 9th session of the Committee (REP14/CF, paras. 113-114).

CCCF9 (2015) noted that the continued support for an ML for methylmercury and agreed that further work on this should continue through the development of another discussion paper to consider expanding the ML to fish species that can accumulate high methylmercury concentrations, other than tuna and that consideration should be given to narrowing down the ML ranges. It was recognised that development of this paper would require additional data and that an exposure assessment based on different MLs should be conducted. The Committee agreed to re-establish the EWG, chaired by Japan and co-chaired by New Zealand to prepare a discussion paper with proposals for ML for methylmercury, including a project document for consideration by the next session. (REP15/CF, paras. 125-126)

CCCF10 (2016) agreed that it would establish an ML for tuna, but that it was not ready at this point to submit a project document to CAC through the CCEXEC for approval of new work, as it was necessary to determine whether it was possible to establish a single ML for tuna or whether it should be set for different species of tuna, and whether it was possible and appropriate to set MLs for canned tuna.

The Committee agreed to establish an EWG, chaired by The Netherlands, and co-chaired by New Zealand and Canada to prepare a discussion paper presenting a proposal for:

- one ML for fresh and frozen tuna, or for MLs for different tuna species, if the need of differentiation is justified;
- an ML for canned tuna, if possible and appropriate, and to determine whether it should be based on occurrence data or derived from the ML(s) for fresh tuna; and

**Metals****Methylmercury**

- the need for MLs for other species of fish, based on the information in CRD18 and other relevant sources, together with a project document (REP16/CF, paras. 160-161).

CCCF11 (2017) discussed following issues:

- Whether to establish the ML for tuna as a whole or for specific tuna species, noting that it was possible to distinguish in subspecies based on methylmercury levels;
- Whether to establish MLs for other identified fish species that accumulate methylmercury;
- Whether the MLs should be based on the ALARA principle or should be guided by risk/benefit;
- Not to establish MLs for canned tuna as levels were generally low and these products were consumed in lower quantities than fresh or frozen fish; and
- Consider setting MLs based on total mercury and not methylmercury. After several discussions, the Committee agreed:
  - To establish an ML for tuna as a group, and that the subspecies of tuna taken into account for this would be indicated;
  - To establish MLs for alfoncino, kingfish/amberjack, marlin, shark, dogfish and swordfish;
  - Not to establish MLs for canned tuna;
  - To continue with the previously decided approach to establish MLs for methylmercury, while screening for total mercury;
  - To establish MLs based on the ALARA principle, which was in line with the criteria for establishing MLs in the GSCTFF; and
  - To put a footnote to the higher MLs would be developed to indicate the need for additional risk management measures, namely consumer advice, to protect health. The Committee noted that MLs should be accompanied by sampling plans and to make this clear in the project document.

The Committee agreed to start new work on MLs for fish (tuna, alfoncino, kingfish/amberjack, marlin, shark, dogfish and swordfish), to submit a project document to CAC for approval and to establish an EWG, chaired by the Netherlands, and co-chaired by Canada and New Zealand subject to approval of new work, would prepare proposals for MLs and associated sampling plans for circulation for comments and consideration by CCCF12. The Codex Secretariat would request further data on total mercury and methylmercury in fish through a CL (REP17/CF, paras. 125-143).

CAC40 (2017) approved new work on MLs for methylmercury in fish species: tuna, alfoncino, kingfish/amberjack, marlin, shark, dogfish and swordfish (REP17/CAC Appendix VI).

CCCF12 (2018) agreed on an ML of 1.2 mg/kg for tuna as a compromise as this was based on the data of all tuna species but with a next lower rejection rate than 5%. EU, Switzerland and Norway expressed their reservation to this decision for the reasons that it could not agree for the time being with any of the MLs proposed as the levels were higher than those currently in force in the EU and would result in higher exposure to mercury which was a public health concern (REP 18/CF, paras. 72, 74-76). The Committee agreed with an ML of 1.5 mg/kg for alfoncino, 1.7 mg/kg for marlin and 1.6 mg/kg for shark which were the proposed MLs based on a next lower rejection rate than 5% and noted the reservation of the EU, Switzerland and Norway for the reasons given in the above (REP 18/CF, paras. 72 and 77).

The Committee agreed to discontinue work on the ML for Amberjack by reason that the average and median concentration of total mercury and methylmercury fall below the 0.3 mg/kg used as selection criterion for selecting fish species for setting MLs, and for swordfish on the ground that no consensus could be reached on an appropriate ML (REP 18/CF, paras. 78, 82 and 83).

**Notes to the MLs**

CCCF12 agreed that no further testing was needed when the total mercury was equal to or less than the ML for methylmercury (REP 18/CF, para, 84).

The Committee agreed to retain the note attached to the current GLs, but to amend the text to indicate that the ML applied also to fresh or frozen fish intended for further processing to ensure that fish not complying with the ML would not be used for canning. CCCF noted that with this amendment, the footnote would not make the ML applicable to canned tuna which was in line with the decision made at the previous session not to set an ML for canned tuna (REP 18/CF, para, 85).

The Committee agreed to the option c proposed by the EWG amended to refer to “women of child-bearing age” noting the clarification from the JECFA Secretariat that the most sensitive period for negative health impacts of methylmercury is very early in foetal development and that JECFA uses the term women of child-bearing age rather than pregnant women (REP 18/CF, para, 86). The Committee noted that for future ML development, data on both methylmercury and total mercury would need to be available, as it was shown that

**Metals****Methylmercury**

for certain fish species the ratio of methylmercury to total mercury was very low and for the data analysis it would not always be assumed that total mercury would be mostly present as methylmercury (REP 18/CF, para, 88).

The Representative of WHO informed CCCF that discussions are ongoing in the context of Minamata Convention on Mercury on methods for monitoring for baseline data and effectiveness monitoring. For signatories to the Convention human biomonitoring is mandatory, fish monitoring has been acknowledged as an important tool and this topic would be discussed at the Conference of the Parties (COP2) in June. WHO encouraged delegates to engage with their colleagues from the environment sector and delegates to the Minamata Convention in order to make them aware of the Codex sampling plan to coordinate fish monitoring for food safety with the monitoring for effectiveness within the Minamata Convention (REP 18/CF, para, 90).

The Committee agreed to:

- i. advance the MLs for tuna, alfonsino, marlin and shark to CAC41 for adoption at Step 5/8
- ii. inform the Commission of discontinuation of work on ML for amberjack and swordfish;
- iii. request revocation of the GLs for methylmercury; and
- iv. send the sampling plan to CCMAS for endorsement together with the following questions.

- The necessary performance criteria for the MLs
- Whether there is evidence that methyl mercury can vary widely between individual fish sampled at the same time. How this would apply to large fish sold as individual units and whether the sampling plan provides enough basis to deal with this; and
- Whether the whole fish should be analyzed or only specific fractions of edible portions. Currently only mention is made that the mid-section should be sampled for some large fish. (REP 18/CF, para. 91 and Appendix IV)

The Committee agreed to establish an EWG chaired by New Zealand and co-chaired by Canada to prepare a discussion paper on the establishment of MLs for additional fish species. The paper should clearly identify the fish species for which MLs should be established and include a project document with proposals for MLs for consideration by CCCF13 (REP 18/CF, paras. 92-and 93).

CAC41(2018) adopted the proposed MLs, noting the reservations expressed by Cuba, Colombia, Ecuador, EU, Norway, Senegal and Switzerland, and agreed that CCCF could consider revising the ML for tuna in the light of additional data after three years, and revoked GLs for methylmercury in predatory and non-predatory fish and discontinued the work on ML for methylmercury in amberjack and sword fish (REP 18/CAC, para. 39, Appendix III, V and VII).

**Sampling plan**

CCMAS39 (2018) did not endorse the sampling plan for MLs for methylmercury in fish and agreed to return the sampling plan to CCCF for further consideration, and to inform CCCF that CCMAS was unable to respond to the questions raised in relation to the sampling plan as the questions were outside the remit of CCMAS. The reasons CCMAS did not endorse the sampling plan are as follows:

- Performance criteria for methods of analysis of mercury and methyl mercury in the sampling plan would need to be revised according to the requirements of the Procedural Manual or should be removed from the sampling plan and replaced with a reference to the Procedural Manual.
- The measurement uncertainty, in the view of some delegations, should not be used in decision rule in Codex standards for acceptance or rejection of lots (section on Interpretation of Results); and this approach was not consistent with other sampling plans already adopted for contaminants in foods.

The Committee endorsed the performance criteria for methods of analysis for methylmercury as amended to meet the format or information currently used in the requirements and format in the Procedural Manual and in the General Standard for Methods of Analysis and Sampling (CXS 234-1999) and agreed to include examples of methods which could meet the criteria. The Committee noted that this list was not exhaustive and served only as examples of methods that meet the criteria for methods for methylmercury and that countries could choose any other methods that meet the criteria (REP 18/MAS, paras. 18-19).

**Metals**

**Methylmercury**

Methylmercury is the most toxic form of mercury and is formed in aquatic environments. Methylmercury therefore is found mainly in aquatic organisms. It can accumulate in the food chain; the levels in large predatory fish species are therefore higher than in other species and fish is the predominant source of human exposure to methylmercury. Methylmercury and also total mercury levels in terrestrial animals and plants are usually very low; the use of fish meal as animal feed can however also lead to higher methyl mercury levels in other animal products.

In all experimental animal species evaluated, methylmercury was readily absorbed (up to 95%) after oral exposure. Methylmercury crossed both the blood–brain barrier and the placenta effectively, resulting in higher concentrations of mercury in the brain of the fetus than of the mother. Methylmercury is eliminated mainly via the bile and faeces, neonatal animals having a lower excretory capacity than adults. Methylmercury is toxic to the nervous system, kidney, liver and reproductive organs, neurotoxicity being the most sensitive endpoint (WHO Food additives Series 52; 2004).

**Metals****Tin**

Reference to JECFA: 10 (1966), 14 (1970), 15 (1971), 19 (1975), 22 (1978), 26(1982), 33(1988), 55 (2000), 64 (2005)  
 Toxicological guidance value: PTWI 14 mg/kg bw (1988, Expressed as Sn; includes tin from food additive uses; maintained in 2000)  
 Contaminant definition: Tin, total (Sn-tot) when not otherwise mentioned; inorganic tin (Sn-in); or other specification  
 Synonyms: Sn  
 Related code of practice: Code of Practice for the Prevention and Reduction of Inorganic Tin Contamination in Canned Foods (CXC 60-2005)  
 Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Canned foods (other than beverages)	250	Adopted	2007	FAC, CF		The ML does not apply to non-tinplate canned cooked cured chopped meat, cooked cured ham, cooked cured pork shoulder, corned beef and luncheon meat. Relevant Codex commodity standards include CXS 62-1981, CXS 254-2007, CXS 296-2009, CXS 242-2003, CXS 297-2009, CXS 78-1981, <del>CXS 159-1987, CXS 42-1981,</del> CXS 60-1981, CXS 99-1981, CXS 160-1987, CXS 66-1981, CXS 13-1981, CXS 115-1981, CXS 57-1981, CXS 145-1981, CXS 98-1981, CXS 96-1981, CXS 97-1981, CXS 88-1981, CXS 89-1981, <i>CXS 3-1981, CXS 17-1981, CXS 37-1991, CXS 70-1981, CXS 73-1981, CXS 90-1981, CXS 94-1981, CXS 119-1981, CXS 241-2003, CXS 319-2015</i>	Reference to CXS 159-1987 and CXS 42-1981 are still retained in the current GSCTFF (amended in 2018) though those were superseded by or incorporated into CXS 319-2015. The CXS indicated in <i>italics</i> are not listed in the current GSCTFF (amended in 2018) as examples.
Canned beverages	150	Adopted	2007	FAC, CF		Relevant Codex commodity standards include CXS 247-2005.	
Cooked cured chopped meat	50	Adopted	CXS 98-1981	PMPP		The ML applies to products in containers other than tinplate containers. Relevant Codex commodity standard is CXS 98-1981.	
Cooked cured ham	50	Adopted	CXS 96-1981	PMPP		The ML applies to products in containers other than tinplate containers. Relevant Codex commodity standard is CXS 96-1981.	
Cooked cured pork shoulder	50	Adopted	CXS 97-1981	PMPP		The ML applies to products in containers other than tinplate containers. Relevant Codex commodity standard is CXS 97-1981.	
Corned beef	50	Adopted	CXS 88-1981	PMPP		The ML applies to products in containers other than tinplate containers. Relevant Codex commodity standard is CXS 88-1981.	
Luncheon	50	Adopted	CXS 89-1981	PMPP		The ML applies to products in containers other than	

**Metals****Tin**

meat

tinplate containers.

Relevant Codex commodity standard is CXS 89-1981.

In previous JECFA meetings it was noted that inorganic tin compounds generally have low systemic toxicity in animals, because of limited absorption from the gastrointestinal tract, low accumulation in tissues, and rapid passage through the gastrointestinal tract. Insoluble tin compounds are less toxic than soluble tin salts.

JECFA33 (1988) established a PTWI for inorganic tin of 14 mg/kg bw.

At JECFA55 (2000), it was concluded that the acute toxicity of inorganic tin in animals and humans results from irritation of the mucosa of the gastrointestinal tract, which may lead to vomiting, diarrhea, anorexia, depression, ataxia, and muscular weakness. There was insufficient data available to establish an ARfD for inorganic tin. The committee did not consider studies on organic tin compounds, since it had concluded at JECFA22 (1978), that these compounds differ considerably from inorganic tin compounds with respect to toxicity and should be considered separately.

The Committee maintained the existing PTWI and reiterated that limited human data available indicated that concentrations of 150mg/kg tin in canned beverages and 250 mg/kg in other canned foods may produce acute manifestations of gastric irritation in certain individuals. This is considered to be a reversible effect however, which may occur in a limited number of sensitive subject only.

Following the discussions in CCFAC34 (2002) and in CCFAC35 (2003) (ALINORM 03/12, para.146 and ALINORM 03/12A, para.160), the proposed MLs were repeatedly returned to Step 3. CCFAC35 changed the terminology of the commodities to which the proposed draft MLs apply, which previously was "liquid canned foods resp. solid foods", to "canned beverages" and "canned foods other than beverages". The Committee decided to ask JECFA to evaluate current tin level in canned foods and to determine an acute reference dose; it was noted that new data would become available. CCFAC36 (2004) decided to hold the proposed MLs and reconsider these MLs in the light of JECFA64 re-evaluation (ALINORM 04/27/12, para.171).

JECFA64 (2005) concluded that the data available indicated that it is inappropriate to establish an ARfD for inorganic tin since whether or not irritation of gastrointestinal tract occur after ingestion of a food containing tin depends on the concentration and nature of in the product, rather than on the dose ingested on a body-weight basis.

CCFAC37 (2005) agreed to circulate the proposed MLs for comments at Step 3 (ALINORM 05/28/12, para.163). CCFAC38 (2006) forwarded the proposed draft MLs to Step 5 (ALINORM 06/29/12 para.183). CAC29 adopted the proposed draft MLs and advanced it to Step 6 (ALINORM 06/29/41 para.106).

CCCCF1 (2007) agreed to forward the draft MLs to CAC30 for adoption at Step 8 and noted that the adoption of the ML for tin in canned foods (other than beverages) would result in consequential changes to MLs for tin in certain canned products (i.e. products in tin-layered cans), currently included in Schedule I (ALINORM 07/30/41, para. 81).

CAC30 adopted these MLs at Step 8 with the understanding that the existing MLs for tin in certain canned foods included in Schedule I of the GSCTF would be replaced by the adopted MLs (ALINORM 07/30/REP).

Tin is mainly used in tinplated containers, but it is also extensively used in solders, in alloys including dental amalgams. Inorganic tin compounds, in which the element may be present in the oxidation states of +2 or +4, are used in a variety of industrial processes for the strengthening of glass, as a base for colours, as catalysts, as stabilizers in perfumes and soaps, and as dental anticariogenic agents. On the whole, contamination of the environment by tin is only slight. Food is the main source of tin for man. Small amounts are found in fresh meat, cereals, and vegetables. Larger amounts of tin may be found in foods stored in plain cans and, occasionally, in foods stored in lacquered cans. Some foods such as asparagus, tomatoes, fruits, and their juices tend to contain high concentrations of tin if stored in unlaquered cans (Environmental health criteria for tin; International Programme on Chemical Safety (IPCS); 1980). Inorganic tin is found in food in the +2 and +4 oxidation states; it may occur in a cationic form (stannous and stannic compounds) or as inorganic anions

**Metals**

**Tin**

(stannites or stannates).



**Mycotoxins****Aflatoxins, Total**

Reference to JECFA:	31 (1987), 46 (1996), 49 (1997), 68 (2007), 83 (2016)
Toxicological guidance value:	Carcinogenic potency estimates for aflatoxins B, G, M (1997, Intake should be reduced to levels as low as reasonably possible.)
Contaminant definition:	Aflatoxins total (B <sub>1</sub> + B <sub>2</sub> + G <sub>1</sub> + G <sub>2</sub> )
Synonyms:	Abbreviations, AFB, AFG, with numbers, to designate specific compounds
Related code of practice:	Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Peanuts (CXC 55-2004) Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Tree Nuts (CXC 59-2005) Code of Practice for the Reduction of Aflatoxin B <sub>1</sub> in Raw Materials and Supplemental Feeding stuffs for Milk Producing Animals (CXC 45-1997) Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Dried Figs (CXC 65-2008) Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Almonds	15	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to almonds intended for further processing (*). For sampling plan, see Annex 2.	TN 0660
Almonds	10	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to almonds "ready-to-eat" (**). For sampling plan, see Annex 2.	TN 0660
Brazil nuts	15	Adopted	2010	CF	Whole commodity	The ML applies to shelled Brazil nuts intended for further processing (*). For sampling plan, see Annex 2.	
Brazil nuts	10	Adopted	2010	CF	Whole commodity	The ML applies to shelled Brazil nuts ready-to-eat (**). For sampling plan, see Annex 2.	
Hazelnuts	15	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to hazelnuts, also known as filberts, intended for further processing (*). For sampling plan, see Annex 2.	TN 0666
Hazelnuts	10	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to hazelnuts, also known as filberts, "ready-to-eat" (**). For sampling plan, see Annex 2.	TN 0666
Peanuts	15	Adopted	1999	FAC	Unless specified, seed or kernels, after removal of shell or husk.	The ML applies for peanuts, also as known as groundnuts, intended for further processing (*). For sampling plan, see Annex 1.	SO 0697

**Mycotoxins****Aflatoxins, Total**

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Peanuts	10	4 (Hold)		CF		The ML applies to peanuts "ready to eat"	REP18/CF, para. 115 Appendix VII
Pistachios	15	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to pistachios intended for further processing (*). For sampling plan, see Annex 2.	TN 0675
Pistachios	10	Adopted	2008	CF	Whole commodity after removal of shell.	The ML applies to pistachios "ready-to-eat" (**). For sampling plan, see Annex 2.	TN 0675
Dried figs	10	Adopted	2012	CF	Whole commodity	The ML applies to dried figs "ready-to-eat" (**). For sampling plan see Annex 3.	DF 0297
Nutmeg, Chili and Paprika, Ginger, Pepper, and Turmeric	20 or 30	4 (Hold)		CF		Relevant Codex commodity standards are CXS 307-2011 and CXS 326-2017	REP18/CF, para. 119 Appendix VIII

(\*) "destined for further processing" means intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption. Processes that have proven to reduce levels of aflatoxins are shelling, blanching followed by colour sorting, and sorting by specific gravity and colour (damage). There is some evidence that roasting reduces aflatoxins in pistachios but for other nuts the evidence is still to be supplied.

(\*\*) "ready-to-eat" means "not intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins before being used as ingredient in foodstuffs, otherwise processed or offered for human consumption."

CCFAC23 (1991) decided to discontinue the development of a ML for aflatoxins in foods in general, and to discuss the problems on a commodity basis.

CCCPL9 (1994) decided not to proceed with the proposed GL for processed peanuts and to advance the proposed GL for raw peanuts (intended for further processing), associated with a specific sampling plan because the contamination is usually very inhomogeneous in a lot. It is assumed that raw peanuts are the major commodity in international trade.

It is acknowledged that for primary plant products the aflatoxin contamination is often not homogeneous and a sampling plan is necessary to assure reasonable application of MLs. A general position paper on aflatoxins in food and feeds (CX/FAC 97/16) was presented to CCFAC29 (1997).

- Maize was included in a Technical Consultation on sampling plans for aflatoxins in commodities. See FAO Food and nutrition Paper 55 (Rome, 1993).
- CCFAC26 (1994) decided to discontinue the establishment of GLs for AFB<sub>1</sub> in supplementary feedingstuffs for milk-producing animals (previously proposed at the level of 5 µg/kg), based on the assumption that the relationship between aflatoxins in milk and feeds is not (completely) clear and that there is not much international trade in (composite) supplementary feedingstuffs. International trade mostly is in the form of individual commodities which can be used as feed components in various quantities, directed to other feed uses than milk producing animals, or to other uses in general, or be decontaminated etc.

Therefore, a Code of practice for the reduction of aflatoxin B<sub>1</sub> in raw materials and supplemental feedingstuffs for milk-producing animals was developed and adopted as CXC 45-

**Mycotoxins****Aflatoxins, Total**

1997.

CCFAC35 (2003) agreed to the elaboration of MLs for aflatoxins in almonds, hazelnuts and pistachios, based on the ALARA principle and with the understanding that related sampling plans need to be established (ALINORM 03/12A para.129). CCFAC37 (2005) advanced the ML for unprocessed almonds, hazelnuts and pistachios while the Committee decided to circulate for comments at Step 3 the ML for processed almonds, hazelnuts and pistachios (ALINORM 05/28/12 para.141).

CCFAC38 (2006) agreed to rename “processed” and “unprocessed” tree nuts to as “ready-to-eat” and tree nuts “for further processing” respectively and to hold at Step 7 the ML in tree nuts for further processing and to advance to Step 5 the ML in ready-to-eat tree nuts (ALINORM 06/29/12 para.132).

CAC29 (2006) adopted ML for ready-to-eat tree nuts at Step 5.

CCFAC38 (2006) agreed to request JECFA to conduct a dietary exposure assessment on ready-to-eat tree nuts and impact on exposure taking into account hypothetical levels of 4, 8, 10 and 15 µg/kg, putting in the context of exposure from other sources and previous exposure assessments on maize and groundnuts. The Committee decided to expand the discussion paper on the aflatoxin level in ready-to-eat tree nuts, considering i) the detailed data on distribution on aflatoxins between lots, ii) consumer health risk assessment of different levels of aflatoxin in ready-to-eat tree nuts, iii) sampling plan for tree nuts, iv) effect of the COP and v) terminology of “ready-to-eat” and “for further processing” for consideration at CCCF1 (ALINORM 06/29/12 paras. 129-130).

CCFAC38 agreed to further elaborate the proposed draft sampling plan once a ML had been established by Committee and to include considerations on the draft sampling plan for tree nuts in the discussion paper on total aflatoxin levels in processed tree-nuts (ALINORM 06/29/12 para.125).

CCCF1 (2007) agreed that the proposed draft Sampling Plan for Aflatoxin Contamination in Almonds, Brazil Nuts, Hazelnuts and Pistachios be returned to Step 2 for redrafting by an EWG, with a view to circulation at Step 3 and consideration at Step 4 at the next session of CCCF. It was also agreed that the working document to be considered at the next session of CCCF incorporate a revised proposed draft Sampling Plan as well as an explanatory text in support of the consideration of the Sampling Plan (ALINORM 07/30/41, para. 62).

JECFA68 (2007) concluded that consumption of almonds, Brazil nuts, hazelnuts, pistachios and dried figs contributes to more than 5% of the total aflatoxin dietary exposure in only five of the 13 GEMS/Food cluster diets (clusters B, C, D, E and M). Setting an ML of 20 µg/kg for these products would only have an impact on the relative contribution to aflatoxin dietary exposure in these clusters (including the high-level consumers of tree nuts). This can solely be attributed to the elevated aflatoxin level in pistachios. For the tree nuts other than pistachios, as well as dried figs, setting an ML has no effect on aflatoxin dietary exposure. Also, enforcing an ML of 4, 8, 10 or 15 µg/kg has little further impact on the overall dietary exposure to aflatoxin compared to an ML of 20 µg/kg.

CCCF2 (2008) forwarded the MLs for Total Aflatoxins in Almonds, Hazelnuts and Pistachios “For further processing” and “Ready-to-eat” to CAC31 for adoption at Step 8 and the Sampling Plans for Aflatoxin Contamination in Ready-to-eat Treenuts and Treenuts Destined for Further Processing: Almonds, Hazelnuts and Pistachios for adoption at Step 5/8 (ALINORM 08/31/41, para. 127 and 142, and Appendix VIII and IX). CAC31 (2008) adopted the MLs as such (ALINORM 08/31/REP, Appendix VII).

CCCF8 (2014) agreed to amend the definition for tree nuts “ready-to-eat” and dried figs “ready-to-eat” to provide further clarification on the description of the products they apply to and that this definition would also apply to peanuts (REP14/CF, para. 91). The Committee also agreed to add the assessments of aflatoxins, already evaluated by JECFA, to the priority list. An update of the risk assessment of aflatoxins may be desirable in view of additional data that have become available since the last full assessment by JECFA. The Committee agreed that the risk assessment of aflatoxins would not be a high priority. (REP14/CF, paras. 129-130, Appendix XIII)

JECFA83 (2016) updated the aflatoxin risk assessment at the request of CCCF. The Committee also evaluated co-exposure to aflatoxins and fumonisins.

The Committee noted that there were limited contamination data from developing countries, which hindered a more comprehensive and global evaluation of aflatoxin occurrence and may have resulted in an underestimate of dietary exposure in these countries. Only five food commodities (maize, peanuts, rice, sorghum and wheat) each contribute more than 10% to international dietary exposure estimates for more than one GEMS/Food cluster diets, for either total aflatoxins (AFT) or AFB<sub>1</sub>. Although overall concentrations of aflatoxins in rice and wheat are lower than concentrations in maize and groundnuts (a traditional focus for aflatoxin risk management), the high consumption of rice and wheat in some countries means

**Mycotoxins****Aflatoxins, Total**

that these cereals may account for up to 80% of dietary aflatoxin exposure for those GEMS/Food cluster diets.

Mean AFB<sub>1</sub> concentrations in sorghum from the GEMS/Food contaminants database are higher than those for maize; combined with high consumption levels of sorghum in some GEMS/Food clusters, this cereal contributes 16–59% of dietary exposure in six GEMS/Food clusters. The database on sorghum is considerably more limited than that on maize. The Committee did not assess acute dietary exposure, but noted that the estimates of chronic dietary exposure are at least 2–5 orders of magnitude lower than the doses associated with acute effects.

The Committee calculated global aflatoxin-related hepatocellular carcinoma (HCC) risk based on the new central and upper-bound cancer potency estimates from the current dose–response analysis and international dietary exposures estimated at the current meeting. Aflatoxin-related cancer rates were calculated, accounting for prevalence of chronic HBsAg positivity, by GEMS/Food clusters. The low end of the range refers to lower-bound estimates at the mean dietary AFB<sub>1</sub> exposure, minimum HBsAg+ rates for countries in the cluster and the central cancer potency estimate. The high end of the range refers to upper-bound estimates at the 90<sup>th</sup> percentile of dietary AFB<sub>1</sub> exposure, maximum HBsAg+ rates for countries in the cluster and upper bound estimates of cancer potency. The lowest cancer risks were estimated for clusters G07 and G08 (European and other developed countries), with cancer risk estimates in the range <0.01–0.10 aflatoxin-induced cancers per year per 100 000 population, with wheat being the major contributing food commodity. For countries within these clusters, HBsAg+ rates were in the range 0.01–1.2%. The highest cancer risks were for cluster G13 (sub-Saharan African countries and Haiti), with cancer risk estimates in the range 0.21–3.94 aflatoxin-induced cancers per year per 100 000 population, with sorghum and maize being the major contributing food commodities. For countries within this cluster, HBsAg+ rates were in the range 5.2–19%. Other clusters with relatively high cancer risks were G03 (sub-Saharan African countries and Paraguay, with maize and sorghum being the major contributing food commodities), G05 (mainly Central and South American countries, with maize, rice, sorghum and wheat being the major contributing food commodities) and G16 (sub-Saharan African countries, with maize and sorghum being the major contributing food commodities). (JECFA/83/SC).

At the request of CCCF, the Committee also evaluated co-exposure to aflatoxins and fumonisins. The Committee concluded that there are few data available to support co-exposure as a contributing factor in human disease. However, the interaction between AFB<sub>1</sub>, a compound with known genotoxic properties, and fumonisins, which have the potential to induce regenerative cell proliferation (particularly at exposures above the PMTDI), remains a concern. This is due to the fact that the incidences of chronic liver disease and stunting are high in the areas of the world where the exposures to both mycotoxins are high and the co-exposure has been confirmed with biomarkers.

**Code of practice for the prevention and reduction of aflatoxin contamination in tree nuts – Brazil nuts**

CCFAC38 agreed to forward the proposed draft Appendix to the Code of practice for the prevention and reduction of aflatoxins contamination in tree nuts – additional measures for the Prevention and Reduction of Aflatoxins in Brazil nuts to CAC29 for adoption at Step 5/8 (ALINORM 06/29/12 para. 123). CAC29 endorsed this decision (ALINORM 06/29/41, Appendix IV).

CCCF3 noted that after the completion of the Standards and Trade Development Facility (STDF) project SafeNut which addressed the factors causing aflatoxin contamination in the Brazil nut production chain and the methods of control available, it appeared that an updating of the provisions on Brazil nuts in the COP was necessary in order to take into account the findings of the project. The Committee agreed to initiate new work on the revision of the Code to incorporate additional measures for the prevention and reduction of aflatoxin contamination in Brazil nuts. It was further agreed that the Proposed Draft Revision prepared by Brazil would be circulated for comments at Step 3 and consideration at the next session (ALINORM 09/32/41, para. 121 and 123, Appendix IX). The proposal of new work was subsequently endorsed by CAC32 (ALINORM 09/32/REP, Appendix VI).

CCCF4 (2010) agreed to forward the proposed draft revision to CAC33 (2010) for adoption at Step 5/8 (with omission of Steps 6 and 7). CAC33 adopted these revisions at Step 8 (ALINORM 10/33/REP, Appendix III).

**Maximum Levels in Brazil Nuts**

CCCF1 agreed that the discussion paper on aflatoxin contamination in Brazil nuts would be updated by the Brazil, incorporating additional data that would become available on the contribution of the shell to aflatoxin contamination of Brazil nuts, for consideration at the next session of the Committee (ALINORM 07/30/41, para. 66).

**Mycotoxins****Aflatoxins, Total**

CCCF2 (2008) agreed to start new work on a Maximum Level for Total Aflatoxins in Brazil Nuts (ALINORM 08/31/41, para. 147).

CCCF3 (2009) agreed to return the Proposed Draft Maximum Levels to Step 2/3 for redrafting by the Brazil for comments and consideration by the next session (ALINORM 09/32/41, para. 78).

CCCF4 (2010) agreed to forward the proposed MLs for Shelled, ready to eat Brazil Nuts and Shelled, destined for further processing Brazil Nuts (including sampling plans) to CAC33 for adoption at Step 5/8 with omission of Steps 6 and 7 and not to set any maximum level for in-shell Brazil nuts (ALINORM 10/33/41, para. 74 and 76, Appendix V). CAC33 adopted the MLs at Step 5/8 (ALINORM 10/33/REP, Appendix III).

**Code of practice for dried figs**

CCCF1 (2007) agreed to forward the project document proposing new work on a Code of practice for aflatoxins in dried figs to CCEXEC59 for critical review and for approval by CAC30. It was also agreed to establish an EWG to prepare a draft proposed Code of practice for the prevention and reduction of aflatoxin contamination in dried figs at Step 2, with a view to its circulation for comments at Step 3 and its consideration at Step 4 at the second session, pending the formal approval of new work by the Commission (ALINORM 07/30/41, paras. 120-121). CAC30 (2007) approved the above new work (ALINORM 07/30/REP, Appendix VII).

CCCF2 (2008) agreed to forward the proposed draft COP to CAC31 for adoption at Step 5/8 with the recommendation to omit Steps 6 and 7 (ALINORM 08/31/41, para. 163 and Appendix XI). CAC31 adopted the Code at Step 5/8 (ALINORM 08/31/REP, Appendix VII).

**Maximum levels in dried figs**

CCCF4 (2010) agreed to initiate new work on maximum levels for total aflatoxins in dried figs. Subject to approval by the Commission, the Committee agreed that the proposed draft maximum levels would be developed by an electronic Working Group led by Turkey, working in English, for comments at Step 3 and consideration at the 5th session of the Committee (ALINORM 10/33/41, para. 114, Appendix IX). CAC33 approved this new work (ALINORM 10/33/REP, Appendix VI).

CCCF5 (2011) agreed to return the Proposed Draft maximum levels for total aflatoxins in dried figs to Step 2/3 so that the sampling plans according to the proposed ML of 10 µg/kg can be developed for consideration by the 6th session of the Committee (REP11/CF, para. 50). CCCF6 (2012) agreed to forward the Proposed Draft ML of 10 µg/kg for Dried Figs including the sampling plan to CAC35 for adoption at Step 5/8 with omission of Steps 6 and 7 (REP12/CF, para. 72 and Appendix VI). CAC35 (2012) adopted the draft ML at Step 5/8 (REP12/CAC, Appendix III).

**Aflatoxins in sorghum**

CCCF6 (2012) agreed to initiate new work on the development of an annex for the management of aflatoxins and ochratoxin A in sorghum to the Code of practice for the prevention and reduction of mycotoxin contamination in cereals (CXC 51-2003). The Committee agreed to establish an EWG to prepare the proposed draft annex for comments at Step 3 and consideration at CCCF07 the 7th session. (REP12/CF, para. 136 and Appendix IX). CAC35 (2012) approved the new work (REP12/CAC, Appendix VI).

CCCF7 (2013) agreed to return the proposed draft Annex to Step 2/3 for further development by the EWG, circulation for comments and further consideration by the 8th session of the Committee (REP13/CF, para. 74).

CCCF8 (2014) agreed that in view of the considerable progress made on the annex that it would be advanced for adoption, with the understanding that the annex would be integrated into the COP and its annexes in the new work on the revision of the COP. The Committee agreed to forward the proposed draft Annex to Step 5/8 (with the omission of Steps 6/7) for adoption by the CAC37 (REP14/CF, paras. 76-77, Appendix V). CAC37 (2014) adopted the annex at Step 5/8 (REP14/CAC, para 47, Appendix III).

**Aflatoxins in cereals**

CCCF6 (2012) agreed to the development of a discussion paper on aflatoxins in cereals through an EWG for consideration and discussion at the 7th session with the view of

**Mycotoxins****Aflatoxins, Total**

identification of possible actions or new work on this issue (REP12/CF, para. 175).

CCCF7 (2013) agreed that JECFA Secretariat would put out a public call for data; that this data would be submitted to GEMS/Food; and that the re-established EWG would review and analyze the data and provide a report and recommendations on how to proceed with aflatoxins in cereals for consideration by the 8th session of the Committee (REP13/CF, para. 140).

CCCF8 (2014) noted that there was general support that rice should remain the focus of work until more data became available on other cereals, but that priority should be given to the revision of the Code of practice for the prevention and reduction of mycotoxin contamination in cereals, noting that an annex on aflatoxins would take into account measures for control aflatoxins in rice and other cereals, rather than on establishing an ML for aflatoxins in rice. The committee agreed that countries would submit data, especially for wheat, maize and sorghum, to GEMS/Food and no further work would be undertaken on the establishment of MLs for aflatoxins in cereals for the time being (REP14/CF, paras. 102-103).

JECFA83 (2016) updated the aflatoxin risk assessment at the request of CCCF and calculated exposure to aflatoxins. The Committee noted that there were limited contamination data from developing countries, which hindered a more comprehensive and global evaluation of aflatoxin occurrence and may have resulted in an underestimate of dietary exposure in these countries. Only five food commodities (maize, peanuts, rice, sorghum and wheat) each contribute more than 10% to international dietary exposure estimates for more than one GEMS/Food cluster diets, for either total aflatoxins (AFT) or AFB<sub>1</sub>.

Although overall concentrations of aflatoxins in rice and wheat are lower than concentrations in maize and groundnuts (a traditional focus for aflatoxin risk management), the high consumption of rice and wheat in some countries means that these cereals may account for up to 80% of dietary aflatoxin exposure for those GEMS/Food cluster diets. Mean AFB<sub>1</sub> concentrations in sorghum from the GEMS/Food contaminants database are higher than those for maize; combined with high consumption levels of sorghum in some GEMS/Food clusters, this cereal contributes 16–59% of dietary exposure in six GEMS/Food clusters. The database on sorghum is considerably more limited than that on maize (JECFA/83/SC).

CCCF11 (2017) agreed, based on the recommendations of the in-session working group on the follow-up to JECFA evaluations, to establish an EWG, led by Brazil, working in English to prepare a discussion paper on aflatoxins and sterigmatocystin in cereals (in particular maize, rice, sorghum and wheat) to enable CCCF to take at CCCF12 an informed decision on the appropriate follow-up as regards possible risk management options for aflatoxins and sterigmatocystin in cereals (REP17/CF, para. 151).

CCCF12 (2018) discussed a proposal for new work on ML(s) for aflatoxins in cereals and cereal-based foods including foods for infants and young children and noted the views that the COP for mycotoxins in cereals (CXC 51-2003) had been revised, including a specific annex for aflatoxins in 2016. It was therefore appropriate that the revised COP should be implemented for some period of time and updated occurrence data collected before beginning work on new MLs, also considering the workload of CCCF and that there were no current concerns for international trade. The Committee noted that it was necessary to distinguish the categories of cereals for which MLs were to be set, to be specific in the commodities and what data were representative of which commodity. It was also necessary to be clear in the scope of the proposed new work that the focus would be on total aflatoxins for grains or on products made from grains, for human consumption and that the impact of proposed MLs on grain availability also be considered. Some Delegations stressed the need to define the types of rice (grain, husked or polished rice) and that aflatoxins were rarely found on white or polished rice (REP 18/CF, para, 134).

The JECFA Secretariat noted concerns from a public health point of view when dealing with such potent contaminants in staple foods. CCCF had specifically requested the work and the call for data had been targeted to these commodities and a large number of occurrence data received from all over the world. It would be appropriate to develop MLs for the key cereals listed for which sufficient data are available and indicating higher levels of contamination (REP 18/CF, para, 134 and 135).

The Committee agreed to establish an EWG, chaired by Brazil and co-chaired by India, reporting to CCCF13, to further develop the discussion paper and provide proposed MLs for total aflatoxins in wheat, maize, sorghum and rice (specifying the categories) for grains for human consumption. The EWG should also propose MLs for flour and cereal-based foods for infants and young children (REP 18/CF, paras. 133-138).

**Aflatoxins in ready-to-eat (RTE) peanuts**

At CCCF7 (2013), a new work on the establishment of a maximum level for total aflatoxins in ready-to-eat peanuts and associated sampling plan was proposed. The Committee agreed to establish an EWG to prepare a discussion paper for consideration at the 8th session that defines the issue, identifies the available data and specifies data requirements for

**Mycotoxins****Aflatoxins, Total**

establishing the ML (REP13/CF, para. 149-151).

CCCF8 (2014) agreed to forward the proposal to initiate new work on MLs for total aflatoxins in RTE peanuts for approval by CAC37 (Appendix X). Russian Federation expressed its reservation to this decision. The Committee agreed to establish an EWG led by India to prepare proposals for MLs for total aflatoxins in RTE peanuts, for comments at Step 3 and consideration at the 9<sup>th</sup> session of the Committee (REP14/CF, paras. 119-120).

CAC37 (2014) adopted the new work (REP14/CAC, para. 96. Appendix VI).

CCCF9 (2015) agreed to request JECFA to conduct an exposure assessment for health impact and calculate violation rates based on the hypothetical MLs of 4, 8, 10 and 15 µg/kg for total aflatoxins in RTE peanuts and agreed that work on the ML for aflatoxins in RTE would be undertaken when the results of the JECFA impact assessment became available. It was clarified that the RTE peanuts include several categories of peanuts, such as raw shelled peanuts, raw-in-shell peanuts, roasted in shell peanuts, roasted/blanched shelled peanuts, fried shelled peanuts with or without skin, coated peanuts in all types of packing (consumer or bulk), and any other products having preparation of more than 20% of peanuts. The Committee noted that the definition for RTE peanuts had been included in the GSCTFF. Noting that the ML should be established for RTE peanuts, the Committee agreed to remove mixed preparations from the list of RTE peanuts. The Committee agreed to hold the proposed draft ML and sampling plan at Step 4 pending the outcome of the JECFA exposure assessment for health impact (REP15/CF, paras. 96-100).

CCCF10 (2016) recalled the MLs for total aflatoxins in RTE peanuts had been held at Step 4 pending the outcome of the JECFA exposure assessment for health impact. Noting that this would be addressed at JECFA83, the Committee agreed that India would prepare proposals for MLs taking into account the outcomes of JECFA83 for consideration by CCCF11 (REP16/CF, paras 170 and 173)

JECFA83 (2016) calculated that five food commodities (maize, peanuts, rice, sorghum and wheat) each contribute more than 10% to international dietary exposure estimates for more than one GEMS/Food cluster diets, for either total aflatoxins (AFT) or AFB1. The Committee performed an impact assessment of different MLs for RTE peanuts and concluded that enforcing an ML of 10, 8 or 4 µg/kg for RTE peanuts would have little further impact on dietary exposure to AFT for the general population, compared with setting an ML of 15 µg/kg. At an ML of 4 µg/kg, the proportion of the world market of RTE peanuts rejected would be approximately double the proportion rejected at an ML of 15 µg/kg (about 20% versus 10%) (JECFA/83/SC).

CCCF11 (2017) discussed the revised proposed draft ML of 15 µg/kg, prepared by India as chair of the EWG based on the outcome of JECFA83. In view of the lack of consensus on the recommendation and the need for further consideration of the JECFA report, the Committee agreed to request comments on the levels of 10 µg/kg or 15 µg/kg at Step 3.

Comments should be accompanied by a rationale for the proposed draft ML and any additional/further information to support the proposed draft ML and to establish an EWG led by India to consider the comments and information received and to prepare a revised proposal for further comments and consideration by CCCF12. (REP17/CF, paras. 104-108 and Appendix IV)

CCCF12 (2018) considered the proposed draft ML of 10 µg/kg for AFT in peanuts RTE. Those in favour expressed the view that the level matched what was achievable in their countries or in their national legislation; that it was consistent with the ML established for tree nuts and that it was important to have a separate ML different from peanuts for further processing which would encourage better practices and better RTE peanuts in the market (REP 18/CF, para, 104 and 105)..

The Representative of FAO reminded CCCF about the importance of Codex standards for international trade. He urged CCCF to focus on the need to find a compromise as the absence of an international standard would not be facilitating trade and might put public health at risk. The Representative emphasized that for the goal of alleviating poverty and eradicating hunger the work of Codex and suitable international food safety standards were critical (REP 18/CF, para, 109).

Noting the lack of consensus, the Committee considered as a compromise an ML of 12 µg/kg, however, the Committee could not reach consensus. The MLs for other tree nuts would need to be revised since the MLs of these nuts are based on a JECFA evaluation with an outcome similar to the one for peanuts. The Committee then considered a proposal from the JECFA Secretariat to hold an ML for aflatoxins in RTE peanuts, while producing countries would make clear efforts to implement the Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Peanuts (CXC 55-2004) and collect occurrence data. The work could then be taken up again in 3 to 5 years once new data were made available and

**Mycotoxins****Aflatoxins, Total**

assessed by JECFA . There was general support for the proposal of the JECFA Secretariat. It was clarified that data should be specifically for RTE peanuts and as moved in trade and that the data should clearly indicate if they referred to RTE or for further processing such as oil production or for feed. (REP 18/CF, para. 111 and 114)

The Committee agreed:

- to hold the proposed draft ML of 10 µg/kg at Step 4 (REP 18/CF, Appendix VII) to ensure implementation of the COP (CXC 55-2004);
- that JECFA would issue a call for data in three-years' time; and
- that an EWG would be re-established, once the data were submitted, to prepare a proposal for consideration by CCCF15. (REP 18/CF, para. 115)

**Aflatoxins in spices**

CCCF8 (2014) discussed proposals for new work on MLs for aflatoxins in spices and AFT and AFB<sub>1</sub> in nutmeg, and associated sampling plans. The Committee had a general discussion on how best to approach the establishment of MLs in spices and considered a proposal by the Chairperson that a review of mycotoxins in spices first be conducted to allow the Committee to understand which mycotoxins to address and in which spices.

Such a study could allow for a possible prioritisation of the work on spices for the Committee. The Committee agreed to establish an EWG, led by India and co-chaired by EU and Indonesia, and working in English only, to prepare a discussion paper as outlined in the proposal by the Chairperson for consideration at the next session (REP14/CF, paras. 134 and 137).

In view of the interest to continue with work on MLs in spices, but the need for further clarity on which mycotoxin/spice(s) combination to establish MLs and the rationale for this, as well as further need for prioritisation of the work, CCCF9 (2015) agreed to re-establish the EWG, led by India and co-chaired by Indonesia and EU to prepare a new discussion paper and project document for establishment of ML for spices. The discussion paper should also include proposals for possible MLs to assist the next session of the Committee to take a decision on new work (REP15/CF, paras. 138-139).

CCCF10 (2016) agreed that further work was needed to expand on the MLs through an EWG chaired by India and co-chaired by the EU with the following terms of reference:

- provide a rationale for selection of spices (chilli, paprika, ginger, nutmeg, pepper, turmeric)
- provide rationale for selection of total aflatoxins and OTA
- take into account the outcome of the JECFA evaluation of 2016
- consider trade aspects of existing national standards
- prepare a Project document for new work with proposals for MLs for spice (REP16/CF, paras. 143-148)

CCCF11 (2017) agreed to start new work on MLs for AFT and OTA in nutmeg, chilli and paprika, ginger, pepper and turmeric and to submit the revised project document for approval by CAC40 and to establish an EWG, led by India subject to approval of new work by CAC40, would prepare a proposal for circulation for comments and consideration by CCCF12.

The Committee also recalled a previous decision that EWG chairs should use data from GEMS/Food database and ensure that any data collected by EWGs should be uploaded to the GEMS/Food database. This was consistent with the recommendation of CCCF9 to use the GEMS/Food platform for data submission and analysis for its work in the development of MLs. When additional information needed to be collected that was not part of the database, (REP17/CF, paras. 118-124) The Committee agreed not to include mycotoxins in spices in the priority list (REP17/CF, para. 149).

CCCF12 (2018) discussed the proposals for MLs for AFT and OTA in nutmeg, chili and paprika, ginger, pepper and turmeric. In view of the range of views, the Committee could not agree on a single figure for the MLs for AFT and OTA in the specified spices.

The Committee agreed:

- i. to suspend work and to hold the ML of 20/30 µg/kg for AFT and 20 µg/kg for OTA in nutmeg, chili and paprika, ginger, pepper and turmeric, respectively, at Step 4 to give time to



**Mycotoxins****Aflatoxins, Total**

- countries to implement the Code of Practice for the prevention and reduction of mycotoxins in spices (CXC 78-2017);
- ii. that JECFA would issue a call for data in three-years' time; and
  - iii. that an EWG would be re-established once the data were submitted to prepare a proposal for consideration by a future CCCF (REP 18/CF, paras. 116-120).

**Code of practice for mycotoxins in spices**

CCCF9 (2015) agreed to request CAC to approve new work on the COP for the Prevention and Reduction of mycotoxin contamination in spices and to forward the project document to the Executive Committee for critical review (Appendix VIII). The Committee also agreed to establish the EWG, chaired by Spain and co-chaired by India and The Netherlands to prepare, subject to approval by the Commission, a proposed draft of COP for circulation for comments at Step 3 and consideration at its next session. The EWG would also prepare a discussion paper to outline the development of possible annexes for mycotoxin/individual spices or groups of spices combinations (REP15/CF, paras. 143-144).

CAC38 (2015) approved the new work (REP15/CAC Appendix VI).

CCCF11 (2017) agreed to advance the proposed draft COP for the prevention and reduction of mycotoxins contamination in spices for adoption at Step 5/8 by CAC and to discontinue work on annexes until further information on management practices specific spices became available. The Committee noted that the Code of Hygienic Practice for Low-moisture Foods (CXC 75-2015) and its annex on spices already covered practices for transport and packaging similar to the advice contained in paragraphs 63-69 and 78 of CX/CF 10/16/12, Appendix I, and agreed that there was no need to refer any text to CCFH for consideration for inclusion in CXC 75-2015. (REP17/CF, paras. 112-117 and Appendix VI)

CAC40 (2017) adopted the COP at Step 5/8 with the amendment to section 2.3.2. (REP17/CAC, paras. 58-59 and Appendix III)

Aflatoxins are a group of highly toxic mycotoxins produced by fungi of the genus *Aspergillus*. The four main aflatoxins found in contaminated plant products are B<sub>1</sub>, B<sub>2</sub>, G<sub>1</sub> and G<sub>2</sub> and are a group of structurally related difuranocoumarin derivatives that usually occur together in varying ratios, AFB<sub>1</sub> usually being the most important one. These compounds pose a substantial hazard to human and animal health. IARC (1992) classified aflatoxin B<sub>1</sub> in Group 1 (human carcinogen) and aflatoxin M<sub>1</sub> in Group 2B (probable human carcinogen). The liver is the primary target organ.

A wide range of foods may be contaminated with aflatoxins; they are most commonly found in groundnuts (peanuts), dried fruit, tree nuts (such as almonds, pecans, walnuts, pistachio and Brazil nuts), spices, figs, crude vegetable oils, cocoa beans, maize, rice, cottonseed and copra. Aflatoxin B<sub>1</sub> present in animal feed can partly be transferred to milk in the form of the metabolite aflatoxin M<sub>1</sub> (mostly 1-2%, but higher percentages are found at low contamination levels in high producing animals.) Aflatoxin contamination is responsible for considerable economic losses and efforts are being made to reduce contamination of food and feedingstuff.

**SAMPLING PLAN FOR TOTAL AFLATOXINS IN PEANUTS INTENDED FOR FURTHER PROCESSING**

**INTRODUCTION**

1. The sampling plan calls for a single 20 kg laboratory sample of shelled peanuts (27 kg of unshelled peanuts) to be taken from a peanut lot (sub-lot) and tested against a maximum level of 15 micrograms per kilogram ( $\mu\text{g}/\text{kg}$ ) total aflatoxins.
2. This sampling plan has been designed for enforcement and controls concerning total aflatoxins in bulk consignments of peanuts traded in the export market. To assist member countries in implementing the Codex sampling plan, sample selection methods, sample preparation methods and analytical methods required to quantify aflatoxin in bulk peanut lots are described in this document.

**A. DEFINITIONS**

<b>Lot</b>	An identifiable quantity of a food commodity delivered at one time and determined by the official to have common characteristics, such as origin, variety, type of packing, packer, consignor or markings.
<b>Sublot</b>	Designated part of a large lot in order to apply the sampling method on that designated part. Each sublot must be physically separate and identifiable.
<b>Sampling plan</b>	Is defined by an aflatoxin test procedure and an accept/reject limit. An aflatoxin test procedure consists of three steps: sample selection, sample preparation and aflatoxin quantification. The accept/reject limit is a tolerance usually equal to the codex maximum limit.
<b>Incremental sample</b>	A quantity of material taken from a single random place in the lot or sublot.
<b>Aggregate sample</b>	The combined total of all the incremental samples taken from the lot or sublot. The aggregate sample has to be at least as large as the 20 kg laboratory sample.
<b>Laboratory sample</b>	The smallest quantity of peanuts comminuted in a mill. The laboratory sample may be a portion of or the entire aggregate sample. If the aggregate sample is larger than 20 kg, a 20 kg laboratory sample should be removed in a random manner from the aggregate sample. The sample should be finely ground and mixed thoroughly using a process that approaches as complete a homogenization as possible.
<b>Test portion</b>	Portion of the comminuted laboratory sample. The entire 20 kg laboratory sample should be comminuted in a mill. A portion of the comminuted 20 kg sample is randomly removed for the extraction of the aflatoxin for chemical analysis. Based upon grinder capacity, the 20 kg aggregate sample can be divided into several equal sized samples, if all results are averaged.

**B. SAMPLING**

**MATERIAL TO BE SAMPLED**

3. Each lot which is to be examined must be sampled separately. Large lots should be subdivided into sublots to be sampled separately. The subdivision can be done following provisions laid down in Table 1 below.
4. Taking into account that the weight of the lot is not always an exact multiple of the weight of the sublots, the weight of the sublot may exceed the mentioned weight by a maximum of 20 %.

**Table 1: Subdivision of large lots into sublots for sampling**

<b>Commodity</b>	<b>Lot weight – tonne (T)</b>	<b>Weight or number of sublots</b>	<b>Number of incremental samples</b>	<b>Laboratory sample weight (kg)</b>
<b>Peanuts</b>	$\geq 500$	100 tonnes	100	20
	$>100$ and $<500$	5 sublots	100	20
	$\geq 25$ and $\leq 100$	25 tonnes	100	20
	$>15$ and $\leq 25$	--1 sublot	100	20

**Mycotoxins****Aflatoxins, Total****NUMBER OF INCREMENTAL SAMPLES FOR LOTS OF LESS THAN 15 TONNES**

5. The number of incremental samples to be taken depends on the weight of the lot, with a minimum of 10 and a maximum of 100. The figures in the following Table 2 may be used to determine the number of incremental samples to be taken. It is necessary that the total sample weight of 20 kg is achieved.

**Table 2: Number of incremental samples to be taken depending on the weight of the lot**

Lot weight tonnes – (T)	N° of incremental samples
$T \leq 1$	10
$1 < T \leq 5$	40
$5 < T \leq 10$	60
$10 < T < 15$	80

**INCREMENTAL SAMPLE SELECTION**

6. Procedures used to take incremental samples from a peanut lot are extremely important. Every individual peanut in the lot should have an equal chance of being chosen. Biases will be introduced by the sample selection methods if equipment and procedures used to select the incremental samples prohibit or reduce the chances of any item in the lot from being chosen.
7. Since there is no way to know if the contaminated peanut kernels are uniformly dispersed throughout the lot, it is essential that the aggregate sample be the accumulation of many small portions or increments of the product selected from different locations throughout the lot. If the aggregate sample is larger than desired, it should be blended and subdivided until the desired laboratory sample size is achieved.

**STATIC LOTS**

8. A static lot can be defined as a large mass of peanuts contained either in a single large container such as a wagon, truck, or railcar or in many small containers such as sacks or boxes and the peanuts are stationary at the time a sample is selected. Selecting a truly random sample from a static lot can be difficult because the container may not allow access to all peanuts.
9. Taking an aggregate sample from a static lot usually requires the use of probing devices to select product from the lot. The probing devices used should be specially designed for the type of container. The probe should (1) be long enough to reach all product, (2) not restrict any item in the lot from being selected, and (3) not alter the items in the lot. As mentioned above, the aggregate sample should be a composite from many small increments of product taken from many different locations throughout the lot.
10. For lots traded in individual packages, the sampling frequency (SF), or number of packages that incremental samples are taken from, is a function of the lot weight (LT), incremental sample weight (IS), aggregate sample weight (AS) and the individual packing weight (IP), as follows:

$$\text{Equation 1: } SF = (LT \times IS) / (AS \times IP).$$

The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.

**DYNAMIC LOTS**

11. True random sampling can be more nearly achieved when selecting an aggregate sample from a moving stream of peanuts as the lot is transferred, for example, by a conveyor belt from one location to another. When sampling from a moving stream, take small increments of product from the entire length of the moving stream; composite the peanuts to obtain an aggregate sample; if the aggregate sample is larger than the required laboratory sample, then blend and subdivide the aggregate sample to obtain the desired size laboratory sample.
12. Automatic sampling equipment such as cross-cut samplers are commercially available with timers that automatically pass a diverter cup through the moving stream at predetermined and uniform intervals. When automatic equipment is not available, a person can be assigned to manually pass a cup through the stream at periodic intervals to collect incremental samples. Whether using automatic or manual methods, small increments of peanuts should be collected and composited at frequent and uniform intervals throughout the entire time peanuts flow past the sampling point.

**Mycotoxins****Aflatoxins, Total**

13. Cross-cut samplers should be installed in the following manner: (1) the plane of the opening of the diverter cup should be perpendicular to the direction of flow; (2) the diverter cup should pass through the entire cross sectional area of the stream; and (3) the opening of the diverter cup should be wide enough to accept all items of interest in the lot. As a general rule, the width of the diverter cup opening should be about three times the largest dimensions of the items in the lot.
14. The size of the aggregate sample (S) in kg, taken from a lot by a cross cut sampler is:  
Equation 2:  $S = (D \times LT) / (T \times V)$ .
- D is the width of the diverter cup opening (in cm), LT is the lot size (in kg), T is interval or time between cup movement through the stream (in seconds), and V is cup velocity (in cm/sec).
15. If the mass flow rate of the moving stream, MR (kg/sec), is known, then the sampling frequency (SF), or number of cuts made by the automatic sampler cup is:  
Equation 3:  $SF = (S \times V) / (D \times MR)$ .
16. Equation 2 can also be used to compute other terms of interest such as the time between cuts (T). For example, the required time (T) between cuts of the diverter cup to obtain a 20 kg aggregate sample from a 30 000 kg lot where the diverter cup width is 5.08 cm (2 inches), and the cup velocity through the stream 30 cm/sec. Solving for T in Equation 2.  
 $T = (5.08 \text{ cm} \times 30\,000 \text{ kg}) / (20 \text{ kg} \times 30 \text{ cm/sec}) = 254 \text{ sec}$
17. If the lot is moving at 500 kg per minute, the entire lot will pass through the sampler in 60 minutes and only 14 cuts (14 incremental samples) will be made by the cup through the lot. This may be considered too infrequent in that too much product passes through the sampler between the time the cup cuts through the stream.

**WEIGHT OF THE INCREMENTAL SAMPLE**

18. The weight of the incremental sample should be approximately 200 g or greater, depending on the total number of increments, to obtain an aggregate sample of 20 kg.

**PACKAGING AND TRANSMISSION OF SAMPLES**

19. Each laboratory sample shall be placed in a clean, inert container offering adequate protection from contamination and against damage in transit. All necessary precautions shall be taken to avoid any change in composition of the laboratory sample which might arise during transportation or storage.

**SEALING AND LABELLING OF SAMPLES**

20. Each laboratory sample taken for official use shall be sealed at the place of sampling and identified. A record must be kept of each sampling, permitting each lot to be identified unambiguously and giving the date and place of sampling together with any additional information likely to be of assistance to the analyst.

**C. SAMPLE PREPARATION****PRECAUTIONS**

21. Daylight should be excluded as much as possible during the procedure, since aflatoxin gradually breaks down under the influence of ultra-violet light.

**HOMOGENISATION – GRINDING**

22. As the distribution of aflatoxin is extremely non-homogeneous, samples should be prepared - and especially homogenised - with extreme care. All laboratory sample obtained from aggregate sample is to be used for the homogenisation/grinding of the sample.
23. The sample should be finely ground and mixed thoroughly using a process that approaches as complete a homogenisation as possible.
24. The use of a hammer mill with a #14 screen (3.1 mm diameter hole in the screen) has been proven to represent a compromise in terms of cost and precision. A better homogenisation (finer grind – slurry) can be obtained by more sophisticated equipment, resulting in a lower sample preparation variance.

**TEST PORTION**

25. A minimum test portion size of 100 g taken from the laboratory sample.

**D. ANALYTICAL METHODS****BACKGROUND**

**Mycotoxins****Aflatoxins, Total**

26. A criteria-based approach, whereby a set of performance criteria is established with which the analytical method used should comply, is appropriate. The criteria-based approach has the advantage that, by avoiding setting down specific details of the method used, developments in methodology can be exploited without having to reconsider or modify the specified method. The performance criteria established for methods should include all the parameters that need to be addressed by each laboratory such as the detection limit, repeatability coefficient of variation, reproducibility coefficient of variation, and the percent recovery necessary for various statutory limits. Utilizing this approach, laboratories would be free to use the analytical method most appropriate for their facilities. Analytical methods that are accepted by chemists internationally (such as AOAC) may be used. These methods are regularly monitored and improved depending upon technology.

**PERFORMANCE CRITERIA FOR METHODS OF ANALYSIS****Table 3: Specific requirements with which methods of analysis should comply**

Criterion	Concentration Range	Recommended Value	Maximum Permitted Value
Blanks	All	Negligible	-
Recovery-Aflatoxins Total	1 - 15 µg/kg	70 to 110 %	
	> 15 µg/kg	80 to 110 %	
Precision RSD <sub>R</sub>	All	As derived from Horwitz Equation	2 x value derived from Horwitz Equation
Precision RSD <sub>i</sub> may be calculated as 0.66 times Precision RSD <sub>R</sub> at the concentration of interest			

- The detection limits of the methods used are not stated as the precision values are given at the concentrations of interest;
- The precision values are calculated from the Horwitz equation, i.e.:

$$RSD_R = 2^{(1-0.5\log C)}$$

where:

- \* RSD<sub>R</sub> is the relative standard deviation calculated from results generated under reproducibility conditions  $[(S_R/\bar{x}) \times 100]$
- \* C is the concentration ratio (i.e. 1 = 100 g/100 g, 0.001 = 1,000 mg/kg)

27. This is a generalized precision equation which has been found to be independent of analyte and matrix but solely dependent on concentration for most routine methods of analysis.

**SAMPLING PLANS FOR AFLATOXIN CONTAMINATION IN READY-TO-EAT TREENUTS AND TREENUTS DESTINED FOR FURTHER PROCESSING: ALMONDS, HAZELNUTS, PISTACHIOS AND SHELLED BRAZIL NUTS**

**DEFINITION**

<b>Lot</b>	An identifiable quantity of a food commodity delivered at one time and determined by the official to have common characteristics, such as origin, variety, type of packing, packer, consignor, or markings.
<b>Sublot</b>	Designated part of a larger lot in order to apply the sampling method on that designated part. Each sublot must be physically separate and identifiable.
<b>Sampling plan</b>	It is defined by an aflatoxin test procedure and an accept/reject limit. An aflatoxin test procedure consists of three steps: sample selection, sample preparation and aflatoxin quantification. The accept/reject limit is a tolerance usually equal to the codex maximum level.
<b>Incremental sample</b>	The quantity of material taken from a single random place in the lot or sublot.
<b>Aggregate sample</b>	The combined total of all the incremental samples that is taken from the lot or sublot. The aggregate sample has to be at least as large as the laboratory sample or samples combined.
<b>Laboratory sample</b>	The smallest quantity of tree nuts comminuted in a mill. The laboratory sample may be a portion of or the entire aggregate sample. If the aggregate sample is larger than the laboratory sample(s), the laboratory sample(s) should be removed in a random manner from the aggregate sample.
<b>Test portion</b>	A portion of the comminuted laboratory sample. The entire laboratory sample should be comminuted in a mill. A portion of the comminuted laboratory sample is randomly removed for the extraction of the aflatoxin for chemical analysis.
<b>Ready-to-eat treenuts</b>	Nuts, which are not intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption.
<b>Treenuts destined for further processing</b>	Nuts, which are intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption. Processes that have proven to reduce levels of aflatoxins are shelling, blanching followed by color sorting, and sorting by specific gravity and color (damage). There is some evidence that roasting reduces aflatoxins in pistachios but for other nuts the evidence is still to be supplied.
<b>Operating characteristic (OC) Curve</b>	A plot of the probability of a accepting a lot versus lot concentration when using a specific sampling plan design. The OC curve provides an estimate of good lots rejected (exporter's risk) and bad lots accepted (importer's risk) by a specific aflatoxin sampling plan design.

**SAMPLING PLAN DESIGN CONSIDERATIONS**

1. Importers may commercially classify treenuts as either "ready-to-eat" (RTE) or "destined for further processing" (DFP). As a result, maximum levels and sampling plans are proposed for both commercial types of treenuts. Maximum levels need to be defined for treenuts destined for further processing and ready-to-eat treenuts before a final decision can be made about a sampling plan design.
2. Treenuts can be marketed either as inshell or shelled nuts. For example, pistachios are predominately marketed as inshell nuts while almonds are predominately marketed as shelled nuts.
3. Sampling statistics, shown in Annex I, are based upon the uncertainty and aflatoxin distribution among laboratory samples of shelled nuts. Because the shelled nut count per kg is different for each of the three treenuts, the laboratory sample size is expressed in number of nuts for statistical purposes. However, the shelled nut count per kg for each treenut, shown in Annex I, can be used to convert laboratory sample size from number of nuts to mass and vice versa.
4. Uncertainty estimates associated with sampling, sample preparation, and analysis, shown in Annex I, and the negative

**Mycotoxins****Aflatoxins, Total**

binomial distribution<sup>1</sup> are used to calculate operating characteristic (OC) curves that describe the performance of the proposed aflatoxin-sampling plans (Annex II).

5. In Annex, the analytical variance reflects a reproducibility relative standard deviation of 22%, which is suggested by Thompson and is based upon Food Analysis Performance Assessment Scheme (FAPAS) data<sup>2</sup>. A relative standard deviation of 22% is considered by FAPAS as an appropriate measure of the best agreement that can be reliably obtained between laboratories. An analytical uncertainty of 22% is larger than the within laboratory variation measured in the sampling studies for the three treenuts<sup>3</sup>.
6. The issue of correcting the analytical test results for the range of acceptable recovery result for recovery is not addressed in this document. However, Table 2 specifies several performance criteria for analytical methods including suggestioy rates.

**AFLATOXIN TEST PROCEDURE AND MAXIMUM LEVELS**

7. An aflatoxin-sampling plan is defined by an aflatoxin test procedure and a maximum level. A value for the proposed maximum level and the aflatoxin test procedure are given below in this section.
8. The maximum levels for total aflatoxins in treenuts (almonds, hazelnuts, pistachios and shelled Brazil nuts) "ready-to-eat" and "destined for further processing" are 10 and 15 µg/kg, respectively.
9. Choice of the number and size of the laboratory sample is a compromise between minimizing risks (false positives and false negatives) and costs related to sampling and restricting trade. For simplicity, it is recommended that the proposed aflatoxin sampling plans use a 20 kg aggregate sample for all three treenuts.
10. The two sampling plans (RTE and DFP) have been designed for enforcement and controls concerning total aflatoxins in bulk consignments (lots) of treenuts traded in the export market.

**Treenuts destined for further processing**

Maximum level	–	15 µg/kg total aflatoxins
Number of laboratory samples	–	1
Laboratory sample size	–	20 kg
Almonds	–	shelled nuts
Hazelnuts	–	shelled nuts
Pistachios	–	inshell nuts (equivalent to about 10 kg shelled nuts that is calculated on the basis of the actual edible portion in the sample)
Brazil nuts	–	shelled nuts
Sample preparation	–	sample shall be finely ground and mixed thoroughly using a process, e.g., dry grind with a vertical cutter mixer type mill, that has been demonstrated to provide the lowest sample preparation variance. Preferably, Brazil nuts should be ground as slurry.
Analytical method	–	performance based (see Table 2)
Decision rule	–	If the aflatoxin test result is less than or equal to 15 µg/kg total aflatoxins, then accept the lot. Otherwise, reject the lot.

The operating characteristic curve describing the performance of the sampling plan for the three treenuts destined for further processing is shown in Annex II.

**Ready-to-eat treenuts**

Maximum level	–	10 µg/kg total aflatoxins
Number of laboratory samples	–	2
Laboratory sample size	–	10 kg
Almonds	–	shelled nuts
Hazelnuts	–	shelled nuts

<sup>1</sup> Whitaker, T., Dickens, J., Monroe, R., and Wiser, E. 1972. Comparison of the negative binomial distribution of aflatoxin in shelled peanuts to the negative binomial distribution. J. American Oil Chemists' Society, 49:590-593.

<sup>2</sup> Thompson, M. 2000. Recent trends in inter-laboratory precision at ppb and sub-ppb concentrations in relation to fitness for purpose criteria in proficiency testing. J. Royal Society of Chemistry, 125:385-386.

<sup>3</sup> The within laboratory analytical uncertainty for each treenut can be found at the website and Brazil nuts in the CONFORCAST

Website: <http://www5.bae.ncsu.edu/usda/www/ResearchActDocs/treenutwg.html>

CONFORCAST: Ferramentas Analíticas para Capacitação do Brasil na Garantia da Conformidade da Castanha-Do-Brasil (Bertholletia Excelsa) quanto ao Perigo aflatoxina. Projeto nº 1.265/05, Aprovado pela FINEP na Chamada Pública, "Ação Transversal - TIB - 06/2005 - Linha 1". MAPA. Ministério da Agricultura, pecuária e do Abastecimento. Secretaria de Defesa Agropecuária - DAS, Departamento de Inspeção de Produtos de Origem Vegetal – DIPOV. Coordenação-Geral de Apoio Laboratorial – CGAL, Laboratório Nacional Agropecuário – LANAGRO/MG, United States Department of Agriculture (Thomas Whitaker and Andy Slate).

**Mycotoxins****Aflatoxins, Total**

- Pistachios – inshell nuts (equivalent to about 5 kg shelled nuts per test sample that is calculated on the basis of the actual edible portion in the sample)
- Brazil nuts – shelled nuts
- Sample preparation – sample shall be finely ground and mixed thoroughly using a process, e.g., dry grind with a vertical cutter mixer type mill, that has been demonstrated to provide the lowest sample preparation variance. Preferably, Brazil nuts should be ground as slurry.
- Analytical method – performance based (see Table 2)
- Decision rule – If the aflatoxin test result is less than or equal to 10 µg/kg total aflatoxin in both test samples, then accept the lot. Otherwise, reject the lot.

The operating characteristic curve describing the performance of the sampling plan for the three ready-to-eat treenuts is shown in Annex II.

11. To assist member countries implement these two Codex sampling plans, sample selection methods, sample preparation methods, and analytical methods required to quantify aflatoxin in laboratory samples taken from bulk treenut lots are described in the following sections.

**SAMPLE SELECTION****MATERIAL TO BE SAMPLED**

12. Each lot, which is to be examined for aflatoxin, must be sampled separately. Lots larger than 25 tonnes should be subdivided into sublots to be sampled separately. If a lot is greater than 25 tonnes, the number of sublots is equal to the lot weight in tonnes divided by 25 tonnes. It is recommended that a lot or a subplot should not exceed 25 tonnes. The minimum lot weight should be 500 kg.
13. Taking into account that the weight of the lot is not always an exact multiple of 25 tonne sublots, the weight of the subplot may exceed the mentioned weight by a maximum of 25%.
14. Samples should be taken from the same lot, i.e. they should have the same batch code or at the very least the same best before date. Any changes which would affect the mycotoxin content, the analytical determination or make the aggregate samples collected unrepresentative should be avoided. For example do not open packaging in adverse weather conditions or expose samples to excessive moisture or sunlight. Avoid cross-contamination from other potentially contaminated consignments nearby.
15. In most cases any truck or container will have to be unloaded to allow representative sampling to be carried out.

**INCREMENTAL SAMPLE SELECTION**

16. Procedures used to take incremental samples from a treenut lot are extremely important. Every individual nut in the lot should have an equal chance of being chosen. Biases will be introduced by sample selection methods if equipment and procedures used to select the incremental samples prohibit or reduce the chances of any item in the lot from being chosen.
17. Since there is no way to know if the contaminated treenut kernels are uniformly dispersed throughout the lot, it is essential that the aggregate sample be the accumulation of many small incremental samples of product selected from different locations throughout the lot. If the aggregate sample is larger than desired, it should be blended and subdivided until the desired laboratory sample size is achieved.

**NUMBER OF INCREMENTAL SAMPLES FOR LOTS OF VARYING WEIGHT**

18. The number and size of the laboratory sample(s) will not vary with lot (subplot) size. However, the number and size of the incremental samples will vary with lot (subplot) size.
19. The number of incremental samples to be taken from a lot (subplot) depends on the weight of the lot. Table 1 shall be used to determine the number of incremental samples to be taken from lots or sublots of various sizes below 25 tonnes. The number of incremental samples varies from a minimum of 10 and to a maximum of 100.

**Table 1. Number and size of incremental samples composited for an aggregate sample of 20 kg<sup>a</sup> as a function of lot (or subplot) weight**

Lot or subplot weight <sup>b</sup> (T in tonnes)	Minimum number of incremental samples	Minimum incremental sample size <sup>c</sup> (g)	Minimum aggregate sample size (kg)
T<1	10	2 000	20
1≤T<5	25	800	20
5≤T<10	50	400	20
10≤T<15	75	267	20



**Mycotoxins****Aflatoxins, Total**

15≤T	100	200	20
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a / Minimum aggregate sample size = laboratory sample size of 20 kg

b / 1 Tonne = 1 000 kg

c / Minimum incremental sample size = laboratory sample size (20 kg) / minimum number of incremental samples, i.e. for 0.5 < T < 1 tonne, 2 000 g = 20 000/10

**WEIGHT OF THE INCREMENTAL SAMPLE**

20. The suggested minimum weight of the incremental sample should be approximately 200 g for lots of 25 metric tonnes (25 000 kg). The number and/or size of incremental samples will have to be larger than that suggested in Table 1 for lots sizes below 25 000 kg in order to obtain an aggregate sample greater than or equal to the 20 kg laboratory sample.

**STATIC LOTS**

21. A static lot can be defined as a large mass of treenuts contained either in a large single container such as a wagon, truck or railcar or in many small containers such as sacks or boxes and the nuts are stationary at the time a sample is selected. Selecting a truly random sample from a static lot can be difficult because all containers in the lot or subplot may not be accessible.
22. Taking incremental samples from a static lot usually requires the use of probing devices to select product from the lot. The probing devices should be specifically designed for the commodity and type of container. The probe should (1) be long enough to reach all products, (2) not restrict any item in the lot from being selected, and (3) not alter the items in the lot. As mentioned above, the aggregate sample should be a composite from many small incremental samples of product taken from many different locations throughout the lot.
23. For lots traded in individual packages, the sampling frequency (SF), or number of packages that incremental samples are taken from, is a function of the lot weight (LT), incremental sample weight (IS), aggregate sample weight (AS) and the individual packing weight (IP), as follows:  
Equation 1:  $SF = (LT \times IS) / (AS \times IP)$ .
24. The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.

**DYNAMIC LOTS**

25. Representative aggregate samples can be more easily produced when selecting incremental samples from a moving stream of treenuts as the lot is transferred from one location to another. When sampling from a moving stream, take small incremental samples of product from the entire length of the moving stream; composite the incremental samples to obtain an aggregate sample; if the aggregate sample is larger than the required laboratory sample(s), then blend and subdivide the aggregate sample to obtain the desired size laboratory sample(s).
26. Automatic sampling equipment such as a cross-cut sampler is commercially available with timers that automatically pass a diverter cup through the moving stream at predetermined and uniform intervals. When automatic sampling equipment is not available, a person can be assigned to manually pass a cup through the stream at periodic intervals to collect incremental samples. Whether using automatic or manual methods, incremental samples should be collected and composited at frequent and uniform intervals throughout the entire time the nuts flow past the sampling point.
27. Cross-cut samplers should be installed in the following manner: (1) the plane of the opening of the diverter cup should be perpendicular to the direction of the flow; (2) the diverter cup should pass through the entire cross sectional area of the stream; and (3) the opening of the diverter cup should be wide enough to accept all items of interest in the lot. As a general rule, the width of the diverter cup opening should be about two to three times the largest dimensions of items in the lot.
28. The size of the aggregate sample (S) in kg, taken from a lot by a cross cut sampler is:  
Equation 2:  $S = (D \times LT) / (T \times V)$ ,  
where D is the width of the diverter cup opening (cm), LT is the lot size (kg), T is interval or time between cup movement through the stream (seconds), and V is cup velocity (cm/sec).
29. If the mass flow rate of the moving stream, MR (kg/sec), is known, then the sampling frequency (SF), or number of cuts made by the automatic sampler cup can be computed from Equation 3 as a function of S, V, D, and MR.  
Equation 3:  $SF = (S \times V) / (D \times MR)$ .
30. Equations 2 and 3 can also be used to compute other terms of interest such as the time between cuts (T). For example, the time (T) required between cuts of the diverter cup to obtain a 20 kg aggregate sample from a 20 000 kg lot where the diverter cup width is 5.0 cm and the cup velocity through the stream 30 cm/sec. Solving for T in Equation 2,

**Mycotoxins****Aflatoxins, Total**

$$T = (5.0 \text{ cm} \times 20\,000 \text{ kg}) / (20 \text{ kg} \times 20 \text{ cm/sec}) = 250 \text{ sec.}$$

31. If the lot is moving at 500 kg per minute, the entire lot will pass through the sampler in 40 minutes (2 400 sec) and only 9.6 cuts (9 incremental samples) will be made by the cup through the lot (Equation 3). This may be considered too infrequent, in that too much product (2 083.3 kg) passes through the sampler between the time the cup cuts through the stream.

**PACKAGING AND TRANSPORTATION OF SAMPLES**

32. Each laboratory sample shall be placed in a clean, inert container offering adequate protection from contamination, sunlight, and against damage in transit. All necessary precautions shall be taken to avoid any change in composition of the laboratory sample, which might arise during transportation or storage. Samples should be stored in a cool dark place.

**SEALING AND LABELLING OF SAMPLES**

33. Each laboratory sample taken for official use shall be sealed at the place of sampling and identified. A record must be kept of each sampling, permitting each lot to be identified unambiguously and giving the date and place of sampling together with any additional information likely to be of assistance to the analyst.

**SAMPLE PREPARATION****PRECAUTIONS**

34. Sunlight should be excluded as much as possible during sample preparation, since aflatoxin gradually breaks down under the influence of ultra-violet light. Also, environmental temperature and relative humidity should be controlled and not favor mold growth and aflatoxin formation.

**HOMOGENIZATION - GRINDING**

35. As the distribution of aflatoxin is extremely non-homogeneous, laboratory samples should be homogenized by grinding the entire laboratory sample received by the laboratory. Homogenization is a procedure that reduces particle size and disperses the contaminated particles evenly throughout the comminuted laboratory sample.
36. The laboratory sample should be finely ground and mixed thoroughly using a process that approaches as complete homogenization as possible. Complete homogenization implies that particle size is extremely small and the variability associated with sample preparation (Annex I) approaches zero. After grinding, the grinder should be cleaned to prevent aflatoxin cross-contamination.
37. The use of vertical cutter mixer type grinders that mix and comminute the laboratory sample into a paste represent a compromise in terms of cost and fineness of grind or particle size reduction<sup>4</sup>. A better homogenization (finer grind), such as a liquid slurry, can be obtained by more sophisticated equipment and should provide the lowest sample preparation variance<sup>5</sup>.

**TEST PORTION**

38. The suggested weight of the test portion taken from the comminuted laboratory sample should be approximately 50 grams. If the laboratory sample is prepared using a liquid slurry, the slurry should contain 50 g of nut mass.
39. Procedures for selecting the 50 g test portion from the comminuted laboratory sample should be a random process. If mixing occurred during or after the comminution process, the 50 g test portion can be selected from any location throughout the comminuted laboratory sample. Otherwise, the 50 g test portion should be the accumulation of several small portions selected throughout the laboratory sample.
40. It is suggested that three test portions be selected from each comminuted laboratory sample. The three test portions will be used for enforcement, appeal, and confirmation if needed.

**ANALYTICAL METHODS****BACKGROUND**

41. A criteria-based approach, whereby a set of performance criteria is established with which the analytical method used should comply, is appropriate. The criteria-based approach has the advantage that, by avoiding setting down specific details of the method used, developments in methodology can be exploited without having to reconsider or modify the specific method. The performance criteria established for methods should include all the parameters that need to be addressed by each laboratory such as the detection limit, repeatability coefficient of variation (within lab), reproducibility coefficient of variation (among lab), and the percent recovery necessary for various statutory limits.

<sup>4</sup> Ozay, G., Seyhan, F., Yilmaz, A., Whitaker, T., Slate, A., and Giesbrecht, F. 2006. Sampling hazelnuts for aflatoxin: Uncertainty associated with sampling, sample preparation, and analysis. *J. Association Official Analytical Chemists, Int.*, 89:1004-1011.

<sup>5</sup> Spanjer, M., Scholten, J., Kastrop, S., Jorissen, U., Schatzki, T., Toyofuku, N. 2006. Sample comminution for mycotoxin analysis: Dry milling or slurry mixing?, *Food Additives and Contaminants*, 23:73-83.

**Mycotoxins****Aflatoxins, Total**

Analytical methods that are accepted by chemists internationally (such as AOAC) may be used. These methods are regularly monitored and improved depending upon technology.

**PERFORMANCE CRITERIA FOR METHODS OF ANALYSIS**

42. A list of criteria and performance levels are shown in Table 2. Utilizing this approach, laboratories would be free to use the analytical method most appropriate for their facilities.

**Table 2: Specific Requirements with which Methods of Analysis Should Comply**

Criterion	Concentration Range (ng/g)	Recommended value	Maximum Permitted Value
Blanks	All	Negligible	n/a
Recovery	1 to 15	70 to 110%	n/a
	>15	80 to 110%	n/a
Precision or Relative Standard Deviation RSD <sub>R</sub> (Reproducibility)	1 to 120	Equation 4 by Thompson	2 x value derived from Equation 4
	>120	Equation 5 by Horwitz	2 x value derived from Equation 5
Precision or Relative Standard Deviation RSD <sub>r</sub> (Repeatability)	1 to 120	Calculated as 0.66 times Precision RSD <sub>R</sub>	n/a
	>120	Calculated as 0.66 times Precision RSD <sub>r</sub>	n/a

n/a = not applicable

43. The detection limits of the methods used are not stated. Only the precision values are given at the concentrations of interest. The precision values are calculated from equations 4 and 5 developed by Thompson<sup>8</sup> and Horwitz and Albert<sup>6</sup>, respectively.

Equation 4:  $RSD_R = 22.0$  (for  $C \leq 120$  ng/g or  $c \leq 120 \times 10^{-9}$ )

Equation 5:  $RSD_R = 2^{(1-0.5 \log c)}$  (for  $C > 120$  ng/g or  $c > 120 \times 10^{-9}$ )

where:

- $RSD_R$  = the relative standard deviation calculated from results generated under reproducibility conditions
- $RSD_r$  = the relative standard deviation calculated from results generated under repeatability conditions  
= 0.66  $RSD_R$
- $c$  = the aflatoxin concentration ratio (i.e. 1 = 100 g/100 g, 0.001 = 1 000 mg/kg)
- $C$  = aflatoxin concentration or mass of aflatoxin to mass of treenuts (i.e. µg/kg)

44. Equations 4 and 5 are generalized precision equations, which have been found to be independent of analyte and matrix but solely dependent on concentration for most routine methods of analysis.
45. Results should be reported on the edible portion of the sample.

<sup>6</sup> Horwitz, W. and Albert, R. 2006. The Horwitz ratio (HorRat): A useful index of method performance with respect to precision. J. Association of Official Analytical Chemists, Int., 89:1095-1109.

**Mycotoxins****Aflatoxins, Total****Annex I****Uncertainty, as measured by the variance, associated with sampling, sample preparation, and analytical steps of the aflatoxin test procedure used to estimate aflatoxin in almonds, hazelnuts, pistachios and shelled Brazil nuts.**

Sampling data for almonds, hazelnuts, pistachios and shelled Brazil nuts were supplied by the United States, Turkey, and Iran, respectively.

Variance estimates and the negative binomial distribution<sup>1</sup> were used to compute operating characteristic curves for each treenut in Annex II. Sampling, sample preparation, and analytical variances associated with testing almonds, hazelnuts, pistachios and shelled Brazil nuts are shown in Table 1 below.

Because of the computational complexities associated with use of the negative binomial distribution to compute operational characteristic (OC) curves for various sampling plan designs, the effect of various laboratory sample sizes, various numbers of laboratory samples, and various maximum levels on the performance (OC curves) of sampling plan designs is provided at the website address <http://www5.bae.ncsu.edu/usda/www/ResearchActDocs/treenutwg.html> and for Brazil nuts in the CONFORCAST.

**Table 1. Variances<sup>a</sup> associated with the aflatoxin test procedure for each treenut.**

Test Procedure	Almonds	Hazelnuts	Pistachios	Shelled Brazil nuts
Sampling <sup>b,c</sup>	$S^2_s = (7,730/ns)5.759C^{1.561}$	$S^2_s = (10,000/ns)4.291C^{1.609}$	$S^2_s = (8,000/ns)7.913C^{1.475}$	$S^2_s = (1,850/ns)4.8616C^{1.889}$
Sample Prep <sup>d</sup>	$S^2_{sp} = (100/nss)0.170C^{1.646}$	$S^2_{sp} = (50/nss)0.021C^{1.545}$	$S^2_{sp} = (25/nss)2.334C^{1.522}$	$S^2_{sp} = (50/nss)0.0306C^{0.632}$
Analytical <sup>e</sup>	$S^2_a = (1/na)0.0484C^{2.0}$	$S^2_a = (1/na)0.0484C^{2.0}$	$S^2_a = (1/na)0.0484C^{2.0}$	experimental $S^2_a = (1/n)0.0164C^{1.117}$ or FAPAS $S^2_a = (1/n)0.0484C^{2.0}$
Total variance	$S^2_s + S^2_{sp} + S^2_a$	$S^2_s + S^2_{sp} + S^2_a$	$S^2_s + S^2_{sp} + S^2_a$	$S^2_s + S^2_{sp} + S^2_a$

a/ Variance =  $S^2$  (s, sp, and a denote sampling, sample preparation, and analytical steps, respectively, of aflatoxin test procedure)

b/ ns = laboratory sample size in number of shelled nuts, nss = test portion size in grams, na = number of aliquots quantified by HPLC, and C = aflatoxin concentration in ng/g total aflatoxin.

c/ Shelled nut count/kg for almonds, hazelnuts, pistachios and Brazil nuts is 773, 1 000, and 1 600, respectively.

d/ Sample preparation for almonds, hazelnuts, and pistachios reflect Hobart, Robot Coupe, and Marjaan Khatman type mills, respectively. Laboratory samples were dry ground into a paste for each treenut except for Brazil nut that were prepared as a slurry Brazil nuts/water 1/1 w/w.

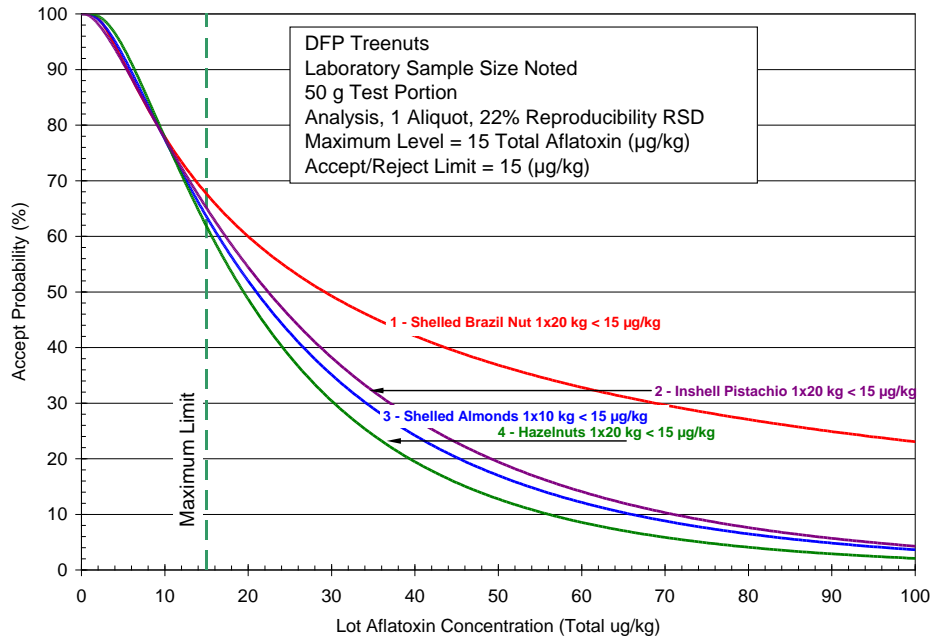
e/ Analytical variances reflect FAPAS recommendation for upper limit of analytical reproducibility uncertainty. A relative standard deviation of 22% is considered by Thompson<sup>2</sup> (based upon FAPAS data) as an appropriate measure of the best agreement that can be obtained between laboratories. An analytical uncertainty of 22% is larger than the within laboratory uncertainty measured in the sampling studies for the three treenuts<sup>3</sup>.

**Annex II**

**Operating Characteristic Curves describing the performance of draft aflatoxin sampling plans for almonds, hazelnuts, pistachios and shelled Brazil nuts.**

**Treenuts Destined for Further Processing**

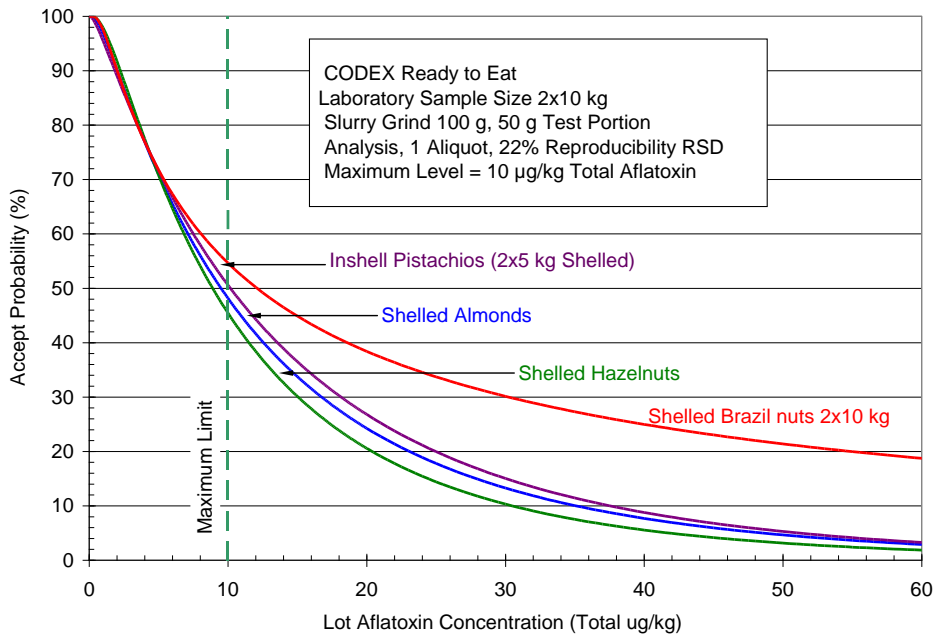
Operating Characteristic curve describing the performance of the aflatoxin sampling plan for almonds, hazelnuts, pistachios and shelled Brazil nuts destined for further processing using a single laboratory sample of 20 kg and a maximum level of 15 ng/g for total aflatoxins. The operating characteristic curve reflects uncertainty associated with a 20 kg laboratory sample of shelled nuts for almonds hazelnuts and shelled Brazil nuts and a 20 kg laboratory sample of inshell nuts (about 10kg shelled nuts) for pistachios, dry grind with a vertical cutter mixer type mill almonds, hazelnuts, pistachio and slurry preparation for shelled Brazil nuts, 50 g test portion, and quantification of aflatoxin in the test portion by HPLC.



**Ready-to-Eats Treenuts**

Operating Characteristic curve describing the performance of the aflatoxin sampling plan for ready-to-eat almonds, hazelnuts, pistachios and shelled Brazil nuts using two laboratory samples of 10 kg each and a maximum level of 10 ng/g for total aflatoxins, dry grind with a vertical cutter mixer type mill almond, hazelnuts, pistachios and slurry preparation for shelled Brazil nuts, 50 g test portion, and quantification of aflatoxin in the test portion by HPLC.

**Mycotoxins**  
**Aflatoxins, Total**



**SAMPLING PLAN FOR AFLATOXIN CONTAMINATION IN DRIED FIGS**

**DEFINITION**

<b>Lot</b>	An identifiable quantity of a food commodity delivered at one time and determined by the official to have common characteristics, such as origin, variety, type of packing, packer, consignor, or markings.
<b>Sublot</b>	Designated part of a larger lot in order to apply the sampling method on that designated part. Each sublot must be physically separate and identifiable.
<b>Sampling plan</b>	It is defined by an aflatoxin test procedure and an accept/reject level. An aflatoxin test procedure consists of three steps: sample selection of sample(s) of a given size, sample preparation and aflatoxin quantification. The accept/reject level is a tolerance usually equal to the Codex maximum level.
<b>Incremental sample</b>	The quantity of material taken from a single random place in the lot or sublot.
<b>Aggregate sample</b>	The combined total of all the incremental samples that is taken from the lot or sublot. The aggregate sample has to be at least as large as the laboratory sample or samples combined.
<b>Laboratory sample</b>	The smallest quantity of dried figs comminuted in a mill. The laboratory sample may be a portion of or the entire aggregate sample. If the aggregate sample is larger than the laboratory sample(s), the laboratory sample(s) should be removed in a random manner from the aggregate sample.
<b>Test portion</b>	A portion of the comminuted laboratory sample. The entire laboratory sample should be comminuted in a mill. A portion of the comminuted laboratory sample is randomly removed for the extraction of the aflatoxin for chemical analysis.
<b>Ready-to-eat dried figs</b>	Dried figs, which are not intended to undergo an additional processing/treatment that have proven to reduce levels of aflatoxin before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption.
<b>Operating characteristic (OC) curve</b>	A plot of the probability of accepting a lot versus lot concentration when using a specific sampling plan design. The OC curve also provides an estimate of good lots rejected (exporter's risk) and bad lots accepted (importer's risk) by a specific aflatoxin sampling plan design.

**SAMPLING PLAN DESIGN CONSIDERATIONS**

1. Importers commercially classify dried figs mostly as "ready-to-eat" (RTE). As a result, maximum levels and sampling plans are proposed for only ready-to-eat dried figs.
2. The performance of the proposed draft sampling plan was computed using the variability and aflatoxin distribution among laboratory samples of dried figs taken from contaminated lots. Because the dried fig count per kg is different for different varieties of dried figs, the laboratory sample size is expressed in number of dried figs for statistical purposes. However, the dried fig count per kg for each variety of dried figs can be used to convert laboratory sample size from number of dried figs to mass and vice versa.
3. Uncertainty estimates (variances) associated with sampling, sample preparation, and analysis and the negative binomial distribution<sup>1</sup> are used to calculate operating characteristic (OC) curves that describe the performance of the proposed aflatoxin-sampling plans for dried figs.
4. The analytical variance measured in the sampling study reflects within laboratory variance and was replaced with an estimate of analytical variance that reflects a reproducibility relative standard deviation of 22%, which is suggested by Thompson and is based upon Food Analysis Performance Assessment Scheme (FAPAS) data<sup>2</sup>. A relative standard deviation of 22% is considered by FAPAS as an appropriate measure of the best agreement that can be reliably obtained between laboratories. An analytical uncertainty of 22% is larger than the within laboratory variation measured in the sampling studies for dried figs.
5. The issue of correcting the analytical test result for recovery is not addressed in this document. However, Table 2 specifies several performance criteria for analytical methods including suggestions for the range of acceptable recovery rates.

**Mycotoxins****Aflatoxins, Total****AFLATOXIN TEST PROCEDURE AND MAXIMUM LEVELS**

6. An aflatoxin-sampling plan is defined by an aflatoxin test procedure and a maximum level. A value for the proposed maximum level and the aflatoxin test procedure are given below in this section.
7. The maximum level for "ready-to-eat" dried figs is 10 µg/kg total aflatoxins.
8. Choice of the number and size of the laboratory sample is a compromise between minimizing risks (false positives and false negatives) and costs related to sampling and restricting trade. For simplicity, it is recommended that the proposed aflatoxin sampling plan uses three 10 kg aggregate samples of dried figs.
9. The RTE sampling plan has been designed for enforcement and controls concerning total aflatoxins in bulk consignments (lots) of dried figs traded in the export market.
 

Maximum level	– 10 µg/kg total aflatoxins
Number of laboratory samples	– 3
Laboratory sample size	– 10 kg
Sample preparation	– water-slurry grind and a test portion that represents 55 g mass of dried figs
Analytical method	– performance based (see Table 2)
Decision rule	– If the aflatoxin test result is less than or equal to 10 µg/kg total aflatoxins for all three 10 kg laboratory samples, then accept the lot. Otherwise, reject the lot.

The operating characteristic curve describing the performance of the sampling plan for the ready-to-eat dried figs is shown in paragraph 46 at the end of this Annex.

10. To assist member countries implement the above Codex sampling plan, sample selection methods, sample preparation methods, and analytical methods required to quantify aflatoxin in laboratory samples taken from bulk dried fig lots are described in the following sections.

**SAMPLE SELECTION****MATERIAL TO BE SAMPLED**

11. Each lot, which is to be examined for aflatoxin, must be sampled separately. Lots larger than 15 tonnes should be subdivided into sublots to be sampled separately. If a lot is greater than 15 tonnes, the number of sublots is equal to the lot weight in tonnes divided by 15 tonnes. It is recommended that a lot or a subplot should not exceed 15 tonnes.
12. Taking into account that the weight of the lot is not always an exact multiple of 15 tonnes, the weight of the subplot may exceed the mentioned weight by a maximum of 25%.
13. Samples should be taken from the same lot, i.e. they should have the same batch code or at the very least the same best before date. Any changes which would affect the mycotoxin content, the analytical determination or make the aggregate samples collected unrepresentative should be avoided. For example do not open packaging in adverse weather conditions or expose samples to excessive moisture or sunlight. Avoid cross-contamination from other potentially contaminated consignments nearby.
14. In most cases any truck or container will have to be unloaded to allow representative sampling to be carried out.

**INCREMENTAL SAMPLE SELECTION**

15. Procedures used to take incremental samples from a dried fig lot are extremely important. Every individual fig in the lot should have an equal chance of being chosen. Biases will be introduced by sample selection methods if equipment and procedures used to select the incremental samples prohibit or reduce the chances of any item in the lot from being chosen.
16. Since there is no way to know if the contaminated figs are uniformly dispersed throughout the lot, it is essential that the aggregate sample be the accumulation of many small incremental samples of product selected from different locations throughout the lot. If the aggregate sample is larger than desired, it should be blended and subdivided until the desired laboratory sample size is achieved.
17. For lots less than 10 tonnes, the size of the aggregate sample is reduced so that the aggregate sample size doesn't exceed a significant portion of the lot or subplot size.

**NUMBER AND SIZE OF INCREMENTAL SAMPLES FOR LOTS OF VARYING WEIGHT**

18. The number of incremental samples to be taken from a lot (subplot) depends on the weight of the lot. Table 1 shall be used to determine the number of incremental samples to be taken from lots or sublots of various sizes. The number of incremental samples varies from 10 to 100 for lots or sublots of various sizes.



**Mycotoxins****Aflatoxins, Total****Table 1. Number and size of incremental samples composited for an aggregate sample of 30kg<sup>a</sup> as a function of lot (or subplot) weight**

Lot or Sublot Weight <sup>b</sup> (T in Tonnes)	Minimum Number of Incremental Samples	Minimum Incremental Sample Size <sup>c</sup> (g)	Minimum Aggregate Sample Size (kg)	Laboratory Sample Size (kg)	Number of Laboratory Samples
15.0 ≥ T > 10.0	100	300	30	10	3
10.0 ≥ T > 5.0	80	300	24	8	3
5.0 ≥ T > 2.0	60	300	18	9	2
2.0 ≥ T > 1.0	40	300	12	6	2
1.0 ≥ T > 0.5	30	300	9	9	1
0.5 ≥ T > 0.2	20	300	6	6	1
0.2 ≥ T > 0.1	15	300	4.5	4.5	1
0.1 ≥ T	10	300	3	3	1

a/ Minimum aggregate sample size = laboratory sample size of 30 kg for lots above 10 tonnes

b/ 1 Tonne = 1000 kg

c/ Minimum incremental sample size = laboratory sample size (30 kg)/minimum number of incremental samples, i.e. for 10 < T ≤ 15 tonne, 300 g = 30000 g/100

19. The suggested minimum weight of the incremental sample is 300 grams for lots and sublots of various sizes.

**STATIC LOTS**

20. A static lot can be defined as a large mass of dried figs contained either in a large single container such as a wagon, truck or railcar or in many small containers such as sacks or boxes and the dried figs are stationary at the time a sample is selected. Selecting a truly random sample from a static lot can be difficult because all containers in the lot or subplot may not be accessible.
21. Taking incremental samples from a static lot usually requires the use of probing devices to select product from the lot. The probing devices should be specifically designed for the commodity and type of container. The probe should (1) be long enough to reach all products, (2) not restrict any item in the lot from being selected, and (3) not alter the items in the lot. As mentioned above, the aggregate sample should be a composite from many small incremental samples of product taken from many different locations throughout the lot.
22. For lots traded in individual packages, the sampling frequency (SF), or number of packages that incremental samples are taken from, is a function of the lot weight (LT), incremental sample weight (IS), aggregate sample weight (AS) and the individual packing weight (IP), as follows:  
Equation 1:  $SF = (LT \times IS) / (AS \times IP)$ .
23. The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.

**DYNAMIC LOTS**

24. Representative aggregate samples can be more easily produced when selecting incremental samples from a moving stream of dried figs as the lot is transferred from one location to another. When sampling from a moving stream, take small incremental samples of product from the entire length of the moving stream; composite the incremental samples to obtain an aggregate sample; if the aggregate sample is larger than the required laboratory sample(s), then blend and subdivide the aggregate sample to obtain the desired size laboratory sample(s).
25. Automatic sampling equipment such as a cross-cut sampler is commercially available with timers that automatically pass a diverter cup through the moving stream at predetermined and uniform intervals. When automatic sampling equipment is not available, a person can be assigned to manually pass a cup through the stream at periodic intervals to collect incremental samples. Whether using automatic or manual methods, incremental samples should be collected and composited at frequent and uniform intervals throughout the entire time the figs flow past the sampling point.
26. Cross-cut samplers should be installed in the following manner: (1) the plane of the opening of the diverter cup should be perpendicular to the direction of the flow; (2) the diverter cup should pass through the entire cross sectional area of the stream; and (3) the opening of the diverter cup should be wide enough to accept all items of interest in the lot. As a general rule, the width of the diverter cup opening should be about two to three times the largest dimensions of items in the lot.
27. The size of the aggregate sample (S) in kg, taken from a lot by a cross cut sampler is:  
Equation 2:  $S = (D \times LT) / (T \times V)$ ,

**Mycotoxins****Aflatoxins, Total**

where D is the width of the diverter cup opening (cm), LT is the lot size (kg), T is interval or time between cup movement through the stream (seconds), and V is cup velocity (cm/sec).

28. If the mass flow rate of the moving stream, MR (kg/sec), is known, then the sampling frequency (SF), or number of cuts made by the automatic sampler cup can be computed from Equation 3 as a function of S, V, D, and MR.  
Equation 3:  $SF = (S \times V) / (D \times MR)$ .
29. Equations 2 and 3 can also be used to compute other terms of interest such as the time between cuts (T). For example, the time (T) required between cuts of the diverter cup to obtain a 30 kg aggregate sample from a 20 000 kg lot where the diverter cup width is 5.0 cm and the cup velocity through the stream 20 cm/sec. Solving for T in Equation 2,  $T = (5.0 \text{ cm} \times 20 \text{ 000 kg}) / (30 \text{ kg} \times 20 \text{ cm/sec}) = 167 \text{ sec}$ .
30. If the lot is moving at 500 kg per minute, the entire lot will pass through the sampler in 40 minutes (2 400 sec) and only 14.4 cuts (14 incremental samples) will be made by the cup through the lot (Equation 3). This may be considered too infrequent, in that too much product (1 388.9 kg) passes through the sampler between the time the cup cuts through the stream.

**PACKAGING AND TRANSPORTATION OF SAMPLES**

31. Each laboratory sample shall be placed in a clean, inert container offering adequate protection from contamination, sunlight, and against damage in transit. All necessary precautions shall be taken to avoid any change in composition of the laboratory sample, which might arise during transportation or storage. Samples should be stored in a cool dark place.

**SEALING AND LABELLING OF SAMPLES**

32. Each laboratory sample taken for official use shall be sealed at the place of sampling and identified. A record must be kept of each sampling, permitting each lot to be identified unambiguously and giving the date and place of sampling together with any additional information likely to be of assistance to the analyst.

**SAMPLE PREPARATION****PRECAUTIONS**

33. Sunlight should be excluded as much as possible during sample preparation, since aflatoxin gradually breaks down under the influence of ultra-violet light. Also, environmental temperature and relative humidity should be controlled and not favor mold growth and aflatoxin formation.

**HOMOGENIZATION – GRINDING**

34. As the distribution of aflatoxin is extremely non-homogeneous, the laboratory samples should be homogenized by grinding the entire laboratory sample received by the laboratory. Homogenization is a procedure that reduces particle size and disperses the contaminated particles evenly throughout the comminuted laboratory sample.
35. The laboratory sample should be finely ground and mixed thoroughly using a process that approaches as complete homogenization as possible. Complete homogenization implies that particle size is extremely small and the variability associated with sample preparation approaches zero. After grinding, the grinder should be cleaned to prevent aflatoxin cross-contamination.
36. The use of vertical cutter mixer type grinders that mix and comminute the laboratory sample into a paste represent a compromise in terms of cost and fineness of grind or particle size reduction<sup>4</sup>. A better homogenization (finer grind), such as a liquid slurry, can be obtained by more sophisticated equipment and should provide the lowest sample preparation variance<sup>5</sup>.

**TEST PORTION**

37. The suggested weight of the test portion taken from the comminuted laboratory sample should be approximately 50 grams. If the laboratory sample is prepared using a liquid slurry, the slurry should contain 50 g of fig mass.
38. Procedures for selecting the 50 g test portion from the comminuted laboratory sample should be a random process. If mixing occurred during or after the comminution process, the 50 g test portion can be selected from any location throughout the comminuted laboratory sample. Otherwise, the 50 g test portion should be the accumulation of several small portions selected throughout the laboratory sample.
39. It is suggested that three test portions be selected from each comminuted laboratory sample. The three test portions will be used for enforcement, appeal, and confirmation if needed.

**ANALYTICAL METHODS****BACKGROUND**

40. A criteria-based approach, whereby a set of performance criteria is established with which the analytical method used should comply, is appropriate. The criteria-based approach has the advantage that, by avoiding setting down specific details of the method used, developments in methodology can be exploited without having to reconsider or modify the specific analytical method. The performance criteria established for analytical methods should include all the parameters that need to be addressed by each laboratory such as the detection limit, repeatability coefficient of

**Mycotoxins****Aflatoxins, Total**

variation (within lab), reproducibility coefficient of variation (among lab), and the percent recovery necessary for various statutory limits. Analytical methods that are accepted by chemists internationally (such as AOAC) may be used. These methods are regularly monitored and improved depending upon technology.

**PERFORMANCE CRITERIA FOR METHODS OF ANALYSIS**

41. A list of criteria and performance levels are shown in Table 2. Utilizing this approach, laboratories would be free to use the analytical method most appropriate for their facilities.

**Table 2: Specific Requirements with which Methods of Analysis Should Comply**

Criterion	Concentration Range (ng/g)	Recommended Value	Maximum Permitted Value
Blanks	All	Negligible	n/a
Recovery	1 to 15	70 to 110%	n/a
	> 15	80 to 110%	n/a
Precision or Relative Standard Deviation RSD <sub>R</sub> (Reproducibility)	1 to 120	Equation 4 by Thompson	2 x value derived from Equation 4
	> 120	Equation 5 by Horwitz	2 x value derived from Equation 5
Precision or Relative Standard Deviation RSD <sub>r</sub> (Repeatability)	1 to 120	Calculated as 0.66 times Precision RSD <sub>R</sub>	n/a
	> 120	Calculated as 0.66 times Precision RSD <sub>r</sub>	n/a

n/a = not applicable

42. The detection limits of the methods used are not stated. Only the precision values are given at the concentrations of interest. The precision values (expressed as a %) are calculated from equations 4 and 5 developed by Thompson and Horwitz and Albert, respectively.

Equation 4:  $RSD_R = 22.0$

Equation 5:  $RSD_R = 45.25C^{-0.15}$

where:

- $RSD_R$  = the relative standard deviation calculated from results generated under reproducibility conditions
- $RSD_r$  = the relative standard deviation calculated from results generated under repeatability conditions  
=  $0.66RSD_R$
- $C$  = aflatoxin concentration or mass of aflatoxin to mass of dried figs (i.e. ng/g)

43. Equations 4 and 5 are generalized precision equations, which have been found to be independent of analyte and matrix but solely dependent on concentration for most routine methods of analysis.
44. Results should be reported on the sample.

**UNCERTAINTY, AS MEASURED BY THE VARIANCE, ASSOCIATED WITH THE SAMPLING, SAMPLE PREPARATION, AND ANALYTICAL STEPS OF THE AFLATOXIN TEST PROCEDURE USED TO DETECT AFLATOXIN IN DRIED FIGS**

45. The sampling, sample preparation, and analytical variances associated with the aflatoxin test procedure for dried figs are shown in Table 3.

**Table 3. Variances<sup>a</sup> associated with the aflatoxin test procedure for each dried figs**

Test Procedure	Variances for Dried Figs
Sampling <sup>b,c</sup>	$S^2_s = (590/ns)2.219C^{1.433}$
Sample Prep <sup>d</sup>	$S^2_{sp} = (55/nss)0.01170C^{1.465}$
Analytical <sup>e</sup>	$S^2_a = (1/na)0.0484C^{2.0}$
Total	$S^2_t = S^2_s + S^2_{sp} + S^2_a$

a / Variance =  $S^2$  (t, s, sp, and a denote total, sampling, sample preparation, and analytical steps, respectively, of aflatoxin test procedure)

b / ns = laboratory sample size in number of dried figs, nss = test portion size in grams of fig mass, na = number of aliquots quantified by HPLC, and C = aflatoxin concentration in ng/g total aflatoxins.

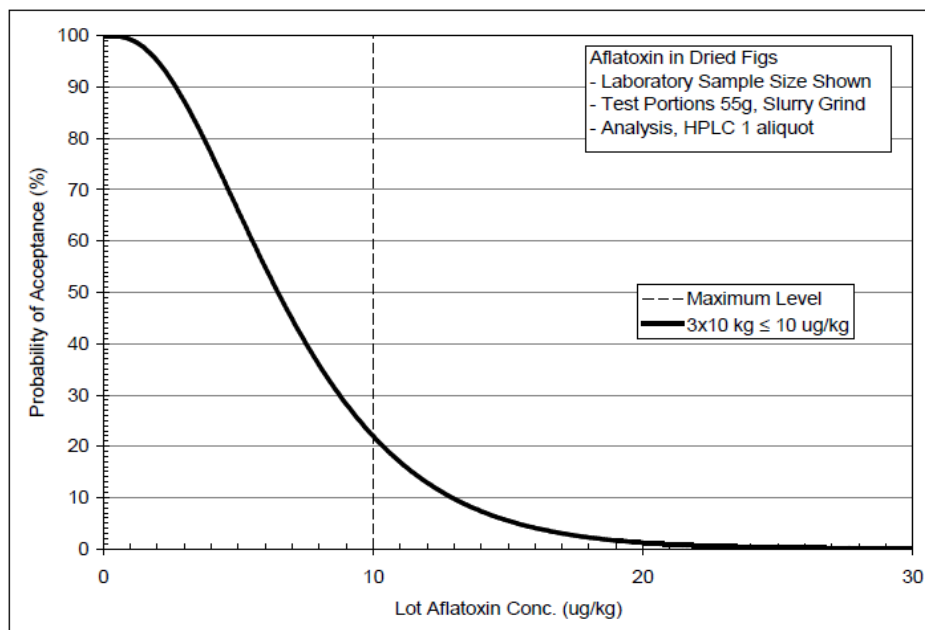
c / Count/kg for dried figs averaged 59/kg.

**Mycotoxins****Aflatoxins, Total**

- d / Sample preparation variance reflects a water-slurry method and a test portion that reflects 55 g fig mass.
- e / Analytical variances reflect FAPAS recommendation for upper limit of analytical reproducibility uncertainty. A relative standard deviation of 22% is considered by Thompson<sup>2</sup> (based upon FAPAS data) as an appropriate measure of the best agreement that can be obtained between laboratories. An analytical uncertainty of 22% is larger than the within laboratory uncertainty measured in the sampling studies for the three dried figs.

**OPERATING CHARACTERISTIC CURVE DESCRIBING THE PERFORMANCE OF THE DRAFT AFLATOXIN SAMPLING PLAN FOR READY-TO-EAT DRIED FIGS**

46. The operating characteristic curve describing the performance of draft aflatoxin sampling plan for ready-to-eat dried figs is shown in Figure 1.



**Figure 1.** Operating characteristic (OC) curve describing the performance of the aflatoxin sampling plan for ready-to-eat dried figs using three laboratory samples of 10 kg each and a maximum level of 10  $\mu\text{g}/\text{kg}$  total aflatoxins, water-slurry comminution method, test portion that reflects 55 g fig mass, and quantification of aflatoxin in the test portion by HPLC.

**Mycotoxins**

**Aflatoxins M<sub>1</sub>**

Reference to JECFA: 56 (2001), 83 (2016)  
 Toxicological guidance value: Cancer potency estimates at specified residue levels (2001, Using worst-case assumptions, the additional risks for liver cancer predicted with use of proposed maximum levels of aflatoxin M<sub>1</sub> of 0.05 and 0.5 µg/kg are very small. The potency of aflatoxin M<sub>1</sub> appears to be so low in HBsAg- individuals that a carcinogenic effect of M<sub>1</sub> intake in those who consume large quantities of milk and milk products in comparison with non-consumers of these products would be impossible to demonstrate. Hepatitis B virus carriers might benefit from a reduction in the aflatoxin concentration in their diet, and the reduction might also offer some protection in hepatitis C virus carriers.)  
 Contaminant definition: Aflatoxin M<sub>1</sub>  
 Synonyms: Abbreviation: AFM<sub>1</sub>  
 Related Code of Practice: Code of Practice for the Reduction of Aflatoxin B<sub>1</sub> in Raw Materials and Supplemental Feedingstuffs for Milk Producing Animals (CXC 45-1997)

Commodity / Product Name	Maximum Level(ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Milks	0.5	Adopted	2001	FAC	Whole commodity	Milk is the normal mammary secretion of milking animals obtained from one or more milkings without either addition to it or extraction from it, intended for consumption as liquid milk or for further processing. A concentration factor applies to partially or wholly Dehydrated milks.	ML0106

CCFAC24 (1993) decided to stop the development of a specific standard for AFM<sub>1</sub> in milk destined for use in baby foods. CCFAC has discussed 2 options for a standard for AFM<sub>1</sub> in milk: 0.05 µg/kg and 0.5 µg/kg.

At the request of CCFAC32 (2000), JECFA56 (2001) examined exposure to AFM<sub>1</sub> and conducted a quantitative risk assessment to compare the consequences of setting the ML in milk at 0.05 µg/kg and 0.5 µg/kg. The estimates of the potency of AFM<sub>1</sub> were combined with estimates of intake from the GEMS/Food European regional diet. The Committee noted that the calculation showed that, with worst case assumptions, the projected risks for liver cancer at the proposed maximum levels of AFM<sub>1</sub> of 0.05 and 0.5 µg/kg are very small. As a result, 0.5 µg/kg was forwarded to CAC24 by CCFAC33 (2001) which adopted this draft ML at Step 8, noting that data supporting the lower level, if and when available, could be examined by CCFAC at a future meeting when necessary. It is acknowledged that the AFM<sub>1</sub> level in milk is related to the AFB<sub>1</sub> level in the animal feed. See notes under Aflatoxins, total.

JECFA83 (2016) noted that given the relative cancer potencies and international dietary exposure estimates for AFB<sub>1</sub> and AFM<sub>1</sub>, AFM<sub>1</sub> will generally make a negligible (<1%) contribution to aflatoxin-induced cancer risk for the general population. (JECFA/83/SC)

Aflatoxin M<sub>1</sub> is the hydroxylated metabolite of aflatoxin B<sub>1</sub> that can occur in milk and milk products from animals consuming contaminated feed. The metabolite is also present in the milk of nursing women who eat foods containing the toxin. Like its parent compound aflatoxin B<sub>1</sub>, aflatoxin M<sub>1</sub> is a carcinogen, but less potent. Aflatoxin M<sub>1</sub> shows 2-10% of the carcinogenic activity of aflatoxin B<sub>1</sub>. In studies of genotoxicity, such as in *Drosophila melanogaster*, aflatoxin M<sub>1</sub> was about 10-fold less mutagenic than aflatoxin B<sub>1</sub>. Epidemiological studies tend to indicate that individuals who are carriers of persistent viral infection with HBV and who are exposed to aflatoxin in their diets are at increased risk for progression to liver cancer as compared with HBV carriers who are not exposed to aflatoxins, but for aflatoxin M<sub>1</sub> this could not be quantified in a dose-response relationship.

Aflatoxin M<sub>1</sub> is cytotoxic, as is aflatoxin B<sub>1</sub>, as shown in human hepatocytes. The short-term toxicity of aflatoxin M<sub>1</sub> is similar to that of aflatoxin B<sub>1</sub>, and it appears to act by the same

***Mycotoxins***

**Aflatoxins M<sub>1</sub>**

mechanism. Aflatoxins may potentiate liver damage caused by bacterial lipopolysaccharide, which may affect acute toxicity in humans and domestic animals. This potentiation of liver damage by aflatoxins may also play a role in the interaction between hepatitis viruses and liver carcinogenesis. (WHO, FAO, Safety evaluation of certain mycotoxins in food, 2001).

**Mycotoxins****Deoxynivalenol**

Reference to JECFA:	56 (2001), 72 (2010)
Toxicological guidance value:	Group PMTDI 0.001 mg/kg bw (2010, for DON and its acetylated derivatives) Group ARfD 0.008 mg/kg bw (2010, for DON and its acetylated derivatives)
Contaminant definition:	Deoxynivalenol
Synonyms:	Vomitoxin; Abbreviation: DON
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Cereal grains (wheat, maize and barley) destined for further processing	2	Adopted	2015	CF		“Destined for further processing” means intended to undergo an additional processing/treatment that has proven to reduce levels of DON before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption. Codex members may define the processes that have been shown to reduce levels. <i>For sampling plan, see Annex.</i>	
Flour, meal, semolina and flakes derived from wheat, maize or barley	1	Adopted	2015	CF		<i>For sampling plan, see Annex.</i>	
Cereal-based foods for infants and young children	0.2	Adopted	2015	CF	ML applies to the commodity on a dry matter basis.	All cereal-based foods intended for infants (up to 12 months) and young children (12 to 36 months). <i>For sampling plan, see Annex.</i>	

The PMTDI is based on a chronic dietary study with mice, applying a safety factor of 100. An intake at the level of the PMTDI is not expected to result in effects of DON on the immune system, growth or reproduction, which are the most critical effects. JECFA in 2001 recommended that toxic equivalency factors relative to DON be developed for the other trichothecenes commonly occurring in cereal grains, if sufficient data become available. The JECFA estimated that the PMTDI for DON could be exceeded in 4 out of 5 GEMS/Food regional diets.

The situation regarding deoxynivalenol has been reviewed in a discussion paper (last version CX/FAC 03/35); CCFAC35 (2003) discontinued the consideration of this discussion paper and agreed to commence work on the elaboration of MLs for DON (ALINORM 03/12A, paras. 180-182).

CAC26 (2003) approved the development of maximum levels for DON as new work (ALINORM 03/41, Appendix VIII).

CCFAC36 (2004) agreed to discontinue the consideration of maximum levels for deoxynivalenol for the time being. Instead, it agreed to request information on: the occurrence of deoxynivalenol in cereals; the influence of processing, decontamination, sorting, etc. to lower the level of DON in a lot; national levels or guideline levels for DON; sampling procedures and methods of analysis; etc. for consideration by CCFAC37 (ALINORM 04/27/12, paras. 156-158).

CCFAC37 (2005) noted that many data on the occurrence of DON in cereals and processed cereal products were already available or would soon be made available on a more global basis. The Committee therefore decided to ask JECFA to conduct an exposure assessment based on the new data. In this regard, the Committee reconfirmed the importance to take

**Mycotoxins****Deoxynivalenol**

into account processed foods and the effects of processing on the level of DON. The Committee decided to establish an electronic Working Group to develop a discussion paper to provide comprehensive relevant data, including the occurrence of deoxynivalenol and the effects of processing on the levels of DON, for consideration at the 38th session (ALINORM 05/28/12, paras. 148-150).

CCFAC38 (2006) agreed to endorse the recommendation of the ad hoc Working Group on Contaminants and Toxins in Foods to update the Discussion Paper on DON with: more data from regions where data on DON levels are missing or inadequate; additional data, especially on DON levels in maize; information on the effect on levels of seasonal variation; and information on the effect of processing on DON levels in foods (ALINORM 06/29/12, paras. 137-138). The Committee also endorsed the recommendations of the Working Group on the Priority List of substances for evaluation by JECFA to maintain the request for evaluation of DON in the Priority List and to add a question regarding the potential toxicity of 3-acetyl and 15-acetyl deoxynivalenol to the existing request (ALINORM 06/29/12, paras. 205-206).

CCCF1 (2007) agreed, in view of the need for more occurrence data, including regional data on incidence and levels of DON in cereals over a period of several years, and for adequate information on consumption patterns for various countries as a pre-requisite to developing international standards, to discontinue consideration of this item for the time being and to encourage countries to submit data on DON contamination to GEMS/Food Databases electronically and in the prescribed format (ALINORM 07/30/41, para. 108). The Committee noted that sufficient data on DON occurrence in food and fate at processing would not be available before the end of 2008 and that no information was provided on the availability of toxicological data. It agreed that DON remain on the priority list (ALINORM 07/30/41, para. 126).

CCCF2 (2008) agreed to maintain the high priority for DON in evaluation by JECFA and noted that occurrence data from ongoing surveys would be made available by the end of 2008 and that some data had already been submitted to the GEMS/Food data base (ALINORM 08/31/41, paras. 173 and 174).

JECFA72 (2010) decided to convert the PMTDI for DON to a group PTMDI of 1 µg/kg bw for DON and its acetylated derivatives (3-Ac-DON and 15-Ac-DON), as 3-acetyl-deoxynivalenol (3-Ac-DON) is converted to DON *in vivo* and therefore contributes to the total DON-induced toxicity. In this regard, the Committee considered the toxicity of the acetylated derivatives equal to that of DON. The Committee concluded that, at this time, there was insufficient information to include DON-3- glucoside in the group PMTDI.

The Committee derived a group acute reference dose (ARfD) of 8 µg/kg bw for DON and its acetylated derivatives, using the lowest lower limit on the benchmark dose for a 10% response (BMDL<sub>10</sub>) of 0.21 mg/kg bw per day for emesis in pigs dosed with DON via the diet and application of an uncertainty factor of 25. Limited data from human case reports indicated that dietary exposures to DON up to 50 µg/kg bw per day are not likely to induce emesis.

The Committee concluded that all of the mean estimates of national exposure to DON were below the group PMTDI of 1 µg/kg-bw. Estimation of dietary exposure was made using data from 42 countries, representing 10 of the 13 GEMS/Food consumption cluster diets, and was therefore considered to be more globally representative than the previous evaluation. National reports showed dietary exposures that were above 1 µg/kg-bw per day in only a few cases, only for children at upper percentiles. For acute dietary exposure, the estimate of 9 µg/kg-bw per day, based on high consumption of bread and a regulatory limit for DON of 1 mg/kg food, was close to the group ARfD. The acetylated derivatives have not been included in the estimates of dietary exposure to DON but the Committee noted that, in general, they are found at levels less than 10% of those for DON, and inclusion would not be expected to significantly change the estimates of dietary exposure to DON. DON-3-glucoside was also not included in the dietary exposure estimates.

The Committee noted that data were limited on the occurrence of DON-3-glucoside, which might be an important contributor to dietary exposure.

During CCCF5 (2011) it was proposed that the Committee proceed with MLs, but that the Committee first focus on MLs for DON together with associated sampling plans before proceeding with MLs for its acetylated derivatives due to the lack of complete data and availability of analytical methods (REP11/CF, para. 38). The Committee agreed to return the proposed draft Maximum Levels for DON to Step 2/3 for further development the EWG led by Canada, circulation for comments and further consideration by the 6th session of the Committee (REP11/CF, para. 43), and that it would at the 8th Session of the Committee consider the extension of the ML to acetylated derivatives of DON (REP11/CF, para. 41).

CCCF6 (2012) agreed to return the proposed draft MLs for DON to Step 2/3 for further development by the electronic Working Group, circulation for comments and further consideration by the 7th session of the Committee (REP12/CF, para. 77).

CCCF7 (2013) agreed to the ML of 2 mg/kg for raw cereals (maize, wheat and barley) prior to sorting and removal of damaged kernels with the associated sampling plan with sample size of 5 kg for maize and 1 kg for wheat and barley. For flour, semolina, meal and flakes derived from wheat, maize or barley, the Committee agreed to establish a ML of 1 mg/kg. For cereal-based foods for infants and young children, the Committee agreed to establish the ML of 0.2 mg/kg and that this ML would apply to cereal-based foods as consumed. The Committee agreed to forward the proposed draft MLs for raw cereal grains including sampling plans, and for flour, semolina, meal and flakes from wheat, maize or barley to Step 5



**Mycotoxins****Deoxynivalenol**

and the proposed draft ML for cereal-based foods for infants and young children to Step 5/8 for adoption by CAC36 (REP13/CF, para. 64-66, 70 and APPENDIX III).

With regard to MLs for bran products, the Committee agreed to encourage members to collect and submit occurrence data for DON in wheat and corn brans for possible future work. (REP13/CF, para. 67)

The Committee recalled its earlier decision taken at the 5th Session of the Committee that it would consider the extension of the MLs for DON to its acetylated derivatives at the 8th Session of the Committee and agreed that an EWG led by Canada and Japan would prepare a discussion paper and proposals for the extension of MLs for DON to its acetylated derivatives for consideration at the 8th session of the Committee (REP13/CF, para. 68).

CAC36 noted that clarification was needed on whether the ML should apply to cereal-based foods for infants and young children “as consumed” or to the “dry matter” and therefore agreed to adopt the proposed draft ML at Step 5 for further consideration in CCCF. The Commission also adopted the draft maximum levels for DON in raw cereal grains (maize, wheat and barley) and associated sampling plan and in flour, semolina, meal and flakes from wheat, maize or barley at Step 5 (REP13/CAC, para. 80, APPENDIX IV).

CCCF8 (2014) noted that it was not possible to reach agreement on the MLs for raw cereal grains (wheat, maize and barley); flour, meal, semolina and flakes derived from wheat, maize or barley, nor for the ML for cereal-based foods for infants and young children and agreed to hold the MLs and associated sampling plans at Step 7 for consideration at the 9th session of the Committee in light of a discussion paper on additional ways of developing MLs, such as phasing in of lower MLs over a defined period of time, to be developed by FAO, WHO and the Codex Secretariat. The Committee agreed that the ML for cereal-based foods for infants and young children should be set on a “dry matter basis”. (REP14/CF, paras. 57-59, Appendix XII).

The Committee, noting the decision taken on MLs for DON and the conclusions of the EWG, agreed that it was premature to continue with work on the extension of the MLs for DON in cereals and cereal products to its acetylated derivatives. The Committee encouraged members to continue collecting and submitting data on occurrence of acetylated DON to GEMS/Food and noted the need for development of an internationally validated method for analysis of acetylated DON. The Committee agreed that no further consideration would be given to acetylated derivatives of DON as a separate item, but that when further information became available, it could be considered as part of the discussion on the MLs for DON in cereals and cereal-based products (REP14/CF, paras. 61-62).

CCCF9 (2015) discussed the note for cereal grains to which the ML applies and agreed to refer to cereal grains “destined for further processing” and to qualify that it meant that additional processing or treatments proven to reduce levels of DON could be applied and that Codex members could define the processes that have been shown to reduce levels. The Committee agreed that the MLs, 2 mg/kg for cereal grains (wheat, maize and barley) for further processing, 1 mg/kg for flour, meal, semolina and flakes derived from wheat, maize or barley, and 0.2 mg/kg on dry matter basis for cereal-based foods for infants and young children, respectively, and agreed to advance the MLs and the associated sampling plans to CAC for adoption at Step 8. The sampling plans and performance criteria for methods of analysis (aligned with fumonisins) being subject to endorsement by CCMAS. The Russian Federation expressed their reservation to all the MLs, while EU and Norway expressed their reservations to the ML for flour, meal, semolina and flakes (REP15/CF, paras. 76-91, Appendix VI).

CAC38 adopted the MLs at Step 8 subject to endorsement of the sampling plans and performance criteria for methods of analysis by CCMAS, as recommended by CCEXEC70. The Commission noted the reservations of the Russian Federation to the ML for cereal-based foods for infants and young children and the reservations of EU, Norway, Jordan and the Russian Federation to the ML for flour, meal, semolina and flakes derived from wheat, maize or barley (REP15/CAC, para. 36).

CCMAS37 (2016) endorsed the sampling plans and performance criteria for methods of analysis as revised by CCCF9 with an amendment to the title to read “Sampling plans and method performance criteria for DON in cereal-based foods for infants and young children in flour, meal, semolina and flakes derived from wheat, maize or barley and in cereal grains (wheat, maize and barley) destined for further processing”(REP16/MAS, para 25 and Appendix II)

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

Deoxynivalenol (DON) is the major compound of a group of chemically related mycotoxins called type B trichothecenes (which are epoxy-sesquiterpenoid compounds) and is produced by certain *Fusarium* species, which are pathogens of several cereal grains. Closely related compounds are e.g. nivalenol and several acetyl-DON derivatives. DON is water-soluble and chemically very stable under most normal food processing conditions. DON contamination is commonly found in various cereals and cereal products. It undergoes rapid

***Mycotoxins***

**Deoxynivalenol**

metabolism and elimination in livestock species and the transfer from feed to animal products is probably negligible. Maximum levels in feed are not needed to protect public health, but are useful for the protection of animal health and productivity. Especially pigs are vulnerable. In animals, decreased feed consumption, diarrhea and vomiting have been observed as acute effects. JECFA recognized that DON can lead to outbreaks of acute illness in humans.

**Mycotoxins****Deoxynivalenol****ANNEX****SAMPLING PLANS AND METHOD PERFORMANCE CRITERIA FOR DEOXYNIVALENOL (DON) IN CEREAL-BASED FOODS FOR INFANTS AND YOUNG CHILDREN IN FLOUR, MEAL, SEMOLINA AND FLAKES DERIVED FROM WHEAT, MAIZE OR BARLEY AND IN CEREAL GRAINS (WHEAT, MAIZE AND BARLEY) DESTINE FOR FURTHER PROCESSING****Cereal grains (wheat, cereal and barley) destined for further processing**

Maximum level	2000 µg/kg DON
Increments	increments of 100 g, depending on the lot weight (≥ 0.5 tonnes)
Sample preparation	dry grind with a suitable mill (particles smaller than 0.85 mm - 20 mesh)
Laboratory sample weight	≥ 1 kg
Number of laboratory samples	1
Test portion	25 g test portion
Method	HPLC
Decision rule	If the DON-sample test result for the laboratory samples is equal or less than 2000 µg/kg, accept the lot. Otherwise, reject the lot.

**Cereal-based foods for infants and young children**

Maximum level	200 µg/kg DON
Increments	10 x 100 g
Sample preparation	None
Laboratory sample weight	1 kg
Number of laboratory samples	1
Test portion	25 g test portion
Method	HPLC
Decision rule	If the DON sample test result is equal or less than 200 µg/kg, accept the lot. Otherwise, reject the lot.

**Flour, semolina, meal and flakes derived from wheat, cereal or barley**

Maximum level	1000 µg/kg DON
Increments	10 x 100 g
Sample preparation	None
Laboratory sample weight	1 kg
Number of laboratory samples	1
Test portion	25 g test portion
Method	HPLC
Decision rule	If the DON sample test result is equal or less than 1000 µg/kg, accept the lot. Otherwise, reject the lot.

**Mycotoxins****Deoxynivalenol****DEFINITION**

<b>Lot</b>	An identifiable quantity of a food commodity delivered at one time and determined by the official to have common characteristics, such as origin, variety, type of packing, packer, consignor, or markings.
<b>Sublot</b>	Designated part of a larger lot in order to apply the sampling method on that designated part. Each sublot must be physically separate and identifiable.
<b>Sampling plan</b>	It is defined by a DON test procedure and an accept/reject level. A DON test procedure consists of three steps: sample selection, sample preparation and analysis or DON quantification. The accept/reject level is a tolerance usually equal to the Codex maximum level (ML).
<b>Incremental sample</b>	The quantity of material taken from a single random place in the lot or sublot
<b>Aggregate sample</b>	The combined total of all the incremental samples that is taken from the lot or sublot. The aggregate sample has to be at least as large as the laboratory sample or samples combined.
<b>Laboratory sample</b>	The smallest quantity of shelled cereal comminuted in a mill. The laboratory sample may be a portion of or the entire aggregate sample. If the aggregate sample is larger than the laboratory sample(s), the laboratory sample(s) should be removed in a random manner from the aggregate sample in such a way to ensure that the laboratory sample is still representative of the sublot sampled
<b>Test portion</b>	A portion of the comminuted laboratory sample. The entire laboratory sample should be comminuted in a mill. A portion of the comminuted laboratory sample is randomly removed for the extraction of the DON for chemical analysis.

**SAMPLING PLAN DESIGN CONSIDERATIONS****MATERIAL TO BE SAMPLED**

- Each lot of cereal, which is to be examined for DON, must be sampled separately. Lots larger than 50 tonnes should be subdivided into sublots to be sampled separately. If a lot is greater than 50 tonnes, the lot should be subdivided into sublots according to Table 1.

**Table 1. Subdivision of cereal sublots according to lot weight**

<b>Lot weight (t)</b>	<b>Maximum Weight or minimum number of sub lots</b>	<b>Number of incremental sample</b>	<b>Minimum laboratory Sample Weight (kg)</b>
≥ 1500	500 tonnes	100	1
> 300 and < 1500	3 sublots	100	1
≥ 100 and ≤ 300	100 tonnes	100	1
≥ 50 and < 100	2 sublots	100	1
< 50	-	3-100*	1

\* see table 2

- Taking into account that the weight of the lot is not always an exact multiple of the weight of sublots, the weight of the sublot may exceed the mentioned weight by a maximum of 20%.

**INCREMENTAL SAMPLE**

- The suggested minimum weight of the incremental sample should be 100 grams for lots ≥ 0.5 tonnes.
- For lots less than 50 tonnes, the sampling plan must be used with 3 to 100 incremental samples, depending on the lot weight. For very small lots (≤ 0.5 tonnes) a lower number of incremental samples may be taken, but the aggregate sample uniting all incremental samples shall be also in that case at least 1 kg. Table 2 may be used to determine the number of incremental samples to be taken.

**Mycotoxins****Deoxynivalenol****Table 2. Number of incremental samples to be taken depending on the weight of the lot of**

Lot weight (t)	Number of incremental sample	Minimum Laboratory Sample Weight (kg)
≤ 0.05	3	1
> 0.05 - ≤ 0.5	5	1
> 0.5 - ≤ 1	10	1
> 1 - ≤ 3	20	1
> 3 - ≤ 10	40	1
> 10 - ≤ 20	60	1
> 20 - < 50	100	1

**STATIC LOTS**

- A static lot can be defined as a large mass of shelled cereal contained either in a large single container such as a wagon, truck or railcar or in many small containers such as sacks or boxes and the cereal is stationary at the time a sample is selected. Selecting a truly random sample from a static lot can be difficult because all containers in the lot or subplot may not be accessible.
- Taking incremental samples from a static lot usually requires the use of probing devices to select product from the lot. The probing devices should be specifically designed for the commodity and type of container. The probe should (1) be long enough to reach all products, (2) not restrict any item in the lot from being selected, and (3) not alter the items in the lot. As mentioned above, the aggregate sample should be a composite from many small incremental samples of product taken from many different locations throughout the lot.
- For lots traded in individual packages, the sampling frequency (SF), or number of packages that incremental samples are taken from, is a function of the lot weight (LT), incremental sample weight (IS), aggregate sample weight (AS) and the individual packing weight (IP), as follows:

$$SF = (LT \times IS) / (AS \times IP).$$

- The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.

**DYNAMIC LOTS**

- Representative aggregate samples can be more easily produced when selecting incremental samples from a moving stream of shelled cereal as the lot is transferred from one location to another. When sampling from a moving stream, take small incremental samples of product from the entire length of the moving stream; composite the incremental samples to obtain an aggregate sample; if the aggregate sample is larger than the required laboratory sample(s), then blend and subdivide the aggregate sample to obtain the desired size laboratory sample(s).
- Automatic sampling equipment such as a cross-cut sampler is commercially available with timers that automatically pass a diverter cup through the moving stream at predetermined and uniform intervals. When automatic sampling equipment is not available, a person can be assigned to manually pass a cup through the stream at periodic intervals to collect incremental samples. Whether using automatic or manual methods, incremental samples should be collected and composited at frequent and uniform intervals throughout the entire time the cereal flow past the sampling point.
- Cross-cut samplers should be installed in the following manner: (1) the plane of the opening of the diverter cup should be perpendicular to the direction of the flow; (2) the diverter cup should pass through the entire cross sectional area of the stream; and (3) the opening of the diverter cup should be wide enough to accept all items of interest in the lot. As a general rule, the width of the diverter cup opening should be about two to three times the largest dimensions of items in the lot.
- The size of the aggregate sample (S) in kg, taken from a lot by a cross cut sampler is:

$$S = (D \times LT) / (T \times V),$$

where D is the width of the diverter cup opening (cm), LT is the lot size (kg), T is interval or time between cup movement through the stream (seconds), and V is cup velocity (cm/sec).

- If the mass flow rate of the moving stream, MR (kg/sec), is known, then the sampling frequency (SF), or number of cuts made by the automatic sampler cup can be computed as a function of S, V, D, and MR.

$$SF = (S \times V) / (D \times MR).$$

**PACKAGING AND TRANSPORTATION OF SAMPLES**

**Mycotoxins****Deoxynivalenol**

14. Each laboratory sample shall be placed in a clean, inert container offering adequate protection from contamination, sunlight, and against damage in transit. All necessary precautions shall be taken to avoid any change in composition of the laboratory sample, which might arise during transportation or storage. Samples should be stored in a cool dark place.
15. Each laboratory sample taken for official use shall be sealed at the place of sampling and identified. A record must be kept of each sampling, permitting each lot to be identified unambiguously and giving the date and place of sampling together with any additional information likely to be of assistance to the analyst.

**SAMPLE PREPARATION**

16. Sunlight should be excluded as much as possible during sample preparation, since DON may gradually break down under the influence of ultra-violet light. Also, environmental temperature and relative humidity should be controlled and not favour mould growth and DON formation.
17. As the distribution of DON is extremely non-homogeneous, laboratory samples should be homogenised by grinding the entire laboratory sample received by the laboratory. Homogenisation is a procedure that reduces particle size and disperses the contaminated particles evenly throughout the comminuted laboratory sample.
18. The laboratory sample should be finely ground and mixed thoroughly using a process that approaches as complete homogenisation as possible. Complete homogenisation implies that particle size is extremely small and the variability associated with sample preparation approaches zero. After grinding, the grinder should be cleaned to prevent DON cross-contamination.

**TEST PORTION**

19. The suggested weight of the test portion taken from the comminuted laboratory sample should be approximately 25 g
20. Procedures for selecting the test portion from the comminuted laboratory sample should be a random process. If mixing occurred during or after the comminuting process, the test portion can be selected from any location throughout the comminuted laboratory sample. Otherwise, the test portion should be the accumulation of several small portions selected throughout the laboratory sample.
21. It is suggested that three test portions be selected from each comminuted laboratory sample. The three test portions will be used for enforcement, appeal, and confirmation if needed.

**ANALYTICAL METHODS**

22. A criteria-based approach, whereby a set of performance criteria is established with which the analytical method used should comply, is appropriate. The criteria-based approach has the advantage that, by avoiding setting down specific details of the method used, developments in methodology can be exploited without having to reconsider or modify the specific method. A list of possible criteria and performance levels are shown in Table 3). Utilizing this approach, laboratories would be free to use the analytical method most appropriate for their facilities.

**Table 3. Method criteria for DON in cereals.**

Commodity	ML (mg/kg)	LOD (mg/kg)	LOQ (mg/kg)	Precision on HorRat	Minimum applicable range (mg/kg)	Recovery
Cereal grains (wheat, cereal and barley) destined for further processing	2.0	≤ 0.2	≤ 0.4	≤ 2	1-3	80 - 110%
Cereal-based foods for infants and young children	0.2	≤ 0.02	≤ 0.04	≤ 2	0.1 – 0.3	80 – 110%
Flour, semolina, meal and flakes derived from wheat, cereal or barley	1.0	≤ 0.1	≤ 0.2	≤ 2	0.5 – 1.5	80 – 110%

**Mycotoxins****Diacetoxyscirpenol**

Reference to JECFA:	83 (2016)
Toxicological guidance value:	Group PMTDI 0.06 µg/kg bw (2016, for T-2, HT-2 and 4, 15-DAS)
Contaminant definition:	
Synonyms:	Abbreviation: DAS, 4,15-DAS
Related Code of Practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level(ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
	No ML						

DAS has been detected with a high prevalence in sorghum samples analysed in the FAO/WHO Mycotoxins in Sorghum Project. This mycotoxin has not been assessed by JECFA and a full safety assessment may be warranted to facilitate the interpretation of the analytical results. CCCF8 (2014) agreed to add a full risk assessment of DAS in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA. (REP14/CF, paras. 125-130 and Appendix XIII)

JECFA83 (2016) evaluated DAS in response to a request from CCCF.

The Committee concluded that there are insufficient toxicological data available to derive a point of departure for the risk assessment of 4,15-DAS alone. There are limitations in the available short-term toxicity studies and no data from chronic exposure and reproductive and developmental toxicity studies. 4,15-DAS and T-2/HT-2 toxin are structurally similar, and there is evidence that they cause similar effects at the biochemical and cellular levels, have similarities in toxic effects in vivo and have an additive dose effect when co-exposure occurs. Therefore, the evidence was considered sufficient by the Committee to support including 4,15-DAS in the group PMTDI for T-2 and HT-2 toxin established at the JECFA56. The PMTDI of 0.06 µg/kg bw for T-2 and HT-2 toxin, alone or in combination, was established based on a LOAEL of 0.03 mg/kg bw per day associated with changes in white blood cell counts following 3 weeks of dietary exposure in pigs and the application of an uncertainty factor of 500. The inclusion of 4,15-DAS in the group PMTDI of 0.06 µg/kg bw is considered to be a conservative approach when taking into consideration the observation that T-2 toxin was consistently more potent than 4,15-DAS when comparing similar in vitro and in vivo end-points.

The Committee noted that only LB dietary exposure estimates for Europe were available for the sum of T-2, HT-2 and 4,15-DAS. From these estimates, the sum of the LB dietary exposure estimates for 4,15-DAS of up to 0.0028 µg/kg bw per day and the total dietary exposures estimated for T-2 plus HT-2 of 0.016 µg/kg bw per day results in a LB mean dietary exposure of 0.019 and in a LB high dietary exposure estimated at 0.038 µg/kg bw per day (twice the mean). The Committee concluded that these LB estimates for Europe do not exceed the group PMTDI for T-2, HT-2 and 4,15-DAS (JECFA/83/SC).

Following the outcome of JECFA83, CCCF11 (2017) agreed to request JECFA to update JECFA56 evaluation of T-2/HT-2 toxin taking into account new toxicity studies (i.e. inclusion in the priority list). Furthermore, the exposure assessment should be based upon more recent occurrence data on the presence of T-2 and HT-2 toxin and 4,15-DAS in food. Member countries are requested to provide recent occurrence data on the presence of T-2, HT-2 toxin and 4,15-DAS to the GEMS/Food contaminants database. (REP17/CF, para. 151)

CCCF12 (2018) listed DAS in the priority list of contaminants and naturally occurring toxicants for evaluation by JECFA (REP 18/CF, appendix X).

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

**Mycotoxins****Diacetoxyscirpenol**

Diacetoxyscirpenol (DAS) is a trichothecene mycotoxin produced by certain species of *Fusarium*, such as *F. poae*, *F. semitectum*, *F. moniliforme*, *F. sporotrichioides* etc. DAS was discovered in 1961 as a phytotoxic compound from a culture of *F. equiseti* and *Gibberella intricans* and its chemical properties and structure have been characterized. According to chemical classification of trichothecenes, DAS as well as T-2 and HT-2 toxins, belongs to group A which is characterized by the absence of a ketone on C-8 position and the absence of a macrocyclic ring. Particularly, it is included in the scirpentriol subgroup which comprises a family of type A trichothecene toxins: scirpentriol, the parent alcohol and its seven acetylated derivatives such as DAS, monoacetoxyscirpenol and triacetoxyscirpenol. Among trichothecenes produced by *Fusarium* spp., DAS is one of the most toxic. The presence of DAS in animal feeds and human foods is a possible health threat to humans and animals in some parts of the world, as historically documented by studies on a variety of animal toxicosis, human alimentary toxic aleukia, Msleni joint disease, and more recently evidenced by studies on human toxicoses and bone and joint disease in China. The toxic effects of DAS in humans and animals are similar and include vomiting, diarrhea, hypotension, and myelosuppression.



**Mycotoxins****Ergot alkaloids**

Reference to JECFA:	-
Toxicological guidance value:	-
Contaminant definition:	-
Synonyms:	abbreviation: EAs
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
No ML							

CCFAC34 (2002) agreed to add ergot alkaloids for full evaluation to the priority list of food additives, contaminants and naturally occurring toxicants proposed for evaluation by JECFA. (ALINORM 03/12, paras. 164-169)

CCFAC38 (2006) agreed to delete ergot alkaloids from the priority list for evaluation by JECFA (details are not noted in the report of the session).

CCCF9 (2015) noted that a proposal had been made for an additional annex on ergot alkaloids to the Code of practice for the prevention and reduction of mycotoxin contamination in cereals (CXC 51-2003) but that further information was needed on which the Committee could take a decision on the inclusion of such an annex. Germany agreed to develop a discussion paper for consideration by the next session of the Committee. (REP15/CF, para.103)

CCCF10 (2016) agreed to circulate the proposed draft annex for comments at Step 3. The Committee further agreed to establish an EWG, chaired by Germany and co-chaired by the United Kingdom to prepare a revised proposed draft taking into account written comments received for consideration by CCCF11 (REP16/CF, para.142).

The Committee agreed to include ergot alkaloids as new proposal in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA (REP16/CF, paras. 164 and 171).

CCCF11 (2017) agreed to advance the annex on ergot and ergot alkaloids in cereal grains for adoption at Step 5/8 by CAC and inclusion in the Code of practice for the prevention and reduction of mycotoxin contamination in cereals (CXC 51-2003) (REP17/CF, paras. 58-59 and Appendix V).

CAC40 (2017) adopted the Annex at Step 5/8. (REP17/CAC Appendix III).

“Ergot” is the term used for the solidified mycelium of the fungus *Claviceps purpurea, africana, fusiformis, sorghi* and related species, which can afflict grasses and cereals of all kinds and may contain ergot alkaloids. A dark, sometimes white ergot (sclerotium) is formed instead of a grain in the ears of cereal infected via the plant’s blossom. These bodies usually differ significantly from the cereal as an overall entity in terms of their shape, colour and composition. The main types of cereal affected are rye and triticale (*Claviceps purpurea*), sorghum (*Claviceps africana, sorghi, sorghicola*) and pearl millet (*Claviceps fusiformis*). In spring seasons with longer moist and cool periods, wheat and barley might also be affected. A contamination of the harvested product with ergot and the toxic compounds – ergot alkaloids (EA) – can occur. Out of 40 known ergot alkaloids the most relevant are ergocornine, ergocristine, ergocryptine, ergometrine, ergosine, ergotamine and their epimers. Moreover, in sorghum ergot also dihydro-ergosine and related alkaloids are relevant components. Sclerotia contain different amounts of EAs, depending on the fungi species, the host, the weather conditions and the geographical region. The total alkaloid content in a single sclerotium varies and can reach up to 0.5%. A total ergot alkaloid mean of 0.08% in ergot bodies has been reported based on European data.

Intoxication induced by ergot alkaloids is commonly known as ergotism or “St. Anthony’s fire”, which was ubiquitous in the middle Ages. Local epidemics have occurred also in more

***Mycotoxins***

**Ergot alkaloids**

recent years in France, India and Ethiopia, respectively. There are two symptomatic forms of ergotism: gangrenous and convulsive. In the gangrenous form, tingling effects are felt in peripheral tissues finally leading to the loss of limbs, whereas in convulsive ergotism the tingling is followed by hallucinations, delirium and epileptic-type seizures.

Chronic intake of moderate quantities of ergot alkaloid can have a negative impact on reproduction (e.g. trigger miscarriage, lower birth weight, deficient lactation).

Chronic oral ingestion of large quantities of ergot alkaloids result in symptoms which correspond to acute ingestion of high quantities of ergot alkaloids. This is known from observations of unwanted effects where certain ergot alkaloids were used as active ingredients in medicines or where, following ingestion of cereal products containing high levels of ergot, people became ill." (Ref. CX/CF 16/10/13)

**Mycotoxins****Fumonisin (B<sub>1</sub> + B<sub>2</sub>)**

Reference to JECFA:	56 (2001), 74 (2011), 83 (2016)
Toxicological guidance value:	Group PMTDI 0.002 mg/kg bw (2001, retained in 2011 and 2016 for FB <sub>1</sub> , FB <sub>2</sub> and FB <sub>3</sub> , alone or in combination)
Contaminant definition:	Fumonisin (B <sub>1</sub> +B <sub>2</sub> )
Synonyms:	(Several related compounds have been described, notably fumonisin B <sub>1</sub> , B <sub>2</sub> and B <sub>3</sub> (abbreviation: FB <sub>1</sub> etc.))
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Raw Maize grain	4000	Adopted	2014	CF	Whole commodity	<i>For sampling plan, see Annex.</i>	
Maize flour and maize meal	2000	Adopted	2014	CF	Whole commodity	<i>For sampling plan, see Annex.</i>	

A position paper had been prepared for fumonisins (last version CX/FAC 00/22). CCFAC32 (2000) asked the USA to finalize the position paper as a potential basis for future work (ALINORM 01/12 paras. 106-109). No MLs had been proposed.

The Representative of WHO, speaking on behalf of the JECFA Secretariats, clarified at CCCF1 (2007) that there was no plan for JECFA to update the risk assessment conducted by JECFA56 and that an updated risk assessment could be conducted only when new data became available (ALINORM 07/30/41, para. 135).

CCCF2 (2008) agreed to establish an electronic working group to prepare a discussion paper, which should include an overview of available data and scope of the problem of fumonisin contamination for consideration at its next session (ALINORM 08/31/41, para. 177).

CCCF3 (2009) agreed to initiate work on establishing maximum levels and developing a sampling plan for fumonisins in maize and maize-based products subject to approval by CAC32. It was further agreed to request JECFA to review the available toxicology and occurrence data in order to carry out a re-evaluation on fumonisins in maize and maize products and that, based on the outcome of JECFA re-evaluation, the maximum level might be revised. It was noted that work would be completed by 2012 noting that JECFA could only consider fumonisins at the earliest at its meeting in 2011 (ALINORM 09/32/41, para. 101). The proposal of new work was subsequently by CAC32 (ALINORM 09/32/REP, Appendix VI).

CCCF4 (2010) agreed to retain the proposed draft ML and sampling plans, as contained in Annex I and Annex II of CX/ CF 10/4/8 respectively, at Step 4 until further advice was provided by JECFA (ALINORM 10/33/41, para. 95). Although occurrence of FB<sub>3</sub> was well documented and that JECFA in 2001 had allocated a PMTDI of 2 µg/kg/ bw/day for FB<sub>1</sub>, FB<sub>2</sub> and FB<sub>3</sub> alone or in combination, it was noted that FB<sub>3</sub> made up only 10% of total intake; that the routine laboratory testing for FB<sub>3</sub> was expensive and that not all countries tested for FB<sub>3</sub>, but that consideration could be given to their inclusion in the standard (ALINORM 10/33/41, para. 90- 91).

JECFA74 (2011) evaluated fumonisins and reviewed all relevant studies performed since 2001. Studies suitable for dose-response analysis have been conducted with rodents employing either purified FB<sub>1</sub> or *F. verticillioides* culture material containing FB<sub>1</sub>. Although naturally contaminated corn would probably be more representative of actual human dietary exposure than either purified FB<sub>1</sub> or culture material, no suitable studies were identified that used naturally contaminated corn as test material.

For culture material, the lowest identified BMDL<sub>10</sub> using FB<sub>1</sub> as a marker was 17 µg/kg bw 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. For pure FB<sub>1</sub>, the lowest identified BMDL<sub>10</sub> was 165 µg/kg bw per day for megalocytic hepatocytes in male mice. Using an uncertainty factor of 100 for intraspecies and interspecies variation, the Committee derived a PMTDI of 2 µg/kg bw. As this was the same value as the previous established group PMTDI, this group PMTDI for FB<sub>1</sub>, FB<sub>2</sub>, and FB<sub>3</sub>, alone or in combination, was retained.

**Mycotoxins****Fumonisin (B<sub>1</sub> + B<sub>2</sub>)**

It was estimated that the dietary exposure to FB<sub>1</sub> for the general population ranges from  $0.12 \times 10^{-3}$  to  $7.6 \mu\text{g/kg bw per day}$  (95th percentile: up to  $33.3 \mu\text{g/kg bw per day}$ ). Dietary exposure to total fumonisins for the general population would range, for a consumer with average consumption, from  $0.087 \times 10^{-3}$  to  $10.6 \mu\text{g/kg bw per day}$ , whereas for consumers with high consumption, exposure would be up to  $44.8 \mu\text{g/kg bw per day}$ . Maize was found to be the predominant source of exposure to FB<sub>1</sub> and total fumonisins. Comparison of the estimated dietary exposure with the group PMTDI indicated 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 is highly desirable, particularly in areas of the world where maize is a major dietary staple food and where high contamination can occur.

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.

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 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. 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.

The Committee recommended that, to be able to fully assess the toxic potential of culture material or naturally contaminated food, characterization and quantification of their mycotoxin content are necessary. Also, to obtain a realistic representation of the effects of "real life" exposure, and in order to compare its toxic potential with the studies used for the final evaluation, naturally contaminated feed should be tested in dose-response studies in animals. In addition, further studies must be performed to elaborate more appropriate analytical methods to obtain additional occurrence data and information on the effects of processing. As dietary exposure to fumonisins may occur together with exposure to other mycotoxins, such as aflatoxins, well-designed laboratory and epidemiological studies are needed to assess interactions. For evaluation of the co-occurrence, in food and feed, of fumonisins with other mycotoxins, levels of fumonisins and other mycotoxins must be provided at the level of the individual analytical sample (i.e. not aggregate data).

Additional data on fumonisin distribution in corn Commodity / Product Names should be collected in order to establish appropriate sampling procedures. To validate the potential candidate urinary FB<sub>1</sub> level for a human biomarker of short-term exposure, large-scale human studies that indicate a well characterized dose-response relationship between urinary FB<sub>1</sub> level and dietary fumonisin exposures are needed. A biomarker for long-term exposure is also needed. To investigate the association of fumonisin exposure with oesophageal cancer risk, child growth impairment and NTDs in humans, studies on fumonisin exposure and incidence of these conditions in individuals (such as a cohort or case-control study) are needed using a validated fumonisin exposure biomarker and controlling for confounders and for known risk factors.

CCCF6 (2012) noted that there was agreement for the need for MLs on raw maize/corn grains and corn/maize flour, but that there was no agreement on the actual MLs and the further proposal to develop a code of practice for fumonisins in maize, the Committee agreed to develop a discussion paper to identify the gaps in the Code of practice for prevention and reduction of mycotoxin contamination in cereals and the need for a separate code of practice for fumonisins in maize and whether there are any other measures to control fumonisins in maize. The Committee agreed to establish an electronic working group lead by Brazil and co-chaired by the United States of America and working to develop the discussion paper for consideration by the next session and to suspend development of the proposed draft MLs for fumonisins until the consideration of the discussion paper by the electronic working group at the 7<sup>th</sup> Session (REP12/CF paras. 92, 93 and 95).

CCCF7 (2013) agreed that it was too early to start new work on the revision of the COP and that it needed more information on the nature of the revision and agreed to re-establish the EWG, led by Brazil and co-chaired by the United States of America, working to further develop the discussion paper based on the discussions at the 7<sup>th</sup> session and, if possible, to prepare a proposed draft revision of the COP for consideration by the 8<sup>th</sup> session. (REP13/CF para 132). It agreed that the proposed draft MLs for fumonisins in maize and maize products and associated sampling plans previously discussed at the 6<sup>th</sup> Session of the Committee (CX/CF 12/6/18) would be circulated for comments and a revised proposal for proposed draft MLs for fumonisins in maize and maize products and associated sampling plans would be prepared by Brazil for comments and consideration by the 8<sup>th</sup> session (REP13/CF para 133).

CCCF8 (2014) agreed that the ML of  $4\ 000 \mu\text{g/kg}$  for raw cereal grains and  $2\ 000 \mu\text{g/kg}$  for maize flour and maize meal were ready for adoption by the Commission. In relation to the ML for maize flour and maize meal, the Committee agreed that these would be advanced for adoption with the understanding that exposure and impact assessment should be

**Mycotoxins****Fumonisin (B<sub>1</sub> + B<sub>2</sub>)**

undertaken by JECFA within three years for reconsideration of the levels. The Committee agreed to forward the proposed draft MLs with associated sampling plans to Step 5/8 (with omission of Steps 6/7) for adoption by CAC37. The sampling plans would be sent for endorsement by CCMAS. (REP14/CF, paras. 71-72, Appendix IV). The Committee also agreed to add the assessments of fumonisins already evaluated by JECFA, to the priority list. An updated exposure assessment for fumonisins shall be performed by JECFA after three years once more occurrence data from countries where limited data are available have been collected. (REP14/CF, paras. 129-130, Appendix XIII)

CAC37 (2014) adopted the adopted the MLs and sampling plans at Step 5/8 while noting that sampling plans should be endorsed by CCMAS. Egypt, supported by Jordan, expressed a reservation that lower MLs would be desirable considering the impact of these mycotoxins on human health, and in particular their cumulative effect in the human body and their carry-over from feed to food. (REP14/CAC, paras. 83 and 85, Appendix III).

CCMAS36 (2015) did not endorse the sampling plans noting that there were several inconsistencies between the tables and text in the sampling plans. The Committee agreed to request CCCF to consider removing the inconsistencies and to present a revised version to the next session of CCMAS. (REP15/MAS, paras. 17-20)

CCCF9 (2015) agreed to send the sampling plans and performance criteria for methods of analysis, revised by in-session WG, to CCMAS for endorsement. (REP15/CF, paras. 11-13, Appendix III)

CCMAS37 (2016) endorsed the sampling plans and performance criteria for methods of analysis as revised by CCCF9 with an amendment to the title to read "Sampling plans and method performance criteria for fumonisins (FB<sub>1</sub> + FB<sub>2</sub>) in maize grain and maize flour and maize meal". (REP16/MAS, para 25 and Appendix II)

JECFA83 (2016) evaluated fumonisins in response to a request from CCCF for an updated exposure assessment. The Committee also evaluated toxicological and epidemiological studies that had become available since the previous evaluation in 2011.

The Committee evaluated the updated toxicological data and concluded that they would not change the overall toxicological assessment performed previously by the Committee. Thus, the previously established group PMTDI of 2 µg/kg bw for FB<sub>1</sub>, FB<sub>2</sub> and FB<sub>3</sub>, alone or in combination, was retained by the current Committee.

LB mean and high (90th percentile) chronic FB<sub>1</sub> exposures in adults were maximally 0.56 and 1.1 µg/kg bw per day, respectively. For total fumonisins, the corresponding exposure estimates were 0.82 and 1.6 µg/kg bw per day. The UB mean and high exposures were estimated to be as high as 1.2 and 2.3 µg/kg bw per day for FB<sub>1</sub>, respectively, and as high as 2.1 and 4.3 µg/kg bw per day for total fumonisins, respectively. In children, the LB mean and high chronic FB<sub>1</sub> exposures were maximally 0.8 and 1.6 µg/kg bw per day, respectively, and for total fumonisins, maximally 1.2 and 2.3 µg/kg bw per day, respectively. In this population group, the UB mean and high exposures were estimated to be as high as 1.6 and 3.9 µg/kg bw per day for FB<sub>1</sub>, respectively, and as high as 3.2 and 6.4 µg/kg bw per day for total fumonisins, respectively. Maize is the predominant source of LB exposure to FB<sub>1</sub> and total fumonisins in most cluster diets. In the UB scenario, wheat was also an important contributor to the exposure to fumonisins in some clusters. Comparison of the estimates of exposure to FB<sub>1</sub> and total fumonisins with the group PMTDI indicates no exceedance at the LB mean exposure level in both children and adults. Assuming that all non-detect samples contained fumonisin at the LOQ, the UB mean exposure to total fumonisins in children exceeded the PMTDI in several countries. This was also true for the high (90<sup>th</sup> percentile) exposure, independent of the fumonisin concentration assigned to the non-detect samples. For adults, only the UB high exposure exceeded the PMTDI.

The Committee noted that, due to the high percentage of non-detect samples in the concentration database (around 70%) and the wide range of LOQs reported in the GEMS/Food contaminants database for fumonisins, the UB estimates may be interpreted as a worst-case estimate of exposure based on the data available.

The Committee noted that the international exposure estimates for FB<sub>1</sub> and total fumonisins were lower than those estimated by the Committee at its 74<sup>th</sup> meeting in 2011. In the current assessment, a larger part of the occurrence data was from countries belonging to the WHO European Region compared with 2011, resulting in lower overall fumonisin levels in maize. In the current assessment, no information on fumonisin levels in maize was available from countries belonging to the African, Eastern Mediterranean or South-East Asia regions, where higher fumonisin concentrations are typically detected. Given these limitations of the occurrence data used in the exposure assessment and high exposures reported in the literature in some countries, it is likely that the exposures to fumonisins in areas where maize is a staple food and high contamination with fumonisins can occur are higher than those estimated by the Committee at this meeting, as can be seen in the previous evaluation, which was based on a larger and more representative data set.

At the request of CCCF, the Committee also evaluated co-exposure to aflatoxins and fumonisins. The Committee concluded that there are few data available to support co-exposure

**Mycotoxins****Fumonisin (B<sub>1</sub> + B<sub>2</sub>)**

as a contributing factor in human disease. However, the interaction between AFB<sub>1</sub>, a compound with known genotoxic properties, and fumonisins, which have the potential to induce regenerative cell proliferation (particularly at exposures above the PMTDI), remains a concern. This is due to the fact that the incidences of chronic liver disease and stunting are high in the areas of the world where the exposures to both mycotoxins are high and the co-exposure has been confirmed with biomarkers (JECFA/83/SC).

Following the outcome of JECFA83, CCCF11 (2017) agreed to call upon countries belonging to the African, Eastern Mediterranean or South-East Asia regions to provide to GEMS/Food contaminants database information on fumonisin levels in maize. (REP17/CF, para. 151)

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

Fumonisin is a class of recently identified mycotoxins that are produced mainly by certain *Fusarium* species, especially *F. moniliforme* which is a pathogen of corn (*Zea mays*). Fumonisin is a structurally related group of diesters of propane-1,2,3-tricarboxylic acid and various 2-amino-12,16-dimethylpolyhydroxyeicosanes. There are at least 12 fumonisin analogues identified, classified into series A, B, F and P. The B-series, consisting mainly of fumonisin B<sub>1</sub> and fumonisin B<sub>2</sub>, is believed to be the most abundant and most toxic group. A typical ratio between these analogues is B<sub>1</sub>:B<sub>2</sub>:B<sub>3</sub> as 10:3:1. The worldwide occurrence of fumonisins in corn and corn-based products is well documented: sporadic natural occurrence in sorghum, rice and navy beans has been reported. Fumonisin is heat-stable, so cooking and other heat processes do not substantially reduce their levels in foods.

Processing involving treatment of wet milling fractions may, however, lead to elimination of most fumonisin. The human exposure via food can vary to a large extent because of the large range of fumonisin contents found in practice. Fumonisin undergoes rapid metabolism and elimination in livestock species and the transfer from feed to animal products is probably negligible. Maximum levels in feed are not needed to protect public health but are useful for the protection of animal health and productivity. In animals, various adverse effects have been observed. The horse appears to be the most sensitive species, and equine leukoencephalomalacia (ELEM) is the most frequently encountered disease. Fumonisin is also associated with liver damage, often also kidney lesions and changes in certain lipid classes, especially sphingolipids, in all animals studied. Carcinogenic effects have been observed in animals exposed to high dietary levels.

Nephrotoxicity, observed in several strains of rat, was considered by JECFA to be the most sensitive toxic effect. On the basis of the NOEL for renal toxicity and a safety factor of 100, the PMTDI was established. National estimates for the mean or median intake were generally much lower than the PMTDI (the highest being 0.2 µg/kg bw).

**Mycotoxins****Fumonisin (B<sub>1</sub>+B<sub>2</sub>)**

ANNEX

**SAMPLING PLANS AND METHOD PERFORMANCE CRITERIA FOR FUMONISINS (FB<sub>1</sub> + FB<sub>2</sub>) IN MAIZE GRAIN AND MAIZE FLOUR AND MAIZE MEAL****Maize grain, unprocessed**

Maximum level	4 000 µg/kg FB <sub>1</sub> + FB <sub>2</sub>
Increments	increments of 100 g, depending on the lot weight (≥ 0.5 tonnes)
Sample preparation	dry grind with a suitable mill (particles smaller than 0.85 mm - 20 mesh)
Laboratory sample weight	≥ 1 kg
Number of laboratory samples	1
Test portion	25 g test portion
Method	HPLC
Decision rule	If the fumonisin-sample test result for the laboratory samples is equal or less than 4 000 µg/kg, accept the lot. Otherwise, reject the lot.

**Maize flour and maize meal**

Maximum level	2 000 µg/kg FB <sub>1</sub> + FB <sub>2</sub>
Increments	10 x 100 g
Sample preparation	None
Laboratory sample weight	≥ 1 kg
Number of laboratory samples	1
Test portion	25 g test portion
Method	HPLC
Decision rule	If the fumonisin-sample test result is equal or less than 2 000 µg/kg, accept the lot. Otherwise, reject the lot.

**DEFINITION**

<b>Lot</b>	An identifiable quantity of a food commodity delivered at one time and determined by the official to have common characteristics, such as origin, variety, type of packing, packer, consignor, or markings.
<b>Sublot</b>	The designated part of a larger lot in order to apply the sampling method on that designated part. Each sublot must be physically separate and identifiable.
<b>Sampling plan</b>	It is defined by a fumonisin test procedure and an accept/reject level. A fumonisin test procedure consists of three steps: sample selection, sample preparation and analysis or fumonisin quantification. The accept/reject level is a tolerance usually equal to the Codex maximum level (ML).
<b>Incremental sample</b>	The quantity of material taken from a single random place in the lot or sublot.
<b>Aggregate sample</b>	The combined total of all the incremental samples that is taken from the lot or sublot. The aggregate sample has to be at least as large as the laboratory sample or samples combined.
<b>Laboratory sample</b>	The smallest quantity of shelled maize comminuted in a mill. The laboratory sample may be a portion of or the entire aggregate sample. If the aggregate sample is larger than the laboratory sample(s), the laboratory sample(s) should be removed in a random manner from the aggregate sample in such a way to ensure that the laboratory sample is still representative of the sublot sampled.
<b>Test portion</b>	A portion of the comminuted laboratory sample. The entire laboratory sample should be comminuted in a mill. A portion of the comminuted laboratory sample is randomly removed for the extraction of the fumonisin for chemical analysis.

**Mycotoxins****Fumonisin (B<sub>1</sub>+B<sub>2</sub>)****SAMPLING PLAN DESIGN CONSIDERATIONS****MATERIAL TO BE SAMPLED**

- Each lot of maize, which is to be examined for fumonisin, must be sampled separately. Lots larger than 50 tonnes should be subdivided into sublots to be sampled separately. If a lot is greater than 50 tonnes, the lot should be subdivided into sublots according to Table 1.

**Table 1.** Subdivision of maize sublots according to lot weight

Lot weight (t)	Maximum Weight or minimum number of sub lots	Number of incremental sample	Minimum laboratory Sample Weight (kg)
≥ 1500	500 tonnes	100	1
> 300 and < 1500	3 sublots	100	1
≥ 100 and ≤ 300	100 tonnes	100	1
≥ 50 and < 100	2 sublots	100	1
< 50	-	3-100*	1

\* see table 2

- Taking into account that the weight of the lot is not always an exact multiple of the weight of sublots, the weight of the subplot may exceed the mentioned weight by a maximum of 20%.

**INCREMENTAL SAMPLE**

- The suggested minimum weight of the incremental sample should be 100 grams for lots ≥0.5 tonnes.
- For lots less than 50 tonnes, the sampling plan must be used with 3 to 100 incremental samples, depending on the lot weight. For very small lots (≤ 0.5 tonnes) a lower number of incremental samples may be taken, but the aggregate sample uniting all incremental samples shall be also in that case at least 1 kg. Table 2 may be used to determine the number of incremental samples to be taken.

**Table 2.** Number of incremental samples to be taken depending on the weight of the lot

Lot weight (t)	Number of incremental sample	Minimum Laboratory Sample Weight (kg)
≤ 0.05	3	1
> 0.05 - ≤ 0.5	5	1
> 0.5 - ≤ 1	10	1
> 1 - ≤ 3	20	1
> 3 - ≤ 10	40	1
> 10 - ≤ 20	60	1
> 20 - < 50	100	1

**STATIC LOTS**

- A static lot can be defined as a large mass of shelled maize contained either in a large single container such as a wagon, truck or railcar or in many small containers such as sacks or boxes and the maize is stationary at the time a sample is selected. Selecting a truly random sample from a static lot can be difficult because all containers in the lot or subplot may not be accessible.
- Taking incremental samples from a static lot usually requires the use of probing devices to select product from the lot. The probing devices should be specifically designed for the commodity and type of container. The probe should (1) be long enough to reach all products, (2) not restrict any item in the lot from being selected, and (3) not alter the items in the lot. As mentioned above, the aggregate sample should be a composite from many small incremental samples of product taken from many different locations throughout the lot.
- For lots traded in individual packages, the sampling frequency (SF), or number of packages that incremental samples are taken from, is a function of the lot weight (LT), incremental sample weight (IS), aggregate sample weight (AS) and the individual packing weight (IP), as follows:  

$$SF = (LT \times IS) / (AS \times IP)$$
- The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.



**Mycotoxins****Fumonisin (B<sub>1</sub>+B<sub>2</sub>)****DYNAMIC LOTS**

9. Representative aggregate samples can be more easily produced when selecting incremental samples from a moving stream of shelled maize as the lot is transferred from one location to another. When sampling from a moving stream, take small incremental samples of product from the entire length of the moving stream; composite the incremental samples to obtain an aggregate sample; if the aggregate sample is larger than the required laboratory sample(s), then blend and subdivide the aggregate sample to obtain the desired size laboratory sample(s).
10. Automatic sampling equipment such as a cross-cut sampler is commercially available with timers that automatically pass a diverter cup through the moving stream at predetermined and uniform intervals. When automatic sampling equipment is not available, a person can be assigned to manually pass a cup through the stream at periodic intervals to collect incremental samples. Whether using automatic or manual methods, incremental samples should be collected and composited at frequent and uniform intervals throughout the entire time the maize flow past the sampling point.
11. Cross-cut samplers should be installed in the following manner: (1) the plane of the opening of the diverter cup should be perpendicular to the direction of the flow; (2) the diverter cup should pass through the entire cross sectional area of the stream; and (3) the opening of the diverter cup should be wide enough to accept all items of interest in the lot. As a general rule, the width of the diverter cup opening should be about two to three times the largest dimensions of items in the lot.
12. The size of the aggregate sample (S) in kg, taken from a lot by a cross cut sampler is:  
$$S = (D \times LT) / (T \times V),$$
where D is the width of the diverter cup opening (cm), LT is the lot size (kg), T is interval or time between cup movement through the stream (seconds), and V is cup velocity (cm/sec).
13. If the mass flow rate of the moving stream, MR (kg/sec), is known, then the sampling frequency (SF), or number of cuts made by the automatic sampler cup can be computed as a function of S, V, D, and MR.  
$$SF = (S \times V) / (D \times MR).$$

**PACKAGING AND TRANSPORTATION OF SAMPLES**

14. Each laboratory sample shall be placed in a clean, inert container offering adequate protection from contamination, sunlight, and against damage in transit. All necessary precautions shall be taken to avoid any change in composition of the laboratory sample, which might arise during transportation or storage. Samples should be stored in a cool dark place.
15. Each laboratory sample taken for official use shall be sealed at the place of sampling and identified. A record must be kept of each sampling, permitting each lot to be identified unambiguously and giving the date and place of sampling together with any additional information likely to be of assistance to the analyst.

**SAMPLE PREPARATION**

16. Sunlight should be excluded as much as possible during sample preparation, since fumonisin may gradually break down under the influence of ultra-violet light. Also, environmental temperature and relative humidity should be controlled and not favor mold growth and fumonisin formation.
17. As the distribution of fumonisin is extremely non-homogeneous, laboratory samples should be homogenised by grinding the entire laboratory sample received by the laboratory. Homogenisation is a procedure that reduces particle size and disperses the contaminated particles evenly throughout the comminuted laboratory sample.
18. The laboratory sample should be finely ground and mixed thoroughly using a process that approaches as complete homogenisation as possible. Complete homogenisation implies that particle size is extremely small and the variability associated with sample preparation approaches zero. After grinding, the grinder should be cleaned to prevent fumonisin cross-contamination.

**TEST PORTION**

19. The suggested weight of the test portion taken from the comminuted laboratory sample should be approximately 25 g
20. Procedures for selecting the test portion from the comminuted laboratory sample should be a random process. If mixing occurred during or after the comminuting process, the test portion can be selected from any location throughout the comminuted laboratory sample. Otherwise, the test portion should be the accumulation of several small portions selected throughout the laboratory sample.
21. It is suggested that three test portions be selected from each comminuted laboratory sample. The three test portions will be used for enforcement, appeal, and confirmation if needed.

**Mycotoxins****Fumonisin (B<sub>1</sub>+B<sub>2</sub>)****ANALYTICAL METHODS**

22. A criteria-based approach, whereby a set of performance criteria is established with which the analytical method used should comply, is appropriate. The criteria-based approach has the advantage that, by avoiding setting down specific details of the method used, developments in methodology can be exploited without having to reconsider or modify the specific method. A list of possible criteria and performance levels are shown in Table 3). Utilising this approach, laboratories would be free to use the analytical method most appropriate for their facilities.

**Table 3.** Performance criteria for Fumonisin B<sub>1</sub>+ B<sub>2</sub>.**MAIZE GRAIN**

Analyte	ML (mg/kg)	LOD (mg/kg)	LOQ (mg/kg)	RSD <sub>R</sub>	Recovery (%)
FB <sub>1</sub> + FB <sub>2</sub>	4.0	-	-	-	-
FB <sub>1</sub>		≤ 0.3*	≤ 0.6*	HorRat ≤ 2 (< 27%)	80 - 110
FB <sub>2</sub>		≤ 0.15*	≤ 0.3*	HorRat ≤ 2 (< 32%)	80 - 110

\* The LOD and LOQ were derived based upon typical B<sub>1</sub>:B<sub>2</sub> ratio of 5:2 in naturally-contaminated samples

**MAIZE FLOUR/MEAL**

Analyte	ML (mg/kg)	LOD (mg/kg)	LOQ (mg/kg)	RSD <sub>R</sub>	Recovery (%)
FB <sub>1</sub> + FB <sub>2</sub>	2.0	-	-	-	-
FB <sub>1</sub>		≤ 0.15*	≤ 0.3*	HorRat ≤ 2 (< 30%)	80 - 110
FB <sub>2</sub>		≤ 0.06*	≤ 0.15*	HorRat ≤ 2 (< 34%)	80 - 110

\* The LOD and LOQ were derived based upon typical B<sub>1</sub>:B<sub>2</sub> ratio of 5:2 in naturally-contaminated samples

**Mycotoxins****Ochratoxin A**

Reference to JECFA:	37 (1990), 44 (1995), 56 (2001), 68 (2007)
Toxicological guidance value:	PTWI 0.0001mg/kg bw (2001)
Contaminant definition:	Ochratoxin A
Synonyms:	(The term "ochratoxins" includes a number of related mycotoxins (A, B, C and their esters and metabolites), the most important one being ochratoxin A), Abbreviation: OTA
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Ochratoxin A Contamination in Wine (CXC 63-2007) Code of Practice for the Prevention and Reduction of Ochratoxin A Contamination in Coffee (CXC 69-2009) Code of Practice for the Prevention and Reduction of Ochratoxin A Contamination in Cocoa (CXC 72-2013) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Barley	5	Adopted	2008	CF	Whole commodity	The ML applies to raw barley.	GC 0640
Rye	5	Adopted	2008	CF	Whole commodity	The ML applies to raw rye.	GC 0650
Wheat	5	Adopted	2008	CF	Whole commodity	The ML applies to raw common wheat, raw durum wheat, raw spelt and raw emmer.	GC 0654
Nutmeg Chili and Paprika, Ginger, Pepper, and Turmeric	20	4 (Hold)		CF			REP18/CF, para. 119 Appendix VIII

The situation regarding ochratoxins has been reviewed in a position paper (last version CX/FAC 99/14).

The draft ML of 5 µg/kg for OTA in raw wheat, barley and rye and derived products was forwarded for adoption at Step 8 by CCFAC34 (2002) (ALINORM 03/12, paras. 111- 114), on the basis of the assumption that this level was ALARA. CAC26 (2003) discussed this proposal (ALINORM 03/41, paras. 45-47). Many delegations were of the opinion that this proposed ML was too low and, taking account of the evaluation of JECFA56 (2001), noted that a ML of 20 µg/kg could be adequate in terms of public health and safety. CAC concluded that there was a lack of consensus both regarding the appropriate ML and regarding the reference to derived products and returned the standard to Step 6 for further work by CCFAC. CCFAC36 (2004) noted that given the wide range of derived products and that many of them were of little or no importance in international trade, the maximum level should be limited to raw wheat, barley, and rye. The Committee agreed to hold the maximum level of 5 µg/kg for OTA in raw wheat, barley, and rye at Step 7. The Committee also agreed, depending upon the available data, that JECFA should perform a comprehensive risk assessment by 2006, so that the Committee might reconsider this issue in the light of the outcome of the JECFA evaluation at its Session in 2007 (ALINORM 04/27/12, paras. 132-137).

The ad hoc working group of CCFAC38 (2006) agreed to forward to CAC for approval of new work, the project document "Code of practice for the prevention and reduction of OTA contamination in wine", and agreed that MLs for OTA in wine might be considered in future, pending collection of data on levels in wine and the outcomes of the elaboration of the Code. The Committee agreed to endorse the recommendation of the ad hoc Working Group on Contaminants and Toxins in Foods to start new work on the elaboration of the Code and clarified that the scope of this work should be limited to wine only. The Committee also agreed that the proposed draft Code would be circulated for comments at Step 3 and considered at the next session of the Committee. CAC29 (2006) approved the development of the Code as a new work (ALINORM 06/29/12, paras. 139-142).

**Mycotoxins****Ochratoxin A**

The Committee agreed with the recommendations of the ad hoc Working Group to establish two electronic Working Groups to prepare separate discussion papers on OTA in coffee and OTA in cocoa, respectively, for circulation, comments and consideration at its next Session that might allow the Committee to decide if the development of Codes of Practice was appropriate (ALINORM 06/29/12, paras. 143-145).

CCCF1 (2007) agreed to retain the draft MLs at Step 7 and to inform CCEXEC that work on this item would be completed by 2009 (ALINORM 07/30/41, para. 50).

JECFA68 (2007) retained the PTWI of 100 ng/kg bw. The estimated overall dietary exposure to OTA from cereals (mainly European data) was adjusted to 8-17 ng/kg bw/week (processed cereals), compared with the 25 ng/kg bw/week (raw cereals) in the previous assessment. This is well below the PTWI. Moreover, contamination levels in the majority of raw cereal samples were below 5 µg/kg and only a few samples were above the highest proposed limit of 20 µg/kg. The Committee concluded that it would be unlikely that an ML of 5 or

20 µg/kg has an impact on dietary exposure to OTA. The committee was unable to reach a conclusion regarding developing countries due to the lack of adequate data to consider.

CCCF2 (2008) agreed to forward the draft Maximum Level of 5 µg/kg for OTA in raw wheat, barley and rye to CAC31 for adoption at Step 8 and subsequent inclusion in the General Standard for Contaminants and Toxins in Foods (ALINORM 08/31/REP, para. 112 and Appendix VII). CAC31 adopted the draft ML at Step 8 (ALINORM 08/31/REP, para. 26 and Appendix VII).

**OTA in coffee**

CCCF1 (2007) decided to establish an electronic working group, to be chaired by Brazil, to prepare a revised discussion paper for consideration at the second session. The revised discussion paper should incorporate new data and other relevant information including those submitted to the first session, and be accompanied by a project document proposing new work and possibly an outline of the proposed draft COP (ALINORM 07/30/41, para. 113).

CCCF2 (2008) agreed to establish an electronic working group to prepare a draft proposed Code of practice for the prevention and reduction of OTA contamination in coffee at Step 2, with a view to its circulation for comments at Step 3 and its consideration at Step 4 at the next session of the Committee, pending the formal approval of new work by the Commission (ALINORM 08/31/41, para. 168). CAC31 approved this work (ALINORM 08/31/REP, para. 101).

CCCF3 (2009) agreed to forward the proposed draft Code of practice for the prevention and reduction of OTA contamination in coffee at Step 5/8 (ALINORM 09/32/41, para. 95 and Appendix VI). CAC32 approved the proposed draft Code at Step 5/8 (ALINORM 09/32/REP, Appendix III).

**OTA in cocoa**

CCCF1 decided to establish an EWG to be chaired by Ghana to update the discussion paper with new data and other relevant information, and taking into account the comments made at the first session, for consideration at the second session (ALINORM 07/30/41, para. 117).

CCCF2 (2008) agreed to suspend the consideration of this matter with the understanding to re-consider OTA contamination in cocoa in light of the new data available in the near future (ALINORM 08/31/41, para. 170).

CCCF5 (2011) agreed to re-establish the EWG, working in English, led by Ghana, to update the discussion paper with a view to the development a code of practice for cocoa, for consideration by the 6th session of the Committee (REP11/CF, para. 75).

CCCF6 (2012) agreed to initiate a new work on the development of a code of practice for the prevention and reduction of OTA in cocoa. The Committee agreed that the proposed COP would be developed by an EWG led by Ghana for comments at Step 3 and consideration at the 7th session (REP12/CF, para. 141 and Appendix X). CAC35 (2012) approved the new work (REP12/CAC, Appendix VI).

CCCF7 (2013) agreed to forward the proposed draft Code to Step 5/8 for adoption by CAC36 (REP13/CF, para. 79, Appendix IV). CAC36 approved the draft Code at Step 5/8

**Mycotoxins****Ochratoxin A**

(REP13/CAC, Appendix III).

**OTA in sorghum**

CCCF6 (2012) agreed to initiate a new work on the development of an annex for the management of aflatoxins and OTA in sorghum to the Code of practice for the prevention and reduction of mycotoxin contamination in cereals (CXC 51-2003), subject to approval by CAC35. The Committee agreed to establish an EWG led by Nigeria and co-chaired by Sudan to prepare the proposed draft annex for comments at Step 3 and consideration at the 7th session (REP12/CF, para. 136 and Appendix IX). CAC35 (2012) approved the new work (REP12/CAC, Appendix VI).

CCCF7 (2013) agreed to return the proposed draft Annex to Step 2/3 for further development by the EWG, circulation for comments and further consideration by the 8th session of the Committee (REP13/CF, para. 74).

CCCF8 agreed that in view of the considerable progress made on the annex that it would be advanced for adoption, with the understanding that the annex would be integrated into the COP and its annexes in the new work on the revision of the COP. The Committee agreed to forward the proposed draft Annex to Step 5/8 (with the omission of Steps /7) for adoption by CAC37 (REP14/CF, para. 76-77, Appendix V). CAC37 adopted the annex at Step 5/8 (REP14/CAC, para. 47, Appendix III).

**Code of practice OTA in spices (OTA in paprika)**

At CCCF8 (2014), a proposal for new work on a code of practice for the prevention and reduction of OTA in paprika was discussed. The Committee agreed that a more general approach should also be taken for this COP, similar to the Code of practice for the prevention and reduction of mycotoxin Contamination in cereals; and that consideration could be given to development of annexes for specific mycotoxin-spice combinations. The Committee agreed to establish an EWG, led by Spain and co-chaired by the Netherlands, to prepare a discussion paper on the feasibility for a code of practice for mycotoxins in spices with specific annexes for consideration at the 9th session (REP14/CF, paras. 138-140).

CCCF10 (2016) agreed to:

- continue work on the COP and its annexes (for total aflatoxins and for OTA), and to use the categories of spices as a starting point
- issue a CL to request information on all available proven measures used in practice to reduce contamination by mycotoxins in spices that would help guide the development of possible annexes to the COP
- re-establish the EWG, chaired by Spain and co-chaired by The Netherlands and India to continue the drafting of the COP and its annexes taking into account the discussion at this session, written comments submitted to this session; and the information to be provided by the aforementioned CL. (REP16/CF, paras. 129-137)

**MLs OTA in spices**

CCCF8 (2014) discussed proposals for new work on MLs for aflatoxins in spices and total aflatoxins and aflatoxin B<sub>1</sub> in nutmeg, and associated sampling plans. The Committee had a general discussion on how best to approach the establishment of MLs in spices and considered a proposal by the Chairperson that a review of mycotoxins in spices first be conducted to allow the Committee to understand which mycotoxins to address and in which spices. Such a study could allow for a possible prioritisation of the work on spices for the Committee. The Committee agreed to establish an EWG, led by India and co-chaired by EU and Indonesia, and working in English only, to prepare a discussion paper as outlined in the proposal by the Chairperson for consideration at the next session (REP14/CF, paras. 134 and 137).

In view of the interest to continue with work on MLs in spices, but the need for further clarity on which mycotoxin/spice(s) combination to establish MLs and the rationale for this, as well as further need for prioritisation of the work, CCCF9 (2015) agreed to re-establish the EWG, led by India and co-chaired by Indonesia and EU to prepare a new discussion paper and project document for establishment of ML for spices. The discussion paper should also include proposals for possible MLs to assist the next session of the Committee to take a decision on new work (REP15/CF, paras. 138-139).

CCCF10 (2016) also agreed that further work was needed to expand on the MLs through an EWG chaired by India and co-chaired by the EU with the following terms of reference:

**Mycotoxins****Ochratoxin A**

- provide a rationale for selection of spices (chilli, paprika, ginger, nutmeg, pepper, turmeric)
- provide rationale for selection of total aflatoxins and OTA
- take into account the outcome of the JECFA evaluation of 2016
- consider trade aspects of existing national standards
- prepare a Project document for new work with proposals for MLs for spices.(REP16/CF, paras. 143-148)

CCCF11 (2017) agreed to start new work on MLs for AFT and OTA in nutmeg, chilli and paprika, ginger, pepper and turmeric and to submit the revised project document for approval by CAC40 and to establish an EWG, led by India subject to approval of new work by CAC40, would prepare a proposal for circulation for comments and consideration by CCCF12.

The Committee also recalled a previous decision that EWG chairs should use data from GEMS/Food database and ensure that any data collected by EWGs should be uploaded to the GEMS/Food database. This was consistent with the recommendation of CCCF09 to use the GEMS/Food platform for data submission and analysis for its work in the development of MLs. When additional information needed to be collected that was not part of the database, WG chairs should consult with the GEMS/Food Secretariat when developing templates for the collection of data (REP17/CF, paras. 118-124)

CCCF12 (2018) could not agree on a single figure for the MLs for OTA in the specified spices and agreed:

- to suspend work and to hold the ML of 20 µg/kg for OTA in nutmeg, chili and paprika, ginger, pepper and turmeric, respectively, at Step 4 to give time to countries to implement the Code of Practice for the prevention and reduction of mycotoxins in spices (CXC 78-2017);
- that JECFA would issue a call for data in three-years' time; and
- that an EWG would be re-established once the data were submitted to prepare a proposal for consideration by a future CCCF. (REP 18/CF, paras. 118-119, Appendix VIII)

**Code of practice for mycotoxins in spices**

CCCF9 (2015) agreed to request CAC to approve new work on the COP for the Prevention and Reduction of mycotoxin contamination in spices and to forward the project document to the Executive Committee for critical review (Appendix VIII). The Committee also agreed to establish the EWG, chaired by Spain and co-chaired by India and The Netherlands to prepare, subject to approval by the Commission, a proposed draft of COP for circulation for comments at Step 3 and consideration at its next session. The EWG would also prepare a discussion paper to outline the development of possible annexes for mycotoxin/individual spices or groups of spices combinations (REP15/CF, paras. 143-144).

CAC38 (2015) approved the new work (REP15/CAC Appendix VI).

CCCF11 (2017) agreed to advance the proposed draft COP for the prevention and reduction of mycotoxins contamination in spices for adoption at Step 5/8 by CAC and to discontinue work on annexes until further information on management practices specific spices became available. (REP17/CF, paras. 112-117 and Appendix VI)

CCCF12 (2018) noted the high occurrence levels presented to the EWG, there was a need to reduce mycotoxin levels in spices by implementing the recently adopted code of practice for the prevention and reduction of mycotoxins in spices (CXC 78-2017) and that the MLs, if agreed, could be revised based on new occurrence data following implementation of the COP (REP 18/CF, para, 116).

CAC40 (2017) adopted the COP at Step 5/8 with the amendment to section 2.3.2 (REP17/CAC, paras. 58-59 and Appendix III)

Ochratoxin A is the major compound of a group of chemically related mycotoxins produced by species of the genera *Aspergillus* and *Penicillium*. Ochratoxin A contamination is commonly found in various cereals, some pulses, coffee, cocoa, figs, grapes, wine, nuts and coconut products. It can also be transferred through the feed to animal products and concentrates especially in the kidney, but may also be found in meat and milk. Most ochratoxin A is, however, converted to the less harmful ochratoxin-alpha in the rumen of ruminants.

***Mycotoxins***

**Ochratoxin A**

Ochratoxin A is a nephrotoxic mycotoxin, which is carcinogenic to rodents and has also teratogenic, immunotoxic and possibly neurotoxic properties. It has been associated with Balkan Endemic Nephropathy.

**Mycotoxins****Patulin**

Reference to JECFA:	35 (1989), 44 (1995)
Toxicological guidance value:	PMTDI 0.0004 mg/kg bw (1995)
Contaminant definition:	Patulin
Related code of practice:	Code of Practice for the Prevention and Reduction of Patulin Contamination in Apple Juice and Apple Juice Ingredients in Other Beverages (CXC 50-2003)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Apple juice	50	Adopted	2003	FAC	Whole commodity (not concentrated) or commodity reconstituted to the original juice concentration.	Relevant Codex commodity standard include CXS 247-2005 (apple product only). The ML applies also to apple juice used as an ingredient in other beverages.	

The situation regarding patulin was reviewed in a position paper (last version CX/FAC 99/16).

CAC26 (2003) adopted the ML. The possible reduction of the ML from 50 to 25 µg/kg will be reconsidered by CCFAC once the COP has been implemented (i.e., after 4 years). More data are requested on the level of patulin in apple juice and apple juice ingredients for other beverages.

CCCF1 (2007) agreed to take patulin out of the priority list, noting that there was an existing maximum level and this topic was no longer considered a high priority (ALINORM 07/30/41, para. 127).

Patulin is a low molecular weight hemiacetal lactone mycotoxin produced by species of the genera *Aspergillus*, *Penicillium* and *Byssoschlamys*. The major sources of patulin contamination are apples with brown rot and blue mould. Because patulin does not spread much from spoilt tissue, the main human exposure can be expected from processed products, like apple juice and apple sauce, in which the contamination is not visible. Because fermentation destroys patulin, it is not normally present in cider and perry, unless unfermented apple juice has been added after fermentation. Patulin may also be a contaminant of soft fruits, some vegetables, barley, wheat and corn.

Potential health problems related to patulin are connected to cytotoxic, immunotoxic, neurotoxic, gastrointestinal and other effects observed in animals. Patulin is mostly eliminated within a few days after ingestion.

The PMTDI was set by applying a safety factor of 100 to the lowest NOAEL of 43 µg/kg bw/day in rats.



**Mycotoxins****Sterigmatocystin**

Reference to JECFA:	83 (2016)
Toxicological guidance value:	BMDL <sub>10</sub> : 0.16 mg/kg bw per day for hepatic haemangiosarcoma
Contaminant definition:	-
Synonyms:	Abbreviation: STC
Related Code of Practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Maximum Level (ML) (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
No ML							

STC has been detected with a high prevalence in sorghum samples analysed in the FAO/WHO Mycotoxins in Sorghum Project. This mycotoxin has not been assessed by JECFA and a full safety assessment may be warranted to facilitate the interpretation of the analytical results. CCCF08 (2014) agreed to add a full risk assessment of STC in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA. (REP14/CF, paras. 125-130 and Appendix XIII)

JECFA83 (2016) evaluated STC at the request of CCCF. The Committee concluded that STC is genotoxic and carcinogenic, and the critical effect was determined to be carcinogenicity. The Committee selected the BMDL<sub>10</sub> of 0.16 mg/kg bw per day for hepatic haemangiosarcoma in male rats from the restricted log-logistic model as the point of departure for use in the risk assessment. The Committee calculated MOEs for mean and high estimates of dietary exposure to STC. The MOEs for adults range from 9400 to more than 530 000 for mean estimates based on UB and LB assumptions. For high estimates, MOEs for adults range from 4700 to 270 000. The lowest MOEs are observed for the African Region (from 4700 to 5000 for the high exposure UB–LB range, and from 9400 to 10 000 for the mean exposure UB–LB range). The Committee noted that these estimates, which are based only on adult populations and for which only one food commodity (sorghum) was considered, may indicate a human health concern. Margins of exposure were not calculated for Europe or Japan, as STC was not detected in any samples. For all other regions, the Committee considered that the MOEs were not of human health concern even at the high UB exposure. Overall, the Committee concluded that the data used for calculating the margins of exposure had considerable limitations, and that consequently, the derived margins of exposure should be considered only as crude estimates.

The Committee also noted that STC and AFB<sub>1</sub> have the same main target organ (the liver). The comparative animal data on carcinogenicity are very limited, but indicate that STC is less potent than AFB<sub>1</sub> (JECFA/83/SC).

Following the outcome of JECFA83, CCCF11 (2017) agreed to establish an EWG, led by Brazil, to prepare a discussion paper on AFs and STC in cereals (in particular maize, rice, sorghum and wheat) to take at CCCF12 an informed decision on the appropriate follow-up as regards possible risk management options for AFs and STC in cereals. (REP17/CF, para. 151)

In CCCF12 (2018), Brazil as Chair of the EWG introduced the recommendation that it was premature to set MLs for STC due to the lack of an internationally validated analytical method and reference material for this mycotoxin. The Committee agreed to inform the Standards development organizations of the need for an internationally validated method of analysis for STC through CCMAS (REP18/CF, paras 132 and 139).

CCMAS41 (2018) encouraged standards development organizations to develop an international validated method for STC in cereals (REP18/MAS, para. 21).

**Code of practice for mycotoxins in cereals**

In CCCF12 (2018), the Committee noted the recommendation that consideration could be given to development of an annex to Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) if there are specific management practices available for STC in cereals. The Committee agreed that there was insufficient information for the development of an annex and that no action was needed at this stage (REP18/CF, paras 132 and 140).

**Mycotoxins**

**Sterigmatocystin**

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

Sterigmatocystin (STC) is a polyketide mycotoxin that is produced by more than 50 fungal species, including *Aspergillus flavus*, *A. parasiticus*, *A. versicolor* and *A. nidulans*, of which *A. versicolor* is the most common source. STC shares its biosynthetic pathway with aflatoxins. *A. nidulans* and *A. versicolor* are apparently unable to biotransform STC into O-methylsterigmatocystin, the direct precursor of aflatoxin B<sub>1</sub> and G<sub>1</sub>. Consequently, substrates colonised by these fungi can contain high amounts of STC, while substrates invaded by *A. flavus* and *A. parasiticus* contain only low amounts of STC as most is converted into aflatoxins. STC can occur in grains and grain-based products due to fungal infestation at the post-harvest stage.

The IARC (1976 and 1978) has assessed the carcinogenic potential of STC and concluded that STC produced lung tumours in mice and liver tumours in rats following oral administration. The IARC noted that in rats, STC induced skin and liver tumours following its administration to the skin and sarcomas at the site of its subcutaneous injection. No case reports or epidemiological studies were available for evaluation by IARC and it was concluded that STC is possibly carcinogenic to humans (group 2B).

**Mycotoxins****T-2 and HT-2 toxin**

Reference to JECFA:	56 (2001), 83 (2016)
Toxicological guidance value:	PMTDI 0.00006 mg/kg bw (2001), Group PMTDI 0.00006 mg/kg bw for T-2, HT-2 and DAS, alone or in combination (2016))
Contaminant definition:	-
Synonyms:	-
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Level (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
No ML							

JECFA56 (2001) evaluated T2 and HT2 toxin. The Committee established the PMTDI of 0.06 µg/kg bw based on a 3-week dietary study with pigs, applying a safety factor of 500 to a LOEL for changes in white and red cell counts. The average intake of T-2 and HT-2 toxin via the human diet was estimated by JECFA as 8 resp. 9 ng/kg bw, which is lower than the group PMTDI. An intake at the level of the PMTDI was not expected to result in effects of T-2 and HT-2 toxin on the immune system and to haematotoxicity, which are considered critical effects after short-term intake. JECFA recommended that toxic equivalency factors relative to DON be developed for the other trichothecenes commonly occurring in cereal grains, if sufficient data become available.

No further action on T-2 and HT-2 toxin has been recommended by CCFAC33 (2001), probably based on the understanding that the (limited) information available suggested that intakes would not exceed the PMTDI (ALINORM 01/12A, para. 16).

JECFA83 (2016) evaluated DAS in response to a request from CCCF and noted that 4,15-DAS and T-2/HT-2 toxin are structurally similar, and there is evidence that they cause similar effects at the biochemical and cellular levels, have similarities in toxic effects in vivo and have an additive dose effect when co-exposure occurs. Therefore, the evidence was considered sufficient by the Committee to support including 4,15-DAS in the group PMTDI for T-2 and HT-2 toxin established at JECFA56. The PMTDI of 0.06 µg/kg bw for T-2 and HT-2 toxin, alone or in combination, was established based on a LOAEL of 0.03 mg/kg bw per day associated with changes in white blood cell counts following 3 weeks of dietary exposure in pigs and the application of an uncertainty factor of 500. The inclusion of 4,15-DAS in the group PMTDI of 0.06 µg/kg bw was considered to be a conservative approach when taking into consideration the observation that T-2 toxin was consistently more potent than 4,15-DAS when comparing similar in vitro and in vivo end-points.

The Committee noted that only LB dietary exposure estimates for Europe were available for the sum of T-2, HT-2 and 4,15-DAS. From these estimates, the sum of the LB dietary exposure estimates for 4,15-DAS of up to 0.0028 µg/kg bw per day and the total dietary exposures estimated for T-2 plus HT-2 of 0.016 µg/kg bw per day results in a LB mean dietary exposure of 0.019 and in a LB high dietary exposure estimated at 0.038 µg/kg bw per day (twice the mean). The Committee concluded that these LB estimates for Europe do not exceed the group PMTDI for T-2, HT-2 and 4,15-DAS (JECFA/83/SC).

CCCF11 (2017) agreed to request JECFA to update the 2001 JECFA evaluation of T-2/HT-2 toxin taking into account new toxicity studies (i.e. inclusion in the priority list). Furthermore, the exposure assessment should be based upon more recent occurrence data on the presence of T-2 and HT-2 toxin and 4,15-1 Diacetoxyscirpenol (DAS) in food. Member countries are requested to provide recent occurrence data on the presence of T-2, HT-2 toxin and 4,15-DAS to the GEMS/Food contaminants database. For the generation of these occurrence data it is necessary to use methods of analysis with appropriate sensitivity (REP17/CF, para. 151). The Committee therefore listed T-2/HT-2 in the priority list of contaminants and naturally occurring toxicants for evaluation by JECFA (REP 17/CF, appendix XII).

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

**Mycotoxins****T-2 and HT-2 toxin**

T-2 and HT-2 toxin are closely related compounds belonging to a group of chemically related mycotoxins called type A trichothecenes (which are epoxy-sesquiterpenoid compounds) and are produced by certain *Fusarium* species, which are pathogens of several cereal grains. The most important producer is *F. sporotrichioides*, a saprophyte which only will grow at high water activities. As a consequence, T-2 and HT-2 toxins are not normally found in grain at harvest, but result from water damage when it remains wet for longer periods in the field or after harvest. T-2 and HT-2 toxin undergo rapid metabolism and elimination in livestock species and the transfer from feed to animal products is probably negligible. Maximum levels in feed are not needed to protect public health, but are useful for the protection of animal health and productivity. Especially pigs are vulnerable. In animals, decreased feed consumption, diarrhea and vomiting have been observed as acute effects.

T-2 toxin is a potent inhibitor of protein synthesis, both in vivo and in vitro. T-2 toxin is linked to outbreaks of acute poisoning of humans, in which the adverse effects reported include nausea, vomiting, pharyngeal irritation, abdominal pain, diarrhea, bloody stool, dizziness and chills. Co-occurrence of T-2 toxin with other trichothecenes in these cases is likely. T-2 toxin is also associated with food-related poisoning incidents in 1931- 1947 referred to as alimentary toxic aleukia, in the former Soviet Union.

**Mycotoxins****Zearalenone**

Reference to JECFA:	53 (1999)
Toxicological guidance value:	PMTDI 0.0005 mg/kg bw (1999, The total intake of zearalenone and its metabolites (including alpha-zearalenol (zeranol)) should not exceed the PMTDI.)
Synonyms:	(Zearalenone is the most important of a group of related mycotoxins and relevant metabolites. Abbreviation: ZEN. Its metabolite, alpha-zearalenol (zeranol) is used as veterinary drug.)
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) Code of Practice for the Prevention and Reduction of Mycotoxins in Spices (CXC 78-2017)

Commodity / Product Name	Level (µg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
No ML							

The situation regarding ZEN has been reviewed in a position paper (last version CX/FAC 00/19).

Preliminary intake calculations indicate values well below the PMTDI. It is mentioned however that further action seems required to reduce the levels of ZEN in risk products (especially maize containing products) for especially children with a high intake of these products.

CCFAC31 (1999) agreed that, recognizing that there were no identified trade problems with ZEN, Codex MLs were not necessary for the time being. The MRLs for zearalenol (ZAL) in cattle liver and muscle have been established by Codex (CCRVDV) because of recognized use of zeranol in cattle; they are relevant for CCFAC in so far that feed contamination with ZEN can lead to residues of both ZEN and ZAL (and other metabolites) in cattle liver and muscle.

**Code of practice for mycotoxins in spices**

See the section on Aflatoxins, total or Ochratoxin A.

Zearalenone (ZEN) is the most important of a group of resorcylic acid lactone mycotoxins, produced by several species of *Fusarium* moulds. It is found worldwide in a number of cereal crops and also in derived products like beer. It has been implicated in numerous incidents of mycotoxicosis in farm animals, especially pigs. ZEN is rapidly metabolized in and excreted from animals; residues of this mycotoxin in animal products are probably not significant from a health point of view. A metabolite of ZEN, alpha-zearalenol (zeranol, abbreviated here as ZAL) is, however, relevant relating to its potential use as a veterinary drug. Also beta-zearalenol (taleralanol) has hormonal activity. Besides these substances which can be used as anabolic growth promoters, also alpha- and beta-zearalenol (ZAL) and zearalenone (ZEN) are mentioned as possibly occurring metabolites of or co-occurring substances with ZEN.

The PMTDI for ZEN was set by applying a safety factor of 100 from the lowest NOAEL, related to the estrogenic effect in pigs. ZAL has an ADI of 0.5 µg/kg bw (ref. JECFA 26, 27 and 32).

Residues of ZEN and ZAL together in an animal product may be regarded as evidence that the animal feed was contaminated with ZEN. In order to distinguish between contamination of the feed with mycotoxins of the ZEN group or use of ZAL as veterinary drug, it may be necessary to determine the relative proportions of the different residues, e.g. as ZEN + alpha- and beta-ZAL against ZAL. A ratio of 5 or more probably indicates only contamination by mycotoxins.

**Marine biotoxins****Saxitoxin group**

Reference to JECFA: -  
 Toxicological guidance value: ARfD 0.7 µg/kg bw (2004; FAO/IOC/WHO ad hoc Expert Consultation)  
 Synonyms: Abbreviation, STX

Commodity / Product Name	Maximum Level (ML) (mg/kg mollusc flesh)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Live and raw bivalve molluscs	0.8	Adopted	CXS 292-2008	FFP, CF	Edible parts of bivalve molluscs (the whole part or any part intended to be eaten separately)	Relevant Codex commodity standard is CXS 292-2008.	(2HCL) of saxitoxin equivalent. 2)
Live abalone, raw fresh chilled or frozen abalone 1)	No ML	Adopted	CXS 312-2013	FFP		Relevant Codex commodity standard is CXS 312-2013.	2)

- 1) Abalone from some geographical areas have been found to accumulate certain marine biotoxins. It is up to the Competent Authority (using a Risk Assessment) to determine whether a risk exists in any geographical areas under its control and if so, put in the necessary mechanisms to ensure that the part of the abalone to be consumed, meets with the marine biotoxins level in the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008).
- 2) These MLs are not listed in the current GSCTFF (rev. 2018).

The Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxin in Bivalve Molluscs (2004) was asked to perform risk assessments for a number of biotoxins that are present in bivalve molluscs. Since exposure to biotoxins generally involves only occasional consumption, and because most of the available toxicological data involve only acute and short-term studies, priority was given to the establishment of an acute reference dose, and generally insufficient data were available to establish a tolerable daily intake. It must be pointed out that the Expert Consultation did not have enough time to fully evaluate epidemiological data or to assess the effects of cooking or processing for deriving the provisional guidance levels/maximum levels for several toxin groups (especially the AZA and STX groups). The Consultation agreed that there is a need for a further in-depth review of these data to better derive the guidance levels/maximum levels.

CCFFP29 (2008) agreed that at this stage it was not necessary to ask for additional scientific advice from FAO/WHO and that this issue would be kept under review and may be reconsidered when further scientific advice became available.

CCCF2 (2008) agreed to provisionally endorse the proposed levels, with the recommendation that the levels would require complete review in the coming few years with the view to revising these levels where necessary, when more data became available (ALINORM 08/31/41 para. 31).

CAC31 (2008) adopted the Draft Standard for Raw and Live Bivalve Molluscs at Step 8 with a correction to the scope of the Spanish version by replacing "desbullados" with "abiertos" (ALINORM 08/31/REP. para. 36).

At CCCF11 (2017), the Representative of FAO reported on the development of TEFs for marine biotoxins associated with bivalve molluscs. The Representative recalled that the CCFFP has developed the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008) which includes provisions for several marine biotoxins (eg Saxitoxin (STX) group; Domoic acid (DA) group; Brevetoxin (BTX) group; etc). As each of these biotoxin groups includes several analogues with different toxic potencies, in order to be able to assess the total toxicity in the shellfish extract and thus implement the standard, there was the need to derive TEF for each of the biotoxin groups.

At CCFFP's request FAO/WHO organized an expert meeting in 2016 to discuss the issues associated with development of TEFs for marine biotoxins, and to develop a technical paper on the state of science on the subject, including guidance for food safety managers to implement the provisions for biotoxins in the standard at national level. The technical

**Marine biotoxins**

**Saxitoxin group**

paper has been published and also resulted in an article in an international scientific journal (REP17/CF, para 23).

Saxitoxin-group toxins are a group of closely related tetrahydropurines occurring in bivalve molluscs, such as oysters, mussels, scallops and clams. STX-group toxins are neurotoxic and cause paralytic shellfish poisoning (PSP) in humans. PSP can be characterized by symptoms ranging from a slight tingling sensation or numbness around the lips, tongue and mouth to fatal respiratory paralysis. From the different STX analogues that have been identified seem STX, NeoSTX, GTX1 and dc-STX to be the most toxic ones. A provisional ARfD was calculated by the FAO/IOC/WHO ad hoc Expert Consultation based on a dose of 2 µg STX eq/kg bw derived from epidemiological data as LOAEL. Because mild illness at lower doses is readily reversible and the data on PSP represent a range of individuals with varying susceptibilities, a safety factor of 3 was considered appropriate to derive a provisional ARfD. The provisional ARfD is therefore calculated to be 0.7 µg STX eq/kg bw. An additional note was however made that further effort is needed to evaluate epidemiological data fully or to assess the effects of cooking or processing for deriving the ARfD and provisional guidance levels/maximum levels for the STX group.

**Marine biotoxins****Okadaic acid group**

Reference to JECFA: -

Toxicological guidance value: ARfD 0.33 µg/kg bw (2004; FAO/IOC/WHO ad hoc Expert Consultation)

Synonyms: Abbreviation, OA

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Live and raw bivalve molluscs	0.16	Adopted	CXS 292-2008	FFP, CF	Edible parts of bivalve molluscs (the whole part or any part intended to be eaten separately)	Relevant Codex commodity standard is CXS 292-2008.	Okadaic acid equivalent. 2)
Live abalone, raw fresh chilled or frozen abalone 1)	No ML	Adopted	CXS 312-2013	FFP		Relevant Codex commodity standard is CXS 312-2013.	2)

- 1) Abalone from some geographical areas have been found to accumulate certain marine biotoxins. It is up to the Competent Authority (using a Risk Assessment) to determine whether a risk exists in any geographical areas under its control and if so, put in the necessary mechanisms to ensure that the part of the abalone to be consumed, meets with the marine biotoxins level in the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008).
- 2) These MLs are not listed in the current GSCTFF (ver. 2018).

The Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxin in Bivalve Molluscs (2004) was asked to perform risk assessments for a number of biotoxins that are present in bivalve molluscs. Since exposure to biotoxins generally involves only occasional consumption, and because most of the available toxicological data involve only acute and short-term studies, priority was given to the establishment of an acute reference dose, and generally insufficient data were available to establish a tolerable daily intake. It must be pointed out that the Expert Consultation did not have enough time to fully evaluate epidemiological data or to assess the effects of cooking or processing for deriving the provisional guidance levels/maximum levels for several toxin groups (especially the AZA and STX groups). The Consultation agreed that there is a need for a further in-depth review of these data to better derive the guidance levels/maximum levels.

CCFFP29 (2008) agreed that at this stage it was not necessary to ask for additional scientific advice from FAO/WHO and that this issue would be kept under review and may be reconsidered when further scientific advice became available.

CCCF2 (2008) agreed to provisionally endorse the proposed levels, with the recommendation that the levels would require complete review in the coming few years with the view to revising these levels where necessary, when more data became available (ALINORM 08/31/41 para. 31).

CAC31 (2008) adopted the Draft Standard for Raw and Live Bivalve Molluscs at Step 8 with a correction to the scope of the Spanish version by replacing "desbullados" with "abiertos" (ALINORM 08/31/REP, para. 36).]

At CCCF11 (2017), the Representative of FAO reported on the development of TEFs for marine biotoxins associated with bivalve molluscs. The Representative recalled that the CCFFP has developed the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008) which includes provisions for several marine biotoxins (e.g. Saxitoxin (STX) group; Domoic acid (DA) group; Brevetoxin (BTX) group; etc). As each of these biotoxin groups includes several analogues with different toxic potencies, in order to be able to assess the total toxicity in the shellfish extract and thus implement the standard, there was the need to derive TEF for each of the biotoxin groups.

At CCFFP's request FAO/WHO organized an expert meeting in 2016 to discuss the issues associated with development of TEFs for marine biotoxins, and to develop a technical paper on the state of science on the subject, including guidance for food safety managers to implement the provisions for biotoxins in the standard at national level. The technical paper has been published and also resulted in an article in an international scientific journal (REP17/CF, para 23)



**Marine biotoxins**

**Okadaic acid group**

Okadaic acid (OA) forms together with its analogues the dinophysins toxins (DTX), the group of OA toxins. OA toxins can be found in microalgae and various species of shellfish, mainly in filter-feeding bivalve molluscs such as oysters, mussels, scallops and clams and can cause diarrhoeic shellfish poisoning (DSP). DSP is characterized by symptoms such as diarrhea, nausea, vomiting and abdominal pain. The onset of DSP in humans is shortly after consumption. OA toxins possess tumour promoting activity, and okadaic acid itself also shows genotoxic and immunotoxic activity. It is unlikely that a substantial risk of cancer exists in consumers of shellfish because of these toxins, but still the question may be raised what the human health risks are of (sub)chronic exposure to low levels.

A provisional ARfD of 0.33 µg OA eq/kg bw could be established. This value is based on a LOAEL of 1.0 µg OA eq/kg bw and a safety factor of 3 because of documentation of human cases including more than 40 persons and because DSP symptoms are readily reversible.

More studies on pharmacokinetics, data on long-term/carcinogenicity and further studies on genotoxicity and reproductive toxicity are needed for establishing a TDI.

**Marine biotoxins****Domoic acid group**

Reference to JECFA: -  
 Toxicological guidance value: ARfD 100 µg/kg bw (2004; FAO/IOC/WHO ad hoc Expert Consultation)  
 Synonyms: Abbreviation, DA

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Live and raw bivalve molluscs	20	Adopted	CXS 292-2008	FFP, CF	Edible parts of bivalve molluscs (the whole part or any part intended to be eaten separately)	Relevant Codex commodity standard is CXS 292-2008.	Domoic acid. 2)
Live abalone, raw fresh chilled or frozen abalone 1)	No ML	Adopted	CXS 312-2013	FFP		Relevant Codex commodity standard is CXS 312-2013.	2)

- 1) Abalone from some geographical areas have been found to accumulate certain marine biotoxins. It is up to the Competent Authority (using a Risk Assessment) to determine whether a risk exists in any geographical areas under its control and if so, put in the necessary mechanisms to ensure that the part of the abalone to be consumed, meets with the marine biotoxins level in the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008).
- 2) These MLs are not listed in the current GSCTFF (ver. 2018).

The Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotoxin in Bivalve Molluscs (2004) was asked to perform risk assessments for a number of biotoxins that are present in bivalve molluscs. Since exposure to biotoxins generally involves only occasional consumption, and because most of the available toxicological data involve only acute and short-term studies, priority was given to the establishment of an acute reference dose, and generally insufficient data were available to establish a tolerable daily intake. It must be pointed out that the Expert Consultation did not have enough time to fully evaluate epidemiological data or to assess the effects of cooking or processing for deriving the provisional guidance levels/maximum levels for several toxin groups (especially the AZA and STX groups). The Consultation agreed that there is a need for a further in-depth review of these data to better derive the guidance levels/maximum levels.

CCFFP29 (2008) agreed that at this stage it was not necessary to ask for additional scientific advice from FAO/WHO and that this issue would be kept under review and may be reconsidered when further scientific advice became available.

CCCF2 (2008) agreed to provisionally endorse the proposed levels, with the recommendation that the levels would require complete review in the coming few years with the view to revising these levels where necessary, when more data became available (ALINORM 08/31/41 para. 31).

CAC31 (2008) adopted the Draft Standard for Raw and Live Bivalve Molluscs at Step 8 with a correction to the scope of the Spanish version by replacing "desbullados" with "abiertos" (ALINORM 08/31/REP. para. 36).

At CCCF11 (2017), the Representative of FAO reported on the development of TEFs for marine biotoxins associated with bivalve molluscs. The Representative recalled that the CCFFP has developed the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008) which includes provisions for several marine biotoxins (eg Saxitoxin (STX) group; Domoic acid (DA) group; Brevetoxin (BTX) group; etc). As each of these biotoxin groups includes several analogues with different toxic potencies, in order to be able to assess the total toxicity in the shellfish extract and thus implement the standard, there was the need to derive TEF for each of the biotoxin groups.

At CCFFP's request FAO/WHO organized an expert meeting in 2016 to discuss the issues associated with development of TEFs for marine biotoxins, and to develop a technical paper on the state of science on the subject, including guidance for food safety managers to implement the provisions for biotoxins in the standard at national level. The technical paper has been published and also resulted in an article in an international scientific journal (REP17/CF, para 23)

**Marine biotoxins**

**Domoic acid group**

Domoic acid (DA) and its isomers may cause amnesic shellfish poisoning (ASP) in humans. Symptoms include gastrointestinal symptoms such as vomiting, diarrhoe or abdominal cramps, and/or neurological symptoms such as confusion, loss of memory or other serious signs such as seizure or coma. These symptoms generally occur within 24-48 hours after consuming contaminated shellfish or other types of seafood.

The toxicological database for DA is limited. Neurotoxicity is the critical toxicological effect identified in experimental animals as well as in humans. Based on the results of the first outbreak of ASP in Canada in 1987, an ARfD could be established. In this outbreak, a dose-related increase in severity of the signs and symptoms was observed in patients consuming between 1 mg/kg bw and 5 mg/kg bw. These findings are supported by studies in rodents and monkeys. The LOAEL of 1 mg/kg bw was divided by a safety factor of 10 to cover intrahuman susceptibility and account for the fact that the starting point was a LOAEL, to derive a provisional ARfD of 100 µg/kg bw.

The Joint FAO/IOC/WHO ad hoc Expert Consultation noted that although very few animal studies have been conducted on the subchronic and chronic toxicity of DA, these limited data suggest that cumulative effects of low doses of DA are unlikely. Hence, their conclusion was that the ARfD may also be considered as a provisional chronic TDI.

**Marine biotoxins****Brevetoxin group**

Reference to JECFA: -  
 Toxicological guidance value: -  
 Synonyms: Abbreviation, BTX

Commodity / Product Name	Maximum Level (ML) (mouse units/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Live and raw bivalve molluscs	200	Adopted	CXS 292-2008	FFP, CF	Edible parts of bivalve molluscs (the whole part or any part intended to be eaten separately)	Relevant Codex commodity standard is CXS 292-2008.	Mouse units or equivalent. 2)
Live abalone, raw fresh chilled or frozen abalone 1)	No ML	Adopted	CXS 312-2013	FFP		Relevant Codex commodity standard is CXS 312-2013.	2)

- 1) Abalone from some geographical areas have been found to accumulate certain marine biotoxins. It is up to the Competent Authority (using a Risk Assessment) to determine whether a risk exists in any geographical areas under its control and if so, put in the necessary mechanisms to ensure that the part of the abalone to be consumed, meets with the marine biotoxins level in the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008).
- 2) These MLs are not listed in the current GSCTFF (ver. 2018).

The Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotxin in Bivalve Molluscs (2004) was asked to perform risk assessments for a number of biotoxins that are present in bivalve molluscs. Since exposure to biotoxins generally involves only occasional consumption, and because most of the available toxicological data involve only acute and short-term studies, priority was given to the establishment of an acute reference dose, and generally insufficient data were available to establish a tolerable daily intake. It must be pointed out that the Expert Consultation did not have enough time to fully evaluate epidemiological data or to assess the effects of cooking or processing for deriving the provisional guidance levels/maximum levels for several toxin groups (especially the AZA and STX groups). The Consultation agreed that there is a need for a further in-depth review of these data to better derive the guidance levels/maximum levels.

CCFFP29 (2008) agreed that at this stage it was not necessary to ask for additional scientific advice from FAO/WHO and that this issue would be kept under review and may be reconsidered when further scientific advice became available.

CCCF2 (2008) agreed to provisionally endorse the proposed levels, with the recommendation that the levels would require complete review in the coming few years with the view to revising these levels where necessary, when more data became available (ALINORM 08/31/41 para. 31).

CAC31 (2008) adopted the Draft Standard for Raw and Live Bivalve Molluscs at Step 8 with a correction to the scope of the Spanish version by replacing "desbullados" with "abiertos" (ALINORM 08/31/REP. para. 36).

At CCCF11 (2017), the Representative of FAO reported on the development of TEFs for marine biotoxins associated with bivalve molluscs. The Representative recalled that the CCFFP has developed the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008) which includes provisions for several marine biotoxins (eg Saxitoxin (STX) group; Domoic acid (DA) group; Brevetoxin (BTX) group; etc). As each of these biotoxin groups includes several analogues with different toxic potencies, in order to be able to assess the total toxicity in the shellfish extract and thus implement the standard, there was the need to derive TEF for each of the biotoxin groups. At CCFFP's request FAO/WHO organized an expert meeting in 2016 to discuss the issues associated with development of TEFs for marine biotoxins, and to develop a technical paper on the state of science on the subject, including guidance for food safety managers to implement the provisions for biotoxins in the standard at national level. The technical paper has been published and also resulted in an article in an international scientific journal (REP17/CF, para 23)

***Marine biotoxins***

**Brevetoxin group**

Brevetoxins (BTX) can accumulate in shellfish and fish. BTX-toxins can cause neurologic shellfish poisoning (NSP) which is characterized by symptoms and signs such as nausea, vomiting, diarrhea, parasthesia, cramps, bronchoconstriction, paralysis, seizures and coma.

The toxicological database for BTX-toxins is limited, comprising mostly acute toxicity studies. Quantitative data of human poisonings are also very limited. There is some evidence that BTX-2 forms DNA adducts raising concerns about possible carcinogenicity and consequential long term effects. In view of the lack of data, the Joint FAO/IOC/WHO ad hoc Expert Consultation concluded that there is a need for further investigations into the mechanisms of action of BTXs and its analogues, and an accurate assessment of long term effects because of low-dose and/or repeated ingestion of BTXs and its analogues in animal experiments. In particular, studies of the possible health effects of chronic low-level exposure are needed in humans and animals.

**Marine biotoxins****Azaspiracid group**

Reference to JECFA: -

Toxicological guidance value: ARfD 0.04 µg/kg bw (2004; FAO/IOC/WHO ad hoc Expert Consultation)

Synonyms: Abbreviation, AZP

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
Live and raw bivalve molluscs	0.16	Adopted	CXS 292-2008	FFP, CF	Edible parts of bivalve molluscs (the whole part or any part intended to be eaten separately)	Relevant Codex commodity standard is CXS 292-2008.	2)
Live abalone, raw fresh chilled or frozen abalone 1)	No ML	Adopted	CXS 312-2013	FFP			2)

- 1) Abalone from some geographical areas have been found to accumulate certain marine biotoxins. It is up to the Competent Authority (using a Risk Assessment) to determine whether a risk exists in any geographical areas under its control and if so, put in the necessary mechanisms to ensure that the part of the abalone to be consumed, meets with the marine biotoxins level in the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008).
- 2) These MLs are not listed in the current GSCTFF (ver. 2018).

The Joint FAO/IOC/WHO ad hoc Expert Consultation on Biotxin in Bivalve Molluscs (2004) was asked to perform risk assessments for a number of biotoxins that are present in bivalve molluscs. Since exposure to biotoxins generally involves only occasional consumption, and because most of the available toxicological data involve only acute and short-term studies, priority was given to the establishment of an acute reference dose, and generally insufficient data were available to establish a tolerable daily intake. It must be pointed out that the Expert Consultation did not have enough time to fully evaluate epidemiological data or to assess the effects of cooking or processing for deriving the provisional guidance levels/maximum levels for several toxin groups (especially the AZA and STX groups). The Consultation agreed that there is a need for a further in-depth review of these data to better derive the guidance levels/maximum levels.

CCFFP29 (2008) agreed that at this stage it was not necessary to ask for additional scientific advice from FAO/WHO and that this issue would be kept under review and may be reconsidered when further scientific advice became available.

CCCF2 (2008) agreed to provisionally endorse the proposed levels, with the recommendation that the levels would require complete review in the coming few years with the view to revising these levels where necessary, when more data became available (ALINORM 08/31/41 para. 31).

CAC31 (2008) adopted the Draft Standard for Raw and Live Bivalve Molluscs at Step 8 with a correction to the scope of the Spanish version by replacing “desbullados” with “abiertos” (ALINORM 08/31/REP. para. 36).

At CCCF11 (2017), the Representative of FAO reported on the development of TEFs for marine biotoxins associated with bivalve molluscs. The Representative recalled that the CCFFP has developed the Standard for Live and Raw Bivalve Molluscs (CXS 292-2008) which includes provisions for several marine biotoxins (eg Saxitoxin (STX) group; Domoic acid (DA) group; Brevetoxin (BTX) group; etc). As each of these biotoxin groups includes several analogues with different toxic potencies, in order to be able to assess the total toxicity in the shellfish extract and thus implement the standard, there was the need to derive TEF for each of the biotoxin groups. At CCFFP’s request FAO/WHO organized an expert meeting in 2016 to discuss the issues associated with development of TEFs for marine biotoxins, and to develop a technical paper on the state of science on the subject, including guidance for food safety managers to implement the provisions for biotoxins in the standard at national level. The technical paper has been published and also resulted in an article in an international scientific journal (REP17/CF, para 23)

**Marine biotoxins**

**Azspiracid group**

Azspiracids (AZAs) are a group of shellfish toxins causing AZA poisoning (AZP). AZP is characterized by symptoms such as nausea, vomiting, diarrhea and stomach cramps. AZAs can be found in various species of filter-feeding bivalve molluscs such as oysters, mussels, scallops and clams. Monitoring data shows that mussels are the most affected species for this group of toxins.

The toxicological database for AZAs is limited and comprises mostly studies on the acute toxicity of AZAs. Limited data in humans indicate an LOAEL between 23 and 86 µg/person for acute gastrointestinal effects. The Joint FAO/IOC/WHO ad hoc Expert Consultation established a provisional ARfD of 0.04 µg/kg bw, based on the LOAEL of 23 µg/person and a bodyweight of 60 kg, using a tenfold safety factor to take into consideration the small number of people involved. Because of insufficient data on the chronic effects of AZA, no TDI could be established.

The Joint FAO/IOC/WHO ad hoc Expert Consultation further noted that some preliminary studies indicate the possibility of severe and prolonged toxic effects at low doses. Repeated studies involving administration of AZA by feeding are therefore required. In addition, information on absorption, excretion and metabolism, on long-term carcinogenicity and genotoxicity and reproductive toxicity are needed.

**Marine biotoxins**

**Ciguatoxins**

Reference to JECFA: Joint FAO/WHO Expert meeting on Ciguatera fish poisoning (CFP) (2018)  
 Toxicological guidance value: -  
 Synonyms: Ciguatera toxins, Abbreviation, CTX

Commodity / Product Name	Maximum Level (ML)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML Applies	Notes/Remarks	Notes for CCCF
No ML							

At CCCF11 (2017), the Representative of FAO introduced FAO's and WHO's work on ciguatera fish poisoning (CFP) and current challenges. He noted that CFP was one of the most common food-borne illnesses related to finfish consumption. While its true incidence was not known, it was estimated that 10,000–50,000 people per year suffer from this food borne illness, making it one of the most common types of marine food-borne poisoning worldwide. He highlighted that analytical methods for detection and quantification of ciguatera to-date are not harmonized and it was unclear which, if any, of the available methods of detection would be suitable as routine methods of analysis.

The Representative invited the Committee to consider requesting FAO/WHO for scientific advice, in particular to carry out a risk assessment of ciguatera toxins and based on this provide guidance for the development of risk management options; and to review existing analytical methods for ciguatoxin detection and quantification, with a view to recommending those useful for routine analysis and surveillance.

There was general support for the proposal to request scientific advice from FAO/WHO to allow the Committee to develop appropriate risk management options. Delegations pointed out the importance of this matter to their countries, noting that due to climate change the traditional occurrence areas were changing and that consideration of ciguatoxins should not be limited to C-CTX-1 and P-CTX-1, but also to I-CTX. A delegation noted that their country does not currently recommend routine surveillance and sampling to meet specified MLs as risk management measure, but uses guidelines for outbreak management.

The Committee:

- agreed to request scientific advice from FAO/WHO to allow the Committee to develop appropriate risk management options;
- noted that the in-session WG on the priority list of contaminants and naturally occurring toxicants for evaluation by JECFA would consider this matter further (REP17/CF, paras. 33-38, Appendix XII).

At CCCF12 (2018), JECFA Secretariat highlighted the upcoming meeting of the FAO/WHO joint scientific advice program on Ciguatera Fish Poisoning scheduled for November 2018 and urged countries to explore all opportunities to submit suitable responses to the call for data and call for experts (REP18/CF, para. 16).

Ciguatera fish poisoning (CFP) is caused by the consumption of herbivorous fish that have become toxic from feeding on toxic benthic dinoflagellates (*Gambierdicus toxicus*) or from carnivorous fish that have consumed toxic herbivorous fish that have fed on the dinoflagellate. *Gambierdicus toxicus* is found primarily in the tropics in association with macro algae usually attached to dead corals. More than 400 species of fish are known to be vectors of ciguatera (FAO Food and Nutrition Paper 80, 2004).

Gastrointestinal symptoms involving vomiting, diarrhoea, nausea and abdominal pain (>~50% of cases) typically occur early in the course of the disease and often, but not always, accompany the neurological disturbances. Neurological disturbances invariably occur in ciguatera and include tingling of the lips, hands and feet, unusual temperature perception disturbances where cold objects give a dry-ice sensation, and a severe localized itch of the skin (>~70 percent of cases). These symptoms and a profound feeling of fatigue (90 percent of cases) can occur throughout the illness. Muscle (>80 percent), joint (>70 percent) and teeth aches (>30 percent) occur to varying extents, and mood disorders including depression and anxiety (50 percent) occur less frequently. Severe cases can involve hypotension with bradycardia, respiratory difficulties and paralysis but deaths are uncommon (less than 1 percent according to Lehane, 2000, cited by FAO Food and Nutrition Paper 80, 2004). The low fatality rate (2 percent) appears to arise because fish rarely accumulate



**Marine biotoxins**

**Ciguatoxins**

sufficient levels of ciguatoxin to be lethal at a single meal, perhaps because fish succumb to the lethal effects of higher ciguatoxin levels (Lewis, 2001, cited by FAO Food and Nutrition Paper 80, 2004).

The mechanism of action of ciguatoxins is related to its direct effect on excitable membranes. Such membranes are critical to the function of nerve and muscle, mainly in their ability to generate and propagate action potentials. Ciguatoxins are characterized by their affinity binding to voltage sensitive sodium channels, causing them to open at normal cell resting membrane potentials. This results in an influx of Na<sup>+</sup> ions, cell depolarization and the appearance of spontaneous action potentials in excitable cells. Ciguatoxin acts at the same receptor site (site 5) of the Na<sup>+</sup> channel as brevetoxin, but the affinity of CTX-1 for voltage-dependent Na<sup>+</sup> channels was around 30 times higher than that of brevetoxin, while CTX-4B had about the same affinity as brevetoxin. (Lehane and Lewis, 2000 and De Fouw et al., 2001, cited by FAO Food and Nutrition Paper 80, 2004)

Ciguatoxins are fat soluble and absorption from the gut is rapid and substantial, although an early onset of vomiting and diarrhoea may exist in expelling some of the toxins before they are absorbed. Since cleaning ciguateric fish can cause tingling of the hands and eating them can cause altered sensation in the oral cavity and dysphagia, it would appear that ciguatoxins can penetrate the skin and mucous membranes. The related brevetoxins also have this property. Ciguatoxins are carried in the blood bound to human serum albumin and moderate (unspecified) levels of ciguatoxin in serum of a patient were reported 22 weeks after consuming ciguatoxic fish. Ciguatoxins are also transmitted in breast milk and are able to cross the placenta and affect the foetus. Because of their similar structure, ciguatoxins are supposed to behave in a similar pharmacokinetic manner to brevetoxins. This means that the biliary/faecal route is the major route of elimination for ciguatoxins as was demonstrated for brevetoxins (Lehane and Lewis, 2000, cited by FAO Food and Nutrition Paper 80, 2004).

**Plant toxins****Hydrocyanic acid**

Reference to JECFA:	39 (1992), 74 (2011)
Toxicological guidance value:	ARfD 0.09 mg/kg bw as cyanide (2011, this cyanide-equivalent ARfD applies only to foods containing cyanogenic glycosides as the main source of cyanide PMTDI 0.02 mg/kg bw as cyanide (2011)
Contaminant definition:	See explanatory notes in the column "Notes/Remarks"
Synonyms:	HCN
Related code of practice:	Code of practice for the reduction of hydrocyanic acid (HCN) in cassava and cassava products (CXC 73-2013)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Cassava flour	10	Adopted	CXS 176-1989 2013	CPL CF		The ML is expressed as total hydrocyanic acid. Relevant Codex commodity standards include CXS 176-1989.	
Gari	2	Adopted	CXS 151-1989 2013	CPL CF	Whole commodity	The ML is expressed as free hydrocyanic acid. Relevant Codex commodity standards include CXS 151-1989.	
Sweet cassava		Adopted	CXS 238-2003	FFV		1)	
Bitter cassava		Adopted	CXS 300-2010	FFV		1)	
Natural mineral waters	0.07 mg/l	Adopted	CXS 108-1981	NMW		2)	

- 1) In the absence of a Codex maximum level for hydrogen cyanide, an acceptable maximum level shall be set on a safety basis by the national legislation of the importing country.
- 2) The Standard for Natural Mineral Waters contains the level in the Section 3.2 "Health-related limits for certain substances". CCCF2 (2008) temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41 para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).

Excessive dietary exposure to cyanogenic glycosides has been assessed at JECFA39 (1992). Due to the lack of quantitative toxicological and epidemiological information no safe level of dietary exposure could be determined. However, it was concluded that a level up to 10 mg/kg HCN in the Standard for Edible Cassava Flour (CXS 176-1989) was not associated with acute toxicity.

CAC31 (2008) agreed with the recommendation of CCEXEC59 (2007) to adopt the Draft Standard for Bitter Cassava (a cyanogenic glycoside food) as elaborated by CCFFV). In the Draft Standard the proposed levels for HCN (a breakdown product of cyanogenic glycosides) are indicated as follow: 'bitter varieties of cassava are those that contain more than 50 mg/kg but less than 200 mg/kg HCN (fresh weight basis). In any case, cassava must be peeled and fully cooked before being consumed'. However, CAC31 recognized safety concerns if cassava is consumed without adequate processing; CCCF should consider the safety levels of hydrogen cyanide (HCN) as proposed in the standard with a view to a re-evaluation of cyanogenic glycosides by JECFA (ALINORM 08/31/REP).

CCCF2 (2008) considered the need for a re-evaluation of cyanogenic glycosides by JECFA and agreed to establish an electronic working group to prepare a discussion paper which

**Plant toxins****Hydrocyanic acid**

should include an overview of available data on cyanogenic glycosides with a view to possible re-evaluation by JECFA. (ALINORM 08/31/41, para. 180)

CCCCF3 (2009) agreed to request JECFA to review data available on occurrence of cyanogenic glycosides in foods and feeds, the mechanisms of releasing hydrogen cyanide in the human body, the effects of processing on reducing levels of hydrogen cyanide in the final product, and report back to the Committee in future. (ALINORM 09/32/41, para 108).

JECFA74 re-evaluated cyanogenic glycosides in 2011. The Committee recognized that human exposure to HCN from cyanogenic glycosides in food commodities would be from a combination of intact glycoside and totally degraded glycoside. The Committee concluded that there were no appropriate studies on which a long-term health-based guidance value could be based. However, as the potential toxicity of ingested cyanogenic glycosides was considered to be directly related to the *in situ* generation of HCN, the Committee concluded that animal studies with cyanide compounds could serve as the basis for establishing a PMTDI. Also, an ARfD could be determined.

The Committee established a cyanide-equivalent ARfD of 0.09 mg/kg bw. This ARfD is based on a BMDL<sub>10</sub> for linamarin of 85 mg/kg bw for increased skeletal defects in developing hamster fetuses following acute exposure of maternal animals. Following application of a 100-fold uncertainty factor, the Committee established an ARfD for linamarin of 0.9 mg/kg bw (equivalent to 0.09 mg/kg bw as cyanide). This cyanide-equivalent ARfD applies only to foods containing cyanogenic glycosides as the main source of cyanide.

The Committee noted that the ARfD was exceeded 3-fold for cassava for adults, 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. The available occurrence data for cyanogenic glycosides were deemed not to be appropriate to determine international estimates of dietary exposure to total HCN.

A PMTDI of 20 µg/kg bw was recommended by applying a 100-fold uncertainty factor for interspecies and intraspecies differences to a BMDL<sub>1SD</sub> of 1.9 mg/kg bw per day. This BMDL<sub>1SD</sub> was derived from a 13-week NTP study in which male rats displayed decreased cauda epididymis weights after exposure to sodium cyanide via drinking-water. 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 acute nature of cyanide toxicity and the sensitivity of the effect (i.e. the reduction of absolute cauda epididymis weight).

It was noted that, based on national estimates of chronic dietary exposure to total HCN, there is potential to exceed the PMTDI for populations reliant on cassava as a staple food: between 1- and 3-fold in children and between 1- and 2-fold in adults. This would also be possible for populations not reliant on cassava: between 1- and 5-fold for children and between 1- and 3-fold for adults.

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 did 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 were no estimates of dietary exposure available that exceed the ARfD or PMTDI. This was supported by the maximum amount of food that could 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.

The Committee recommended that further research is needed to quantify how nutritional factors ultimately contribute to the human diseases observed in populations whose diets consist mainly of improperly processed cassava. There is also need for more extensive occurrence data for cyanogenic glycosides including data showing the ratio of cyanogenic glycosides to cyanohydrins to HCN in raw and processed foods containing cyanogenic glycosides. Distributions of occurrence data could then be used for probabilistic dietary exposure assessments. More consumption data for cassava and cassava products from a broader range of countries would enable more detailed estimates of dietary exposure to be conducted or refined.

CCCCF6 (2012) agreed to establish an electronic Working Group led by Australia and co-chaired by Nigeria to start new work on a COP and MLs for hydrocyanic acid in cassava and cassava products for comment at Step 3 and consideration by the next session. The Committee agreed that the electronic Working Group would:

- undertake a review of the MLs for hydrocyanic acid in existing Codex commodity standards for bitter cassava and sweet cassava with a view of the possible revision of these MLs and the establishment of new MLs for additional commodities, such as ready-to-eat cassava chips;

**Plant toxins****Hydrocyanic acid**

- develop a code of practice to reduce the presence of hydrocyanic acid in cassava in which the agricultural aspects and the methods of processing are addressed; and
- identify methods of analysis suitable for analysis of hydrocyanic acid in foods (REP12/CF, paras. 165-167).

CCCF7 (2013) agreed to discontinue work on the revision or establishment of MLs for cassava and cassava products and to inform CAC36 accordingly. The Committee agreed to transfer the MLs for HCN for cassava flour and gari to the GSCTFF with the current descriptors for the content of HCN in these products. In taking this decision, the Committee agreed to introduce consequential amendments to the standards for edible cassava flour and gari to remove these MLs from the standard and to include a general reference to the GSCTFF in the section on contaminants. Along these lines, the Committee also agreed to make a consequential amendment in the section on contaminants in the Standard for Sweet Cassava to refer the ML for HCN to the national legislation of the importing country (REP13/CF, paras. 87-88 and Appendix V).

CAC36 (2013) approved discontinuation of work on proposed draft maximum levels hydrocyanic acid in cassava and cassava products and adopted consequential amendments to the Standard for Edible Cassava Flour, Gari and Sweet Cassava.

CCCF7 agreed to forward the proposed draft Code of practice for the reduction of hydrocyanic acid (HCN) in cassava and cassava products to CAC36 for adoption at Step 5/8 (REP13/CF, para. 92).

CAC36 adopted the Code of practice for the reduction of hydrocyanic acid in cassava and cassava products.

CCCF11 (2017) considered the proposal by CCAFRICA on an ML for HCN in fermented cooked cassava-based products and noted the following comments:

- It is inappropriate to apply the ML for gari to other fermented cooked cassava based-products without considering more information on occurrence of HCN in fermented cassava products, influence of processing such as fermentation and cooking on the level of HCN in the final product. Different types Fermented cooked cassava-based products and consumption patterns have to be considered to represent all fermentation processes worldwide.
- There is a need to harmonize the expression of HCN, noting that it is expressed as free HCN in the case of gari, but as total HCN in the case of cassava flour.
- The GSCTFF states that MLs should only be established if there is a health concern and/or a trade issue;
- The COP provides guidance on how to produce cassava products with safe concentrations of HCN.

The Committee agreed to establish an EWG led by Nigeria to prepare a discussion paper to advise on the need and feasibility to establish an ML for HCN in all fermented cassava products and address the issue of harmonizing the expression of HCN levels, i.e. free or total HCN. The Codex Secretariat would issue a circular letter (CL) requesting data on occurrence of HCN and other relevant information in fermented cassava products. The Committee also agreed that the EWG would consolidate information on mycotoxin occurrence in these products, and other relevant information, to allow CCCF to determine if mycotoxin contamination in these products would be a health concern in order to provide a more informed reply to CCAFRICA (REP17/CF, paras. 10-15)

CCCF12 (2018) recalled that CCCF11 agreed to establish an EWG chaired by Nigeria to address HCN and mycotoxin contamination in cassava and cassava-based products and deferred the discussion until next year in the absence of the EWG Chair to present the item at the current session and encouraged Codex members to continue submitting data to GEMS/Food (REP18/CF, para. 125).

Cyanogenic glycosides (CG) may be defined chemically as glycosides of the beta-hydroxy nitriles and are secondary metabolites produced by plants. CG occur in at least 2000 plant species of which many are used as food, such as cassava, lima beans, sorghum, almonds, stone fruits, bamboo shoots, flax seed and elderberries. CG can be broken down to hydrogen cyanide (HCN) as a result of enzymatic hydrolysis by beta-glucosidases following structure disruption of plant cells or by the action of gut microflora. The cyanogenic glycoside content of foods is often reported as mg/kg of HCN in the food. Levels of HCN in a respective food may vary depending on variety, growing conditions (altitude, geographical location, seasonal condition) and production conditions. Acute toxicity results when the rate of HCN is such that the metabolic detoxification capacity of the body is exceeded.

The toxicity of a cyanogenic plant depends on the potential that its consumption will produce a toxic concentration of HCN, HCN causing the inhibition of mitochondrial oxidation. This

***Plant toxins***

**Hydrocyanic acid**

will cause energy deprivation and result in non-specific symptoms that reflect oxygen deprivation of the brain and heart, such as headache, nausea, vomiting, dizziness, palpitations, hyperpnoea then dyspnoea, bradycardia, unconsciousness and convulsions, followed by death. Chronic uptake of HCN in sub-acutely toxic doses, may be involved in disturbance of thyroid function and neuropathies. However, suitable long-term toxicity studies are lacking. No ADI or ARfD has been established yet, however, as HCN clearance is rapid and its half life is short, cumulative toxicity is not expected and the appropriate toxicological reference value must reflect acute rather than cumulative toxicity.

**Plant toxins****Pyrrrolizidine alkaloids**

Reference to JECFA:	80 (2015)
Toxicological guidance value:	BMDL <sub>10</sub> (for riddelliine) 182 µg/kg bw/day; MOE for high adult consumers of tea and honey and for average tea consumption by children indicated a concern
Contaminant definition:	Pyrrrolizidine alkaloids
Synonyms:	PA
Related code of practice:	Code of Practice for Weed Control to prevent and reduce Pyrrrolizidine Alkaloid Contamination in Food and Feed (CXC 74-2014)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
	No ML						

CCCF6 (2012) agreed to initiate new work on the development of a Code of practice for weed control to prevent and reduce pyrrrolizidine alkaloid contamination in food and feed. Subject to approval by the Commission, the Committee agreed that the proposed COP would be developed by an electronic Working Group led by the Netherlands for comments at Step 3 and consideration at the next session.

The Committee also agreed that this electronic Working Group would prepare a discussion paper for consideration by the next session on the topics 'Management practices to reduce exposure of animals to PAs', 'Management practices to reduce exposure of food-producing animals to PA-containing plants – livestock and bees' and 'Management practices to reduce presence of PAs in commodities – raw and processed' to explore their possible inclusion in the proposed COP (REP12/CF, paras. 114-115 and Appendix VII). CAC35 (2012) approved the new work (REP12/CAC, Appendix VI).

CCCF7 (2013) agreed to return the Code to Step 2/3 for redrafting, circulation for comments and consideration at the 8th session of the Committee. The Committee also agreed to resume the consideration on management practices to reduce exposure of food-producing animals (livestock and bees) to PAs; and to reduce presence of PAs in commodities (raw and processed) if more information would become available e.g. in 2 or 3 years time (REP13/CF, para. 96 and 112).

The Committee agreed with the recommendations of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for Evaluation by JECFA to maintain Pyrrrolizidine alkaloids in the Priority List (REP13/CF, para 142 and APPENDIX VII).

CCCF8 (2014) agreed to forward the proposed draft COP to Step 5/8 (with omission of Steps 6/7) for adoption by CAC37. The Committee agreed that for the time-being it would keep the reference to the non-exhaustive list of PA-containing plants (Annex I of CX/CF 11/15/14) in the report for further consultation noting that reports of Codex committee meetings are available to Codex members and the general public on the Codex website (REP14/CF, paras. 78-82, Appendix VI). CAC37 adopted the COP at Step 5/8 (REP14/CAC, para. 47, Appendix III).

JECFA80 (2015) evaluated PAs. A systematic review approach was used to gather data. As the approach proved to be very labour intensive and there was insufficient time left before the JECFA meeting, stages of the systematic review subsequent to the title/abstract selection were not performed according to the systematic review protocol, and full text selection was done using the critical appraisal method regularly used in the preparation of JECFA monographs. Because of the narrow time frame between the work on the selection of references and the JECFA meeting, the evaluation could not be completed at the meeting, but the Committee considered the information sufficient to determine an approach for the evaluation and to agree upon preliminary results, which will need confirmation later when all studies have been quality assessed and described in detail.

The Committee considered that the genotoxic mode of action does not allow derivation of a health-based guidance value for chronic toxicity and a lower limit on the benchmark dose for a 10% response (BMDL<sub>10</sub>) of 182 µg/kg bw per day for liver haemangiosarcoma in female rats treated with riddelliine was used as the point of departure in an MOE approach. Dietary exposures were estimated based on limited data for exposure to PAs through honey and tea consumption, for adults and children. The calculated MOEs for high adult consumers of tea and honey and for average tea consumption by children indicated a concern.

**Plant toxins**

**Pyrrolizidine alkaloids**

Available data were not sufficient to identify relative potency factors for different 1,2-unsaturated PAs in order to evaluate the possible effects of combined exposure. The Committee considered that acute toxicity is of concern, and data, in particular human case reports, would be reviewed in detail for their potential use in the derivation of dose levels of concern.

CCCF10 (2016) agreed to discuss PAs at CCCF11 once the full JECFA evaluation becomes available. (REP16/CF, paras. 169 and 173)

At CCCF11 (2017), the JECFA Secretariat committed that the monograph on PAs would be published before the CCCF12 and further work on PAs could be considered at the next session (REP17/CF, para. 150)

CCCF12 (2018) did not consider a work on PAs following the JECFA80 evaluation due to unavailability of the monograph.

Pyrrolizidine alkaloids (PAs) are toxins found naturally in a wide variety of plant species. PAs are heterocyclic compounds and most of them are derived from four necine bases: retronecine, heliotridine, otonecine and platynecine; the platynecine type PAs are considered non-toxic. Over 350 different tertiary amine PA structures are known, most of the naturally occurring PAs in plants are esterified necines or alkaloid N-oxides (except for the otonecine-type alkaloids), whereas non-esterified PAs occur less frequently in plants.

PAs are widely distributed natural toxins and affect wildlife, livestock and humans. Human cases of poisoning can result from the direct and deliberate use of toxic plant species as herbal teas or traditional medicines, or direct contamination of foods with PA-containing plants. Animal mediated contamination of food includes transfer of PAs from feed to animal products like milk, and contamination of honey by PA-containing pollen.

PAs have a common toxicity profile; liver is the main target organ of toxicity. Major signs of toxicity in all animal species include various degrees of progressive liver damage (centrolobular hepatocellular necrosis), and veno-occlusive disease. Furthermore, bile duct proliferation, hepatic megalocytosis, and liver fibrosis are reported. Also effects on other organs such as lungs (pulmonary hypertension), the cardiovascular system (cardiac right ventricular hypertrophy) and degenerative injury in the kidneys are seen. IPCS evaluated PAs in 1988. IPCS concluded that a daily intake of PAs as low as the equivalent of 0.01 mg/kg heliotrine may cause disease in humans and that humans might be more sensitive to PA toxicity than rats; however, they stated also that these estimates were of uncertain reliability. Still, it was recommended to minimize exposure if possible. IARC has classified three PAs, lasiocarpine, monocrotaline and riddelliine, as 'possibly carcinogenic to humans' (Group 2B).

**Plant toxins****Scopoletin**

Reference to JECFA: -  
 Toxicological guidance value: -  
 Contaminant definition: -  
 Synonyms: -  
 Related code of practice: -

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

CCNASWP13 (2014) considered the request for determination of safe intake levels for scopoletin in fermented noni juice. The Coordinating Committee agreed to request advice from CCCF on a safe maximum level for scopoletin as well as a method of analysis.

CCCF9 (2015) considered the above request and agreed with an inclusion of of scopoletin for a full risk assessment in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA. (REP15/CF, paras. 145-152, Appendix X).

Scopoletin is a coumarin found in the root of plants in the genus *Scopolia* such as *Scopolia carniolica* and *Scopolia japonica*, in chicory, in *Artemisia scoparia*, in the roots and leaves of Stinging Nettle (*Urtica dioica*), in the passion flower, in Brunfelsia, in *Viburnum prunifolium*, in *Solanum nigrum*, in *Mallotus resinousus*, or and in *Kleinhovia hospita*.



**Other Chemical Contaminants (except radionuclides)****Acrylamide**

Reference to JECFA:	64 (2005), 72 (2010)
Toxicological guidance value:	(Intake estimates: mean 0.001 mg/kg bw/day; high 0.004 mg/kg bw/day)
Margin of exposure (MOE):	morphological changes in nerves (NOEL 0.2 mg/kg bw/day), mean intake 200, high intake 50; MOE mammary tumours in rats (BMDL <sub>10</sub> 0.31 mg/kg bw/day), mean intake 310, high intake 78 MOE Harderian gland tumours in mice (BMDL <sub>10</sub> 0.18 mg/kg bw/day), mean intake 180, high intake 45.)
Related code of practice:	Code of Practice for the Reduction of Acrylamide in Foods (CXC 67-2009)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

JECFA was asked by CCFAC36 (2004) to evaluate acrylamide.

JECFA64 (2005) concluded that a dietary intake of 1 µg/kg/day of acrylamide represents the average for the general population and an intake of 4 µg/kg bw/day represents the high consumers; this includes children. Comparison of these intakes with the NOEL of 0.2 mg/kg bw/day for morphological changes in nerves would provide MOEs of 200 and 50, respectively. Comparison with the NOEL of 2 mg/kg bw/day for reproductive, developmental and other non-neoplastic effects would provide MOEs of 2000 and 500, respectively. For the induction of tumors, the MOE is calculated by comparing those intakes with the BMDL of 0.3 mg/kg bw/day for mammary tumours in rats to be 300 and 75, respectively.

The Committee concluded that adverse effects on morphological changes in nerves and on reproductive, developmental and other non-neoplastic effects are unlikely at the estimated average intakes, but that morphological changes in nerves cannot be excluded for some individuals with very high intakes. It considered the MOEs (induction of tumors - mean and high intakes) to be low for a compound that is genotoxic and carcinogenic and that they may indicate a human health concern. Therefore, appropriate efforts to reduce acrylamide concentrations in food stuffs should continue.

**Recommendations by JECFA64:**

- Acrylamide be re-evaluated when results of ongoing carcinogenicity and long-term neurotoxicity studies become available.
- Work should be continued on using PBPK modeling to better link human biomarker data with exposure assessments and toxicological effects in experimental animals.
- Appropriate efforts to reduce acrylamide concentrations in food should continue.
- In addition, the Committee noted that it would be useful to have occurrence data on acrylamide in foods as consumed in developing countries. This information will be useful in conducting intake assessments as well as considering mitigation approaches to reduce human exposure (Sixty-fourth Report of the Joint FAO/WHO Expert Committee on Food Additives, pages 8-26).

CCFAC37 (2005) agreed to revise the discussion paper which would include an outline of a COP and a project document for starting new work on the elaboration of the COP, taking into account the JECFA64 evaluation of acrylamide; national mitigation strategies; and the role of food processors, catering services, and consumers (ALINORM 05/28/12, paras. 193- 196).

CCFAC38 (2006) agreed to forward to CAC for approval as new work the project document on the elaboration of a Code of practice for the reduction of acrylamide in food, and agreed that, subject to the approval of CAC, an electronic working group would elaborate an initial draft COP for comment at Step 3 (ALINORM 06/29/12, paras. 184 & 185).

CCCF1 (2007) decided to maintain recommendations to national authorities on consumer practices since consumer practices were considered to add significantly to acrylamide exposure and similar recommendations had already been incorporated in other codes of practice.

The Committee, noting the opinion of the ad hoc physical working group that the document was not yet ready for advancement in the Codex Procedure, agreed that a revised proposed draft should be prepared, taking account of additional data and information which would become available in the coming year from ongoing studies. The Committee agreed to return

**Other Chemical Contaminants (except radionuclides)****Acrylamide**

the proposed draft COP to Step 2 for redrafting by an electronic working group chaired by the USA and the UK on the basis of the written comments received and the discussion in the ad hoc Working Group and the in CCCF1, with a view to circulation for comments at Step 3 and consideration at Step 4 at the next session of the Committee (ALINORM 07/30/41, paras. 95, 96, 97).

CCCF2 (2008) agreed to forward the proposed draft COP, which focus mainly on foods produced from potatoes and cereals reflecting their importance in terms of dietary exposure to acrylamide, to CAC31 for adoption at Step 5 (ALINORM 08/31/41, paras. 75 and 95).

CAC31 adopted the proposed draft COP and advanced it to Step 6 (ALINORM 08/31/REP, para. 65).

JECFA72 (2010) noted that neither the estimated average acrylamide exposure for the general population (0.001 mg/kg bw per day) nor the exposure for consumers with high dietary exposure (0.004 mg/kg bw per day) had changed since the sixty-fourth meeting. The MOE calculated relative to the no-observed-adverse-effect level (NOAEL) of 0.2 mg/kg bw per day for morphological changes in nerves in rats therefore remains unchanged. For the general population and consumers with high dietary exposure, the MOE values are 200 and 50, respectively. Consistent with the conclusion made at the 64<sup>th</sup> meeting, the Committee noted that while adverse neurological effects are unlikely at the estimated average exposure, morphological changes in nerves cannot be excluded for individuals with a high dietary exposure to acrylamide.

When average and high dietary exposures are compared with the BMDL<sub>10</sub> (the BMDL for a 10% response) of 0.31 mg/kg bw per day for the induction of mammary tumours in rats, the MOE values are 310 and 78, respectively. For Harderian gland tumours in mice, the BMDL<sub>10</sub> is 0.18 mg/kg bw per day, and the MOE values are 180 and 45 for average and high exposures, respectively. The Committee considered that for a compound that is both genotoxic and carcinogenic, these MOEs indicate a human health concern. The Committee recognized that these MOE values were similar to those determined at the 64<sup>th</sup> meeting and that the extensive new data from cancer bioassays in rats and mice, physiologically based pharmacokinetic modelling of internal dosimetry, a large number of epidemiological studies and updated dietary exposure assessments support the previous evaluation.

To better estimate the cancer risk from acrylamide in food for humans, the Committee recommended that longitudinal studies on intra-individual levels of acrylamide and glycidamide hemoglobin adducts be measured over time in relation to concurrent dietary. Such data would provide a better estimate of acrylamide exposure for epidemiological studies designed to assess the risk associated with consumption of certain foods.

CCCF3 (2009) agreed to forward the draft Code of practice for the reduction of acrylamide in foods to CAC32 for adoption at Step 8 (ALINORM 09/32/41, para. 64 and Appendix IV). CAC32 (2009) adopted the Code of practice for the reduction of acrylamide in foods (ALINORM 09/32/REP, Appendix III).

CCCF4 (2010) discussed Part 2 of the report of the in-session Working Group on Priorities: Follow-up on results of JECFA evaluations for CCCF, and agreed with the recommendations:

- To encourage the use of the COP to reduce acrylamide formation;
- To stimulate research on the mitigation measures and their impact on acrylamide production;
- To reconsider work on acrylamide in future to allow sufficient time for the implementation of the COP.

Acrylamide is an important industrial chemical used since the mid 1950s as a chemical intermediate in the production of polyacrylamides, which are used as flocculants for clarifying drinking water and other industrial applications. Recently, attention was drawn to the formation of acrylamide at high temperatures during frying, baking or other thermal processing of a variety of foods, typically plant commodities high in carbohydrates and low in protein. In this Maillard reaction, the most important precursor amino acid asparagine reacts with reducing sugars. After its formation acrylamide seems to be stable in a large majority of the affected foods. Acrylamide levels in commodities are highly variable because its formation is dependent on the exact conditions of time and temperature used to heat process the food and the composition of the food. Research on acrylamide formation is ongoing; mitigation could be accomplished by adjustments in existing production procedures.

In experimental animals, acrylamide is rapidly and extensively absorbed following oral administration and widely distributed to the tissues, as well as the fetus. It has also been found in breast milk. The major metabolite is glycidamide, formed by a CYP2E1-mediated oxidation, which is much more reactive with DNA than acrylamide itself. Acrylamide and metabolites

**Other Chemical Contaminants (except radionuclides)**

**Acrylamide**

are rapidly eliminated via urine.

The neurotoxicity of acrylamide in humans is well-known from occupational and accidental exposures. In addition, experimental studies in animals have shown reproductive, genotoxic and carcinogenic properties. The nervous system is the principal site of toxic actions of acrylamide, which is expressed by morphological changes. Degenerative changes in nerves (NOEL 0.2 mg/kg/day, based on a study in rats). Reproduction studies showed reduced fertility, adverse effects on sperm-count and -morphology in male rodents, however, no adverse effects have been observed in female rodents (NOEL 2 mg/kg/day). Furthermore, acrylamide was not teratogenic in mice or rats. Acrylamide is genotoxic, however, metabolism to glycidamide appears to be a prerequisite.

Acrylamide was evaluated by IARC in 1994 and classified as probably carcinogenic to humans on the basis of a positive cancer bioassay and evidence that acrylamide is efficiently biotransformed to the genotoxic metabolite glycidamide. BMDL for 10% extra risk of tumors was established by JECFA to be 0.3 mg/kg/day.

A wide range of commodities may be contaminated with acrylamide, such as cereals and cereals-based products, fish and seafood, meat and offals, milk and milk products, nuts and oilseeds, pulses, potato and potato products, coffee, sugars and honey, vegetables.

Studies conducted in Sweden in 2002 showed the formation of high levels of acrylamide during frying or baking of a variety of food.

**Other Chemical Contaminants (except radionuclides)****Acrylonitrile**

Reference to JECFA:	28 (1984)
Toxicological guidance value:	Provisional Acceptance (1984, the use of food-contact materials from which acrylonitrile may migrate is provisionally accepted on condition that the amount of the substance migrating into food is reduced to the lowest level technologically attainable.)
Contaminant definition:	acrylonitrile (monomer)
Synonyms:	2-Propenenitrile; vinyl cyanide (VCN); cyanoethylene; abbreviations, AN, CAN.
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Guideline Level (GL) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Food	0.02	Adopted	2006	FAC			

Guideline Levels for Acrylonitrile in Food and Vinyl Chloride Monomer in Food and Food Packaging Materials were adopted by CAC19 (1991) with the understanding that the AOAC and the ISO would be requested to elaborate appropriate sampling plans and methods of analysis. (ALINORM 91/40, paras. 203-204)

CAC29 (2006) adopted the GSCTF, including Schedule 1 and revoked Guideline Levels for Vinyl Chloride Monomer and Acrylonitrile in Food and Packaging Material (CXG 6-1991) (ALINORM 06/29/41).

Acrylonitrile monomer is the starting substance for the manufacture of polymers which are used as fibres, resins, rubbers and also as packaging material for foods. Acrylonitrile is not known to occur as a natural product. Acrylonitrile is classified by IARC as possibly carcinogenic to humans (Group 2B). Polymers derived from acrylonitrile may still contain small amounts of free monomer. Migration of possibly harmful substances from food contact materials has been discussed in the CCFA/CCFAC in the period 1986-1991. (IARC Vol. 71, 43- 108)

**Other Chemical Contaminants (except radionuclides)****Benzene**

Reference to JECFA: This compound has not been evaluated by JECFA

Toxicological guidance value: -

Contaminant definition: -

Synonyms: -

Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Guideline Level (GL) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
	No ML						

In the first edition of the WHO Guidelines for Drinking-water Quality, published in 1984, a health-based guideline value of 0.01 mg/liter was recommended for benzene based on human leukaemia data from inhalation exposure applied to a linear multistage extrapolation model. The 1993 Guidelines estimated the range of benzene concentrations in drinking-water corresponding to an upper-bound excess lifetime cancer risk of 10<sup>-5</sup> to be 0.01–0.08 mg/liter based on carcinogenicity in female mice and male rats. As the lower end of this estimate corresponds to the estimate derived from epidemiological data, which formed the basis for the previous guideline value of 0.01 mg/liter associated with a 10<sup>-5</sup> upper-bound excess lifetime cancer risk, the guideline value of 0.01 mg/liter was retained.

CCCF3 noted that benzene in soft drinks was not a major contributor to overall benzene exposure and in view of the considerable guidance available to industry to limit formation of benzene in soft drinks, in particular, the guidance by the International Council of Beverages Associations (ICBA) which is available in various languages, a COP was not necessary at this time. The Committee, however, agreed to encourage member countries, especially those in the tropics to continue data collection on the occurrence of benzene in soft drinks (ALINORM 09/32/41, para 104).

Benzene is colourless liquid at room temperature, which evaporates rapidly. It is slightly soluble in water and miscible with most organic solvents. Benzene is a naturally occurring chemical found in crude petroleum, but it is also produced in large quantities. Emissions arise during the processing of petroleum products, in the coking of coal, during the production of industrial solvents (toluene, xylene and other aromatic compounds) and from its use in consumer products as a chemical intermediate and as a component of gasoline (petrol). Human exposure occurs mainly by outdoor environmental levels of benzene (gasoline, industrial solvents), cigarette smoke, and occupationally when not protected.

In EHC 150 (1993) it is reported that benzene appears to be of low acute toxicity after oral exposure in various animal species. There are only a limited number of oral studies available on benzene. Exposure to benzene at high levels (by inhalation at the working place) is dose-dependently associated with bone marrow depression resulting in anemia. Benzene can easily cross the placental barrier, however, numerous animal experiments show no evidence of benzene being teratogenic even at maternally toxic doses, though in inhalation studies fetal toxicity has been demonstrated in mice and rats. Neurotoxicity and immunotoxicity of benzene has not been well studied in experimental animals or humans. IARC (1987) classified benzene in Group 1 (human carcinogenic).

**Other Chemical Contaminants (except radionuclides)****Chloropropanols**

Reference to JECFA:	41 (1993; for 1,3-dichloro-2-propanol only), 57 (2001), 67 (2006), 83 (2016; for 3-MCPD esters)
Toxicological guidance value:	Group PMTDI 4 µg/kg bw (2016, for for 3-MCPD and 3-MCPD esters singly or in combination (expressed as 3-MCPD equivalents)) Establishment of tolerable intake was considered to be inappropriate for 1,3-dichloro-2-propanol because of the nature of the toxicity (tumorigenic in various organs in rats and the contaminant can interact with chromosomes and/or DNA.) BMDL <sub>10</sub> cancer, 3.3 mg/kg bw/day (for 1,3-dichloro-2-propanol); MOE, 65 000 (general population), 24 000 (high level intake, including young children)
Contaminant definition:	3-MCPD
Synonyms:	Two substances are the most important members of this group: 3-monochloropropane-1,2-diol (3-MCPD, also referred to as 3-monochloro-1,2-propanediol) and 1,3-dichloro-2-propanol (1,3-DCP)
Related code of practice:	Code of Practice for the Reduction of 3-Monochloropropane-1,2-diol (3-MCPD) during the Production of Acid-Hydrolyzed Vegetable Protein (Acid-HVPs) and Products that Contain Acid-HVPs (CXC 64-2008)

Commodity / Product Name	Maximum Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Liquid condiments containing acid-hydrolyzed vegetable protein	0.4	Adopted	2008	CF		The ML does not apply to naturally fermented soy sauces.	

JECFA57 (2001) noted that the dose that caused tumours in rats (19 mg/kg bw/day) was about 20,000 times the highest estimated intake of 1,3-DCP by consumers of soya sauce (1mg/kg bw/day). The available evidence suggests that 1,3-DCP is associated with high concentrations of 3-MCPD in food. Regulatory control of the latter would therefore obviate the need for specific controls on 1,3-DCP. (57th Report of the Joint FAO/WHO Expert Committee on Food Additives, pages 118-121)

High levels of chloropropanols (up to 100 mg/kg and more) have especially been found in products like non-traditionally fermented soy sauces and hydrolyzed vegetable proteins (HVP). There is an obvious connection with the conditions of the production method; levels of chloropropanols in these products are shown to be declining in the last decade since the problem was noticed and measures have been taken to reduce the formation of chloropropanols. These compounds have also been found, however, in many other foods, including baked goods, bread, cooked/cured meat/fish and malt ingredients. There are (inconclusive) indications that cooking/grilling (high temperature treatment) could result in some formation of 3-MCPD. Also the resins in packaging materials and paper used for processing of food may contain 3-MCPD and could contribute to exposure via food, this has led to the development of resins with significantly lower levels of 3-MCPD. The available evidence suggests that 1,3-DCP occurs at lower levels than 3-MCPD in soy sauce (and related products) and in acid-HVP food ingredients. However, in meat products the concentrations of 1,3-DCP are generally higher than the levels of 3-MCPD as concluded at the JECFA57. Further information is required on the levels of chloropropanols in foods and food ingredients, on the dietary exposure to these compounds, on the origin and formation and on production methods which can be utilized to avoid chloropropanol contamination of foodstuffs.

CCFAC37 (2005) agreed to request JECFA to conduct an exposure assessment for chloropropanols from all sources (ALINORM 05/28/12, para. 189).

JECFA67 (2006) estimated the average exposure to 3-MCPD (at the national level in a wide range of foods including soya-sauce and soya-sauce related products) to be 1% to 35% of the PMTDI in the general population. For consumers at the 95<sup>th</sup> percentile the estimated intakes ranged from 3% to 85%, and for young children up to 115% of the PMTDI. The Committee noted that a reduction in the concentration of 3-MCPD in soya sauce and related products made with acid-HVP could substantially reduce the intake of this contaminant by certain consumers.

The Committee concluded that the critical effect of 1,3-DCP is carcinogenicity. Negative results were found in two new studies on genotoxicity in vivo. However, limitations in these studies, positive findings in in vitro test for genotoxicity as well as lack of knowledge on the modes of action operative at the various tumor locations led the Committee to the conclusion

**Other Chemical Contaminants (except radionuclides)****Chloropropanols**

that a genotoxic mode of action could not be excluded.

The estimated intake of 1,3-DCP was calculated at 0.051 µg/kg bw/day and 0.136 µg/kg bw/day, respectively for the general population and the high-level intake (including young children). Comparison of these intakes with the lowest BMDL<sub>10</sub> of 3.3 mg/kg bw/day (incidence data on tumour-bearing animals for all treatment-affected locations) resulted in a margin of exposure (MOE) of approximately 65,000 and 24,000, respectively. Based on these MOEs the Committee concluded that the estimated intakes of 1,3-DCP were of low concern for human health.

The Committee recommended that studies should be undertaken to evaluate the intake or toxicological significance of fatty acid esters of 3-MCPD, which have been reported to be present in foods.

CCCF8 (2014) agreed with the recommendations of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for Evaluation by JECFA to maintain 3-MCPD esters in the Priority List (REP14/CF, paras. 126 and 130 and APPENDIX XIII).

JECFA83 (2016) evaluated 3-MCPD esters in response to a request from CCCF8. (JECFA/83/SC) (see 3-MCPD esters)

**Discussions on MLs**

A position paper was written; CCFAC35 (2003) agreed that the paper should be revised on the basis of the discussions and of submitted comments and data (ALINORM 03/12A, para. 179). The setting of MLs for 3-MCPD in foodstuffs was asked to be considered at CCFAC35. CCFAC could not reach a consensus on a ML of 1 mg/kg for acid-HVP soy sauce as proposed, and deferred the elaboration of MLs in different foodstuffs until its next session; the revised position paper should include proposals for the elaboration of MLs for chloropropanols in relevant foods (ALINORM 03/12A, paras. 173-179).

CCFAC36 (2004) agreed to commence work on the establishment of a maximum level for 3-MCPD in acid-HVPs and acid-HVP containing products subject to approval as new work. In addition, CCFAC agreed that a working group would prepare an updated discussion paper (ALINORM 04/27/12, paras. 193-194).

CCFAC37 (2005) agreed to use as a starting point a maximum level of 0.4 mg/kg for 3-MCPD in liquid condiments containing acid-HVP (excluding naturally fermented soya sauce). Due to the need to better define the products for which maximum levels should be set, the Committee agreed to prepare a discussion paper that will define the different acid HVP containing products and collect information on other products that contain 3-MCPD (ALINORM 05/28/12, paras. 188 and 189).

CCFAC38 (2006) agreed to update the discussion paper in view of the results of the JECFA evaluation and other information relevant for discussions on the Maximum Levels and to maintain the proposed draft Maximum Level at Step 4 (ALINORM 06/29/12, paras. 176 and 177).

CCCF1 agreed to forward the proposed draft ML of 0.4 mg/kg to CAC30 for adoption at Step 5. It was agreed that the draft ML should be further considered in light of finalization and implementation of the Codex of Practice for the Reduction of 3-MCPD during the Production of Acid-Hydrolyzed Vegetable Proteins (acid-HVPs) and Products that Contain Acid-HVPs (ALINORM 07/30/41).

**Discussions on COP**

CCFA37 (2005) agreed to forward to the Commission for approval as new work the project document on the elaboration of a Code of practice for the reduction of chloropropanols during the production of acid HVPs and products that contain acid HVPs and pending the approval of the Commission, to elaborate the proposed draft COP (ALINORM 05/28/12, para. 183).

CCFAC38 (2006) agreed to urge professional organisations and governments to provide additional data on measures to reduce the presence of chloropropanols in acid HVP produced under industrial conditions, thereby considering, in particular, that which was feasible from an organoleptic point-of-view and the Committee also agreed to revise the proposed draft. In revising the COP, the electronic Working Group should consider revision of the title to specifically refer to 3-MCPD, on account of the co-occurrence of 3-MCPD and other chloropropanols (ALINORM 06/29/12, paras. 172 and 173).

**Other Chemical Contaminants (except radionuclides)**

**Chloropropanols**

CCCF1 (2007) agreed to most of the amendments proposed by the ad hoc physical working group and two additional changes and forwarded the proposed draft COP, as amended at the session, to CAC30 for adoption at Step 5 (ALINORM 07/30/41, paras. 92-93).

CAC30 (2007) adopted the proposed draft Code and ML at Step 5 (ALINORM 07/30/REP, paras. 80 and 94).

CAC31 (2008) adopted the Code of practice for the reduction of 3-MCPD during the production of acid-HVPs and products that contain acid- HVPs The Committee also adopted the draft Maximum Level of 0.4 mg/kg for 3-MCPD in Liquid Condiments containing acid-HVPs (Excluding Naturally Fermented Soy Sauce) at Step 8 (ALINORM 08/31/REP, para. 24 and APPENDIX XII).

Chloropropanols can be formed in foods as a result of specific processing and storage conditions. The main source is acid hydrolyzation of vegetable proteins for the production of savoury food ingredients (e.g. soy sauce). In this process the use of hydrochloric acid at high temperatures can result in chlorination of lipids present in the protein starting materials. 3- MCPD has been shown to be a precursor for 1,3-DCP-formation and control of the levels of 3-MCPD is expected to obviate the need for specific control on 1,3-DCP.

Toxicity of 3-MCPD:

3-MCPD crosses the blood-testis barrier and the blood-brain barrier and is widely distributed in the body fluids. The parent compound is partly detoxified by conjugation with glutathione, resulting in excretion of the corresponding mercapturic acid, and is partly oxidized further to oxalic acid. Intermediate formation of an epoxide has been postulated but not proven. The incidence of tubule hyperplasia in the kidneys of treated rats was the most sensitive end-point for deriving a tolerable intake. This effect was seen in the long-term study of toxicity and carcinogenicity in rats in a dose-related manner. 3-MCPD is neither genotoxic in vitro at concentrations at which other toxic effects are observed, nor genotoxic in vivo. (Fifty-seventh Report of the Joint FAO/WHO Expert Committee on Food Additives, pages 114-118)

Toxicity of 1,3-DCP:

Although only a few studies of kinetics, metabolism, short- and long-term toxicity and reproductive toxicity were available for evaluation, the results clearly indicated that 1,3-dichloro-2- propanol was genotoxic in vitro, was hepatotoxic and induced a variety of tumours in various organs in rats. JECFA concluded that it would be inappropriate to estimate a tolerable intake because of the nature of the toxicity observed:

- The results of the long-term study of toxicity and carcinogenicity showed significant increases in the incidences of both benign and malignant neoplasms in at least three different tissues.
- It has been shown unequivocally that this contaminant can interact with chromosomes and/or DNA; however, the tests were confined to bacterial and mammalian test systems in vitro, and there were no data on intact mammalian organisms or humans (57th Report of the Joint FAO/WHO Expert Committee on Food Additives, pages 118-121).



**Other Chemical Contaminants (except radionuclides)****3-MCPD esters**

Reference to JECFA:	83 (2016) (see also Chloropropanols)
Toxicological guidance value:	Group PMTDI 4 µg/kg bw (2016, for for 3-MCPD and 3-MCPD esters singly or in combination (expressed as 3-MCPD equivalents))
Contaminant definition:	-
Synonyms:	abbreviation, MCPDE
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001) Code of Practice for the Reduction of 3-Monochloropropane-1,2-diol (3-MCPD) during the Production of Acid-Hydrolyzed Vegetable Protein (Acid-HVPs) and Products that Contain Acid-HVPs (CXC 64-2008)

Commodity / Product Name	Guideline Level (GL) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

JECFA67 (2006) evaluated 3-MCPD and noted that it has been reported that fatty acid esters of 3-MCPD are present in foods, but there were insufficient data to enable either their intake or toxicological significance to be evaluated. The Expert Committee recommended that studies be undertaken to address this question.

At CCCF2 (2008), Germany reported that recent data show levels of MCPD esters in refined vegetable oils that may lead to exceeding of the PMTDI for 3-MCPD, if assuming full hydrolysis and uptake. The Committee agreed to include 3-MCPD ester in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA, but not to assign a high priority, due to the fact that there were currently only limited data available and kinetic studies and collection of exposure data were still ongoing.

JECFA83 (2016) evaluated 3-MCPD esters in response to a request from CCCF. The main target organs for 3-MCPD and its esters in rats and for 3-MCPD in mice are the kidneys and the male reproductive organs. 3-MCPD was carcinogenic in two rat strains, but not in mice. No genotoxic potential has been demonstrated in vivo for 3-MCPD. Two long-term carcinogenicity studies with 3-MCPD in rats were identified as pivotal studies, and renal tubular hyperplasia was identified as the most sensitive end-point. The lowest BMDL<sub>10</sub> (restricted log-logistic model) for renal tubular hyperplasia was calculated to be 0.87 mg/kg bw per day for male rats. After application of a 200-fold uncertainty factor, the Committee established a group PMTDI of 4 µg/kg bw for 3-MCPD and 3-MCPD esters singly or in combination (expressed as 3-MCPD equivalents). The overall uncertainty factor of 200 incorporates a factor of 2 related to the inadequacies in the studies of reproductive toxicity. The previous PMTDI of 2 µg/kg bw for 3-MCPD, established at the 57th meeting and retained at the 67th meeting, was withdrawn.

Experimental evidence indicates that 3-MCPD esters are substantially hydrolysed to 3-MCPD in the gastrointestinal tract and elicit toxicity as free 3-MCPD. The Committee therefore based its evaluation on the conservative assumption of complete hydrolysis of 3-MCPD esters to 3-MCPD, also for neonates. The Committee noted that estimated dietary exposures to 3-MCPD for the general population, even for high consumers (up to 3.8 µg/kg bw per day), did not exceed the new PMTDI. Estimates of mean dietary exposure to 3-MCPD for formula-fed infants, however, could exceed the PMTDI by up to 2.5-fold for certain countries (e.g. 10 µg/kg bw per day in the first month of life) (JECFA/83/SC).

Following up the outcome of JECFA83, CCCF11 (2017) agreed to endorse the proposal for new work for adoption by CAC on a Code of practice for the reduction of 3-MCPD esters and glycidyl esters in refined oils and products made with refined oils, especially infant formula and to establish an EWG, chaired by USA and co-chaired by EU and Malaysia to follow-up on this new work (REP17/CF, paras. 150-151 and Appendix X).

CAC40 (2017) approved the new work. (REP17/CAC, Appendix VI).

CCCF12 (2018) agreed:

- that the scope of the COP covers refined oils and food products made with refined oils;
- to forward the COP (with the sections in square brackets related to the points on specific practices on matters such as: low lipase activity, irrigation water, polar solvents, degumming, bleaching clay, or the inclusion of specific references to fish oils) to CAC41 for adoption at Step 5 (Appendix VI); and

**Other Chemical Contaminants (except radionuclides)**

**3-MCPD esters**

- to establish an EWG chaired by the United States of America, co-chaired by EU and Malaysia, to revise the COP based on the comments and information submitted by Codex members and observers and to resolve all outstanding issues in order to submit a new draft for consideration by CCCF13 (REP18/CF, paras. 99-102). CAC41 (2018) adopted the COP at Step 5 with note of comment that some provisions in the COP were based on inappropriate experimental measures while others were not practical, increased production costs and incurred excessive waste water with potential environmental impacts, and risk-management measures to reduce contamination with these chemicals should be science-based, proven to be effective at large scale, and widely applicable (REP18/CAC, paras. 63-64 and Appendix IV).

3-Chloro-1,2-propanediol is formed when chloride ions react with lipid components in foods under a variety of conditions, including food processing, cooking, and storage. The compound has been found as a contaminant in various foods and food ingredients, most notably in acid-hydrolysed vegetable protein and soy sauces.

**Other Chemical Contaminants (except radionuclides)****Dioxins**

Reference to JECFA:	57 (2001)
Toxicological guidance value:	PTMI 70 pg TEQ/kg bw (2001, Including coplanar PCBs)
Synonyms:	Polychlorinated dibenzo-dioxins and -furans
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001) Code of Practice for the Prevention and Reduction of Dioxin and Dioxin-like PCB Contamination in Food and Feeds (CXC 62-2006)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

The situation regarding dioxins has been reviewed in a discussion paper (last version CX/FAC 00/26). CCFAC32 (2000) requested an additional position paper in which recent intake assessments and national regulations regarding dioxins are assembled. This was presented to CCFAC33 (2001). A revision of this document was requested, with also data on dioxin levels in food and feedingstuffs and breast-milk; the latest version is CX/FAC 03/32. CCFAC34 (2002) agreed that it should not draft MLs for dioxins at the time. CCFAC35 (2003) requested a revision of the position paper, including the insertion of a new section to cover ranges of data on background levels of dioxins and dioxin-like PCBs in food and feed.

CCFAC36 (2004) encouraged Codex members to submit data on dioxins and dioxin-like PCBs in foods, and it agreed to request WHO to report in a detailed way to the Committee on the data submitted within three years time. In view of this, CCFAC agreed to discontinue the consideration of the position paper (ALINORM 04/27/12, paras. 188-189).

CAC29 (2006) agreed to invite CCMAS to review the sections on sampling and analytical methods and assess the need for future revisions of the Code, taking into account the comments made at CAC29 (ALINORM 06/29/41, paras. 60-62).

CCMAS29 (2008) agreed that the Germany would lead an EWG in order to update document CX/MAS 06/27/8 in the light of the remarks made by CCCF; answer the questions on the applicability of the methods for the indicated ranges and commodities concerned; review the validation data for the methods; and set criteria for dioxin analysis. (ALINORM 08/31/23 para. 128). CCMAS30 agreed to forward this discussion paper for consideration by CCCF (ALINORM 09/32/23 para.140).

CCCF3 (2009) considered the discussion paper prepared by CCMAS on methods of analysis for dioxins and dioxin-like PCBs, following the earlier request of the Committee in relation to the development of the Code of practice for the prevention and reduction of dioxins and dioxin-like PCBs and further clarification provided on the ranges for the determination of dioxins and dioxin-like PCBs. The document considered the methods currently used and the criteria for the methods, as well as information provided by governments and organizations which participated in the preparation of the discussion paper. The Committee noted that the document provided useful information that could be used by governments at the national level as a reference for the purpose of monitoring contamination by dioxins and dioxin-like PCBs. The Committee recalled its earlier decision not to establish MLs for dioxins in foods and discussed how to proceed further, in view of the lack of new data since 2004 on dioxin and dioxin-like PCB contamination in the GEMS/Foods database at this moment. Several delegations informed the Committee that they had collected data on the occurrence of dioxins in foods and feeds or had initiated surveys for that purpose and indicated that they could send their data to GEMS/Foods. The JECFA Secretary pointed out that very limited data submitted since 2004 in GEMS/Foods and that there was a need for more data originating from different regions in order to consider exposure to dioxins. The Committee invited all countries to submit relevant data to GEMS/Foods and agreed that the question of dioxins and PCBs would not be discussed further in the Committee, with the understanding that it could be reconsidered when relevant data became available (ALINORM 09/32/41 para. 9-13).

CCCF6 (2012) discussed the report of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for evaluation by JECFA. With regard to the request for re-evaluation of dioxins and dioxin-like PCBs, the JECFA Secretariat stated that dioxins were a known public health problem and that it might not be the best use of JECFA resources to perform a re-evaluation, but that it would be important for countries to implement source directed measures to reduce formation and release of dioxins into the environment, thereby reducing human exposure. The Committee agreed to not request a re-evaluation of dioxins and dioxin-like PCBs at this point (REP12/CF, para. 160 and 162).

CCCF9 (2015) discussed the report of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for evaluation by JECFA and agreed to

**Other Chemical Contaminants (except radionuclides)**

**Dioxins**

include dioxins for update of the risk assessment. The Committee noted that this would not be a high priority, considering that extensive re-assessment was being undertaken by national and regional agencies, and as such the JECFA assessment could build on this work once completed (REP15/CF, para. 147-148).

The term dioxins refers to a group of polychlorinated planar aromatic compounds. The group consists of 75 dibenzo-p-dioxins (PCDD) and 135 dibenzofurans (PCDF). The most studied and toxic dioxins are 17 congeners with a 2,3,7,8-chlorosubstitution pattern, of which 2,3,7,8-tetra-CDD (TCDD) is the most toxic and most studied congener. Dioxins are ubiquitously present as contaminants in the environment and in food, be it in minute amounts. Dioxins are lipophilic compounds which bind to sediment and organic matter in the environment and tend to be absorbed in animal and human fatty tissue. They are extremely resistant towards chemical and biological transformation processes and are consequently persistent in the environment and accumulate in the food chain. Dioxins are formed as unwanted by-products in combustion processes or industrial processes. Most of the dioxins enter the environment by emission to air. The Ah receptor is an important factor in the toxicological effects of dioxins. Activation of this receptor can result in endocrine and paracrine disturbances and alterations in cell functions including growth and differentiation.

Developmental neurobehavioral (cognitive) and reproductive effects and immunotoxic effects belong to the most sensitive endpoints of dioxin toxicology. TCDD is classified by IARC as Group 1 human carcinogen. It has been shown to be carcinogenic in several animal species at multiple sites, but TCDD is not an initiator of carcinogenesis and the tumour promotion in animal studies indicated a non-genotoxic mechanism.

The toxic equivalency concept has been developed for application to dioxins in order to assess the toxicity of a mixture of congeners as it exists in practice. Toxic Equivalency Factors (TEFs) have been established in relation to TCDD and the total toxicity of a mixture can thus be calculated as total toxic equivalents (TEQs). It has been shown that also some PCB-congeners (those with a planar dioxin-like structure) have effects on the Ah receptor and thus they are given TEFs and can be combined with the dioxins for the calculation of total TEQ of a sample.

**Other Chemical Contaminants (except radionuclides)****Ethyl carbamate**

Reference to JECFA:	64 (2005)
Toxicological guidance value:	(Intake estimates: from food (=mean) 15 ng/kg bw/day; from food and alcoholic beverages (=high) 80 ng/kg bw/day Margin of Exposure (MOE): cancer (BMDL 0.3 mg/kg bw/day), mean intake 20 000, high intake 3 800.)
Synonyms:	Urethane; abbreviation, EC
Related code of practice:	Code of Practice for the Prevention and Reduction of Ethyl Carbamate Contamination in Stone Fruit Distillates (CXC 70-2011)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

When ethyl carbamate was discussed in CCFAC in 1991, a Danish national TDI of 0.2 µg/kg bw was reported. The intake of a person consuming some of the higher contaminated food products was estimated to be more than 50% of this TDI. Therefore, measures aimed at reducing the EC formation were seen as necessary. No specific health effects by ethyl carbamate in humans related to dietary exposure are reported however.

Some countries mentioned national GLs for EC. No trade problems are reported however. CCFAC27 (1995) decided that no further action was needed at present.

JECFA64 (2005) evaluated the national estimates of intake submitted to the Committee by Denmark, Switzerland, USA (assessments conducted in the early 1990s) and South Korea, Australia, New Zealand (assessments conducted more recently). The committee noted that mitigation measures have been effective in reducing residual concentrations of ethyl carbamate, and that, consequently the older data published in the early 1990s and used to make the initial estimates of intake of ethyl carbamate no longer accurately reflect current intake from alcoholic beverages. The committee estimated the mean intake of ethyl carbamate from food to be approximately 15 ng/kg bw/day, this was based on the relevant foods, including bread, fermented milk products and soy sauce; alcoholic beverages were not included. With the inclusion of alcohol beverages, the estimated intake is 80 ng/kg bw/day. High consumption of stone-fruit brandies could lead to higher intakes of ethyl carbamate.

The Committee concluded that intake of ethyl carbamate from foods excluding alcoholic beverages would be of low concern (MOE: 20 000). However, the MOE from all intakes, food and alcoholic beverages combined (MOE: 3800), is of concern and therefore mitigation measures to reduce concentrations of ethyl carbamate in some alcoholic beverages should be continued. The Committee had concluded that health risks for the general population were low and that only sub-populations consuming a high quantity of specific alcoholic beverages might be exposed to certain health risks (ALINORM 07/30/41, para. 137).

CCFAC37 (2005) observed the matter of ethyl carbamate was relevant but not of a high priority and that, due to the limited resources, it should be taken up at a later stage (ALINORM 05/28/12, para. 41).

CCCF2 (2008) agreed that the Germany would prepare a discussion paper on ethyl carbamate in alcoholic beverages for consideration by the next session of CCCF with a view to determining how and to what extent this matter could be approached within CCCF (ALINORM 08/31/41, para. 191).

CCCF3 (2009) agreed to start new work on a proposed draft Code of practice for the reduction of ethyl carbamate in stone fruit distillates which will not include a signal value subject to approval by the Commission. It further agreed that the Germany would prepare a proposed the draft COP for comments at Step 3 and consideration by the next session of the Committee. (ALINORM 09/32/41, paras. 115 and 116). The proposal for new work was subsequently approved by CAC32 (ALINORM 09/32/REP, Appendix VI).

CCCF5 (2011) agreed to forward the proposed draft COP to CAC34 for adoption at Step 5/8 with omission of Steps 6 and 7 (REP11/CF, para. 26 and Appendix II).

CAC34 (2011) adopted the Code of practice for the prevention and reduction of ethyl carbamate contamination in stone fruit distillates at Step 5/8 (REP11/CAC, Appendix III).

**Other Chemical Contaminants (except radionuclides)****Ethyl carbamate**

Ethyl carbamate can be formed from various substances derived from food and beverages, including hydrogen cyanide, urea, citrulline and other N-carbamyl compounds. Cyanate is probably the ultimate precursor, reacting with ethanol to form the carbamate ester. Over the past years, major reductions in concentrations of EC have been achieved using two approaches: first, by reducing the concentration of the main precursor substances in the food and beverages; second, by reducing the tendency for these precursor substances to react to form cyanate, e.g. by the exclusion of light from bottled spirits. Also, diethylpyrocarbonate, an inhibitor of fermentation, and azodicarbonamide, a blowing agent for sealing gaskets, can form ethyl carbamate. Diethylpyrocarbonate was revoked by JECFA17, azodicarbonamide is not recommended for bottling alcoholic beverages.

Ethyl carbamate is well absorbed from the gastrointestinal tract and is rapidly distributed throughout the body. Elimination is also rapid, with most being excreted as carbon dioxide as studied in mice. CYP2E1 activity is responsible for most of the metabolism of EC to carbon dioxide. EC may also undergo metabolic activation to vinyl carbamate epoxide, which binds covalently to nucleic acids and proteins. Moreover, hydrolysis to ethanol and ammonia may occur.

The acute oral toxicity of EC is low; however, high doses caused anesthesia in rodents. Effects on lung, liver, kidney, heart, spleen, lymph nodes, thymus, bone marrow and ovaries were seen during chronic exposure to EC, as studied in mice and rats. Reproduction studies showed high rates of embryonic/fetal mortality and malformations. Ethyl carbamate is genotoxic and carcinogenic. Single doses, short-term and long-term oral dosing of ethyl carbamate have been shown to induce tumors in all species tested (BMDL 0.3 mg/kg bw/day). IARC classified ethyl carbamate in Group 2B, possibly carcinogenic to humans (1974). No quality data for humans are available.

**Other Chemical Contaminants (except radionuclides)****Furan**

Reference to JECFA:	72 (2010)
Toxicological guidance value:	(Intake estimates: mean 0.001 mg/kg bw/day; high 0.002 mg/kg bw/day, Margin of exposure (MOE): hepatocellular adenomas and carcinomas in female mice (BMDL <sub>10</sub> 0.96 mg/kg bw/day), mean intake 960, high intake 480.)
Contaminant definition:	-
Synonyms:	furfuran
Related code of practice:	-

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

Information available to JECFA72 (2010) suggested that the major route of exposure to furan in the human population is through consumption of heat-treated foods and beverages.

MOEs were calculated at dietary exposures of 0.001 mg/kg bw per day, to represent the average dietary exposure to furan for the general population, and 0.002 mg/kg bw per day, to represent the dietary exposure to furan for consumers with high dietary exposure. This estimate will also cover dietary exposure of children. Comparison of these dietary exposures with the BMDL<sub>10</sub> of 1.3 mg/kg bw, corresponding to 0.96 mg/kg bw per day when adjusted from a 5 day/week dosing schedule to an average daily dose, for induction of hepatocellular adenomas and carcinomas in female mice gives MOEs of 960 and 480 for average and high dietary exposures, respectively. The Committee considered that these MOEs indicate a human health concern for a carcinogenic compound that might act via a DNA-reactive genotoxic metabolite.

The furan levels can be reduced in some foods through volatilization (e.g. by heating and stirring canned or jarred foods in an open saucepan). However, there is currently a lack of quantitative data for all foods, and no information is available on other mitigation methods.

CCCF4 (2010) agreed that a discussion paper prepared by an electronic Working Group, led by USA would be presented to the next session of the Committee for consideration (ALINORM 10/33/41, para. 116).

CCCF5 (2011) agreed that this work could be taken up in the future when more adequate data became available and that at that time the re-establishment of the electronic Working Group to further develop the discussion paper could be considered (REP11/CF, para. 79).

Furan (C<sub>4</sub>H<sub>4</sub>O) (CAS No. 110-00-9) is a highly volatile cyclic ether that can be formed unintentionally in foods during processing from precursors that are natural food components. Furan is hepatotoxic and hepatocarcinogenic in rats & mice; JECFA considered carcinogenicity the critical endpoint for use in human health risk assessment.

**Other Chemical Contaminants (except radionuclides)****Glycidyl ester**

Reference to JECFA:	83 (2016)
Toxicological guidance value:	BMDL <sub>10</sub> : 2.4 mg/kg bw/day (mesotheliomas in the tunica vaginalis/peritoneum in male rats) MOE (adults): mean 8000-24000, high 3000-12000 MOE (Children): mean 2400-12000, high 1100-6000 MOE (Infants): mean 670-24000, high 490-8000
Contaminant definition:	-
Synonyms:	glycidol ester; abbreviation, GE
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

CCCF5 (2011), Germany requested to include glycidyl esters in the 3-MCPD ester evaluation by JECFA. The Committee agreed to include glycidol esters in the priority list of contaminants and naturally occurring toxicants proposed for evaluation by JECFA, but separate from the 3-MCPD esters. (REP11/CF, paras. 91-93)

JECFA83 (2016) evaluated glycidol esters in response to a request from CCCF.

The Committee concluded that glycidol is a genotoxic compound and considered its carcinogenicity as the most sensitive end-point on which to base a point of departure. The lowest BMDL<sub>10</sub> was 2.4 mg/kg bw per day for mesotheliomas in the tunica vaginalis/peritoneum in male rats observed in the NTP (1990) carcinogenicity study. Experimental evidence indicated that glycidyl esters are substantially hydrolysed to glycidol in the gastrointestinal tract and elicit toxicity as glycidol. The Committee therefore based its evaluation on the conservative assumption of complete hydrolysis of glycidyl esters to glycidol, also for neonates. National estimates of dietary exposure were used for determining the margins of exposure. The national dietary exposures were considered to be reliable estimates, as they were based on consumption data from national dietary surveys of which the majority include 2 or more days of data, and the estimates were based on a range of foods in the diet and included the key foods in which glycidol contamination is known to occur – namely, fats and oils. The Committee considered that the lower ends of the ranges of the MOEs for infants, children and adults (670, 2400, 8000) were low for a compound that is genotoxic and carcinogenic and that they may indicate a human health concern. (JECFA/83/SC)

Following up the outcome of JECFA83, CCCF11 (2017) agreed to endorse the proposal for new work for adoption by CAC on a Code of practice for the reduction of 3-MCPD esters and glycidyl esters in refined oils and products made with refined oils, especially infant formula and to establish an EWG, chaired by USA and co-chaired by EU and Malaysia to follow-up on this new work (REP17/CF, paras. 150-151 and Appendix X)

CAC40 (2017) approved the new work. (REP17/CAC, Appendix VI)

CCCF12 (2018) agreed:

- that the scope of the COP covers refined oils and food products made with refined oils;
- to forward the COP (with the sections in square brackets related to the points on specific practices on matters such as: low lipase activity, irrigation water, polar solvents, degumming, bleaching clay, or the inclusion of specific references to fish oils) to CAC41 for adoption at Step 5 (Appendix VI); and
- to establish an EWG chaired by the United States of America, co-chaired by EU and Malaysia, to revise the COP based on the comments and information submitted by Codex members and observers and to resolve all outstanding issues in order to submit a new draft for consideration by CCCF13 (REP18/CF, paras. 99-102).

CAC41 (2018) adopted the COP at Step 5 with note of comment that some provisions in the COP were based on inappropriate experimental measures while others were not practical, increased production costs and incurred excessive waste water with potential environmental impacts, and risk-management measures to reduce contamination with these chemicals



**Other Chemical Contaminants (except radionuclides)**

**Glycidyl ester**

should be science-based, proven to be effective at large scale, and widely applicable (REP18/CAC, paras. 63-64 and Appendix IV).

Glycidol is an epoxide used as a chemical intermediate in the production of functional epoxides, glycidyl urethanes, pharmaceuticals and other products. The IARC (2000) has assessed the carcinogenic potential of glycidol and concluded that glycidol is probably carcinogenic to humans (Group 2A).

Glycidyl esters are compounds formed independently from 3-MCPD esters during the processing of all oils and fats. They are likely formed from the diglycerides naturally present in all oils when heated to high temperatures. They are consequently found in foods that contain refined oils and fats.

**Other Chemical Contaminants (except radionuclides)****Halogenated solvents**

Reference to JECFA:	39 (1992), 51 (1998) (dichloromethane)
Toxicological guidance value:	ADI "should be limited to current uses" (dichloromethane)
Contaminant definition:	halogenated solvent
Synonyms:	Methylene chloride, methylene dichloride
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Olive oils and pomace oils	0.1 (individual) 0.2 (sum)	Adopted	CXS 33-1981	FO		Relevant Codex commodity standard is CXS 33-1981	1)

1) The ML does not listed in the current version of GSCTFF (ver. 2018)

CCCF7 (2013) considered a request from CCFO on the transfer of MLs for halogenated solvents from the Standard for Olive Oils and Pomace Oils (CXS 33-1981) to the GSCTFF and agreed that EU would prepare a discussion paper on what substances were included under the term "halogenated solvents" and whether the MLs in section 5.8 of CXS 33-1981 related to food safety or food quality (REP13/CF, para. 11).

CCCF8 (2014) noted the work done by the EU and was informed that these MLs referred to the use of these substances as processing aids/extraction solvents when such substances were allowed in the production of these oils. It was further noted that JECFA had evaluated halogenated solvents and had limited their use to extraction solvent for spice oleoresins and decaffeination of coffee and tea and that there was no information on presence of halogenated solvents in olive oils or pomace oils from other uses than as extraction solvents, however their use as such was no longer allowed in the production of these oils. In addition, there was no information on potential public health implications resulting from exposure to halogenated solvents in olive oil and olive pomace oils nor information on environmental contamination resulting from the use of these substances in food products.

Following this presentation, the Committee noted that there was no support for the transfer of the levels for halogenated solvents from the Standard for Olive Oils and Pomace Oils (CXS 33-1981) to the GSCTFF, however it agreed to recommend CCFO to maintain these levels in CXS 33-1981 until such time more information on environmental contamination became available that would allow CCCF to make a decision on this matter. EU agreed to follow-up on this issue and report back to the Committee in the future (REP14/CF paras. 122-124).

A halogenated solvent refers to an organic solvent which contains halogenic atoms (chlorine, fluorine, bromine or iodine). Examples include compounds such as bromoform, chloroform and trichloroethylene. Halogenated solvents have been widely used in many industrial and commercial applications due to their excellent ability to dissolve oils, their fast evaporation rates and their chemical stability. Major uses were as dry cleaning fluids, degreasing solvents, electrical cleaning solvents, paint strippers, propellants and refrigerants. However, because halogenated organic solvents are often environmental and health hazards, their use in open applications has now been banned worldwide. They are still widely used by chemical and pharmaceutical industries in closed applications. Some halogenated solvents are naturally occurring, especially in marine environments.

Health effects from direct exposure to halogenated solvents are well known and include toxicity to the nervous system, reproductive damage, liver and kidney damage, respiratory impairment, cancer and dermatitis. Human health effects from low environmental exposures are unknown. Halogenated solvents generally do not persist in soil or water but some of the widely used substances, such as trichloroethene, can contaminate surface and ground water. Also chlorination can result in contamination of water with halogenated solvents, mainly trihalomethanes. For these reasons, maximum levels (ML) for certain halogenated solvents in drinking water have been set by many jurisdictions, including the WHO. (WHO Guidelines for drinking water quality 4th edition—Chapter 8 [http://whqlibdoc.who.int/publications/2011/9789241548151\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241548151_eng.pdf)).

JECFA evaluated dichloromethane in 1992 and specifications have been set and revised by JECFA in 1998. JECFA concluded in its evaluation in 1992 that "the use should be limited to current uses as an extraction solvent for spice oleoresins and the decaffeination of coffee and tea, and for food additives in which previous specifications drawn up by the Committee

***Other Chemical Contaminants (except radionuclides)***

**Halogenated solvents**

included residues of dichloromethane"
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**Other Chemical Contaminants (except radionuclides)****Melamine**

Reference to JECFA: FAO/WHO Expert Meeting (2008)  
 Toxicological guidance value: TDI 0.2 mg/kg bw (2008)  
 Contaminant definition: melamine

Commodity / Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Foods (other than infant formula) and feed	2.5	Adopted	2010	CF		<p>The ML applies to food other than infant formula.</p> <p>The ML applies to levels of melamine resulting from its non-intentional and unavoidable presence in feed and food.</p> <p>The ML does not apply to feed and food for which it can be proven that the level of melamine higher than 2.5 mg/kg is the consequence of</p> <ul style="list-style-type: none"> <li>- authorised use of cyromazine as insecticide. The melamine level shall not exceed the level of cyromazine</li> <li>- migration from food contact materials taking account of any nationally authorised migration limit.</li> </ul> <p>The ML does not apply to melamine that could be present in the following feed ingredients/additives: guanidino acetic acid (GAA), urea and biuret, as a result of normal production process.</p>	
Liquid Infant formula	0.15	Adopted	2012	CF		The ML applies to liquid infant formula as consumed.	
Powdered Infant formula	1	Adopted	2010	CF			

An FAO/WHO Expert Meeting in December 2008 established a tolerable daily intake (TDI) of 0.2 mg/kg body weight for melamine, based on dose–response assessment of subchronic rat studies, modelling of the incidence of bladder stones and application of a safety factor of 200 to account for extrapolation from rats to humans, variation within humans and uncertainties associated with the data. The TDI is applicable to the whole population, including infants, and applicable to exposure to melamine alone.

Available data indicated that simultaneous exposure to melamine and cyanuric acid is more toxic than exposures to each compound individually. Data were not adequate to allow the calculation of a health-based guidance value for this co-exposure. A TDI of 1.5 mg/kg body weight for cyanuric acid had previously been derived by WHO.

#### Maximum Levels for Melamine in Food and Feed

CCCF3 (2009) agreed to start new work on MLs for Melamine in Food and Feed (ALINORM 09/32/41, para. 126 and Appendix X). CAC32 approved this new work.

CCCF4 (2010) agreed to forward the proposed draft maximum levels for liquid infant formula to Step 3 for comments and consideration by the next session (ALINORM 10/33/41, para. 68).

CCCF5 (2011) agreed to forward the proposed draft maximum level for liquid infant formula to CAC34 for adoption at Step 5/8 with omission of Steps 6 and 7 (ALINORM 11/34/41,

**Other Chemical Contaminants (except radionuclides)**

**Melamine**

Appendix III). CAC34 (2011) agreed to adopt the ML at Step 5, to advance to Step 6 for comments and discussion in CCCF.

CCCF6 (2012) agreed to forward the proposed draft maximum level for liquid infant formula to CAC35 for adoption at Step 8 (REP12/CF, para58 and Appendix V). CAC35 (2012) adopted the ML at Step 8 (REP12/CAC, Appendix III).

Melamine is an industrially synthesized chemical used for a wide variety of applications, such as laminates, coatings and plastics. Commercially produced melamine may contain structural analogues, such as cyanuric acid, ammelide and ammeline.

Humans are exposed to melamine and its analogues from a number of different sources, including food and environmental sources. Sources range from breakdown of the pesticide cyromazine which is approved for use in many countries, to migration from approved food packaging material to the adulteration of specific foods from the (mostly non-approved) presence of melamine in animal feed or feed ingredients. Data have shown carry-over from feed to products of animal origin (e.g. milk, eggs, meat), including fish.

Melamine produces crystals in urine when its concentration exceeds a threshold. This results in renal failure from both intrarenal crystal-associated obstruction and an elevation in renal pressure that reduces renal blood flow and glomerular filtration.

**Other Chemical Contaminants (except radionuclides)****Perchlorate**

Reference to JECFA: 72 (2010)  
 Toxicological guidance value: PMTDI 0.01 mg/kg bw  
 Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
	No ML						

JECFA72 (2010) considered appropriate to derive a PMTDI as perchlorate has a very short half-life and is rapidly cleared from the body. The BMDL<sub>50</sub> of 0.11 mg/kg bw per day for inhibition of uptake of radiolabelled iodide by the thyroid in a clinical study in healthy adult volunteers was chosen as the POD for derivation of a PMTDI. As it was based on human data, there was no need to apply any interspecies uncertainty factor. The Committee concluded that it was not necessary to apply an uncertainty factor to account for the short duration of the pivotal study. The Committee concluded that an uncertainty factor of 10 would be appropriate to cover any differences in the general population, including those in potentially vulnerable subgroups. Applying this 10-fold factor to the BMDL<sub>50</sub> and rounding to one significant figure, a PMTDI of 0.01 mg/kg bw was established for perchlorate. The estimated dietary exposures of 0.7 µg/kg bw per day (highest) and 0.1 µg/kg bw per day (mean), including both food and drinking-water, are well below the PMTDI. The Committee considered that these estimated dietary exposures were not of health concern.

CCCF5 (2011) agreed that no follow-up was necessary since no health concern was identified at current estimated levels of exposure from food and drinking water (REP11/CF, para. 99).

The perchlorate ion ( $\text{ClO}_4^-$ ) is very stable in water, and its salts are highly soluble in water. Perchlorate occurs naturally in the environment, in deposits of nitrate and potash, and can be formed in the atmosphere and precipitate into soil and groundwater. It also occurs as an environmental contaminant arising from the use of nitrate fertilizers and from the manufacture, use and disposal of ammonium perchlorate (CAS No. 7790-98-9) used in rocket propellants, explosives, fireworks, flares and air-bag inflators and in other industrial processes. Perchlorate can also be formed during the degradation of sodium hypochlorite used to disinfect water and can contaminate the water supply. Water, soil and fertilizers are considered to be potential sources of perchlorate contamination in food. Potassium perchlorate (CAS No. 7778-74-7) has been used as a human therapeutic medicine to treat thyroid disease. The primary effect of perchlorate is its ability to competitively inhibit uptake of iodide by the thyroid gland.

**Other Chemical Contaminants (except radionuclides)**

**Polybrominated diphenyl ethers**

Reference to JECFA: 64 (2005)  
 Toxicological guidance value: (Intake estimates: mean approximately 4 ng/kg bw/day  
 Based on limited toxicity data, the 64th JECFA concluded that there appeared to be a large MOE for a non-genotoxic compound which, despite the inadequacy of the data on toxicity and intake, gave reassurance that intakes of PBDEs are not likely to be a significant health concern.)  
 Synonyms: PBDEs  
 Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

In 1994, WHO published an Environmental Health Criteria document on PBDEs. Recent analysis of samples from environment and from human collected over the last 3-4 decades demonstrated significant increases in concentrations of PBDEs. CCFAC35 requested to evaluate the potential risks associated with the presence of PBDEs in food.

JECFA64 (2005) noted that the available data on PBDEs were not adequate to allocate a PTWI or PMTDI, because:

- PBDEs represent a complex group of related chemicals and the pattern of PDBE congeners in food is not clearly defined by a single commercial mixture;
- Data are inadequate to establish a common mechanism of action that would allow a single congener to be used as a surrogate for total exposure or, alternatively, as the basis for establishing toxic equivalence factors;
- There is no systematic database on toxicity including long-term studies on the main congeners present in diet, using standardized testing protocols that could be used to define a NOEL for individual PBDEs of importance;
- Several of the reported effects are biological outcomes for which the toxicological significance remains unclear;
- Studies with purified PBDE congeners in vitro have shown a lack of Ah receptor activation, however, many of the adverse effects reported are similar to those found with dioxin-like contaminants, suggesting that some toxicity data may be confounded by the presence of traces of impurities that are potent Ah receptor agonists.

The Committee recognized the preliminary nature of the data on concentrations of PBDEs in food and human milk and estimated the dietary intake for the sum of all measured PBDE congeners to be approximately 4 ng/kg bw/day, while intake by breastfeeding infants could be up to 100 ng/kg bw/day. Adverse effects for PBDE congeners would be unlikely to occur at doses of less than approximately 100 µg/kg bw/day.

Based on limited toxicity data, the Committee concluded that there appeared to be a large MOE for a non-genotoxic compound which, despite the inadequacy of the data on toxicity and intake, gave reassurance that intakes of PBDEs are not likely to be a significant health concern. The committee considered that continuing studies of PBDEs in samples from humans, including human milk, would be useful in assessing the overall exposures to PBDEs in foods and other possible sources.

CCFAC37 (2005) endorsed the recommendations of the ad hoc Working Group on the Contaminants and Toxins that no action was required for PBDEs (ALINORM 05/28/12, para. 41 and Appendix IV).

Polybrominated diphenyl ethers (PBDEs) are anthropogenic chemicals that are added to a wide variety of consumer/commercial products (e.g. plastics, polyurethane foam, textiles) in order to improve their fire resistance. Theoretically, 209 distinct PBDE isomers are possible, however, each commercial mixture usually only contains a limited number of congeners from each homologue group. PDBEs have been produced primarily as three main commercial products (mixtures): pentabromodiphenyl oxide or ether (PentaBDE), octabromodiphenyl oxide or ether (OctaBDE) and decabromodiphenyl oxide or ether (DecaBDE). Some variability in composition is known to exist between products from different manufacturers. The

**Other Chemical Contaminants (except radionuclides)**

**Polybrominated diphenyl ethers**

worldwide demand for PBDEs in 2001 was estimated to be almost 70 000 tonnes, with DecaBDE accounting for almost 80% of the total market.

Absorption of PBDEs is directly related to the extent of bromination of the parent diphenyl ether; as a general rule, greater substitution of bromine leads to a decrease in bioavailability. The metabolism of PBDEs consists of hydroxylation and methoxylation reactions and, in the case of congeners with a higher degree of bromination, oxidative debromination. Faecal excretion appears to be the dominant route of elimination, however, species differences exist. Limited data are available regarding the half-lives, however, preliminary values ranged from 30 to 90 days for the tetra- to hexa-substituted congeners. Moreover, limited pharmacokinetic data are available for humans, however, based on the observed increase in concentrations of PBDEs in tissue in time, PDBEs are absorbed and bioaccumulate.

The acute toxicity of mixtures of PBDEs is low in rodents, however, increased mortality, neurobehavioral effects, changes in gross pathology, induction of enzymes, changes in levels of hormones have been observed. In short-term studies the main effects of mixtures of PBDEs were seen in the liver (enlargement, 'round bodies', vacuolization, necrosis), kidney (hyaline degenerative cytoplasmic changes) and thyroid (hyperplasia). Embryo and fetus may be more sensitive to PBDEs than maternal animals; exposure to OctaBDE mixtures caused an increase in the incidence of developmental abnormalities. The results of the majority of tests for genotoxicity indicated that PBDE mixtures and single congeners are not genotoxic. The only long-term study was conducted with the DecaBDE mixture in mice and rat, however, evidence for the carcinogenicity of DecaBDE is limited. No information is available on the carcinogenic potential of other PBDE mixtures. Available studies in humans are not adequate to evaluate whether exposure to PBDEs is associated with adverse health effects. Some toxicity data may be confounded by the presence of traces of impurities that are Ah-receptor agonists (e.g. dioxin).



**Other Chemical Contaminants (except radionuclides)****Polychlorinated biphenyls**

Reference to JECFA:	35 (PCBs) (1989), 80 (NDL-PCBs) (2015)
Toxicological guidance value:	MOEs for adults ranging from 4.5 to 5000, MOEs for breastfed infants, which may have a body burden up to 2-fold higher than that of adults, would be approximately half of the adult values. The MOEs for children would be expected to be intermediate between those for adults and those for breastfed infants, owing to the initial contribution from breastfeeding and the subsequent lower dietary contribution compared with human milk. (For coplanar PCBs (dioxin-like PCBs), see the toxicological guidance value of Dioxins)
Synonyms:	Abbreviations, polychlorinated biphenyls: PCBs, non dioxin like polychlorinated biphenyls: NDL-PCBs
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001) Code of practice for the prevention and reduction of dioxins and dioxin-like pcb contamination in food and feed (CXC 62-2006)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

PCBs were discussed by JECFA35 (1989); it was difficult to come to clear conclusions about the toxicity of PCBs as such because impurities such as dioxins and related compounds (e.g., PCDFs) probably were present in the PCB-mixtures used for the animal studies. The Committee concluded that 0.04 mg/kg bw was the NOEL in monkey studies. However, because of the limitations of the data and the ill-defined nature of the materials used in the study, no tolerable intake for humans could be established. One of the complications is that humans are exposed to biologically filtered mixtures of congeners, which are rather different from the industrial PCB-mixtures that were used for the studies. No toxicological monograph was prepared (see however EHC 140).

The major foods in which contamination with PCBs can be significant are fish, milk and dairy products, meat and eggs. Because PCBs bioaccumulate, the levels will usually be higher in animals which are higher in the food chain, but local pollution and feed composition may have major influence on the levels in animal products. Humans with a considerable intake of animal fats also may accumulate high levels of PCBs and as a consequence also PCB-levels in breast milk and in human adipose fat may be high. The Committee, however, considered that the advantages to the infant of breast-feeding outweigh any potential hazards due to the PCB-content of breast milk. The Committee recommended that PCB-levels in foods are monitored, preferably by quantifying the most important individual congeners. Safety studies should be carried out on the toxicological potential of the PCB-congeners which are predominantly present in foods. It is evident that in relation to the persistent nature of PCBs and ongoing environmental contamination, it is still valid to pay due attention to PCBs. The Committee pointed out that a long-term goal should be the reduction of PCBs in the diet to a minimum.

PCBs are related to other chlorinated hydrocarbons, such as polybrominated biphenyls (PBBs), polychlorinated terphenyls (PCTs), tetrachlorobenzyltoluenes, and polychlorinated dibenzodioxins and dibenzofurans. Coplanar PCBs were integrated included in the toxicological evaluation of dioxins (see the PTMI of 3.08 Dioxins), but it has to be borne in mind that the toxicological effects of PCBs are broader than the dioxin-related effects. CCFAC discussed PCBs from 1990 to 1994 on the basis of CX/FAC 90/20-Add.1 and further related documents. It was noted that several countries have established MLs for PCBs in food, so that trade issues might arise. Some of these countries have introduced MLs for the sum of some specific PCB-congeners, which is probably the best defined way of analyzing and reporting PCBs. The most important congeners for analysis of the general content of PCBs in foods are usually considered to be IUPAC numbers 28, 52, 101, 118, 138, 153 and 180.

CCFAC also acknowledged that source-directed measures were most important to reduce contamination with PCBs. The Committee agreed in 1992 that it was premature to set (maximum) levels for these contaminants at this stage. The discussions later were focused on dioxins and the dioxin-related PCBs.

FAO and WHO organized an expert consultation on the risks and benefits of fish consumption, taking into consideration the health risks associated with methylmercury (MeHg), dioxin and dioxin-like PCBs (DLC) and the nutritive and health benefits of eating fish, in response to the request of CAC29 (ALINORM 09/32/41, para. 24). The Expert Consultation was held in January 2010. It was concluded that consumption of fish provides energy, protein, and a range of other important nutrients, including the long-chain n-3 poly unsaturated fatty acids (LC n-3 PUFA), that eating fish was part of the cultural traditions of many peoples and that in some populations fish was a major source of food and essential nutrients.

**Other Chemical Contaminants (except radionuclides)****Polychlorinated biphenyls**

The Consultation concluded that among the general adult population, consumption of fish, particularly oily fish, lowers the risk of coronary heart disease (CHD) mortality and that potential cancer risks of DLCs were well below established CHD benefits. At levels of maternal DLC intake (from fish and other dietary sources) that exceed the the provisional tolerable monthly intake (PTMI) of 70 picograms/kg bodyweight/month established by JECFA, neurodevelopmental risk may not be negligible. Among infants, young children, and adolescents, the available data were insufficient to derive a quantitative framework of health risks and benefits of eating fish. However, the Consultation stated that healthy dietary patterns that include fish and are established early in life influence dietary habits and health during adult life. To minimize risks in target populations, the Consultation recommended a series of steps that member states should take to better assess and manage the risks and benefits of fish consumption and more effectively communicate with their citizens.

**NDL-PCBs**

CCCCF8 (2014) agreed with the recommendations of the in-session Working Group on the Priority List of Contaminants and Naturally Occurring Toxicants for Evaluation by JECFA to maintain Non-dioxin like PCBs in the Priority List (REP14/CF, paraa. 126 and 130 and APPENDIX XIII).

JECFA80 (2015) evaluated NDL-PCBs. For this evaluation, the Committee decided to focus on the six indicator PCBs (PCB 28, PCB 52, PCB 101, PCB 138, PCB 153 and PCB 180), as there were sufficient data (toxicological, biomonitoring, occurrence and dietary exposure) available for review. Other NDL-PCBs were also considered where adequate data were available to make a risk characterization, as was found in the case of PCB 128.

National estimates of dietary exposure to the sum of the six indicator PCBs ranged, for mean exposure, from <1 to 82 ng/kg bw per day and, for high percentile exposure, from <1 to 163 ng/kg bw per day. International estimates based on Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme (GEMS/Food) consumption cluster diets are in the same range. For the sum of the six indicator PCBs, the contribution of each of the individual congeners differs between countries and population groups. However, for both dietary exposure and body burden estimates (which also take into consideration kinetics and half-lives), the main contributor is PCB 153, followed by PCB 180, then PCB 101 and PCB 28, with the lowest contribution from PCB 52.

The Committee concluded that none of the available studies on the six indicator PCBs and PCB 128 was suitable for derivation of health-based guidance values or for assessment of the relative potency of the NDL-PCBs compared with a reference compound. Therefore, a comparative approach using the minimal effect doses was developed in order to estimate MOEs to provide guidance on human health risk. Based on the available toxicological data on individual congeners, subtle changes in liver and thyroid histopathology were evident from the lowest doses tested of 2.8–7 µg/kg bw per day and were similar across the short-term and long-term studies of toxicity. The Committee decided to take the lower end of the range of test doses used for each congener at which these subtle changes occurred as a conservative point of departure for estimating MOEs, after conversion of external doses to internal doses (body burdens), based on reported NDL-PCB congener concentrations in adipose tissue.

Owing to the long half-lives and to eliminate interspecies differences in toxicokinetics, the Committee considered it appropriate to estimate body burdens rather than using external dose (dietary exposure) for the risk characterization. From human biomonitoring studies, the Committee derived equivalent body burdens based on the reported range of NDL-PCB concentrations in human milk for each congener. In addition, using a one-compartment kinetic dietary exposure model, body burdens were simulated for each congener using dietary exposure data from countries.

Comparison of the human body burden estimates (derived from human milk concentrations) with the body burden estimates from animal studies derived as points of departure for each congener resulted in MOEs for adults ranging from 4.5 to 5000. MOEs for breastfed infants, which may have a body burden up to 2-fold higher than that of adults, would be approximately half of the adult values. The MOEs for children would be expected to be intermediate between those for adults and those for breastfed infants, owing to the initial contribution from breastfeeding and the subsequent lower dietary contribution compared with human milk. Because the MOEs are based on minimal effect doses, they were considered to give some assurance that dietary exposures to NDL-PCBs are unlikely to be of health concern for adults and children, based on the available data. For breastfed infants, the MOEs would be expected to be lower. However, based on present knowledge, the benefits of breastfeeding are considered to outweigh the possible disadvantages that may be associated with the presence of NDL-PCBs in breast milk.

The Committee recognized that there are similarities in some of the reported effects for NDL-PCBs and therefore that risk estimates for combined exposure are desirable. The Committee concluded that this cannot be done on the basis of currently available data. The Committee also noted that the end-point selected for derivation of the MOEs was particularly

**Other Chemical Contaminants (except radionuclides)****Polychlorinated biphenyls**

conservative, as it was not of clear toxicological significance, it was a minimal change, and the lowest doses at which it was seen were used for the point of departure, combined with upper-bound estimates of body burden.

CCCF10 (2016) agreed that an EWG chaired by EU would prepare a discussion paper on the review of the Code of practice for the prevention and reduction of dioxin and dioxin-like PCB contamination in food and feeds (CXC 62-2006) to evaluate if recommendations from the JECFA assessment on non-dioxin like PCBs could be included. (REP16/CF, para. 168).

CCCF11 (2017) agreed to start a new work on the revision of the Code of practice for the prevention and reduction of dioxin and PCB contamination in food and feed (CXC 62-2006), to forward the project document (Appendix IX) to CAC for approval and to establish an EWG, chaired by the EU to revise the COP for comments and consideration at its next session. (REP17/CF, paras. 144-147)

CAC40 (2017) approved the new work. (REP17/CAC, Appendix VI)

CCCF12 (2018) agreed to advance the proposed draft COP for the Prevention and Reduction of dioxins, and dioxin-like PCBs and non dioxin-like PCB Contamination in Food and Feed to CAC41 for adoption at Step 5/8 (REP18/CF, para. 98 and Appendix V).

CAC41 (2018) adopted the Code of Practice for the prevention and reduction of dioxins, dioxin-like PCBs and non-dioxin-like PCB contamination in food and feed (REP18/CAC, Appendix III).

**PCBs in Natural Mineral Waters**

CCCF2 (2008) considered the proposed draft amendments to Section 3.2 "Health-Related Limits for Certain Substances" of the Codex Standard for Natural Mineral Waters, referred by CCNMW8. The Committee also considered whether the health-related provision in Section 3.2 should be included in Schedule I of the GSCTF. It was pointed out that iron, zinc and copper had been considered as quality factors rather than safety factors and therefore the levels for those substances had been currently not included in Schedule I of the GSCTF. It was noted that some delegations believed that the level for copper was based on both safety and quality parameters of mineral water.

The Committee temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41, para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).

The Standard contains the following wording for Section 3.2 "Health-related limits for certain substances":

"The following substances shall be below the limit of quantification when tested, in accordance with the methods prescribed in Section 7: 3.2.18 Pesticides and PCBs"

PCBs are a class of stable chlorinated aromatic hydrocarbons which (mostly prior to the 1970s) have been produced since 1930 and used extensively in a wide range of industrial applications. One of the main uses which still persists is as dielectric and heat exchange fluids. Despite increasing withdrawal of the use and restrictions on the production, large amounts of PCBs continue to be present in the environment, either in use in existing industrial systems, or in waste materials, or dispersed as persistent pollutants. PCBs are mixtures of related chemicals which are formed by the chlorination of biphenyl. Theoretically, 209 congeners are possible; in practice about 130 are likely to occur in commercial products. Also related by-products are formed, such as polychlorinated dibenzofurans (PCDFs), and may be found in technical PCB-mixtures. Some of the trade names for technical PCB-mixtures as they were produced are Aroclor, Clophen, Kanechlor. The different congeners in PCB-mixtures can be designated by their IUPAC number, and different industrial PCB-mixtures can be characterized by their composition in terms of the relative percentages of the congeners.

Degradation of PCBs in the environment depends on the degree of chlorination (higher chlorinated compounds are generally more persistent against photolytic, microbial and animal

**Other Chemical Contaminants (except radionuclides)****Polychlorinated biphenyls**

metabolic degradation) and on the position of the chlorine atoms in the molecule. All congeners are lipophilic and accumulate in the food chain.

PCBs were evaluated by IARC in 1978 and 1987. The conclusion was that PCBs are carcinogenic for laboratory animals and are probably carcinogenic for humans (IARC, 1987). Extensive documentation about PCBs is gathered in EHC 140 (WHO, 1993).

The PCB-congeners that most easily adopt a co-planar configuration (the non-ortho substituted PCBs, numbers 77, 126 and 169) are potent Ah receptor agonists. Mono-ortho substituted PCBs are less potent but are included with a TEQ-factor for dioxin-like activity (nos 105, 114, 118, 123, 156, 157, 167, 189). Sometimes also PCB 81 and two di-ortho substituted PCBs (170 and 180) were included in the discussion about the TEF-approach for dioxins because of their ability to induce P4501A1 enzymes and their occurrence and persistence in the environment; they however were not incorporated in the WHO-recommendation about the TEF-approach for dioxin-related compounds (1998). The PCBs with a TEF form usually only a few percent of the total PCBs, but are relevant because of this specific toxicity, which can form an important contribution to the total TEQ for dioxins in a sample of food and in the human diet.

(NDL-PCBs)

Two linked benzene rings in which 1–10 chlorine atoms substitute the hydrogen atoms on the benzene rings comprise the class of chemicals known as PCBs. There are a total of 209 possible PCB congeners, based on the substitution positions along the phenyl rings. PCBs were intentionally produced in considerable amounts between the 1930s and 1970s and were used for a wide range of applications. Although there are 209 possible PCB congeners, of which 197 are NDL-PCBs, only about 130 have been reported in commercial mixtures. The congener profiles observed in commercial mixtures are not reflective of the congener profiles present in environmental compartments, food or human tissues. PCBs are thermally stable, persist in the environment and are found at large distances from their area of release. PCBs are lipophilic compounds and accumulate in the tissues of living organisms; they are taken up by humans primarily through the consumption of food, with foods of animal origin being the primary source of human exposure.

PCBs exhibit different toxicological effects depending on the site of chlorine substitution on the phenyl rings. The position of chlorine substitution on the ring structure is important, because the receptor interaction profile is highly dependent on it. Congeners having chlorine substitution in both para and at least two meta positions and also having zero or one chlorine atom present in an ortho position have the highest binding affinity for the aryl hydrocarbon receptor (AhR) and induce typical dioxin-like toxicity. These congeners, of which there are 12, are known as the DL-PCBs and have been assigned WHO toxic equivalency factors (TEFs). Congeners with two or more chlorine atoms in the ortho position are generally considered to be NDL-PCBs. The NDL-PCBs have a different spectrum of toxicological activity relative to DL-PCBs and PCDDs/ PCDFs. International bodies have identified seven PCBs that can be used to characterize the presence of PCB contamination. Six of these seven are NDLPBs (PCB 28, PCB 52, PCB 101, PCB 138, PCB 153 and PCB 180), and one is a DL-PCB (PCB 118). The six NDL-PCBs are often called “indicator PCBs”

**Other Chemical Contaminants (except radionuclides)****Polycyclic aromatic hydrocarbons**

Reference to JECFA:	37 (1990), 64 (2005)
Toxicological guidance value:	(Intake estimates for benzo[a]pyrene as marker for PAHs: mean 4 ng/kg bw/day; high 10 ng/kg b/day Margin of exposure (MOE): Cancer (BMDL for benzo[a]pyrene as marker for mixtures of PAHs 100 000 ng/kg bw/day), mean intake 25 000; high intake 10 000.)
Synonyms:	PAHs, Polynuclear aromatic hydrocarbons
Related code of practice:	Code of Practice for the Reduction of Contamination of Food with Polycyclic Aromatic Hydrocarbons (PAH) from Smoking and Direct Drying Processes. (CXC 68-2009) Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

JECFA37 (1990) evaluated benzo[a]pyrene and recognized that it was one member of a family of PAHs that should be considered as a class. The most significant toxicological effect was carcinogenicity and it was noted that the estimated average daily intake of benzo[a]pyrene by humans was about four orders of magnitude lower than that reported to be without effect on the incidence of tumors in rats. However, the committee was unable to establish a tolerable intake for benzo[a]pyrene, based on the available data.

JECFA64 (2005) evaluated 33 compounds. Some were found to be clearly genotoxic and carcinogenic (benzo[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, chrysene, dibenz[a,h]anthracene, dibenzo[a,e]pyrene, dibenzo[a,h]pyrene, dibenzo[a,l]pyrene, dibenzo[a,i]pyrene, indeno[1,2,3-cd]pyrene, 5-methylchrysene), whereas others were not. There is limited or no evidence on the reproductive toxicity of individual PAHs, other than benzo[a]pyrene, which showed impaired fertility in the offspring of female mice. Developmental toxicity after oral administration has been reported for benzo[a]anthracene, benzo[a]pyrene, dibenz[a,h]anthracene and naphthalene. A NOEL for reproductive toxicity has not been established. Using parenteral administration, it was shown that PAHs exert immunosuppressive effects, probably via the Ah receptor. The NOEL for immunosuppressive effects of benzo[a]pyrene was 3 mg/kg bw/day. No quality data for humans are available.

To evaluate the combined toxicity of PAHs, JECFA64 decided to use a surrogate approach, with benzo[a]pyrene being used as a marker of exposure to, and effect of the 13 genotoxic and carcinogenic PAHs. A BMDL equivalent to 0.1 mg benzo[a]pyrene kg bw/day was derived for mixtures of PAHs in food. The committee concluded that a representative mean intake of benzo[a]pyrene of 0.004 µg/kg bw/day and high-level intake of 0.01 µg/kg bw/day could be used in the evaluation. Comparison of these mean and high-level intakes with the BMDL indicates MOEs of 25 000 and 10 000, respectively. Based on these MOEs, the committee concluded that the estimated intakes of PAHs were of low concern for human health. Measures to reduce intake of PAHs could include avoiding contact of foods with flames, and cooking with the heat source above rather than below the food. Efforts should be made to reduce contamination with PAHs during drying and smoking processes by replacing direct smoking (with smoke developed in the smoking chamber, traditionally in smokehouses) with indirect smoking. Washing or peeling fruit and vegetable before consumption would help to remove surface contaminants.

Recommendations by JECFA64:

- Future monitoring should include, but not be restricted to, analysis of the 13 PAHs identified as being genotoxic and carcinogenic.

CCFAC37 (2005) agreed to revise the discussion paper with particular attention to JECFA64 evaluation (ALINORM 05/28/12, para.199). CCFAC38 (2006) agreed to the elaboration of a Code of practice for the reduction of PAH contamination in food and to limit its scope to smoking and direct drying process (ALINORM 06/29/12, para.187). An initial draft COP is to be considered at the 1st session of CCCF.

CCCF1 (2007) agreed to address smoke flavours in the introductory part only in the Code. CCCF agreed to return the proposed draft COP to Step 2 for redrafting by an electronic working group led by Denmark with a view to circulation for comments at Step 3 and consideration at Step 4 at its next session (ALINORM 07/30/41, para. 102).

**Other Chemical Contaminants (except radionuclides)****Polycyclic aromatic hydrocarbons**

CCCF2 (2008) agreed to forward the proposed draft COP to CAC31 for adoption at Step 5 (ALINORM 08/31/41, para. 109). CAC31 adopted the proposed draft code and advanced it to Step 6 (ALINORM 08.31/REP, para. 65).

CCCF3 (2009) agreed to forward the draft Code to CAC32 for adoption at Step 8 (ALINORM 09/32/41, para. 67 and Appendix V). CAC32 adopted the draft Code at Step 8 (ALINORM 09/32/REP, APPENDIX III).

**PAHs in Natural Mineral Waters**

CCCF2 (2008) considered the proposed draft amendments to Section 3.2 “Health-Related Limits for Certain Substances” of the Codex Standard for Natural Mineral Waters, referred by the CCNMW08. The Committee also considered whether the health-related provision in Section 3.2 should be included in Schedule I of the GSCTF. It was pointed out that iron, zinc and copper had been considered as quality factors rather than safety factors and therefore the levels for those substances had been currently not included in Schedule I of the GSCTF. It was noted that some delegations believed that the level for copper was based on both safety and quality parameters of mineral water. CCCF2 temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41, para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, paras. 89-90).

The Standard contains the following wording for Section 3.2 “Health-related limits for certain substances”:

“The following substances shall be below the limit of quantification when tested, in accordance with the methods prescribed in Section 7: 3.2.20 Polynuclear aromatic hydrocarbons”.

Polycyclic aromatic hydrocarbons (PAHs) constitute a large class of organic compounds containing two or more fused aromatic rings. Foods can be contaminated by two major routes: firstly, by environmental PAHs present in air, soil and water; secondly, PAHs can be formed during processing (drying, smoking) or cooking (grilling, roasting, frying) of foods.

Absorption of dietary PAH is determined by size and lipophilicity of the molecule and the lipid content of the food. PAHs are metabolized by oxidation of the aromatic rings, followed by formation of glutathione, glucuronide and sulfate conjugates. Oxidation can generate electrophilic metabolites that bind covalently to nucleic acids and proteins. Some PAH and PAH metabolites bind to the aryl hydrocarbon (Ah) receptor, resulting in upregulation of enzymes involved in PAH metabolism.

The major foods containing higher concentrations of PAHs are meat and fish products, particularly grilled and barbecued products, oils and fats, cereals and dry foods.

**Other Chemical Contaminants (except radionuclides)****Vinyl chloride monomer**

Reference to JECFA: 28 (1984)

Toxicological guidance value: Provisional Acceptance (1984, the use of food-contact materials from which vinyl chloride may migrate is provisionally accepted, on condition that the amount of the substance migrating into food is reduced to the lowest level technologically)

Contaminant definition: Vinyl chloride monomer

Synonyms: Monochloroethene, chloroethylene; abbreviation VC or VCM

Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

Commodity / Product Name	Guideline Level (GL) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the GL applies	Notes/Remarks	Notes for CCCF
Food	0.01	Adopted	2006	FAC		The GL in food packaging material is 1.0 mg/kg.	

Migration of possibly harmful substances from food contact materials has been discussed in the CCFA/CCFAC in the period 1986-1991. Guideline levels for vinyl chloride monomer and acrylonitrile in food and packaging material were adopted by CAC19 (1991) on the understanding that the AOAC International and the ISO would develop appropriate sampling plans and methods of analysis. CAC29 (2006) adopted the GSCTF, including Schedule 1 and revoked Guideline Levels for Vinyl Chloride Monomer and Acrylonitrile in Food and Packaging Material (CXG 6-1991) (ALINORM 06/29/41).

Vinyl chloride monomer is the main starting substance for the manufacture of polymers which are used as resins, as packaging material for foods. Vinyl chloride is not known to occur as a natural product. Residues of vinyl chloride monomer may be still present in the polymer. Vinyl chloride is considered by IARC to be a human carcinogen (as has been shown in occupational exposure situations). IARC Vol. 19, 377-438 (1979)

**Radionuclides**

Reference to JECFA:	-
Toxicological guidance value:	-
Contaminant definition:	-
Synonyms:	radioisotopes, radioactive nuclides, radioactive elements
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CXC 49-2001)

TABLE 1

Commodity / Product Name	Guideline Level (GL) (Bq/kg)	Representative radionuclides	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the GL applies	Notes/Remarks	Notes for CCCF
Infant foods	1	<sup>238</sup> Pu, <sup>239</sup> Pu, <sup>240</sup> Pu, <sup>241</sup> Am	Adopted	2006	FAC		The GL applies to foods intended for consumption by infants.	
Infant foods	100	<sup>90</sup> Sr, <sup>106</sup> Ru, <sup>129</sup> I, <sup>131</sup> I, <sup>235</sup> U	Adopted	2006	FAC		The GL applies to foods intended for consumption by infants.	
Infant foods	1000	<sup>35</sup> S (*), <sup>60</sup> Co, <sup>89</sup> Sr, <sup>103</sup> Ru, <sup>134</sup> Cs, <sup>137</sup> Cs, <sup>144</sup> Ce, <sup>192</sup> Ir	Adopted	2006	FAC		The GL applies to foods intended for consumption by infants.	
Infant foods	1000	<sup>3</sup> H (**), <sup>14</sup> C, <sup>99</sup> T	Adopted	2006	FAC		The GL applies to foods intended for consumption by infants.	
Foods other than infant foods	10	<sup>238</sup> Pu, <sup>239</sup> Pu, <sup>240</sup> Pu, <sup>241</sup> Am	Adopted	2006	FAC			
Foods other than infant foods	100	<sup>90</sup> Sr, <sup>106</sup> Ru, <sup>129</sup> I, <sup>131</sup> I, <sup>235</sup> U	Adopted	2006	FAC			
Foods other than infant foods	1000	<sup>35</sup> S (*), <sup>60</sup> Co, <sup>89</sup> Sr, <sup>103</sup> Ru, <sup>134</sup> Cs, <sup>137</sup> Cs, <sup>144</sup> Ce, <sup>192</sup> Ir	Adopted	2006	FAC			
Foods other than infant foods	10000	<sup>3</sup> H (**), <sup>14</sup> C, <sup>99</sup> T	Adopted	2006	FAC			

(\*) This represents the value for organically bound sulphur.

(\*\*) This represents the value for organically bound tritium.

**Scope:** The Guideline Levels apply to radionuclides contained in foods destined for human consumption and traded internationally, which have been contaminated following a nuclear or radiological emergency<sup>7</sup>. These guideline levels apply to food after reconstitution or as prepared for consumption, i.e., not to dried or concentrated foods, and are based on an intervention exemption level of 1 mSv in a year.

**Application:** As far as generic radiological protection of food consumers is concerned, when radionuclide levels in food do not exceed the corresponding Guideline Levels, the food should be considered as safe for human consumption. When the Guideline Levels are exceeded, national governments shall decide whether and under what circumstances the food should be distributed within their territory or jurisdiction. National governments may wish to adopt different values for internal use within their own territories where the assumptions concerning food distribution that have been made to derive the Guideline Levels may not apply, e.g., in the case of wide-spread radioactive contamination. For foods that are consumed

<sup>7</sup> For the purposes of this document, the term "emergency" includes both accidents and malevolent actions.



**Radionuclides**

in small quantities, such as spices, that represent a small percentage of total diet and hence a small addition to the total dose, the Guideline Levels may be increased by a factor of 10. **Radionuclides:** The Guideline Levels do not include all radionuclides. Radionuclides included are those important for uptake into the food chain; are usually contained in nuclear installations or used as a radiation source in large enough quantities to be significant potential contributors to levels in foods, and; could be accidentally released into the environment from typical installations or might be employed in malevolent actions. Radionuclides of natural origin are generally excluded from consideration in this document.

In the Table, the radionuclides are grouped according to the guideline levels rounded logarithmically by orders of magnitude. Guideline levels are defined for two separate categories "infant foods" and "other foods". This is because, for a number of radionuclides, the sensitivity of infants could pose a problem. The guideline levels have been checked against age-dependent ingestion dose coefficients defined as committed effective doses per unit intake for each radionuclide, which are taken from the "International Basic Safety Standards" (IAEA, 1996)<sup>8</sup>.

**Multiple radionuclides in foods:** The guideline levels have been developed with the understanding that there is no need to add contributions from radionuclides in different groups. Each group should be treated independently. However, the activity concentrations of each radionuclide within the same group should be added together<sup>9</sup>.

See the textual part of the Guideline Levels for Radionuclides in Foods Contaminated Following A Nuclear or Radiological Emergency for Use in International Trade below.

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<sup>8</sup> Food and Agriculture Organization of the United Nations, International Atomic Energy Agency, International Labour Office, OECD Nuclear Energy Agency, Pan American Health Organization, World Health Organization (1996) International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources, IAEA, Vienna.

<sup>9</sup> For example, if <sup>134</sup>Cs and <sup>137</sup>Cs are contaminants in food, the guideline level of 1 000 Bq/kg refers to the summed activity of both these radionuclides.

**Radionuclides**

## ANNEX 1

**SCIENTIFIC JUSTIFICATION FOR PROPOSED DRAFT REVISED GUIDELINE LEVELS FOR RADIONUCLIDES IN FOODS CONTAMINATED FOLLOWING A NUCLEAR OR RADIOLOGICAL EMERGENCY**

The Guideline Levels for Radionuclides in Foods and specifically the values presented in Table 1 above are based on the following general radiological considerations and experience of application of the existing international and national standards for control of radionuclides in food.

Significant improvements in the assessment of radiation doses resulting from the human intake of radioactive substances have become available since the Guideline Levels were issued by the Codex Alimentarius Commission in 1989<sup>10</sup> (CXG 5-1989).

**Infants and adults:** The levels of human exposure resulting from consumption of foods containing radionuclides listed in Table 1 at the suggested guideline levels have been assessed both for infants and adults and checked for compliance with the appropriate dose criterion.

In order to assess public exposure and the associated health risks from intake of radionuclides in food, estimates of food consumption rates and ingestion dose coefficients are needed. According to Ref. (WHO, 1988) it is assumed that 550 kg of food is consumed by an adult in a year. The value of infant food and milk consumption during first year of life used for infant dose calculation equal to 200 kg is based on contemporary human habit assessments (F. Luykx, 1990<sup>11</sup>; US DoH, 1998<sup>12</sup>; NRPB, 2003<sup>13</sup>). The most conservative values of the radionuclide-specific and age-specific ingestion dose coefficients, i.e. relevant to the chemical forms of radionuclides which are most absorbed from the gastro-intestinal tract and retained in body tissues, are taken from the (IAEA, 1996).

**Radiological criterion:** The appropriate radiological criterion, which has been used for comparison with the dose assessment data below, is a generic intervention exemption level of around 1 mSv for individual annual dose from radionuclides in major commodities, e.g. food, recommended by the International Commission on Radiological Protection as safe for members of the public (ICRP, 1999)<sup>14</sup>.

**Naturally occurring radionuclides:** Radionuclides of natural origin are ubiquitous and as a consequence are present in all foodstuffs to varying degrees. Radiation doses from the consumption of foodstuffs typically range from a few tens to a few hundreds of microsieverts in a year. In essence, the doses from these radionuclides when naturally present in the diet are unamenable to control; the resources that would be required to affect exposures would be out of proportion to the benefits achieved for health. These radionuclides are excluded from consideration in this document as they are not associated with emergencies.

**One-year exposure assessment:** It is conservatively assumed that during the first year after major environmental radioactive contamination caused by a nuclear or radiological emergency it might be difficult to readily replace foods imported from contaminated regions with foods imported from unaffected areas. According to FAO statistical data the mean fraction of major foodstuff quantities imported by all the countries worldwide is 0.1. The values in Table 1 as regards foods consumed by infants and the general population have been derived to ensure that if a country continues to import major foods from areas contaminated with radionuclides, the mean annual internal dose of its inhabitants will not exceed around 1 mSv (see Annex 2). This conclusion might not apply for some radionuclides if the fraction of contaminated food is found to be higher than 0.1, as might be the case for infants who have a diet essentially based on milk with little variety.

**Long-term exposure assessment:** Beyond one year after the emergency the fraction of contaminated food placed on the market will generally decrease as a result of national restrictions (withdrawal from the market), changes to other produce, agricultural countermeasures and decay.

Experience has shown that in the long term the fraction of imported contaminated food will decrease by a factor of a hundred or more. Specific food categories, e.g. wild forest products, may show persistent or even increasing levels of contamination. Other categories of food may gradually be exempted from controls. Nevertheless, it must be anticipated that it may take many years before levels of individual exposure as a result of contaminated food could be qualified as negligible.

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<sup>10</sup> The Codex Alimentarius Commission at its 18th Session (Geneva 1989) adopted Guideline Levels for Radionuclides in Foods Following Accidental Nuclear Contamination for Use in International Trade (CXG 5-1989) applicable for six radionuclides (<sup>90</sup>Sr, <sup>131</sup>I, <sup>137</sup>Cs, <sup>134</sup>Cs, <sup>239</sup>Pu and <sup>241</sup>Am) during one year after the nuclear accident.

<sup>11</sup> F. Luykx (1990) Response of the European Communities to environmental contamination following the Chernobyl accident. In: Environmental Contamination Following a Major Nuclear Accident, IAEA, Vienna, v.2, 269-287.

<sup>12</sup> US DoHHS (1998) Accidental Radioactive Contamination of Human Food and Animal Feeds: Recommendations for State and Local Agencies. Food and Drug Administration, Rockville.

<sup>13</sup> K. Smith and A. Jones (2003) Generalized Habit Data for Radiological Assessments. NRPB Report W41.

<sup>14</sup> International Commission on Radiological Protection (1999). Principles for the Protection of the Public in Situations of Prolonged Exposure. ICRP Publication 82, Annals of the ICRP.

ANNEX 2

**ASSESSMENT OF HUMAN INTERNAL EXPOSURE WHEN THE GUIDELINE LEVELS ARE APPLIED**

For the purpose of assessment of the mean public exposure level in a country caused by the import of food products from foreign areas with residual radioactivity, in implementing the present guideline levels the following data should be used: annual food consumption rates for infants and adults, radionuclide- and age-dependent ingestion dose coefficients and the import/production factors. When assessing the mean internal dose in infants and adults it is suggested that due to monitoring and inspection the radionuclide concentration in imported foods does not exceed the present guideline levels. Using cautious assessment approach it is considered that all the foodstuffs imported from foreign areas with residual radioactivity are contaminated with radionuclides at the present guideline levels.

Then, the mean internal dose of the public,  $E$  (mSv), due to annual consumption of imported foods containing radionuclides can be estimated using the following formula:

$$E = GL(A) \cdot M(A) \cdot e_{ing}(A) \cdot IPF$$

where:

$GL(A)$  is the Guideline Level (Bq/kg)

$M(A)$  is the age-dependent mass of food consumed per year (kg)

$e_{ing}(A)$  is the age-dependent ingestion dose coefficient (mSv/Bq)

$IPF$  is the import/production factor<sup>15</sup> (dimensionless).

Assessment results presented in Table 2 both for infants and adults demonstrate that for all the twenty radionuclides doses from consumption of imported foods during the 1<sup>st</sup> year after major radioactive contamination do not exceed 1 mSv. It should be noted that the doses were calculated on the basis of a value for the IPF equal to 0.1 and that this assumption may not always apply, in particular to infants who have a diet essentially based on milk with little variety.

It should be noted that for <sup>239</sup>Pu as well as for a number of other radionuclides the dose estimate is conservative. This is because elevated gastro-intestinal tract absorption factors and associated ingestion dose coefficients are applied for the whole first year of life whereas this is valid mainly during suckling period recently estimated by ICRP to be as average first six months of life (ICRP, 2005<sup>16</sup>). For the subsequent six months of the first year of life the gut absorption factors are much lower. This is not the case for <sup>3</sup>H, <sup>14</sup>C, <sup>35</sup>S, iodine and cesium isotopes.

As an example, dose assessment for <sup>137</sup>Cs in foods is presented below for the first year after the area contamination with this nuclide.

For adults:  $E = 1000 \text{ Bq/kg} \cdot 550 \text{ kg} \cdot 1.3 \cdot 10^{-5} \text{ mSv/Bq} \cdot 0.1 = 0.7 \text{ mSv}$ ;

For infants:  $E = 1000 \text{ Bq/kg} \cdot 200 \text{ kg} \cdot 2.1 \cdot 10^{-5} \text{ mSv/Bq} \cdot 0.1 = 0.4 \text{ mSv}$

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<sup>15</sup> The import/production factor ( $IPF$ ) is defined as the ratio of the amount of foodstuffs imported per year from areas contaminated with radionuclides to the total amount produced and imported annually in the region or country under consideration.

<sup>16</sup> International Commission on Radiological Protection (2005) Doses to Infants from Radionuclides Ingested in Mothers Milk. To be published.

TABLE 2.

**ASSESSMENT OF EFFECTIVE DOSE FOR INFANTS AND ADULTS FROM INGESTION OF IMPORTED FOODS IN A YEAR**

Radionuclide	Guideline Level (Bq/kg)		Effective dose (mSv)	
	Infant foods	Other foods	1 <sup>st</sup> year after major contamination	
			Infants	Adults
<sup>238</sup> Pu	1	10	0.08	0.1
<sup>239</sup> Pu			0.08	0.1
<sup>240</sup> Pu			0.08	0.1
<sup>241</sup> Am			0.07	0.1
<sup>90</sup> Sr	100	100	0.5	0.2
<sup>106</sup> Ru			0.2	0.04
<sup>129</sup> I			0.4	0.6
<sup>131</sup> I			0.4	0.1
<sup>235</sup> U			0.7	0.3
<sup>35</sup> S*	1000	1000	0.2	0.04
<sup>60</sup> Co			1	0.2
<sup>89</sup> Sr			0.7	0.1
<sup>103</sup> Ru			0.1	0.04
<sup>134</sup> Cs			0.5	1
<sup>137</sup> Cs			0.4	0.7
<sup>144</sup> Ce			1	0.3
<sup>192</sup> Ir			0.3	0.08
<sup>3</sup> H**	1000	10000	0.002	0.02
<sup>14</sup> C			0.03	0.3
<sup>99</sup> Tc			0.2	0.4

\* This represents the value for organically bound sulphur.

\*\* This represents the value for organically bound tritium.

See for "Scientific justification for the Guideline Levels" (Annex 1) and the "Assessment of human internal exposure when the Guideline Levels are applied" (Annex 2).

**Quality factors****Copper**

Reference to JECFA: 10 (1966), 14 (1970), 26 (1982)  
 Toxicological guidance value: PMTDI 0.05 - 0.5 mg/kg bw (1982)  
 Contaminant definition: Copper, total  
 Synonyms: Cu

Commodity/Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Edible fats and oils, refined (not covered by individual standards)	0.1	Adopted	CXS 19-1981	FO		This quality factors is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Edible fats and oils, virgin(not covered by individual standards)	0.4	Adopted	CXS 19-1981	FO		This quality factors is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Edible fats and oils, cold pressed fats and oils (not covered by individual standards)	0.4	Adopted	CXS 19-1981	FO		This quality factors is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Named animal fats	0.4	Adopted	CXS 211-1999	FO		Lard, rendered pork fat, premier jus and edible tallow. This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments. Relevant Codex commodity standard is CXS 211-1999.	1)
Vegetable oils, Crude	0.4	Adopted	CXS 210-1999,	FO		Named vegetable oils from arachis, babassu, coconut, cottonseed, grapeseed, maize, mustardseed, palm kernel, palm, rapeseed, safflowerseed, sesameseed, soya bean, and sunflowerseed, and palm olein, stearin and superolein. Relevant Codex commodity standard is CXS 210-1999.	OC 0172

**Quality factors****Copper**

Commodity/Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Named Vegetable oils, refined	0.1	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	OR 0172 1)
Named vegetable oils, virgin	0.4	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	
Olive oils and olive-pomace oils	0.1	Adopted	CXS 33-1981	FO		These quality and composition factors are supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet these supplementary factors, may still conform to the standard. Relevant Codex commodity standard is CXS 33-1981.	
Milkfat products	0.05	Adopted	CXS 280-1973	MMP		This limit applies to anhydrous milkfat, milkfat, anhydrous butteroil and butter oil and ghee. Relevant Codex commodity standard is CXS 280-1973.	
Casein products	5	Adopted	CXS 290-1995	MMP		This limit applies to edible acid casein, edible rennet caein and edible caseinate, intended for direct consumption or further processing. Relevant Codex commodity standard is CXS 290-1995.	
Salt, food grade	2	Adopted	CXS 150-1985	NFSDU, FA		Relevant Codex commodity standard is CXS 150-1985.	
Natural mineral waters	1 mg/l	Adopted	CXS 108-1981	NMW, CF		Relevant Codex commodity standard is CXS 108-1981.	

- 1) The revised Standards for oils and fats contain the following wording for the mentioned contaminant MLs: "The products covered by the provisions of this Standard shall comply with MLs being established by the CAC but in the meantime the following limits will apply."

Copper as cupric sulfate has been evaluated by JECFA in 1966, 1970, and 1982. The PMTDI was established to be 0.05-0.5 mg/kg bw. A provisional guidance value of 0.5 mg/kg

**Quality factors****Copper**

bw/day was proposed in 1966 on the understanding that a very considerable margin appeared to exist between normal intakes and those that could lead to chronic copper poisoning, and that the dietary levels of those constituents such as molybdenum and zinc, which are known to affect copper metabolism, lie within normal limits. JECFA14 concluded in 1970 from more recent food analyses that the daily intake of 20 mg was likely to be exceeded by significant sections of the population with no apparent deleterious effects. On this basis the tentative assessment of the maximum acceptable daily load of 0.5 mg/kg bodyweight was retained. JECFA26 (1982) reaffirmed the provisional value based on the same rationale.

In EHC 200 (1998) it was concluded that the upper limit of the acceptable range of oral intake (AROI) in adults is uncertain but is most likely in the range of several but not many mg/day in adults (several meaning more than 2 or 3 mg/day). This evaluation was based solely on studies of gastrointestinal effects of copper-contaminated drinking water. The available data on toxicity in animals were not considered helpful in establishing the upper limit of the AROI due to uncertainty about an appropriate model for humans, but they help to establish a mode of action for the response.

WHO established a drinking water guideline of 2 mg/liter in 2003, based on the 1993 Guidelines for Drinking Water Quality, 2nd edition, where a provisional health-based guideline value of 2 mg/liter for copper was derived from the PMTDI of 0.5 mg/kg bw/day as proposed by JECFA26. The document mentioned that this PMTDI was based on a rather old study in dogs, that did not take into account differences in copper metabolism between infants and adults, but this rationale could not be found in the JECFA26 (see above).

**Copper in Natural Mineral Waters**

CCCF2 (2008) considered the proposed draft amendments to Section 3.2 "Health-Related Limits for Certain Substances" of the Codex Standard for Natural Mineral Waters, referred to by CCNMW08. The Committee also considered whether the health-related provision in Section 3.2 should be included in Schedule I of the GSCTF. It was pointed out that iron, zinc and copper had been considered as quality factors rather than safety factors and therefore the levels for those substances had been currently not included in Schedule I of the GSCTF. It was noted that some delegations believed that the level for copper was based on both safety and quality parameters of mineral water. CCCF2 temporarily endorsed the section pending elaboration of appropriate methods of analyses by CCMAS and decided to postpone the decision on inclusion of those substances in the GSCTF (ALINORM 08/31/41, para. 23-27). After establishment of an EWG by CCCF4, CCCF5 (2011) agreed to inform the Commission to remove the footnote which indicated the temporary endorsement (footnote 3) from the Standard on Natural Mineral Waters (CXS 108-1981) as there was no need for the endorsement of these sections since there was no safety concern associated with these compounds at the proposed levels. The Committee did not integrate the levels in the GSCTFF (REP11/CF, para 89-90).

**Copper in salt, food grade**

CCFA43 (2011) started a new work on the revision of the Standard for Food Grade Salt (CXS 150-1985). The copper had been moved to section 3.2 "Naturally present secondary products and contaminants". Copper had no entry in the GSCTFF and was also a micronutrient and its level in food was considered to reflect quality aspects rather than safety issues. Its presence as a contaminant might result from the use of copper-based equipment in salt production.

The Committee did not support proposals to increase the maximum level for copper to 10 mg/kg because there were not sufficient data to justify this. The Committee agreed to forward the revised proposed draft Standard to CAC34 for adoption at Step 5. (REP11/FA, paras. 131 and 136)

CAC34 (2011) adopted the revised proposed draft Standard at Step 5 and CAC35 (2012) adopted the the revised draft Standard at Step 8. (REP11/CAC, para. 116, and REP12/CAC, para. 145)

Copper is both an essential nutrient and a drinking-water contaminant. It has many commercial uses. It is used to make pipes, valves and fittings and is present in alloys and coatings. Copper sulfate pentahydrate is sometimes added to surface water for the control of algae. Dissolved copper can sometimes impart a light blue or blue-green colour and an unpleasant metallic, bitter taste to drinking-water.

Dietary copper intake will vary with the types of food consumed, the condition of the soils the foods are produced on (e.g. copper content) and drinking-water characteristics. Copper is ubiquitously distributed in foods, but the richest sources of copper in food are liver, seafood (especially shellfish and crustaceans), grains, cereal products and potatoes, which

**Quality factors**

**Copper**

contribute to about 65% of total dietary intake. Also, drinking-water may contribute for a considerable part to the total daily intake of copper. The average daily intake of copper has been estimated to range from 0.5 to 0.7 mg for infants 6 months of age or less up to 2-3 mg for adults, however this level is likely to be exceeded in arid areas where there may be a high intake of water containing high levels of copper.

Sensitivity to the toxic effects of excess dietary copper is influenced by its chemical form, species, and interaction with other dietary minerals. High levels can cause symptoms of acute toxicity, including nausea, abdominal discomfort (diarrhea), emesis, haemoglobinuria and/or haematuria, jaundice, oliguria/anuria, hypotension, coma and death. Histopathological effects were observed in the gastrointestinal tract, liver and kidney. WHO (1974) concluded that the fatal oral human dose is about 200 mg/kg. There is limited information on chronic copper toxicity. However, copper does not appear to be a cumulative toxic hazard for man, except for individuals suffering from Wilson's disease. Copper is not considered to be mutagenic, carcinogenic or affect reproduction. Teratogenicity/embryotoxicity is observed in some animal studies.



**Quality factors****Iron**

Reference to JECFA: 27 (1983)

Toxicological guidance value: PMTDI 0.8 mg/kg bw (1983, Group PMTDI, applies to iron from all sources except for iron oxides used as colouring agent, supplemental iron taken during pregnancy and lactation, and supplemental iron for specific clinical requirements)

Contaminant definition: Iron, total

Synonyms: Fe

Commodity/Product Name	Maximum Level (ML) (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
Edible fats and oils, refined (not covered by individual standards)	2.5	Adopted	CXS 19-1981	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Edible fats and oils, virgin (not covered by individual standards)	5.0	Adopted	CXS 19-1981	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Edible fats and oils, cold pressed (not covered by individual standards)	5.0	Adopted	CXS 19-1981	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 19-1981.	
Named vegetable oils, virgin	5.0	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	OC 0172
Named vegetable oils, refine	1.5	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	OR 0172

**Quality factors****Iron**

<b>Commodity/Product Name</b>	<b>Maximum Level (ML) (mg/kg)</b>	<b>Step</b>	<b>Reference or Adoption year</b>	<b>Ref to CC</b>	<b>Portion of the Commodity/Product to which the ML applies</b>	<b>Notes/Remarks</b>	<b>Notes for CCCF</b>
Crude palm kernel olein	5.0	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	
Crude palm kernel stearin	7.0	Adopted	CXS 210-1999	FO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 210-1999.	
Olive oils and olive-pomace oils	3	Adopted	CXS 33-1981	PO		This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 33-1981.	
Named animal fats	1.5	Adopted	CXS 211-1999	FO		Lard, rendered pork fat, premier jus and edible tallow. This quality factor is supplementary information to the essential composition and quality factors of the standard. A product, which meets the essential quality and composition factors but does not meet this supplementary factor, may still conform to the standard. Relevant Codex commodity standard is CXS 211-1999.	
Milkfat products	0.2	Adopted	CXS 280-1973	MMP		This limit applies to anhydrous milkfat, milkfat, anhydrous butteroil and butter oil and ghee. Relevant Codex commodity standard is CXS 280-1973.	
Casein products	20	Adopted	CXS 290-1995	MMP		50 mg/kg in roller dried caseinates. This limit applies to edible acid casein, edible rennet casein and edible caseinate, intended for direct consumption or further processing. Relevant Codex commodity standard is CXS 290-1995.	

Iron has been evaluated by JECFA in 1983. The PMTDI is established to 0.8 mg/kg bw as a precaution against storage in the body of excessive iron. (Hydrated) iron oxides have

**Quality factors****Iron**

been evaluated by JECFA in 1974, 1978 and 1979 (based on their use as colouring agents). An ADI of 0.5 mg/kg bw was established for these iron forms.

WHO did not propose a health-based guideline value for iron in drinking-water 1993 Guidelines for Drinking Water Quality, but it was mentioned that a value of about 2 mg/litre can be derived from the PMTDI established in 1983 by JECFA as a precaution against storage in the body of excessive iron.

Iron is one of the most abundant metals in the Earth's crust. It is found in natural fresh waters at levels ranging from 0.5 to 50 mg/liter. Iron may also be present in drinking-water as a result of the use of iron coagulants or the corrosion of steel and cast iron pipes during water distribution.

Iron is an essential trace element required by all forms of life. In man it is required for the synthesis of haem proteins and in many enzyme systems. Various groups (male, female, children, pregnant, lactating) differ in requirement for iron, iron deficiency is one of the most common nutritional deficiencies in children, in women of child bearing age, and pregnant women. It rarely occurs in adult men, except in cases of chronic bleeding.

Iron occurs as a natural constituent of all foods of plant and animal origin, and may also be present in drinking water. In food it occurs as iron oxides, inorganic and organic salts or organic complexes such as haem iron. Processing may affect the chemical form of iron. Levels of iron range from low for many fruits, vegetables and fats, to medium for red meats, chicken, eggs, whole wheat flour, to high for organ tissues, fish, green vegetables and tomatoes. Meat and grain contribute to a great part of diet-derived iron. Other important dietary sources include water, beverages and iron medication. The average daily intake of iron has been estimated to be 17 mg/day for males and 9-12 mg/day for females. Iron fortification of food, but also contamination of food during its preparation (iron-rich soil) could increase the intake of iron. The chemical form of the dietary iron is important for determining the amount of iron available for absorption, but also the source of iron (plant or animal), its interaction with other food components and the body's need for iron (mucosal regulation) affect absorption.

The effects of toxic doses of iron in animal studies are characterized by initial depression, coma, convulsion, respiratory failure and cardiac arrest. Post-mortem examination reveals adverse effects on the gastrointestinal tract. No long-term feeding studies are available, however, injection-site tumors have been observed in several animals studies after injection with iron preparations. Some iron-forms were found positive in mutagenicity tests. No teratogenic effects or effects on reproduction were observed.

In human, acute toxicity of iron ingested from normal dietary sources has not been reported; the amount of iron absorbed in normal subjects is subject to mucosal regulation so that excessive iron is not stored in the body. However, subjects with impaired ability to regulate iron absorption (i.e. suffering from idiopathic haemochromatosis), will be at risk from excessive exposure to iron. Excess iron intake may result in siderosis (deposition of iron in tissue) in liver, pancreas, adrenals, thyroid, pituitary and heart depending on the chemical form. Haemochromatosis patients suffer from liver cirrhosis, adrenal insufficiency, heart failure or diabetes. It is unknown whether excessive iron in the diet of individuals with impaired ability to regulate iron absorption will accelerate the clinical symptoms of the disease or increase the incidence of preclinical haemochromatosis.

**Quality factors**

**Zinc**

Reference to JECFA: 10 (1966), 26 (1982)  
 Toxicological guidance value: PMTDI 0.3-1 mg/kg bw (1982)  
 Contaminant definition: Zinc, total  
 Synonyms: Zn

Commodity / Product Name	Level (mg/kg)	Step	Reference or Adoption year	Ref to CC	Portion of the Commodity/Product to which the ML applies	Notes/Remarks	Notes for CCCF
No ML							

Zinc has been evaluated by JECFA in 1966 and 1982. The PMTDI is established to 0.3-1 mg/kg bw, based on clinical studies in which up to 600 mg of zinc sulfate (equivalent to 200 mg elemental zinc) has been administered daily in divided doses for a period of several months, without any reported adverse effects, including effects on blood counts and serum biochemistry. There is a wide margin between nutritionally required amounts of zinc and toxic levels.

WHO proposed in 2003 that, taking into account recent studies on humans, the derivation of a guideline value was not required at the time. It was stated however, that drinking-water containing zinc at levels above 3 mg/litre may not be acceptable to consumers based on taste considerations.

Zinc is a ubiquitous metal present in the environment, most rocks and many minerals contain zinc which can be used for the zinc industry. Zinc is utilized as protective coating of other metals, dye casting, construction industry, for alloys, dry cell batteries, dental, medical and household applications, fungicide, topical antibiotics and lubricants. Natural emissions results from erosion and forest fires. Anthropogenic sources are mining, zinc production facilities, iron and steel production, corrosion of galvanized structures, coal and fuel combustion, waste disposal and the use of zinc-containing fertilizers and pesticides.

Zinc is an essential trace element; the requirement for zinc changes throughout life and health effects associated with zinc deficiency are numerous. Zinc occurs as a natural constituent in all plant and animal tissues and functions as an integral part of several enzyme systems. Protein foods are important dietary sources of zinc. Levels range from high for oysters with lesser amounts in other seafood, muscle meats, nuts, whole cereals. Sugar, citrus fruits and non-leafy vegetables are poor sources of zinc. The interaction with other dietary factors affects the absorption of zinc. The average daily intake of zinc has been estimated to be maximally 20 mg/day for adults.

In animal studies, zinc in toxic doses caused weakness, anorexia, anemia, diminished growth, loss of hair, lowered food utilization, changes in the levels of liver and serum enzymes, morphological and enzymatic changes in the brain, and histological and functional changes in the kidney. The haematopoietic system, kidney and pancreas were found to be the target organs after long-term oral exposure to zinc. Genotoxicity tests failed to prove that zinc is mutagenic and only (very) high levels of zinc showed teratogenic effects or effects on reproduction.

In human, high levels of zinc cause acute effects such as vomiting and gastrointestinal irritation (nausea, cramps, diarrhea), however when bound to food components (i.e. meat, oysters) these effects are expected to be less. No information is available on toxic effects in man due to chronic excessive intake of zinc, however impaired copper uptake in humans has been noted following the chronic elevated intake of zinc. Some effects of zinc therefore may be secondary to impaired copper utilization (i.e. anemia).