CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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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 the 38th Session of the Codex Committee on Food Additives and Contaminants[1] and on the basis of the Document CX/CF 07/1/6 published for the First Codex Committee on Contaminants in Foods (CCCF) held in 2007. It incorporates all the decisions made at the Fifth CCCF[2] and subsequently adopted by the 34th Codex Alimentarius Commission in 2011[3]: the results of the 74th JECFA meeting on Fumonisins and Cyanogenic glycosides have been incorporated.

2. As the Third Session of CCCF agreed to discontinue work on the food categorization system to be used for the purpose of the General Standard for Contaminants and Toxins in Foods and Feeds (GSCTF) [4], 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 Codex Code for the commodity, the Codex Code was removed if it was added after the adoption.

Some texts were added in the Explanatory Notes to indicate whether and where commodity descriptions are found.

2. 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.

3. The list of maximum levels for contaminants and toxins in foods is attached to this document (starting from page 2). Schedule I is no longer included in this Information Document as agreed by the Fourth CCCF but is available in the GSCTFF (CODEX STAN 193-1995).

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1 ALINORM 06/29/12, para. 116
2 REP11/CF
3 REP11/CAC
4 ALINORM 09/31/41, para. 37

Working Document for Information and Use in Discussions on the GSCTF

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 the 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, the 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 the CCCF.

INDEX OF CONTAMINANTS IN ALPHABETICAL ORDER

Background of the Working Document

The Working Document was established in its current form when the 36th Codex Committee on Food Additives and Contaminants (CCFAC) 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 Part2) 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 32nd CCFAC 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 36th CCFAC, 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 delegations of the Netherlands and Japan to perform this task (ALINORM 04/27/12, paras 118 and 119). The current Working Document is the subsequent result.

EXPLANATORY NOTES

Reference to JECFA:	References to 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 milligrammes (mg) per kg body weight (bw). The year of recommendations and additional explanation are included.
Residue definition:	Definition of the contaminant in the form of which the ML applies or which may or should be analyzed in commodities.
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 code:	The code for food commodities are according to the food categorization system as contained in Annex IV of the GSCTF or the Codex Classification of Foods and Animal Feeds as contained in Volume 2 of the Codex Alimentarius. The food/feed categorization system also specifies the part of commodity which should be analyzed and to which the ML applies, unless a specific commodity definition is provided as an annex to the ML. For those maximum levels contained in Codex commodity standards, the relevant standard numbers are referred, if the code numbers are not readily available for these commodities.
Type:	Indicates whether the value is Codex maximum level (ML) or Codex guideline level (GL). See also the definitions of these terms in the preamble of the GSCTF.
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).

Qualification of MLs

C:	In canned products only

Description of commodities

Commodity with Codex code	The description of commodity and the portion of commodity to which the ML or GL applies and which is analyzed are found in the relevant section of the Codex Classification of Foods and Animal Feeds (Codex MISC 4)
Commidity for which Codex commodity standard was adopted	The description of commodity is found in the “Description” section of the relevant Codex commodity standard.
Other than the above	No detailed description has been considered by CCFAC/CCCF.

Definitions of some toxicological terms

PMTDI:	*(Provisional Maximum Tolerable Daily Intake). 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.* The endpoint used for contaminants that are known not to accumulate in the body Its value represents permissible human exposure as a result of the background 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.
PTWI:	*(Provisional Tolerable Weekly Intake) 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* 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.
PTMI:	*(Provisional Tolerable Monthly Intake)* 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
BMDL:	*(Benchmark Dose Lower Limit)* 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.
MOE	*(Margin of Exposure)* 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.

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/chem/principles/en/index1.html#content

Compounds that have not been toxicologically evaluated by JECFA

1. Benzene

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^{-5} 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^{-5} upper-bound excess lifetime cancer risk, the guideline value of 0.01 mg/liter was retained.

The Third CCCF 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 code of practice 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 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).

2. Pyrrolizidine alkaloids

The Fifth CCCF agreed to re-establish the electronic Working Group, led by Netherland working in English, to update the discussion paper based on the last Committee's consideration in particular to undertake further compilation of existing management practices and to evaluate the possibility to develop a code of practice for consideration at its next session. .

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 probably the most 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 carry-over from PAs in 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).

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 (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	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 fro human exposure to aluminium. (ALINORM 07/30/41, para. 31)

The 67th JECFA 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 JECFA 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 the JECFA confirmed that the resulting health-based guidance value should be expressed as a PTWI.

The JECFA 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. The JECFA also noted that dietary exposure to Al is expected to be very high for infants fed on soya-based formula.

The 67th JECFA 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 the 74th JECFA 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 neurobehavioural 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. JECFA 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.

Metals

Aluminium

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

The 74th JECFA 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: BMDL0.5 3.0 µg/kg bw per day (2-7 µg/kg bw per day based on the range of estimated total dietary exposure)(2010, for inorganic arsenic)
Residue definition: Arsenic: total when not otherwise mentioned or inorganic arsenic; or other specification
Synonyms: As
Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Edible fats and oils	0.1	ML	Adopted	CS 19-1981	FO	Edible fats and oils not covered by individual standards	1)
	Fat spreads and blended spreads	0.1	ML	Adopted	CS 256-2007	FO		1)
	Named animal fats	0.1	ML	Adopted	CS 211-1999	FO	Lard, rendered pork fat, premier jus and edible tallow.	1)
	Olive oil, refined	0.1	ML	Adopted	CS 33-1981	FO		
	Olive oil, virgin	0.1	ML	Adopted	CS 33-1981	FO		
	Olive, pomace oil	0.1	ML	Adopted	CS 33-1981	FO	Olive pomace oil	
	Vegetable oils, Crude	0.1	ML	Adopted	CS 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.	
	Vegetable oils, Edible	0.1	ML	Adopted	CS 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.	1)
	Natural mineral water	0.01	ML	Adopted	CS 108-1981	NMW	Expressed in total As mg/l	Changed from 0.05 mg/l in 2001.
	Salt, food grade	0.5	ML	Adopted	CS 150-1985	NFSDU		
	Brown rice or Polished rice	0.3 or 0.2	ML	3		CF	for total As or inorganic As or for inorganic As	CX/CF 12/6/8

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." CS for Edible Fats and Oils Not Covered by Individual Standards contains the same contaminant provision as the other recent Standards for oils and fats (only applying to Pb and As).

Metals

Arsenic

A position document CX/FAC 99/22 on arsenic discussed in the 31st CCFAC in 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 CCFAC 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).

The 72nd JECFA in February 2010 derived an inorganic arsenic BMDL for a 0.5% increased incidence of lung cancer (BMDL0.5) by using a range of assumptions to estimate exposure from drinking-water and food, with differing concentrations of inorganic arsenic. The BMDL0.5 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 BMDL0.5 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 BMDL0.5 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 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 World Health Organization 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 72nd JECFA 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.

The 5th CCCF (2011) agreed to initiate new work on maximum levels for arsenic in rice subject to approval by the 34th Session of the Commission and also agreed to re-convene the electronic Working Group, led by China and working in English, 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.

The 34th CAC (2011) approved the new work (REP11/CAC, para.142).

Metals

Arsenic

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 ug/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 6x 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)
Toxicological guidance value:	PTMI 25 µg/kg bw (2010)
Residue definition:	Cadmium, total
Synonyms:	Cd
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
VB 0040	Brassica vegetables	0.05	ML	Adopted	2005	FAC		
VA 0035	Bulb vegetables	0.05	ML	Adopted	2005	FAC		
VC 0045	Fruiting vegetables, cucurbits	0.05	ML	Adopted	2005	FAC		
VO 0050	Fruiting vegetables, other than cucurbits	0.05	ML	Adopted	2005	FAC	Excluding tomatoes and edible fungi.	
VL 0053	Leafy vegetables	0.2	ML	Adopted	2005	FAC		
VP 0060	Legume vegetables	0.1	ML	Adopted	2001	FAC		
VR 0589	Potato	0.1	ML	Adopted	2005	FAC	Peeled	
VD 0070	Pulses	0.1	ML	Adopted	2001	FAC	Excluding soya bean (dry)	
VR 0075	Root and tuber vegetables	0.1	ML	Adopted	2005	FAC	Excluding potato and celeriac	
VS 0078	Stalk and stem vegetables	0.1	ML	Adopted	2005	FAC		
GC 0081	Cereal grains, except buckwheat, canihua and quinoa	0.1	ML	Adopted	2001	FAC	Excluding wheat and rice; and bran and germ	
CM 1205	Rice, polished	0.4	ML	Adopted	2006	FAC		
GC 0654	Wheat	0.2	ML	Adopted	2005	FAC		
IM 0152	Cephalopods	2	ML	Adopted	2006	FAC	Without viscera	
IM 0151	Marine bivalve molluscs	2	ML	Adopted	2006	FAC	Excluding oysters and scallops	
	Natural mineral waters	0.003	ML	Adopted	CS 108-1981	NMW	Expressed in mg/l	
	Salt, food grade	0.5	ML	Adopted	CS 150-1985	NFSDU		

At the 61th JECFA (2003) it was estimated that the total intake of cadmium ranged from 2.8 to 4.2 µg/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 µg/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.

The 36th CCFAC (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).

Metals

Cadmium

The 64th JECFA (2005) conducted intake and impact assessment requested by the 36th session of CCFAC for the seven commodity groups; rice, wheat, potatoes, stem and root vegetables, leafy vegetables, other vegetables and molluscs taking into account different MLs. The JECFA concluded that the effect of different MLs on the overall intake of cadmium would be very small.

The 73rd JECFA (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 β2-microglobulin level was chosen as the most suitable biomarker for cadmium toxicity because it was widely recognized as a marker for renal pathology and 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 β2-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) μg of cadmium per gram creatinine was estimated. Using a one-compartment toxicokinetic model, a corresponding dietary cadmium exposure of 0.8 μg/kg body weight per day or 25 μg/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 μg/kg body weight and established a PTMI of 25 μg/kg body weight,
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 the Committee were below this PTMI.

The 5th CCCF agreed that no follow-up was necessary.

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 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; International Programme on Chemical Safety (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; International Programme on Chemical Safety (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)
Residue definition:	Lead, total
Synonyms:	Pb
Related code of practice:	Code of Practice for the Prevention and Reduction of Lead Contamination in Foods (CAC/RCP 56-2004) Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
FT 0026	Assorted (sub)tropical fruits, edible peel	0.1	ML	Adopted	2001	FAC		
FI 0030	Assorted (sub)tropical fruits, inedible peel	0.1	ML	Adopted	2001	FAC		
FB 0018	Berries and other small fruits	0.2	ML	Adopted	2001	FAC		
FC 0001	Citrus fruits	0.1	ML	Adopted	2001	FAC		
FP 0009	Pome fruits	0.1	ML	Adopted	2001	FAC		
FS 0012	Stone fruits	0.1	ML	Adopted	2001	FAC		
VB 0040	Brassica vegetables	0.3	ML	Adopted	2001	FAC	Excluding kale	
VA 0035	Bulb vegetables	0.1	ML	Adopted	2001	FAC		
VC 0045	Fruiting vegetables, Cucurbits	0.1	ML	Adopted	2001	FAC		
VO 0050	Fruiting vegetables, other than Cucurbits	0.1	ML	Adopted	2001	FAC	Excluding mushrooms	
VL 0053	Leafy vegetables	0.3	ML	Adopted	2001	FAC	Including Brassica leafy vegetables but excluding spinach.	
VP 0060	Legume vegetables	0.2	ML	Adopted	2001	FAC		
VD 0070	Pulses	0.2	ML	Adopted	2001	FAC		
VR 0075	Root and tuber vegetables	0.1	ML	Adopted	2001	FAC	Including peeled potatoes	
	Canned fruit cocktail	1	ML	Adopted	CS 78-1981	PFV		
	Canned mangoes	1	ML	Adopted	CS 159-1987	PFV		
	Canned pineapple	1	ML	Adopted	CS 42-1981	PFV		
	Canned raspberries	1	ML	Adopted	CS 60-1981	PFV		
	Canned strawberries	1	ML	Adopted	CS 62-1981	PFV		
	Canned tropical fruit salad	1	ML	Adopted	CS 99-1981	PFV		
	Mango chutney	1	ML	Adopted	CS 160-1987	PFV		
	Table olives	1	ML	Adopted	CS 66-1981	PFV		
	Canned tomatoes	1	ML	Adopted	CS 13-1981	PFV		
	Pickled cucumbers	1	ML	Adopted	CS 115-1981	PFV		

Metals

Lead

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	(cucumber pickles)							
	Processed tomato concentrates	1.5	ML	Adopted	CS 57-1981	PFV		
JF 0175	Fruit juices	0.05	ML	Adopted		FAC	Including nectars; Ready to drink	
GC 0081	Cereal grains, except buckwheat, canihua and quinoa	0.2	ML	Adopted	2001	FAC		
	Canned chestnuts and canned chestnuts puree	1	ML	Adopted	CS 145-1985	PFV		
MM 0097	Meat of cattle, pigs and sheep	0.1	ML	Adopted	2001	FAC	Also applies to the fat from meat	
PM 0110	Poultry meat	0.1	ML	Adopted	2001	FAC		
MO 0812	Cattle, Edible offal of	0.5	ML	Adopted	2001	FAC		
MO 0818	Pig, Edible offal of	0.5	ML	Adopted	2001	FAC		
PO 0111	Poultry, Edible offal of	0.5	ML	Adopted	2001	FAC		
	Fish	0.3	ML	Adopted	2006	FAC		
	Edible fats and oils	0.1	ML	Adopted	CS 19-1981,	FO	Edible fats and oils apply to any oil or fat not covered by individual standards	1)
	Fat spreads and blended spreads	0.1	ML	Adopted	CS 256-2007	FO		1)
	Named animal fats	0.1	ML	Adopted	CS 211-1999	FO	Lard, rendered pork fat, premier jus and edible tallow.	
	Olive oil, refined	0.1	ML	Adopted	CS 33-1981	FO		
	Olive oil, virgin	0.1	ML	Adopted	CS 33-1981	FO		
	Olive, pomace oil	0.1	ML	Adopted	CS 33-1981	FO	Olive pomace oil	
PF 0111	Poultry fats	0.1	ML	Adopted	2001	FAC		
OC 0172	Vegetable oils, Crude	0.1	ML	Adopted	CS 210-1999, 2001	FO, FAC	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.	
OR 0172	Vegetable oils, Edible	0.1	ML	Adopted	CS 210-1999, 2001	FO, FAC	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.	

Metals

Lead

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
ML 0106	Milks	0.02	ML	Adopted	2001	FAC	A concentration factor applies to partially or wholly dehydrated milks.	The previous footnote "For dairy products, an appropriate concentration factor should apply" was changed by the 35th CCFAC.2)
	Secondary milk products	0.02	ML	Adopted	2001	FAC	As consumed	
	Natural mineral waters	0.01	ML	Adopted	CS 108-1981	NMW	Expressed in mg/l	
	Infant formula	0.02	ML	Adopted	2001	FAC	Ready to use	CCNFSDU is revising at Step 6 the Codex Standard for Infant formula which includes an ML for lead at the same level.
	Salt, food grade	2	ML	Adopted	CS 150-1985	NFSDU		
	Wine	0.2	ML	Adopted	2001	FAC		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).

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." The Codex Standard for Edible Fats and Oils Not Covered by Individual Standards contains the same contaminant provisions as the other recent Standards for oils and fats (only applying to Pb and As).
2) The 32nd CAC (2001) requested reevaluation of the lead MLs in milk and milk fat (ALINORM 01/41, para. 121); see also ALINORM 03/12 para. 135-137. The 35th CCFAC (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 the 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).

The 4th CCCF considered whether the levels for lead applied to the more general standards with particular regard to whether these levels could also be extended to other processed commodities in these general standards for which levels had not previously been established. The Committee agreed to not take action until the 73rd JECFA in June 2010 had completed its evaluation (ALINORM 10/33/41, para. 18-22).

The 73rd JECFA 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

Lead

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.

The 5th CCCF agreed to establish an electronic Working Group, led by the United States of America and working in English only, to: (i) reconsider the existing maximum levels 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.

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 (WHO Food Additives Series 44, 2000 with reference to Environmental health criteria for inorganic lead, International Programme on Chemical Safety (IPCS), 1995).

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 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. (WHO Food Additives Series 44, 2000 with reference to Environmental health criteria for inorganic lead, International Programme on Chemical Safety (IPCS), 1995)

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 was considered to be the most critical effect. (Food Additives Series 44, 2000 with reference to Environmental health criteria for inorganic lead, International Programme on Chemical Safety (IPCS), 1995).

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)
Residue definition:	Mercury, Total
Synonyms:	Hg
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Natural mineral waters	0.001	ML	Adopted	CS 108-1981	NMW	Expressed in mg/l	
	Salt, food grade	0.1	ML	Adopted	CS 150-1985	NFSDU		

No CCFAC position document was available about mercury.

The 72nd JECFA in February 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 BMDL10 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 72nd JECFA 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,)
Residue definition:	Methylmercury
Related code of practice:	Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Fish	0.5	GL	Adopted	1991	FAC, FFP	Except predatory fish Intended for methylmercury in fresh or processed fish and fish products moving in international trade. a)	
	Predatory fish	1	GL	Adopted	1991	FAC, FFP	Predatory fish such as shark (WS 0131), swordfish, tuna (WS 0132), pike (WF 0865) and others. Intended for methylmercury in fresh or processed fish and fish products moving in international trade. a)	1)

1) The GLs for methylmercury in fish were adopted by the CAC-19 in 1991 (ALINORM 91/40, para. 202), on the understanding that the levels would be kept under review by the CCFAC as well as the CCFFP, especially as to the identification of predatory species of fish to which the higher GL applies.

The 53rd JECFA（1999）calculated the human exposure to methylmercury in regional diets to range from 0.3-1.5 ug/kg bw/week. Nationally reported dietary exposures are in the range 0.1 –2.0 mcg/kg bw/week. The 53rd JECFA maintained the PTWI of 3.3 ug bw for methylmercury set in the previous meetings of the 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 JECFA 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.

The 67th JECFA 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 67th JECFA 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.

Metals

Methylmercury

The 24th CCFAC (1992) informed the CAC and the CCFFP that the recommended GLs for mercury in fish referred to total mercury rather than methylmercury. The 20th CAC (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 the CCFAC at its next meeting. The 26th CCFAC (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. The 29th CCFAC (1997) noted that the 43rd CXEXEC (1996) had recommended that the 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. The 32nd CCFAC (2000) took note of these recommendations made by the 53rd JECFA.

The 37th CCFAC 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).

The 38th CCFAC agreed: to forward a request to the 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).

The First CCCF 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 First CCCF reaffirmed the decision made by the 38th Session of the CCFAC 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)

The 30th Commission recalled that its 29th Session 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 and dioxin-like PCBs (DLC) and the nutritive and health benefits of eating fish, in response to the request of the 29th session of the Commission. (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.

Methylmercury

The 5th CCCF (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.

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 end-point (WHO Food additives Series 52; 2004).

a) Lots should be considered as being in compliance with the guideline levels if the level of methylmercury in the analytical sample, derived from the composite bulk sample, does not exceed the above levels. Where these Guideline levels are exceeded, governments should decide whether and under what circumstances, the food should be distributed within their territory or jurisdiction and what recommendations, if any, should be given as regards restrictions on consumption, especially by vulnerable groups such as pregnant women.

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)
Residue 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 (CAC/RCP 60-2005)
Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)		Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Canned beverages	150	C	ML	Adopted	2007	FAC 99-07		Changed from 200 mg/kg in 2005.
	Cooked cured chopped meat	50		ML	Adopted	CS 98-1981	PMPP	For products in other containers than tinplate container	
	Cooked cured ham	50		ML	Adopted	CS 96-1981	PMPP	For products in other containers than tinplate container	
	Cooked cured pork shoulder	50		ML	Adopted	CS 97-1981	PMPP	For products in other containers than tinplate container	
	Corned beef	50		ML	Adopted	CS 88-1981	PMPP	For products in other containers than tinplate container	
	Luncheon meat	50		ML	Adopted	CS 89-1981	PMPP	For products in other containers than tinplate container	
	Canned foods (other than beverages)	250	C	ML	Adopted	2007	FAC 99-07		
	Canned citrus fruits	250	C	ML	Adopted	2009	PFV, CF	The ML covers canned mandarin oranges, canned grapefruits, canned pummelos and canned sweet oranges offered for direct consumption, including for catering purposes or for repacking if required.	
	Jams, jellies and marmalades	250		ML	Adopted	2009	PFV, CF	Jam, jellies and marmalades made from all fruits and vegetables offered for direct consumption, including for catering purposes or for repacking if required excluding: a. products when indicated as being intended for further processing such as those intended for use in the manufacture of fine bakery wares, pastries or biscuits; b. products which are clearly intended or labelled as intended for special dietary uses;	

Metals

Tin

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
							c. reduced sugar products or those with a very low sugar content; d. products where the foodstuffs with sweetening properties have been replaced wholly or partially by food additive sweeteners.	
	Canned vegetables	250 C	ML	Adopted	2009	PFV, CF	The ML covers canned asparagus, canned carrots, canned green peas, canned green beans and wax beans, canned mature processed peas, canned palmito, canned sweet corn and canned baby corn offered for direct consumption, including for catering purposes or for repacking if required.	
	Canned stone fruits	250 C	ML	Adopted	2009	PFV, CF	The ML covers canned peaches, canned plums, canned apricots and canned cherries offered for direct consumption, including for catering purposes or for repacking if required.	

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.

The 33rd JECFA (1988) established a PTWI for inorganic tin of 14 mg/kg bw.

At the 55th JECFA (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 the 22nd JECFA (1978), that these compounds differ considerably from inorganic tin compounds with respect to toxicity and should be considered separately.

The 55th JECFA (2000) 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 the 34th CCFAC (2002) and in the 35th CCFAC (2003) (ALINORM 03/12, para.146 and ALINORM 03/12A, para.160), the proposed MLs were repeatedly returned to step 3. The 35th CCFAC 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. The 36th CCFAC (2004) decided to hold the proposed MLs and reconsider these MLs in the light of the 64th JECFA re-evaluation (ALINORM 04/27/12, para.171).

Tin

The 64th JECFA (2005) concluded that the data available indicated that it is inappropriate to establish and 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.

The First CCCF (2007) agreed to forward the draft MLs to the 30th Commission 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 1. (ALINORM 07/30/41, para. 81).

The 30th Commission 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 (stannites or stannates).

Mycotoxins

Aflatoxins, Total

Reference to JECFA:	31 (1987), 46 (1996), 49 (1997) , 68 (2007)
Toxicological guidance value:	Carcinogenic potency estimates for aflatoxins B, G, M (1997, Intake should be reduced to levels as low as reasonably possible.)
Residue definition:	Aflatoxins total (B1 +B2 + G1 + G2)
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 (CAC/RCP 55-2004) Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Tree Nuts (CAC/RCP 59-2005) Code of Practice for the Reduction of Aflatoxin B1 in Raw Materials and Supplemental Feedingstuffs for Milk Producing Animals (CAC/RCP 45-1997) Code of Practice for the Prevention and Reduction of Aflatoxin Contamination in Dried Figs (CAC/RCP 65-2008)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
TN 0660	Almonds	15	ML	Adopted	2008	CF	For further processing. For sampling plan, see Schedule I.	
TN 0660	Almonds	10	ML	Adopted	2008	CF	Ready-to-eat. For sampling plan, see Schedule I.	
	Brazil nuts	15	ML	Adopted	2010	CF	For further processing	
	Brazil nuts	10	ML	Adopted	2010	CF	Ready-to-eat	
TN 0666	Hazelnuts	15	ML	Adopted	2008	CF	For further processing. For sampling plan, see Schedule I.	
TN 0666	Hazelnuts	10	ML	Adopted	2008	CF	Ready-to-eat. For sampling plan, see Schedule I.	
SO 0697	Peanut	15	ML	Adopted	1999	FAC	Applies to peanuts intended for further processing. For sampling plan, see Schedule I.	
TN 0675	Pistachio nut	15	ML	Adopted	2008	CF	For further processing. For sampling plan, see Schedule I.	
TN 0675	Pistachio nut	10	ML	Adopted	2008	CF	Ready-to-eat. For sampling plan, see Schedule I.	
DF 0297	Dried figs	10	ML	3	1)	CF	Ready-to-eat	1)

1) CX/CF 12/6/10 (Annex I)

The 23rd CCFAC (1991) decided to discontinue the development of a ML for aflatoxins in foods in general, and to discuss the problems on a commodity basis.

The CCCPL in 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 the 29th CCFAC (1997).
- Corn was included in a Technical Consultation on sampling plans for aflatoxins in commodities. See FAO Food and nutrition Paper 55 (Rome, 1993).

Mycotoxins

Aflatoxins, Total

- The 26th CCFAC (1994) decided to discontinue the establishment of GLs for AFB1 in supplementary feedingstuffs for milk-producing animals (previously proposed at the level of 5 ug/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 B1 in raw materials and supplemental feedingstuffs for milk-producing animals was developed and adopted as RCP 045-1997.

The 68th JECFA 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.

The 5th CCCF (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 10µg/kg can be developed for consideration by the next session of the Committee (REP11/CF, para. 50).

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 B1, B2, G1 and G2 and are a group of structurally related difuranocoumarin derivatives that usually occur together in varying ratios, AFB1 usually being the most important one. These compounds pose a substantial hazard to human and animal health. IARC (1992) classified aflatoxin B1 in Group 1 (human carcinogen) and aflatoxin M 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 B1 present in animal feed can partly be transferred to milk in the form of the metabolite aflatoxin M1 (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 (µg/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.

Aflatoxins, Total

A. Definitions

Lot:	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.
Sublot:	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.
Sampling plan:	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.
Incremental sample:	a quantity of material taken from a single random place in the lot or sublot.
Aggregate sample:	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.
Laboratory sample:	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.
Test portion:	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 %.

Aflatoxins, Total

Table 1: Subdivision of Large Lots into Sublots for Sampling

Commodity	Lot weight – tonne (T)	Weight or number of sublots	Number of incremental samples	Laboratory sample weight (kg)
Peanuts	≥ 500	100 tonnes	100	20
	>100 and <500	5 sublots	100	20
	≥ 25 and ≤ 100	25 tonnes	100	20
	>15 and <= 25	--1 sublot	100	20

<u>Number of Incremental Samples for Lots of Less than 15 Tonnes</u>

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≤ 1	10
1 <T ≤ 5	40
5< T ≤ 10	60
10<T < 15	80

<u>Incremental Sample Selection</u>

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.

Aflatoxins, Total

<u>*Static Lots*</u>

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 :

Equation 1 : SF = (LT x IS)/(AS x IP). The sampling frequency (SF) is the number of packages sampled. All weights should be in the same mass units such as kg.

<u>*Dynamic Lots*</u>

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 though 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.

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 x LT) / (T x 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).

Aflatoxins, Total

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 x V) / (D x 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 cm x 30,000 kg)/(20 kg x 30 cm/sec) = 254 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 grams or greater, depending on the total number of increments, to obtain an aggregate sample of 20kg.

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.

Homogenization – Grinding

22. As the distribution of aflatoxin is extremely non-homogeneous, samples should be prepared - and especially homogenized - with extreme care. All laboratory sample obtained from aggregate sample is to be used for the homogenization/grinding of the sample.

Aflatoxins, Total

23. The sample should be finely ground and mixed thoroughly using a process that approaches as complete a homogenization 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 homogenization (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

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_R	All	As derived from Horwitz Equation	2 x value derived from Horwitz Equation
Precision RSD_r may be calculated as 0.66 times Precision RSD_R 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.:

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

where:

* RSD_R is the relative standard deviation calculated from results generated under reproducibility conditions [(s_R / _) x 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

Lot - 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.

Sublot - 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.

Sampling plan - 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.

Incremental sample – the quantity of material taken from a single random place in the lot or sublot.

Aggregate sample - 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.

Laboratory sample – 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.

Test portion – 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.

Aflatoxins, Total

Ready-to-eat treenuts – nuts, which are not intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins.

Treenuts destined for further processing – 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.

Operating Characteristic (OC) Curve – 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 binomial distribution[5],[6],[7] are used to calculate operating characteristic (OC) curves that describe the performance of the proposed aflatoxin-sampling plans (Annex II).
5. In Annex I, 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[8]. A relative standard deviation of 22% is considered by FAPAS as an appropriate measure of the best agreement

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[5] 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.
[6] 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.
[7] 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. Minist~erio da Agricultura, pecuária e do Abasteciento. 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).

Aflatoxins, Total

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. The within laboratory analytical uncertainty for each treenut can be found at the website http://www5.bae.ncsu.edu/usda/www/ResearchActDocs/treenutwg.html and for Brazil nuts in the CONFORCAST[7].

6. The issue of correcting the analytical test ns for the range of acceptable recoverresult 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 ng/g, 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 ng/g total aflatoxins

Number of laboratory samples – 1

Laboratory sample size - 20 kg
Almonds – shelled nuts
Hazelnuts – shelled nuts
Pistachios – inshell nuts (equivalent to about 10kg 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.

Aflatoxins, Total

Analytical method – performance based (see Table 2)

Decision rule – If the aflatoxin test result is less than or equal to 15 ng/g 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 ng/g total aflatoxins

Number of laboratory samples – 2

Laboratory sample size - 10 kg
Almonds – shelled nuts
Hazelnuts – shelled nuts
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 ng/g 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 sublot 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 sublot may exceed the mentioned weight by a maximum of 25%.

Aflatoxins, Total

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 (sublot) size. However, the number and size of the incremental samples will vary with lot (sublot) size.
19. The number of incremental samples to be taken from a lot (sublot) 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[a] as a function of lot (or sublot) weight.

Lot or Sublot Weight[b] (T in Tonnes)	Minimum Number of Incremental Samples	Minimum Incremental Sample Size[c] (g)	Minimum Aggregate Sample Size (kg)
$T<1$	10	2000	20
$1\leq T<5$	25	800	20
$5\leq T<10$	50	400	20
$10\leq T<15$	75	267	20
$15\leq T$	100	200	20

Aflatoxins, Total

a/ Minimum aggregate sample size = laboratory sample size of 20 kg
b/ 1 Tonne = 1000 kg
c/ Minimum incremental sample size = laboratory sample size (20 kg)/minimum number of incremental samples, i.e. for 0.5<T< 1 tonne, 2000 g = 20000/10

Weight of the Incremental Sample

20. The suggested minimum weight of the incremental sample should be approximately 200 grams 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 sublot 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 x IS)/(AS x 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).

Aflatoxins, Total

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 x LT) / (T x 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 x V) / (D x 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,

    T = (5.0 cm x 20,000 kg)/(20 kg x 20 cm/sec) = 250 sec.

31. If the lot is moving at 500 kg per minute, the entire lot will pass through the sampler in 40 minutes (2400 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.

<u>Packaging and Transportation of Samples</u>

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.

Aflatoxins, Total

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[9]. 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[10].

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.

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[9] 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.

[10] Spanjer, M., Scholten, J., Kastrup, 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.

Aflatoxins, Total

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. 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_R (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_r (Repeatability)	1 to 120	Calculated as 0.66 times Precision RSD_R	n/a
	>120	Calculated as 0.66 times Precision RSD_r	n/a

n/a = not applicable

Aflatoxins, Total

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[2] and Horwitz and Albert[11], respectively.

Equation 4: $RSD_R = 22.0$ (for $C \leq 120$ ng/g or $c \leq 120x10^{-9}$)

Equation 5: $RSD_R = 2^{(1-0.5logc)}$ (for $C > 120$ ng/g or $c > 120x10^{-9}$)

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 = $0.66RSD_R$
- c = the aflatoxin concentration ratio (i.e. 1 = 100g/100g, 0.001 = 1,000 mg/kg)
- C = aflatoxin concentration or mass of aflatoxin to mass of treenuts (i.e. ng/g)

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.

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[1] 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[7].

[11] 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.

Aflatoxins, Total

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Table 1. Variances[a] associated with the aflatoxin test procedure for each treenut.

Test Procedure	Almonds	Hazelnuts	Pistachios	Shelled Brazil nuts
Sampling[b,c]	$S^2_s = (7{,}730/ns)5.759C^{1.561}$	$S^2_s = (10{,}000/ns)4.291C^{1.609}$	$S^2_s = (8{,}000/ns)7.913C^{1.475}$	$S^2_s = (1{,}850/ns)4.8616C^{1.889}$
Sample Prep[d]	$S^2_{sp} = (100/nss)0.170C^{1.646}$	$S^2_{sp} = (50/nss)0.021C^{1.545}$	$S^2_{sp} = (25/nss)2.334C^{1.522}$	$S^2_{sp} = (50/nss)0.0306C^{0.632}$
Analytical[e]	$S^2_a = (1/na)0.0484C^{2.0}$	$S^2_a = (1/na)0.0484C^{2.0}$	$S^2_a = (1/na)0.0484C^{2.0}$	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, 1000, and 1600, 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[2] (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.

Aflatoxins, Total

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.

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Aflatoxins, Total

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.

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Aflatoxin M1

Reference to JECFA:	56 (2001)
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 M1 of 0.05 and 0.5 µg/kg are very small. The potency of aflatoxin M1 appears to be so low in HBsAg- individuals that a carcinogenic effect of M1 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.)
Residue definition:	Aflatoxin M1
Synonyms:	AFM1
Related Code of Practice:	Code of Practice for the Reduction of Aflatoxin B1 in Raw Materials and Supplemental Feedingstuffs for Milk Producing Animals (CAC/RCP 45-1997)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
ML 0106	Milks	0.5	ML	Adopted	2001	FAC		

The 24th CCFAC (1993) decided to stop the development of a specific standard for aflatoxin M1 in milk destined for use in baby foods. The CCFAC has discussed 2 options for a standard for aflatoxin M1 in milk: 0.05 ug/kg and 0.5 ug/kg. At the request of the 32nd CCFAC (2000), the 56th JECFA (2001) examined exposure to aflatoxin M1 and conducted a quantitative risk assessment to compare the consequences of setting the maximum level in milk at 0.05 ug/kg and 0.5 ug/kg. The estimates of the potency of aflatoxin M1 were combined with estimates of intake from the GEMS/Food European regional diet. JECFA noted that the calculation showed that, with worst case assumptions, the projected risks for liver cancer at the proposed maximum levels of aflatoxin M1 of 0.05 and 0.5 ug/kg are very small. As a result, 0.5 ug/kg was forwarded to the 33rd CCFAC (2001) which adopted this draft ML, noting that data supporting the lower level, if and when available, could be examined by the CCFAC at a future meeting when necessary.

It is acknowledged that the aflatoxin M1 level in milk is related to the aflatoxin B1 level in the animal feed. See notes under Aflatoxins, total.

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 derivates) Group ARfD 0.008 mg/kg bw (2010, for DON and its acetylated derivates)
Synonyms:	Vomitoxin; Abbreviation, DON
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes (CAC/RCP 51-2003)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Raw cereal grains (wheat, maize and barley)	2		3		CF	Raw wheat, maize and barley grain to be subject to sorting or other physical treatment before human consumption or before use as an ingredient in other foods	CX/CF 12/6/9
	Semi-processed products derived from wheat, maize and barley	1		3		CF	Flour, semolina, meal, grits, flakes, starch	CX/CF 12/6/9
	Cereal-based foods for infants (up to 12 months) and young children (12 to 36 months)	0.5		3		CF	Cereal-based foods for infants and young children (e.g., infant cereals, biscuits for infants and young children, pasta for infants and young children)	CX/CF 12/6/9

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); the 35th CCFAC (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).

The 26th CAC (2003) approved the development of maximum levels for DON as new work (ALINORM 03/41, Appendix VIII).

The 36th CCFAC (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 the 37th Session of the Committee (ALINORM 04/27/12, paras 156-158).

The 37th CCFAC (2005) 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).

Mycotoxins

Deoxynivalenol

The 38th CCFAC (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).

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 prerequisite to developing international standards, the First CCCF agreed 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 1st CCCF 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)

The 2nd CCCF 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)

The 72nd JECFA in February 2010 decided to convert the provisional maximum tolerable daily intake (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 deoxynivalenol (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 (BMDL10) 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 Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme (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 72nd JECFA noted that data are limited on the occurrence of DON-3-glucoside, which might be an important contributor to dietary exposure.

The 5th CCCF (2011) agreed to return the proposed draft Maximum Levels for DON to Step2/3 for further development the electronic Working Group led by Canada, circulation for comments and further consideration by the next session of the Committee (REP11/CF, para. 43).

Deoxynivalenol

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 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 product 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

Fumonisins (B1+B2+B3)

Reference to JECFA:	56 (2001), 74 (2011)
Toxicological guidance value:	PMTDI 0.002 mg/kg bw (2001, 2011)
Synonyms:	(Several related compounds have been described, notably fumonisin B1, B2 and B3 (abbreviation: FB1 etc.))
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes (CAC/RCP 51-2003)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Corn/maize grain, unprocessed	5		4		CF		1)
	Corn/maize flour/meal	2		4		CF		1)
	Popcorn grain	2		4		CF		1)
	Maize-based baby food	0.5		4		CF		1)
	Maize based breakfast cereals, snack and chips	1		4		CF		1)

1) Fumonisin (B1 and B2)

A position paper has been prepared for fumonisins (last version CX/FAC 00/22). The 32nd CCFAC (2000) asked the USA to finalize the position paper as a potential basis for future work (ALINORM 01/12 paras 106-109). No MLs have been proposed.

The Representative of WHO, speaking on behalf of the JECFA Secretariats, clarified at the First CCCF that there was no plan for JECFA to update the risk assessment conducted by the 56th JECFA meeting and that an updated risk assessment could be conducted only when new data became available. (ALINORM 07/30/41, para. 135)

The Second CCCF 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)

Discussion paper on Fumonisins

The Third CCCF 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 the 32nd Session of the Commission. 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 the Commission at its 32nd Session.(ALINORM 09/32/REP, Appendix VI)

The 4th CCCF 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).

The 74th JECFA evaluated fumonisins and reviewed all relevant studies performed since 2001. Studies suitable for dose-response analysis have been conducted with rodents employing either purified FB1 or F. verticillioides culture material containing FB1. Although naturally contaminated corn would probably be more representative of actual human dietary exposure than either purified FB1 or culture material, no suitable studies were identified that used naturally contaminated corn as test material.

Fumonisins (B1+B2+B3)

For culture material, the lowest identified BMDL10 using FB1 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 FB1, the lowest identified BMDL10 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 FB1, FB2, and FB3, alone or in combination, was retained.

It was estimated that the dietary exposure to FB1 for the general population ranges from 0.12 x 10-3 to 7.6 µg/kg bw per day (95th percentile: up to 33.3 µg/kg bw per day). Dietary exposure to total fumonisins for the general population would range, for a consumer with average consumption, from 0.087 x 10-3 to 10.6 µg/kg bw per day, whereas for consumers with high consumption, exposure would be up to 44.8 µg/kg bw per day. Maize was found to be the predominant source of exposure to FB1 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 74th JECFA 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 74th JECFA 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 food products should be collected in order to establish appropriate sampling procedures. To validate the potential candidate urinary FB1 level for a human biomarker of short-term exposure, large-scale human studies that indicate a well characterized dose–response relationship between urinary FB1 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.

Fumonisins (B1+B2+B3)

Fumonisins are 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). Fumonisins are 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 B1 and fumonisin B2, is believed to be the most abundant and most toxic group. A typical ratio between these analogues is B1:B2:B3 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. Fumonisins are 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. Fumonisins 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. 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. Fumonisins are 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 ug/kg bw).

Ochratoxin A

Reference to JECFA:	37 (1990), 44 (1995), 56 (2001), 68 (2007)
Toxicological guidance value:	PTWI 0.0001mg/kg bw (2001)
Residue 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)
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes (CAC/RCP 51-2003)
	Code of Practice for the Prevention and Reduction of Ochratoxin A Contamination in Wine (CAC/RCP 63-2007)
	Code of Practice for the Prevention and Reduction of Ochratoxin A Contamination in Coffee (CAC/RCP 69-2009)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
GC 0640	Barley	5	ML	Adopted	2008	CF		
GC 0650	Rye	5	ML	Adopted	2008	CF		
GC 0654	Wheat	5	ML	Adopted	2008	CF		

The 68th JECFA (2007) retained the PTWI of 100 ng/kg bw. The estimated overall dietary exposure to Ochratoxin A 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 68th JECFA concluded that it would be unlikely that an ML of 5 or 20 µg/kg has an impact on dietary exposure to Ochratoxin A. The committee was unable to reach a conclusion regarding developing countries due to the lack of adequate data to consider.

<u>Discussion paper on OTA in cocoa</u>

The 1st CCCF decided to establish and electronic working group, 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)

The 2nd CCCF agreed to suspend the consideration of this matter with the understanding to re-consider ochratoxin A contamination in cocoa in light of the new data available in the near future. (ALINORM 08/31/41, para. 170)

The 5th CCCF (2011) agreed to re-establish the electronic Working Group, working in English, led by Ghana, to update the discussion paper with a view to the development a code of practice, for consideration by the next session of the Committee (REP11/CF, para. 75).

Ochratoxin A

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. 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.

Patulin

Reference to JECFA:	35 (1989), 44 (1995)
Toxicological guidance value:	PMTDI 0.0004 mg/kg bw (1995)
Residue 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 (CAC/RCP 50-2003)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Apple juice	50	ML	Adopted	2003	FAC	The ML also covers apple juice as ingredient in other beverages.	

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

The 26th CAC in 2003 adopted the ML. The possible reduction of the ML from 50 to 25 ug/kg will be reconsidered by the CCFAC once the Code of Practice 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.

The First CCCF 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 Byssochlamys. 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 ug/kg bw/day in rats.

T2 and HT-2 Toxin

Reference to JECFA:	56 (2001)
Toxicological guidance value:	PMTDI 0.00006 mg/kg bw (2001, Group PMTDI for T-2 and HT-2 toxins, alone or in combination)
Related code of practice:	Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes (CAC/RCP 51-2003)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

No further action on T-2 and HT-2 toxin has been recommended by the 33rd CCFAC (2001), probably based on the understanding that the (limited) information available suggested that intakes would not exceed the PMTDI (ALINORM 01/12A, para. 16).

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.

The PMTDI is 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 is 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.

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, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes (CAC/RCP 51-2003)

Code	Food/product	Level (ug/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	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.

The 31st CCFAC (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 ZAL in cattle liver and muscle have been established by Codex (CCRVDF) because of recognized use of zeranol in cattle; they are relevant for the 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.

Zearalenone (ZEN) is the most important of a group of resorcyclic 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 (taleranol) has hormonal activity. Besides these substances which can be used as anabolic growth promoters, also alpha- and beta-zearalenol (ZEL) and zearalenone (ZAN) 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 ug/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-ZEL against ZAL. A ratio of 5 or more probably indicates only contamination by mycotoxins.

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 (BMDL10 0.31 mg/kg bw/day), mean intake 310, high intake 78 MOE Harderian gland tumours in mice (BMDL10 0.18 mg/kg bw/day), mean intake 180, high intaken 45.)
Related code of practice:	Code of Practice for the Reduction of Acrylamide in Foods (CAC/RCP 67-2009)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

JECFA was asked by the 36th Session of CCFAC (2004) to evaluate acrylamide.

The 64th JECFA (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/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 64th JECFA (2005) 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 the 64th JECFA:
- 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).

The 72nd JECFA in February 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 sixty-fourth 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.

Acrylamide

When average and high dietary exposures are compared with the BMDL10 (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 BMDL10 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 sixty-fourth 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 72nd JECFA recommended that longitudinal studies on intra-individual levels of acrylamide and glycidamide haemoglobin 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.

The 32nd CAC (2009) adopted the code of practice for the reduction of acrylamide in foods (ALINORM 09/32/REP).

The 4th CCCF agreed with the recommendations proposed by the working group:
- To encourage the use of the Code of Practice 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 Code of Practice.

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 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 the 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.

Acrylamide

Studies conducted in Sweden in 2002 showed the formation of high levels of acrylamide during frying or baking of a variety of food.

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.)
Residue definition:	acrylonitrile (monomer)
Synonyms:	2-Propenenitrile; vinyl cyanide (VCN); cyanoethylene; abbreviations, AN, CAN.

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Food	0.02	GL	Adopted	1991	FAC		

Guideline Levels for Acrylonitrile in Food and Vinyl Chloride Monomer in Food and Food Packaging Materials were adopted by the CAC at its 19th session (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)

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)

Chloropropanols

Reference to JECFA:	41 (1993; for 1,3-dichloro-2-propanol only), 57 (2001), 67 (2006)
Toxicological guidance value:	PMTDI 0.002 mg/kg bw (2001, for 3-chloro-1,2-propanediol; maintained in 2006. Establishment of tolerable intake was considered to be inappropriate for 1,3-dichloro-2-propanol because of the nature of the toxicity (tumorogenic in various organs in rats and the contaminant can interact with chromosomes and/or DNA.) BMDL 10 cancer, 3.3 mg/kg bw/day (for 1,3-dichloro-2-propanol); MOE, 65000 (general population), 2400 (high level intake, including young children))
Residue 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 (CAC/RCP 64-2008)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Liquid condiments containing acid-hydrolyzed vegetable protein (excluding naturally fermented soy sauce)	0.4	ML	Adopted	2008	CF		

The 57th JECFA (2001) noted that the dose that caused tumours in rats (19 mg/kg bw/day) was about 20000 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 65th JECFA. 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.

The 67th JECFA (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 95th 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.

Chloropropanols

The 67th JECFA 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 that a genotoxic mode of action could not be excluded.

The estimated intake of 1,3-DCP was calculated at 0.051µg/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 BMDL10 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 65000 and 24000, respectively. Based on these MOEs the Committee concluded that the estimated intakes of 1,3-DCP were of low concern for human health.

The 67th JECFA 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.

The 31st CAC (2008) adopted the 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 (ALINORM 08/31/REP 107).

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. The 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)

Cyanogenic glycosides

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)
Synonyms:	HCN

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

Excessive dietary exposure to cyanogenic glycosides has been assessed at the 39th JECFA (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 (CODEX STAN 176-1989) was not associated with acute toxicity.
The CAC agreed with the recommendation of the 59th Executive Committee (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, the CAC (2008) recognized safety concerns if cassava is consumed without adequate processing; the 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 .

The Second CCCF 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 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)

The Third CCCF 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).

The 74th JECFA re-evaluated cyanogenic glycosides in 2011. JECFA 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 bedirectly 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 JECFA established a cyanide-equivalent ARfD of 0.09 mg/kg bw. This ARfD is based on a BMDL10 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 JECFA 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.

Cyanogenic glycosides

A PMTDI of 20 µg/kg bw was recommended by applying a 100-fold uncertainty factor for interspecies and intraspecies differences to a BMDL1SD of 1.9 mg/kg bw per day. This BMDL1SD 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 JECFA 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.

Cyanogenic glycosides (CG) may be defined chemically as glycosides of the α-hydroxynitriles 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 β-glucosidases following structure disrupture 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 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.

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 the Prevention and Reduction of Dioxin and Dioxin-like PCB Contamination in Food and Feeds (CAC/RCP 62-2006)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

The situation regarding dioxins has been reviewed in a discussion paper (last version CX/FAC 00/26). The 32nd CCFAC (2000) requested an additional position paper in which recent intake assessments and national regulations regarding dioxins are assembled. This was presented to the 33rd CCFAC (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. The 34th CCFAC (2002) agreed that it should not draft MLs for dioxins at the time. The 35th CCFAC (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. The 36th CCFAC (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, the CCFAC agreed to discontinue the consideration of the position paper (ALINORM 04/27/12, paras 188-189).

The 29th CAC (2006) agreed to invite the 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 the 29th CAC (ALINORM 06/29/41, paras 60-62)

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.

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 (CAC/RCP 70-2011)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

When ethyl carbamate was discussed in the CCFAC in 1991, a Danish national TDI of 0.2 ug/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. The 27th CCFAC (1995) decided that no further action was needed at present.

The 64th JECFA 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 64th JECFA 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 64th JECFA 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.

The 3rd CCCF 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 (ALINORM 09/32/41, para 115).

The 34th CAC (2011) adopted the Code of Practice for the Prevention and Reduction of Ethyl Carbamate Contamination in Stone Fruit Distillates (REP11/CAC, Appendix III).

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 is revoked by the JECFA at its 17th meeting, 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

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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 (BMDL10 0.96 mg/kg bw/day), mean intake 960, high intake 480.)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

Information available to 72nd JECFA in 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 BMDL10 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.

The 4th CCCF (2010) agreed that a discussion paper prepared by an electronic Working Group, working in English, led by the Delegation of the United States of America would be presented to the next session of the Committee for consideration (ALINORM 10/33/41, para. 116).

The 5th CCCF (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_4H_4O) (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.

Melamine

Reference to JECFA:
Toxicological guidance value: TDI 0.2 mg/kg bw (2008; FAO/WHO Expert Meeting)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Liquid Infant formula	0.15	ML	6	1)	CF		
	Powdered Infant formula	1	ML	Adopted	2010	CF		
	Foods (other than infant formula)	2.5	ML	Adopted	2010	CF	Note 1 The maximum level applies to levels of melamine resulting from its non-intentional and unavoidable presence in feed and food. The maximum level 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 - authorised use of cyromazine as insecticide. The melamine level shall not exceed the level of cyromazine - migration from food contact materials taking account of any nationally authorised migration limit. Note 2 The maximum level 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.	
	Animal feed	2.5	ML	Adopted	2010	CF		

1) REP11/CAC (para. 62).

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.

Melamine

Maximum Levels for Melamine in Food and Feed

The 4th CCCF 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).

The 5th CCCF agreed to forward the proposed draft maximum level for liquid infant formula to the 34th Session of the Codex Alimentarius Commission for adoption at Step 5/8 (with omission of Steps 6 and 7) (Appendix III).

The 34th CAC agreed to adopt the ML at Step 5, to advance to Step 6 for comments and discussion in the Committee on Contaminants in Foods.

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.

Perchlorate

Reference to JECFA: 72 (2010)
Toxicological guidance value: PMTDI 0.01 mg/kg bw

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

The 72nd JECFA considered appropriate to derive a PMTDI as perchlorate has a very short half-life and is rapidly cleared from the body. The BMDL50 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 BMDL50 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.

The 5th CCCF 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 (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.

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 (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	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. At its 35th session the CCFAC requested to evaluate the potential risks associated with the presence of PBDEs in food.

The 64th JECFA 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 64th JECFA 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 ug/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. 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.

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 worldwide demand for PBDEs in 2001 was estimated to be almost 70 000 tonnes, with DecaBDE accounting for almost 80% of the total market.

Polybrominated diphenyl ethers

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).

Polychlorinated biphenyls

Reference to JECFA: 35 (1989)
Toxicological guidance value: Not established (, For coplanar PCBs (dioxin-like PCBs), see the toxicological guidance value of Dioxins)
Synonyms: Abbreviations, PCBs
Related code of practice: Code of Practice for Source Directed Measures to Reduce Contamination of Food with Chemicals (CAC/RCP 49-2001)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

PCBs were discussed by the 35th JECFA (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 JECFA, however, considered that the advantages to the infant of breast-feeding outweigh any potential hazards due to the PCB-content of breast milk. The JECFA 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. JECFA 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. The 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.
The 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 the 29th session of the Commission. (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 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

Polychlorinated biphenyls

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.

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 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.

Polycyclic aromatic hydrocarbons

Reference to JECFA:	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
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. (CAC/RCP 68-2009)

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
No ML								

At the 37th JECFA the committee 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.

The 64th JECFA evaluated 33 compounds. Some were found to be clearly genotoxic and carcinogenic (benz[a]anthracene, benzo[b]fluoranthene, benzo[j]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,l]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 benz[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, the 64th JECFA 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 64th JECFA:
- Future monitoring should include, but not be restricted to, analysis of the 13 PAHs identified as being genotoxic and carcinogenic.

The 37th CCFAC (2005) agreed to revise the discussion paper with particular attention to the 64th JECFA evaluation (ALINORM 05/28/12 para.199). The 38th CCFAC (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 Code of Practice is to be considered at the 1st session of CCCF.

The First CCCF (2007) agreed to address smoke flavours in the introductory part only in the Code. The CCCF agreed to return the proposed draft Code of Practice 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)

Polycyclic aromatic hydrocarbons

The Second CCCF agreed to forward the proposed draft Code of Practice to the 31st Session of the Codex Alimentarius Commission for adoption at Step 5. (ALINORM 08/31/41, para. 109)

The 31st Commission adopted the proposed draft code and advanced it to Step 6. (ALINORM 08.31/REP, para. 65)

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.

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
Residue definition: Vinyl chloride monomer
Synonyms: Monochloroethene, chloroethylene; abbreviation VC or VCM

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Food	0.01	GL	Adopted	1991	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 the CAC at its 19th session (1991) on the understanding that the AOAC International and the ISO would develop appropriate sampling plans and methods of analysis.

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)

^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Am

Residue definition: ^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Am

Code	Food/product	Level (Bq/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Foods other than infant foods	10	GL	Adopted	2006	FAC		
	Infant foods	1	GL	Adopted	2006	FAC	When intended for use as such.	

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.

Radionuclides

^{90}Sr, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U

Residue definition: ^{90}Sr, ^{106}Ru, ^{129}I, ^{131}I, ^{235}U

Code	Food/product	Level (Bq/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Foods other than infant foods	100	GL	Adopted	2006	FAC		
	Infant foods	100	GL	Adopted	2006	FAC	When intended for use as such.	

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.

^{35}S, ^{60}Co, ^{89}Sr, ^{103}Ru, ^{134}Cs, ^{137}Cs, ^{144}Ce, ^{192}Ir

Residue definition: ^{35}S, ^{60}Co, ^{89}Sr, ^{103}Ru, ^{134}Cs, ^{137}Cs, ^{144}Ce, ^{192}Ir; ^{35}S represents the value for organically bound sulphur.

Code	Food/product	Level (Bq/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Foods other than infant foods	1000	GL	Adopted	2006	FAC		
	Infant foods	1000	GL	Adopted	2006	FAC	When intended for use as such.	

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.

Radionuclides

^{3}H, ^{14}C, ^{99}Tc

Residue definition: ^{3}H, ^{14}C, ^{99}Tc; ^{3}H represents the value for organically bound tritium.

Code	Food/product	Level (Bq/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Foods other than infant foods	10000	GL	Adopted	2006	FAC		
	Infant foods	1000	GL	Adopted	2006	FAC	When intended for use as such.	

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.

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[12]. 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 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)[13].

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[14].

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12 For the purposes of this document, the term “emergency” includes both accidents and malevolent actions.

13 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.

14 For example, if ^{134}Cs and ^{137}Cs are contaminants in food, the guideline level of 1000 Bq/kg refers to the summed activity of both these radionuclides.

ANNEX 1

SCIENTIFIC JUSTIFICATION FOR PROPOSED DRAFT REVISED GUIDELINE LEVELS FOR RADIONUCLIDES IN FOODS CONTAMINATED FOLLOWING A NUCLEAR OR RADIOLOGICAL EMERGENCY

The proposed draft revised 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[15] (CAC/GL 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[16]; US DoH, 1998[17]; NRPB, 2003[18]). 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)[19].

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15 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 (CAC/GL 5-1989) applicable for six radionuclides (^{90}Sr, ^{131}I, ^{137}Cs, ^{134}Cs, ^{239}Pu and ^{241}Am) during one year after the nuclear accident.

16 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.

17 US DoHHS (1998) Accidental Radioactive Contamination of Human Food and Animal Feeds: Recommendations for State and Local Agencies. Food and Drug Administration, Rockville.

18 K. Smith and A. Jones (2003) Generalized Habit Data for Radiological Assessments. NRPB Report W41.

19 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.

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.

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[20] (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 1st 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 ^{239}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[21]). For the subsequent six months of the first year of life the gut absorption factors are much lower. This is not the case for ^{3}H, ^{14}C, ^{35}S, iodine and cesium isotopes.

As an example, dose assessment for ^{137}Cs in foods is presented below for the first year after the area contamination with this nuclide.

For adults: E = 1000 Bq/kg ·550 kg ·1.3·10^{-5} mSv/Bq ·0.1 = 0.7 mSv;
For infants: E = 1000 Bq/kg ·200 kg ·2.1·10^{-5} mSv/Bq ·0.1 = 0.4 mSv

[20] 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.

[21] International Commission on Radiological Protection (2005) Doses to Infants from Radionuclides Ingested in Mothers Milk. To be published.

TABLE. ASSESSMENT OF EFFECTIVE DOSE FOR INFANTS AND ADULTS FROM INGESTION OF IMPORTED FOODS IN A YEAR

Radionuclide	Guideline Level (Bq/kg)		Effective dose (mSv) 1st year after major contamination	
	Infant foods	Other foods	Infants	Adults
^{238}Pu	1	10	0.08	0.1
^{239}Pu			0.08	0.1
^{240}Pu			0.08	0.1
^{241}Am			0.07	0.1
^{90}Sr	100	100	0.5	0.2
^{106}Ru			0.2	0.04
^{129}I			0.4	0.6
^{131}I			0.4	0.1
^{235}U			0.7	0.3

Radionuclide	Guideline Level (Bq/kg)		Effective dose (mSv) 1st year after major contamination	
	Infant foods	Other foods	Infants	Adults
^{35}S*	1000	1000	0.2	0.04
^{60}Co			1	0.2
^{89}Sr			0.7	0.1
^{103}Ru			0.1	0.04
^{134}Cs			0.5	1
^{137}Cs			0.4	0.7
^{144}Ce			1	0.3
^{192}Ir			0.3	0.08
^{3}H**	1000	10000	0.002	0.02
^{14}C			0.03	0.3
^{99}Tc			0.2	0.4

* This represents the value for organically bound sulphur.

** This represents the value for organically bound tritium.

Copper

Reference to JECFA: 10 (1966), 14 (1970), 26 (1982)
Toxicological guidance value: PMTDI 0.05-0.5 mg/kg bw (1982)
Residue definition: Copper, total
Synonyms: Cu

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Edible fats and oils, refined (not covered by other standards)	0.1	ML	Adopted	CS 19-1981	FO	Edible fats and oils not covered by individual standards. This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments.	
	Edible fats and oils, virgin and cold pressed (not covered by other standards)	0.4	ML	Adopted	CS 19-1981	FO	This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments.	
	Named animal fats	0.4	ML	Adopted	CS 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.	1)
OC 0172	Vegetable oils, Crude	0.4	ML	Adopted	CS 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.	
OR 0172	Vegetable oils, Edible	0.1	ML	Adopted	CS 210-1999	FO	Named vegetable oils from arachis, babasu, coconut, cottonseed, grapeseed, maize, mustardseed, palm kernel, palm, rapeseed, safflowerseed, sesameseed, soya bean, and sunflowerseed, and palm olein, stearin and superolein. This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments.	1)
	Natural mineral waters	1 mg/l	ML	Adopted	CS 108-1981	NMW		

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

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 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. The 26th JECFA 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. The 26th JECFA 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 JECFA in 1982. 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 JECFA evaluation of 1982 (see above).

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 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.

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)
Residue definition: Iron, total
Synonyms: Fe

Code	Food/product	Level (mg/kg)	Type	Step	Reference or Adoption year	Ref to CC	Notes/Remarks for Codex Alimentarius	Notes for CCCF
	Edible fats and oils, refined (not covered by other standards)	2.5	ML	Adopted	CS 19-1981	FO	This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments.	
	Edible fats and oils, virgin and cold pressed	5	ML	Adopted	CS 19-1981	FO	This ML is mentioned to be a quality characteristic, for voluntary application by commercial partners and not for application by governments.	
OC 0172	Vegetable oils, Crude	5	ML	Adopted	CS 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.	
OR 0172	Vegetable oils, Edible	2.5	ML	Adopted	CS 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.	

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 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

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 flower, 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.

Zinc

Reference to JECFA:	10 (1966), 26 (1982)
Toxicological guidance value:	PMTDI 0.3-1 mg/kg bw (1982)
Residue definition:	Zinc, total
Synonyms:	Zn

Commodity/Product Code	Name	Level mg/kg	Suffix	Type	Step	Reference	Ref to CC	Notes/Remarks for Codex Alimentarius	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).