Expert advice on appropriate criteria and limits for contaminants in Ready to Use Therapeutic Foods (RUTF)

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Contents

1. Abstract

In connection with the development of a Codex RUTF guideline for Ready to Use Therapeutic Foods (RUTF), the risks of contaminants present in the raw ingredients used to make RUTF was assessed. The objectives of the report were to identify possible contaminants in the raw ingredients used in RUTFs together with considerations of the validity of Codex Maximum Levels (MLs) for RUTF and its target group. Possible contaminants that can occur in raw ingredients used in the production of existing and future RUTF products were identified as aflatoxins (B1, B2, G1,G2 and M1), arsenic, DON, lead, cadmium, mercury, glycidol, dioxin and PCBs (polychlorinated biphenyl), PAH (Polycyclic aromatic hydrocarbons), zearalenone, fumonisins, T-2 and HT-2 toxin, erucic acid and ochratoxin A. Based upon the current knowledge and the assumptions and criteria applied when developing MLs (taken into account lifetime exposure) and other measures, it is assumed that established Codex MLs provides sufficient margin of safety also to include the target group for RUTF products.

In general, it is recommended that all Codex MLs for contaminants and all relevant Codex codes of practice for reducing contaminants in food should be applied for raw ingredients that are and can be used in RUTF products. MLs set by Codex are in general considered to best reflect global dietary patterns and food chemical contamination. It's important to note that in general MLs are only set for raw ingredients in which the contaminant may be found in amounts that are significant for the total exposure of the consumer. Specifically, for aflatoxin (total) it is recommended to apply the ML proposal for ready-to-eat peanuts of 10 µg/kg for peanuts used in RUTF products. In addition, the Codex ML of 0.5 µg/kg for aflatoxin M1 for milks should be applied as milk and other dairy products (milk powder and whey powder) are used as raw ingredients in RUTF products. As JECFA (2016) highlighted a need for future risk management activities for aflatoxins in cereals, it is expected that further measures will be proposed to reduce aflatoxin in cereals. This will need to be taken into account, also for RUTFs, when available. Glycidol is a contaminant that can be found in refined fats and oils and is relevant as refined oils are used in RUTF products. JECFA has recommended that measures to reduce glycidol) in fats and oils continue, particularly when used in infant formula. This will need to be taken into account when a risk management decision is made by Codex. Finally, for the contaminant erucic acid which might end up in RUTF products neither JECFA or Codex activities have been initiated. It is proposed to request JECFA for scientific advice. Erucic acid occurs in common food commodities as vegetable oil. A request for scientific advice is not especially related to RUTF products, but to food in general. However, if JECFA identifies a need for further risk management measures and Codex then establish a ML for erucic acid or code of practice it should also apply to RUTF.

2. Introduction

UNICEF is a major buyer of therapeutic foods and related products which are used for management of children suffering from Severe Acute Malnutrition (SAM). As there are no official standards for RUTF, the process for a Codex guideline has been initiated, to provide the needed normative standards for this kind of products. The Codex Alimentarius food standards, guidelines and codes of practice are internationally recognized technical reference documents that contribute to the safety, quality and fairness of international food trade and Codex standards serve in many cases as a basis for national legislation.

UNICEF, in collaboration with key partners, is supporting the development of a Codex guideline for RUTF. Within the scope of the development of this guideline, the risks of contaminants present in the ingredients used to make RUTF will need to be defined for the target population, who are infants and children with SAM.

The Codex RUTF guideline will be used by agencies that procure RUTF, such as UNICEF, WFP (World Food Programme). Medecins sans frontiers (MSF) and United States Agency for International Development (USAID) and the normative bodies regulating these products.

3. General considerations

The focus of this consultancy concerns identification of the chemical hazards in the supply chain of the ingredients used in RUTF that may result in chemical contamination of the finished product. Thereafter, initial recommendations for maximum criteria for these contaminants shall be made.

The objectives of this report were to identify possible contaminants in the raw ingredients used in RUTFs together with considerations of the validity of these MLs for RUTF and its target group. Recommendation regarding relevant contaminants to manage and control in RUTF products and recommended limits for the identified contaminants are provided.

The consultancy included the following briefly described work steps:

- UNICEF and suppliers of RUTF products provided information about raw ingredients currently used or intended to be used in RUTF in the future.
- Compilation of appropriate Codex standards and references relevant for the CODEX RUTF guideline and comparing Codex standards with other regulatory bodies (U.S Food and Drug Administration (FDA) and EU) standards for contaminants in raw ingredients used in RUTF. In general EU regulation for contaminants in food has been used for comparing known contaminants and MLs with Codex standard as EU has an elaborated and advanced legislation in place that manage food contaminants in food.
- Considerations on gaps and limitations of Codex standards and references with respect to RUTF and its target group.

The Codex definition of contaminants has been used when evaluating which raw ingredients would be investigated for possible contaminants. This excludes e.g. pesticides, biocides and veterinary drug residues, food additives and vitamins for which other risk management regimes apply.

Codex defines a contaminant as follows:

> "Any substance not intentionally added to food or feed for food producing animals, which is present in such food or feed as a result of the production (including operations carried out in crop husbandry, animal husbandry and veterinary medicine), manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food or feed, or as a result of environmental"

The Codex definition of a contaminant implicitly includes naturally occurring toxicants including toxic metabolites of certain microfungi that are not intentionally added to food and feed (mycotoxins).

4. Identification of known contaminants in raw ingredients to be used in Ready to use Therapeutic Foods (RUTF)

As previously described, the Codex definition of contaminants has been applied for the raw materials relevant for investigation of known contaminants.

Only raw ingredients used in RUTF products or where information has been obtained that a raw material might be used in the future have been included in this evaluation.

Raw ingredients used in existing and future innovative RUTF products have been derived from the proposed Draft Guidelines for Ready to use Therapeutic Foods (RUTF) (CX/NFSDU 18/40/6) and the draft Technical Card Templates for existing and innovative product provided by UNICEF (both included in Annex I). The description of the raw materials are in general briefly stated with respect to which form and processes it might have undergone in the above mentioned documents, however some additional information from UNICEF and suppliers and producers of existing RUTF products has also been taken into consideration. From these documents it has been noted that cereals (milled), legumes and pulses must be dry to keep the moisture level in the finished RUTF low and are typically milled (flour) and further processed (e.g. sorted, dehulling, cleaned, roasted). It is also observed that the raw ingredients used in RUTF products are common food commodities with well-known food contaminants.

The following raw ingredients have been investigated for known contaminants:

- Milk and other dairy products as milk and whey powder
- Peanuts and peanut paste
- Legumes, cereals and seeds (including oil seeds) such as soybeans, lentils, chickpeas, cowpeas, beans, peanut, sesame and other types of legumes and seeds

- Oils (edible refined vegetable oil)
- Animal source foods such as fish (dried) and eggs (dried)
- Carbohydrates such as lactose, plant starch, sucrose and maltodextrin should be the preferred carbohydrates in RUTF. Honey has not been included as it is not to be used in RUTF due to the risk of Botulism.

Fish was included in the contaminants review, as UNICEF has been informed of future RUTF products that will include small, locally caught fish as a source of protein.

Meat is mentioned as animal source in the proposed Draft Guidelines for Ready to use Therapeutic Foods. However for the time being UNICEF decided not to include meat products in this review. If meat is included in future RUTF products known contaminants in meat products such as certain metals, dioxin and PCB should be considered.

In the following section all contaminants that have been identified as being relevant for raw materials used in RUTF products will be listed individually with existing ML and toxicological guidance value.

Specific contaminants

Contaminant: Deoxynivalenol (DON) and its acetylated derivates

Mycotoxins are secondary fungal metabolites with diverse structures and toxicological properties that induce a variety of toxic effects in humans and animals. In particular, fungi of the genera *Aspergillus*, *Penicillium* and *Fusarium* are significant in foods and feed all over the world. *Fusarium* produce various trichothecenes including deoxynivalenole (DON, vomitoxin), HT-2 toxin (HT-2) and T-2 toxin (T-2) which might be present in cereal grain intended for human consumption. Increased levels of DON in cereal grains are often observed in harvest years with frequent rainfall and high humidity during the flowering period and timing, rather than the amount of rain being the most critical factor (12). Published DON data (68% from Europe, 17% from Asia, 6% from North America, 5% from South America and 3% from Africa) showed that DON remains a common contaminant in cereals (wheat, maize, oats, rye, barley, rice) and their products. Highest reported mean levels were for raw cereals (13). Contamination levels vary widely between and within regions. Relatively lower levels have been detected in processed products (such as baby food, beer, bread, biscuits, pasta, muesli, couscous, flours and fermented soya bean) most likely due to the decrease in contamination resulting from cereal milling and processing, (13).

DON produces acute effects (e.g vomiting, abdominal cramps, headache, nausea) and longer term effects. JECFA established a provisional maximum tolerable daily intake (PMTDI) of 1 µg/kg body weight on the basis of the no observed- effect level (NOEL) 1 of 100 µg/kg bw per day for decreased body weight gain reported in a 2-year feeding study in mice and application of a safety factor of 100. The Committee concluded that intake at this level would not result in effects of DON on the immune system, growth or reproduction. JECFA noted that the available data did not suggest that DON presents a carcinogenic hazard.

Cereals contained in RUTF products are in the form of flour applying various kinds of processing.

Codex has established an ML of 1000 µg/kg for DON in flour from wheat, maize and barley while in EU an ML of 750 µg/kg for DON in cereal flour, bran and germ as end product marketed for direct human consumption has been established, see table 4.1.

Table 4.1. Established Maximum Levels for DON

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2001/2010)**
Flour, meal, semolina and flakes derived from wheat, maize or barley[1]	1000	n.a		1 µg/kg bw/day (TDI)[2] 0.008 mg/kg bw/day (ARfD)[3]
COMMISSION REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level[4] (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2002)**
Cereals intended for direct human consumption, cereal flour, bran and germ as end product marketed for direct human consumption	750	n.a		1 µg/kg bw/day (TDI) Note: In 2002 Scientific Committee on Food (SCF) (4) confirmed the temporary TDI = 1 µg/kg bw/day for DON (from 1999) based on a NOAEL (0.1 mg/kg bw/day) in the chronic dietary study with mice with the application of an uncertainty factor of 100. This TDI-value would also protect against the other sub-chronic and reproductive effects as well as the acute vomiting effect of DON.
Deoxynivalenol is not listed in the U. S. FDA list of contaminants recommended to be controlled.				

n.a= not applicable

Contaminant: T-2 and HT-2 toxin

T-2 toxin and HT-2 toxin are mycotoxins of the group trichothecenes and are commonly found in various cereal crops (wheat, maize, barley, oats, and rye) and processed grains (malt, beer and bread). T-2-and HT-2 toxin often occur together in infected cereals. The fungi producing trichothecenes are soil fungi and are important plant pathogens which grow on the crop in the field (22). There was substantial evidence of immunotoxicity and haematotoxicity after short term intake in several animal species after exposure for T-2 toxin and HT-2 toxin and that these are critical effects after short-term.

Cereals (milled) are proposed to be used as raw ingredients in future/innovative RUTF products.

[1] An ML for cereal grains for further processing exists as the provided information indicates the use of milled cereals in RUTFs.
[2] TDI= Tolerable daily intake.
[3] Reference dose for acute effects.
[4] For the purpose of the application of maximum levels for deoxynivalenol, rice is not included in 'cereals' and rice products are not included in 'cereal products'.

JECFA evaluated the mycotoxins T-2 and HT-2 (trichlothcenes) in 2002 and 2016 and concluded that the total of the average intakes of T-2 toxin and HT-2 toxin (8 ng/kg bw/day and 9 ng/kg bw/day, respectively) was not expected to exceed the group PMTDI 60 ng/kg bw per day. No ML was established. Update of the risk assessment including exposure assessment is on JECFA´s priority list of contaminants and naturally occurring toxicants to be evaluated (20).

EU has evaluated the mycotoxins and no ML is listed in EU Regulation (EC) No 1881/2006.

T-2 and HT-2 toxin are not listed in the U. S. FDA list of contaminants recommended to be controlled.

Contaminant: AFLATOXINS, TOTAL (Aflatoxin B1 + B2 + G1 + G2)
***Peanuts and cereals*:**

Two closely related species of fungi (*Aspergillus flavus* & *A. parasiticus)* are mainly responsible for producing aflatoxins of public health significance in food on a global basis. Under favorable conditions typically found in tropical and subtropical regions, including high temperatures and high humidity, these molds, normally found on dead and decaying vegetation, can invade food crops. The aflatoxin B1, B2, G1 and G2 are particularly dangerous to humans and animals as they have been found in all major food crops; but most human exposure comes from contaminated nuts, grains and their derived products. Additionally, aflatoxin M1, a product of aflatoxin B1, metabolism, can be found in milk in areas of high aflatoxin exposure. Subsequently humans may be exposed to this aflatoxin through milk and milk products, including breast milk, especially in areas where the poorest quality grain is used for animal feed (14, 15).

The consumption of food containing aflatoxin concentrations of 1 mg/kg (corresponding to 1000 ug/kg; a 100 fold higher value than the ML of 10 ug/kg for 'ready-to-eat' peanuts) or higher has been suspected to cause acute poisoning (aflatoxicosis). National estimates of dietary exposure to aflatoxins indicate differences between developed and developing countries. In developed countries, mean aflatoxin dietary exposures are generally less than 1 ng/kg body weight (bw) per day, whereas estimates for some sub-Saharan African countries exceed 100 ng/kg bw per day, although these latter estimates are often based on very few data. Estimates of dietary exposure to aflatoxin M1 (in milk) have rarely exceeded 1 ng/kg bw per day in any country (15).

JECFA confirmed in 2016 that aflatoxins are considered to be genotoxic carcinogens that induce tumors in the liver of animals and humans. For this type of carcinogen, it is generally assumed that there is no threshold dose below which no tumour formation would occur. In other words, only a zero level of exposure will result in no risk and therefore As Low As Reasonably Achievable (ALARA) principle has been applied the intake should be reduced to ALARA levels. Aflatoxin B1 is the most potent carcinogen of the aflatoxins; most of the toxicological data available are related to aflatoxin B1.

The following raw ingredients; peanuts and peanut paste, milled cereals and flour of maize or rice are used or can be contained in future RUTFs.

The currently Codex established ML for total aflatoxin in peanuts for further processing is 15 µg/kg. A Codex ML proposal for ready-to-eat peanuts of 10 µg/kg has recently been discussed (2018), but is yet not adopted. Ready-to-eat" means not intended to undergo an additional processing/treatment that has proven to reduce levels of aflatoxins in peanuts before being used as ingredient in foodstuffs, otherwise processed or offered for human consumption. This ML is considered relevant for the raw material used in the existing RUTF (peanuts and peanut paste) when adopted. Communication in 2011 between WHO and UNICEF (information provided by UNICEF) regarding recommended maximum level in peanuts used in RUTF products for severely malnourished children recommended a limit of 10 µg/kg (using the limit for tree nuts 'ready-to-eat' at the time). Implementing a ML of 10 µg/kg for peanuts used in RUTF products instead of ML of 15 µg/kg for peanuts used as raw ingredient in RUTFs will increase the level of protection which is also in line with the ALARA principle for genotoxic carcinogens. Furthermore a ML of 10 µg/kg for aflatoxin in RUTF products seems achievable as such a ML corresponds to the ML that will apply for aflatoxin in ready-to-eat peanuts.

No MLs has been set for cereals and flour of rice and maize within the Codex system. In the latest JECFA evaluation (2016) it was stressed, based on high consumption of rice and wheat in some areas of the world, that these food commodities need to be considered in future risk management activities for aflatoxins.

In EU a similar ML of 15 ug/kg are applicable for total aflatoxins in groundnuts (peanuts) and other oilseeds for further processing before human consumption. A ML of 4 ug/kg are set for peanuts and other oilseeds and processed products thereof intended for direct human consumption or use as an ingredient in foodstuffs

In addition, EU has set MLs of 4 µg/kg for cereal and cereal products (except rice and maize) for further treatment before human consumption. In maize and rice to be subjected to sorting or other physical treatment before human consumption or use as an ingredient in foodstuffs an ML of 10 µg/kg applies (table 4.2).

U.S. FDA has set a ML of 20 ug/kg for peanuts and peanuts products.

UNICEF has provided analytical data (attached in Annex I named "RUTF test data 2016") on aflatoxin levels in RUTF/RUSF[5] products collected in 2016 from 19 suppliers. Out of a total of 438 tested batches from 13 different suppliers 3/438 batches had aflatoxin levels between 2-10 ppb (2-10 µg/kg) while 1/438 batches had aflatoxin levels above 10 ppb, all originated from the same supplier. Another 158 tested batches from 6 suppliers showed 20/158 of the tested batches had levels between 2-10 ppb (80% came from 1 supplier) and 1/158 above 10 ppb. It seems that in general the contamination of RUTF/RUSF products (2016) with aflatoxin were below the proposed Codex ML for 'ready-to-eat' peanuts of 10 ug aflatoxin/kg.

[5] Ready to Use Supplementary Food (RUSF)

Table 4.2. Established Maximum Levels for aflatoxin in peanuts and cereals.

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 1987/96/97 & 2007//2016)**
Peanuts	15	Unless specified, seed or kernels, after removal of shell or husk.	The ML applies for peanuts, also known as groundnuts, intended for further processing. "Further processing" means intended to undergo an additional processing/treatment that have proven to reduce levels of aflatoxins before being used as an ingredient in foodstuffs, otherwise processed or offered for human consumption. Processes that have proven to reduce levels of aflatoxins are shelling, blanching followed by colour sorting, and sorting by specific gravity and colour (damage). There is some evidence that roasting reduces aflatoxins in pistachios but for other nuts the evidence is still to be supplied.	Carcinogenic potency estimates for aflatoxins B, G, M. Intake should be reduced to levels As Low As Reasonably Achievable) (ALARA principle).
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity /Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 1994/2007)**
Groundnuts (peanuts) and other oilseeds, to be subjected to sorting, or other physical treatment, before human consumption or use as an ingredient in foodstuffs, with the exception of: groundnuts (peanuts) and other oilseeds for crushing for refined vegetable oil production	B1: 8.0 Aflatoxin B1 + B2 + G1 + G2 : 15	The maximum levels refer to the edible part of groundnuts (peanuts) and tree nuts. If groundnuts (peanuts) and tree nuts 'in shell' are analysed, it is assumed when calculating the aflatoxin content all the contamination is on the edible part, except in the case of Brazil nuts.		SCF concluded: "Aflatoxins are genotoxic carcinogens. For this type of carcinogen, it is generally felt that there is no threshold dose below which no tumour formation would occur. In other words, only a zero level of exposure will result in no risk. It agreed with the recent evaluations of International Agency for Research on Cancer (1993) with respect to the carcinogenicity and genotoxicity of the aflatoxins. From the many reports on risk assessment, it can be concluded that even very low levels of exposure to aflatoxins, contribute to the risk of liver cancer." For aflatoxin M1, the Scientific Committee for Food concluded that there is sufficient evidence that aflatoxin M1 is a genotoxic carcinogen; its carcinogenic potency is estimated to be approximately 10 times lower than aflatoxin B1.
Groundnuts (peanuts) and other oilseeds and processed products thereof, intended for direct human consumption or use as an ingredient in foodstuffs, with the exception of: — crude vegetable oils destined for refining — refined vegetable oils	B1: 2.0 Aflatoxin B1 + B2 + G1 + G2: 4.0	n.a		
All cereals and all products derived	B1: 2.0	n.a		

from cereals, including processed cereal products, with the exception of foodstuffs listed below	Aflatoxin B1 + B2 + G1 + G2 : 4.0			Based on that opinion, it is appropriate to limit the total aflatoxin content of food (sum of aflatoxins B1, B2 , G1 and G2) as well as the aflatoxin B 1 content alone.
Maize and rice to be subjected to sorting or other physical treatment before human consumption or use as an ingredient in foodstuffs	B1: 5.0 Aflatoxin B1 + B2 + G1 + G2 : 10.0	n.a		
U.S. FDA				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value**
Peanuts and Peanut products	20	n.a	-	-

Contaminant: Aflatoxin M1

Aflatoxin M1, a product of aflatoxin B1 metabolism, can be found in milk in areas of high aflatoxin exposure (15). For aflatoxin M1, the SCF (EU) concluded that there is sufficient evidence that aflatoxin M1 is a genotoxic carcinogen; its carcinogenic potency is estimated to be approximately 10 times lower than aflatoxin B1.

Milk and milk products:

According to information provided by UNICEF, RUTF products can contain milk powder or whey powder as raw ingredients.

Codex and U.S. FDA have set ML of 0.5 µg/kg for aflatoxin M1 in milks.

Codex/JECFA (2002) concluded that by using the EU proposed ML of 0.05 µg/kg for aflatoxin M1 in the risk assessment, the predicted risk for developing liver cancer was only marginally increased.

EU has set a ML of 0.050 µg/kg for raw milk, heat-treated milk and milk for the manufacture of milk-based products.

Table 4.3. Established Maximum Levels for aflatoxin in milk and milk products.

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2002)**
Milks	0.5	Whole commodity	Milk is the normal mammary secretion of milking animals obtained from one or more milkings without either addition to it or extraction from it, intended for consumption as liquid milk or for further processing. A concentration factor applies to partially or wholly dehydrated milks.	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 were very small. The potency of aflatoxin M1 appears to be so low in HBsAg-individuals[6] 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.
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU)**
Raw milk, heat-treated milk and milk for the manufacture of milk-based products	0.050[7]	n.a		Please refer to text above and under aflatoxin total.
U.S. FDA				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value**
Milk	0.5	n.a	-	-

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

Arsenic (As) is a ubiquitous element, which is introduced to the environment from both natural and anthropogenic sources. The crust of the Earth contains arsenic, which is released through weathering of rocks and volcanic activity. The toxicity of arsenic compounds strongly depends on their chemical forms (speciation).

[6] HBsAg- individuals: The "surface antigen" is part of the hepatitis B virus that is found in the blood of someone who is infected.

[7] Applicable for liquid milk and milk products, which are dried or processed, taken into account the concentration caused by the drying process or by processing.

Inorganic arsenic is considered the most toxic of the arsenic species present in food. Peeling of vegetables and polishing of rice reduce the content of total arsenic. Arsenic is a carcinogenic metal (11).

Rice (as flour) and edible fats and oils have been proposed to be used in RUTF products.

A Codex MLs of 0.35 mg/kg for husked rice, 0.2 mg/kg for polished rice and 0.1 mg/kg for edible fats and oils have been set for inorganic arsenic (As-in).

In EU comparable MLs have been set for rice, see table 4.4.

Table 4.4. Established Maximum Levels for arsenic

CODEX				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 1988/2011)**
Edible fats and oils	0.1	Whole commodity	For fish oils covered by CXS 329-2017, the ML is for fish oils (As-in).	BMDL0.5: 3 µg/kg bw/day (lung cancer); 0.5% increased incidence of lung cancer (BMDL 0.5) was determined from epidemiological studies to be 3.0 µg/kg bw/day (2–7 µg/kg bw/day based on the range of estimated total dietary exposure) using a range of assumptions to estimate total dietary exposure to inorganic arsenic from drinking-water and food.
Rice, husked	0.35	Whole commodity	The ML is for inorganic arsenic (As-in). Countries or importers may decide to use their own screening when applying the ML for As-in in rice by analyzing total arsenic (As-tot) in rice. If the As-tot concentration is below or equal to the ML for As-in, no further testing is required and the sample is determined to be compliant with the ML. If the As-tot concentration is above the ML for As-in, follow-up testing shall be conducted to determine if the As-in concentration is above the ML.	
Rice, polished	0.2	Whole commodity	The ML is for inorganic arsenic (As-in). Countries or importers may decide to use their own screening when applying the ML for As-in in rice by analysing total arsenic (As-tot) in rice. If the As-tot concentration is below or equal to the ML for As-in, no further testing is required and the sample is determined to be compliant with the ML. If the As-tot concentration is above the ML for As-in, follow-up testing shall be conducted to determine if the As-in concentration is above the ML.	
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2009/2010)**
Non-parboiled milled rice (polished or white rice)[a]	0.2	n.a		The EFSA CONTAM Panel modeled the dose-response data from key epidemiological studies

Parboiled rice and husked rice	0.25	n.a		and selected a benchmark response of 1 % extra risk. The CONTAM Panel concluded that the overall range of BMDL01 values of 0.3 to 8 µg/kg bw/day should be used instead of a single reference point in the risk characterization for inorganic arsenic. The lowest BMDL01 values are for lung cancer (23).
U.S. FDA				
Arsenic is not listed in the U. S. FDA list of contaminants recommended to be controlled.				

[a]Rice, husked rice, milled rice and parboiled rice as defined in Codex Standard 198-1995.

BMDL: lower confidence limit of the benchmark dose

Contaminant: Lead: total

Lead (Pb) is a ubiquitous element, found naturally in the Earth's crust at an average level of 10 mg/kg. It is widespread in the environment due to its use in various industrial applications (11). Lead contamination of food arises mainly from the environment or from food processing, food handling and food packaging. Atmospheric lead can contaminate food through deposition on agricultural crops. Water is another source of lead contamination of food. Although lead exists in both organic and inorganic forms, only inorganic lead has been detected in food. Lead is a metal causing neurodevelopmental effects in children and affects the systolic blood pressure in adults (16).

The following raw ingredients such as fish (dried), milk, pulses, legumes and seeds, cereals (typically as flour) and fats and oils have been proposed to be included RUTF products.

Codex MLs for lead have been established for fish of 0.3 mg/kg, milk and secondary milk products of 0.02 mg/kg, edible fats and oils of 0.08 mg/kg, for pulses of 0.1 mg/kg and cereal grains of 0.2 mg/kg.

Comparable MLs exists in EU, see table 4.5.

Table 4.5. Established Maximum Levels for lead

CODEX				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 1999/2011)**
Fish	0.3	Whole commodity (in general after removing the digestive tract)		The Committee considered the neurodevelopmental effects of lead to be pivotal in its assessment for children (based on the results of a meta-analysis of epidemiological data) Point of departure doses: 0.6 µg/kg/day loss of 1 IQ point in children; 1.2 µg/kg bw/day for 1 mmHg increase in blood pressure (adults)
Milk and secondary milk products	0.02	Whole commodity	Milk is the normal mammary secretion of milking animals obtained from one or more milkings without either addition to it or extraction from it, intended for consumption as liquid milk or for further processing. A concentration factor applies to partially or wholly dehydrated milks	
Edible fats and oils	0.08	Whole commodity as prepared for wholesale or retail distribution.		
Pulses	0.1	Whole commodity		
Cereal grains	0.2	Whole commodity	The ML does not apply to buckwheat cañihua and quinoa.	
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) mg/kg (wet weight)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2010/2013)**
Raw milk, heat-treated milk and milk for the manufacture of milk-based products	0.02	n.a		0.5 µg/kg/day for children (BMDL01; 1% change in full scale IQ score) 1.5 µg/kg bw/day (BMDL01; 1% increase in blood pressure) for adults
Muscle meat of fish	0.3	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category.	
Cereals and pulses	0.2	n.a		
Fats and oils, including milk fat	0.1	n.a		
U.S. FDA				
Lead in food commodities is not listed in the U. S. FDA list of contaminants recommended to be controlled.				

BMDL: lower confidence limit of the benchmark dose

Contaminant: Cadmium: total

Cadmium (Cd) is a toxic trace element found as an environmental contaminant, both through natural occurrence and from industrial and agricultural sources. Cadmium has no known biological function in humans. Foods are the main source of cadmium exposure for the non-smoking population. Tobacco smoking and work place air have also been identified as major contributors to cadmium exposure (12). Cadmium has a range of toxic effects on organs particular to kidneys, the skeletal system (loss of bone density), the reproductive system and the respiratory system (24).

The following raw ingredients such as fish (dried), milk, pulses, legumes and seeds, cereals (typically as flour) and fats and oils have been proposed to include in RUTF products.

Codex has established MLs for cadmium in pulses and cereal grains of 0.1 mg/kg, rice (polished) of 0.4 mg/kg and in wheat of 0.2 mg/kg.

EU has set the following MLs for cereal grains (except rice and wheat) of 0.1 mg/kg, 0.2 mg/kg for rice and wheat and soy bean and for muscle meat of fish ranges from 0.05-0.25 mg/kg depending of the fish species (table 4.6).

Table 4.6. Established Maximum Levels for cadmium

CODEX				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA latest 2010)**
Pulses	0.1	Whole commodity	The ML does not apply to soya bean (dry).	In view of the long half-life of cadmium, daily ingestion in food has a small or even a negligible effect on overall exposure. In order to assess long- or short-term risks to health due to cadmium exposure, dietary intake should be assessed over months, and tolerable intake should be assessed over a period of at least 1 month. JECFA (2010) decided to express the tolerable intake as a monthly value in the form of a provisional tolerable monthly intake (PTMI) and established a PTMI of 25 µg/kg bw/month
Cereal grains	0.1	Whole commodity	The ML does not apply to buckwheat, cañihua, quinoa, wheat and rice	
Rice, polished	0.4	Whole commodity		
Wheat	0.2	Whole commodity	The ML applies to common wheat, durum wheat, spelt and emmer.	
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) mg/kg (wet weight)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2006/2011)**
Cereal grains excluding wheat and rice	0.1			TWI of 2.5 µg/kg bw/week [8] JECFA and EU used the same epidemiological dataset.
Wheat grains, rice grains Wheat bran and wheat germ for direct consumption Soy beans	0.2			
Muscle meat of fish, excluding species listed below	0.050	Where fish are intended to be eaten whole, the maximum	See note (24) in EC No 1881/2006 for further condition regarding fish category.	

[8] Statement on Tolerable weekly intake for cadmium (https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.1975)

		level shall apply to the whole fish.		
Muscle meat of the following fish : mackerel , Tuna & bichique	0.1	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category.	
Muscle meat of the following fish: bullet tuna	0.15	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category.	
Muscle meat of the following fish: anchovy, swordfish sardine	0.25	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category.	
U.S. FDA				
Cadmium in food commodities is not listed in the U. S. FDA list of contaminants recommended to be controlled.				

TWI: tolerable weekly intake

Contaminant: Mercury (total)

Mercury (Hg) is naturally present in the Earth's crust usually at levels around 0.02 mg/kg. The element can be found in various chemical forms, both inorganic and organic (methylmercury), it is the organic form which is considered most toxic. It is used in various industrial applications and the main anthropogenic source of mercury is the incineration of waste (12). Mercury is toxic to the kidneys (kidney damage and nephropathy). The most critical effect of methyl mercury is developmental neurotoxicity in humans (neurobehavioral disturbances; reduced intelligence), (25).

Fish (dried) has been proposed to be used as raw ingredients in future/innovative RUTF products.

Codex has established MLs of 1.2, 1.6, 1.5 and 1.7 mg/kg for methyl mercury in tuna, shark, alfonsino and marlin respectively. Future work in Codex includes discussion of establishment of MLs for additional fish species (20).

Whereas EU has only established ML of 0.5 mg/kg for total mercury for fishery products and muscle meat of fish (some fish species excluded).

U.S. FDA has established a ML of 1 ppm (1 mg/kg) for methyl mercury for fish, shellfish, crustaceans, other aquatic animals (fresh, frozen or processed).

Table 4.8. Established Maximum Levels for mercury

CODEX				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA latest 2011)**
No ML for food commodities relevant to raw ingredients in RUTFs.				JECFA (2011) established a new Provisional Tolerable Weekly Intake (PTWI) for inorganic mercury of 4 µg/kg bw. 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.
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) mg/kg (wet weight)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2012/ April 2018)**
Fishery products and muscle meat of fish, with the exception of certain listed fish species for which 1 mg/kg applies	0.5	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category. For listed fish species exempted please refer to EC No 1881/2006 with amendments (Annex section 3.3.2)	A tolerable weekly intake (TWI) for inorganic mercury of 4 µg/kg bw/week expressed as mercury was established.
U.S. FDA				
Fish, shellfish, crustaceans, other aquatic animals (fresh, frozen or processed) 1 ppm (1 mg/kg) methyl mercury in edible portion.				

Contaminant: Methyl mercury

Please refer to text above.

Table 4.9. Established Maximum Levels for methyl mercury

CODEX				
Raw material/ Commodity	**Maximum Level (ML) mg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 1978/88/99 &2003/2006)**
Tuna	1.2	Whole commodity fresh or frozen (in general after removing the digestive tract)	Countries or importers may decide to use their own screening when applying the ML for methyl mercury in fish by analysing total mercury in fish. If the total mercury concentration is below or equal to the ML for methyl mercury, no further testing is required and the sample is determined to be compliant with the ML. If the total mercury concentration is above the ML for methyl mercury, follow-up testing shall be conducted to determine if the methyl mercury concentration is above the ML. The ML also applies to fresh or frozen fish intended for further processing. Countries should consider developing nationally relevant consumer advice for women of childbearing age and young children to supplement the ML.	PTWI : 1.6 µg/kg bw/week (Provisional Tolerable Weekly Intake 2003; confirmed 2006)
Shark	1.6			
Alfonsino	1.5			
Marlin	1.7			
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) mg/kg (wet weight)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2012/2018)**
Currently only Total Mercury has been listed with ML in the currently consolidated EU Regulation. However European Food Safety Authority (EFSA)[9] proposed in 2012/ April 2018 a new TWI for methyl mercury A tolerable weekly intake (TWI) for methyl mercury of 1.3 µg/kg bw expressed as mercury, was proposed.				
U.S. FDA				
Fish, shellfish, crustaceans, other aquatic animals (fresh, frozen or processed) 1 ppm (1 mg/kg) methyl mercury in edible portion.				

Contaminant: Glycidyl fatty acid esters expressed as glycidol

Glycidyl esters are processing-induced contaminants primarily found in refined fats and oils and foods containing fats and oils. Experimental evidence indicates that glycidyl esters are substantially hydrolysed to glycidol in the gastrointestinal tract and elicit toxicity as glycidol. The JECFA therefore based its evaluation on the conservative assumption of complete hydrolysis of glycidyl esters to glycidol. JECFA concluded that glycidol is a genotoxic compound and considered its carcinogenicity as the most sensitive end-point on which to base a point of departure (14).

[9] EFSA is a European agency funded by the European Union and is the source of scientific advice on risks associated with the food chain.

Oil (edible refined vegetable oil) is used as raw ingredients in RUTF products.

Glycidyl esters are currently under review by JECFA/Codex. In the JECFA evaluation it was recommended that measures to reduce glycidyl esters (glycidol) in fats and oils continue, particularly when used in infant formula.

EU has set a ML of 1000 µg/kg for vegetable oils and fats see table 4.10.

Table 4.10. Established Maximum Levels for glycidyl fatty acid esters

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2016)**
Currently under review. The JECFA evaluation recommended that measures to reduce glycidyl esters (glycidol) in fats and oils continue, particularly when used in infant formula.				Genotoxic carcinogen
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2016)**
Vegetable oils and fats placed on the market for the final consumer or for use as an ingredient in food	1000	n.a		Based on the EFSA Guidance on substances that are genotoxic and carcinogenic, T25 values were calculated for the incidence of tumours observed in rats and mice following long-term exposure to glycidol. A T25 of 10.2 mg/kg bw/day for peritoneal mesothelioma in male rats was used as the reference point.
U.S. FDA				
Not listed.				

Contaminant: Dioxins and polychlorinated biphenyls (PCB)s

Dioxins, including polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) are toxic chemicals that persist in the environment and accumulate in the food chain. Their presence in the environment in Europe has declined since the 1970s, following concerted efforts by public authorities and industry. Dioxins have no technological or other use, but are generated in a number of thermal and industrial processes as unwanted and often unavoidable by-products. In contrast to dioxins, PCBs had widespread use in numerous industrial applications, and were produced in large quantities for several decades, until they were banned in most countries by the 1980s (27). They are lipophilic chemicals and dioxins and dioxins like PCBs persist in the environment and accumulate in biological systems, as such there continues to be public concern about the health hazards arising from them. For the general population, the primary source of exposure to dioxins and related compounds is food. These compounds are detectable in almost all types of food with the highest concentrations found in meat, fish, eggs and dairy products (26).

Food of animal origin is the predominant route of human exposure to dioxins and PCBs with approximately 80–90% of the total exposure via fats in fish, meat and dairy products. Levels of dioxins and PCBs in animal fat may be related to contamination of the local environment and to contamination of feed (e.g. fish-oil and fish-meal) or to certain production processes (e.g. artificial drying) (20).

Long-term exposure to these substances has been shown to cause a range of adverse effects on the nervous, immune and endocrine systems, and impair reproductive function. They may also cause cancer. Their persistence and the fact that they accumulate in the food chain, notably in animal fat, therefore continues to cause safety concerns (27).

Current RUTF products include milk and dairy products and edible refined vegetable oils and RUTF products in the future may contain dried fish and eggs.

Codex has no ML for dioxin or PCB but has instead issued a Code of Practice for the Prevention and Reduction of Dioxin and Dioxin-like PCB Contamination in Food and Feeds to reduce contamination. The code of practice recommends various management measures that help to reduce the contamination of food from animal origin including measures to reduce contamination of animal feed. A proposed draft revision of the existing version is currently ongoing (20).

In EU MLs for fish, milk, egg, and vegetable oils have been established (table 4.11).

Table 4.11. Established Maximum levels for Dioxins and PCBs

CODEX				
Raw material/ Commodity	**Maximum Level (ML)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2002[10])**
No ML. 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 of Practice for Source Directed Measures to Reduce Contamination of Foods with Chemicals (CAC/RCP 49-2001)				PTMI 70 pg/kg bw/month PTMI= Provisional Tolerable Monthly intake
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML)**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2001/2006)**
Muscle meat of fish and fishery products and products thereof with the exception of certain listed fish species	3.5 pg/g wet weight [a] 6.5 pg/g wet weight [b] 75 ng/g wet weight [c]	Where fish are intended to be eaten whole, the maximum level shall apply to the whole fish.	See note (24) in EC No 1881/2006 for further condition regarding fish category. For listed fish species exempted please refer to EC No 1881/2006 with amendments (Annex section 5)	TWI: 14 pg 2,3,7,8-TCDD/kg bw/week TWI= tolerable weekly intake
Raw milk and dairy products, including butter fat	2.5 pg/g fat [a] 5.5 pg/g fat [b] 40 ng/g fat [c]	n.a		
Hen eggs and egg products	2.5 pg/g fat [a] 5.5 pg/g fat [b] 40 ng/g fat [c]	n.a		
Vegetable oils and fats	0.75 pg/g fat [a] 1.25 pg/g fat [b] 40 ng/g fat [c]	n.a		
U.S. FDA				
Not listed				

[a] Sum of dioxins (WHO-PCDD/ F-TEQ), [b] Sum of dioxins and dioxin-like PCBS (WHO- PCDD/F-PCB- TEQ), [c] Sum of PCB28, PCB52, PCB101, PCB138, PCB153 and PCB180 (ICES –6)

Contaminant: Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAH) constitute a large class of organic chemicals that normally occur in complex mixtures of several hundred compounds. Food can be contaminated from environmental sources and during the processing of foods e.g. drying, smoking and barbecuing. During smoking, drying and barbequing PAH are found bound to particles in the smoke, formed either from the heating source itself (e.g. wood or charcoal burning) or from lipids dripping on the heating source. For non-smokers, food is the main source of human exposure to PAH (12). PAH are genotoxic carcinogens.

In future RUTF products raw ingredients such as fish (dried) and oils (edible refined vegetable oil) are proposed.

Codex has set no ML for PAH based on the JECFA (2006) evaluation. JECFA concluded that the estimated intakes of PAHs were of low concern for human health. Measures to reduce intake of PAHs could include avoiding contact

[10] Includes POLYCHLORINATED DIBENZODIOXINS (PCDDs), POLYCHLORINATED DIBENZOFURANS (PCDFs), AND COPLANAR POLYCHLORINATED BIPHENYLS (PCBs)

of foods with flames, and cooking with the heat source above rather than below the food. Efforts should also be made to reduce contamination with PAHs during drying and smoking processes.

In EU MLs for smoked fish and Oils and fats have been established (table 4.12).

Table 4.12. Established Maximum Levels for PAH

<table>
<tr><th colspan="6">CODEX</th></tr>
<tr><th>Raw material/Commodity</th><th>Maximum Level (ML)</th><th colspan="2">Portion of the Commodity/Product to which the ML applies</th><th>Notes/Remarks</th><th>Toxicological guidance value (CODEX/JECFA 2006)</th></tr>
<tr><td colspan="5">No ML.
The JECFA evaluation calculated margin of exposure values of 25, 000 and 10,000 between the BMDL10 value of 100 µg of benzo[a]pyrene/kg bw/day and mean and 95th-percentile intake levels of 4 and 10 ng/kg bw/day, respectively. Based on the derived margins of exposure, 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.</td><td>Genotoxic carcinogen

BMDL: 100 µg of benzo[a]pyrene/kg bw/day</td></tr>
<tr><th colspan="6">EU REGULATION (EC) No 1881/2006</th></tr>
<tr><th rowspan="2">Raw material/Commodity</th><th colspan="2">Maximum Level (ML) µg/kg</th><th rowspan="2">Portion of the Commodity/Product to which the ML applies</th><th rowspan="2">Notes/Remarks</th><th rowspan="2">Toxicological guidance value (CODEX/JECFA 2008)</th></tr>
<tr><th>Benzo(a)pyrene</th><th>Sum of benzo(a)- pyrene, benz(a)anthracene, benzo(b)fluoranthene and chrysene</th></tr>
<tr><td>Oils and fats (excluding cocoa butter and coconut oil) intended for direct human consumption or use as an ingredient in food</td><td>2.0</td><td>10.0</td><td></td><td></td><td rowspan="3">Carcinogenicity and genotoxicity.

Benchmark dose calculation (BMD10 & BMDL10) for different PAHs.</td></tr>
<tr><td>Coconut oil intended for direct human consumption or use as an ingredient in food</td><td>2.0</td><td>20.0</td><td></td><td></td></tr>
<tr><td>Muscle meat of smoked fish and fish products</td><td>2.0</td><td>12.0</td><td></td><td></td></tr>
<tr><th colspan="6">U.S FDA</th></tr>
<tr><td colspan="6">Not listed</td></tr>
</table>

BMD: Benchmark dose
BMDL:lower confidence limit of the benchmark dose

Contaminant: Erucic (inherent plant toxin)

Erucic acid is a naturally occurring contaminant present in vegetable oil. Erucic acid is a monounsaturated omega-9 fatty acid, which is present in the oil-rich seeds of the Brassicaceae family of plants, particularly rapeseed and mustard. It mainly enters the food chain when rapeseed oil is used in industrial food processing and home cooking in some countries. It is present in pastries, cakes and infant/follow-on formulae and also in some animal feed (e.g. rapeseed meal).

Tests on animals show that ingesting oils containing erucic acid over time can lead to a heart condition called myocardial lipidosis. This is temporary and reversible. Other potential effects observed in animals – including changes in the weight of the liver, kidney and skeletal muscle – occur at slightly higher doses (17).

Oil (edible refined vegetable oil e.g. rapeseed) is used as raw ingredients in RUTF products.

No information is found for this contaminant in JECFA/Codex references.

According to EFSA (2016) erucic acid is not of safety concern for most consumers as average exposure is less than half the safe level. But it may be a long-term health risk for children up to 10 years of age who consume high amounts of foods containing this substance. It was however noted by EFSA, that they are likely to have overestimated this risk to account for limitations in the available scientific information. EFSA recommended further data collection on erucic acid concentrations in processed foods such as fine bakery wares and food for infants and small children (17).

EU has set a ML of 50 g/kg for vegetable oils and fats and for foods containing added vegetable oils and fats.

Considering the short treatment period with RUTF products and that the risk was anticipated as a long-term health risk for individuals consuming high amounts of foods containing erucic and taking into account the uncertainties (likely overestimated the risk) noted by EFSA erucic it is not considered to be as an area of high priority.

Table 4.13. Established Maximum Levels for euricic

CODEX				
Raw material/ Commodity	**Maximum Level (ML) g/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA latest 2010)**
No information found				
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) g/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2016/2017)**
Vegetable oils and fats and foods containing added vegetable oils and fats	50	The maximum level refers to the level of erucic acid, calculated on the total level of fatty acids in the fat component in food.		TDI : 7 mg/kg bw/day for erucic acic
U.S. FDA				
Not listed				

Contaminant: Zearalenone

Zearalenone is a nonsteroidal estrogenic mycotoxin produced by several Fusarium species. It is found worldwide in a number of cereal crops such as maize, barley, oats, wheat, rice and sorghum and also in bread. Zearalenone was shown to be produced on corn by *Fusarium* isolates from the continents of Australia, Europe, and North America as well as in New Zealand and South East Asia (Philippines, Thailand, and Indonesia). The occurrence of zearalenone in food and feed was also demonstrated in South America, Africa, Taiwan, China and Russia (18).

Zearalenone is an estrogenic mycotoxin and elicit hormonal disturbances and has shown to affect fertility especially in pigs (28).

Oil (edible refined vegetable oil) and milled cereals are both proposed to be used as raw ingredients in future/innovative RUTF products.

No MLs has been set by Codex for zearalenone based upon a JECFA evaluation showing average dietary intakes of zearalenone from cereals and legumes to be below the provisional maximum tolerable daily intake (2000).

EU has set a ML of 75 µg/kg for cereals intended for direct human consumption and 400 µg/kg for refined maize oil.

Table 4.13. Established Maximum Levels for zearalenone

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2000)**
No ML. The JECFA evaluation calculated average dietary intakes of zearalenone from cereals and legumes in the GEMS/Food regional to be below the provisional maximum tolerable daily intake.				PMTDI: 0.5 µg/kg bw/day for total intake of zearalenone and its metabolites (including alpha-zearalanol)
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2001)**
Cereals intended for direct human consumption, cereal flour, bran and germ as end product marketed for direct human consumption	75	n.a		TDI: 0.2 µg/kg bw/day
Refined maize oil	400	n.a		
U.S. FDA				
Not listed				

Contaminant: Fumonisins (B1 + B2)

Fumonisins are mycotoxins produced by fungi of the genus *Fusarium*. Fumonisins are common contaminants of maize and have also been found in rice. *Fusarium* toxins have been shown to cause a variety of toxic effects in both experimental animals and livestock (19). In animals, fumonisins are associated with a wide range of health effects including effect on liver and kidneys, particular concern is the cancer causing potential of the toxins. Another concern is potential immunotoxicity. In humans, the potential to contribute to cancer is a main concern but so far there is no scientific evidence for this in humans (29).

Cereals (milled) are proposed to be used as raw ingredients in future/innovative RUTF products.

Codex (2016) has established a ML of 2000 µg/kg for maize flour and maize meal and 4000 µg/kg for raw maize grains.

EU (2007) has set an ML of 1000 µg/kg for maize and maize-based food for direct human consumption.

Table 4.14. Established Maximum Levels for fumonisins

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 2001/2011/2016)**
Maize flour and maize meal	2000	Whole commodity		PMTDI: 2 µg/kg bw/ day (group PMTDI)
Raw maize grain	4 000	Whole commodity		
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 2007)**
Maize intended for direct human consumption, maize-based foods for direct human consumption	1000	n.a		TDI of 2 µg/kg bw/day
U.S FDA				
Not listed				

PMTDI (provisional maximum tolerable daily intake)

Contaminant: Ochratoxin A

Ochratoxin A is produced by various *Penicillium* and *Aspergillus* species and represents a well-known hazard to human and animal health. The ochratoxin A is typically found in meat product, cereals, coffee and wine. The key to controlling ochratoxin A in cereals is rapid drying; however, in cool temperate zones, grain is often harvested during moist or rainy conditions, and rapid drying may be difficult in practice. There are limited data available on cereals grown in tropical zones, but ochratoxin A has been found to occur in sorghum, maize and millet (21).

Ochratoxin A is a kidney carcinogen in rodents and accumulates in the kidney. The kidneys have been identified to be the most sensitive organ with respect to the toxicity of this mycotoxin (21).

Cereals (milled) are proposed to be used as raw ingredients in future/innovative RUTF products.

Codex (2007) has established MLs of 5 mg/kg for wheat, barley and rye.

Comparable MLs exists in EU for cereals and cereal products.

Table 4.15. Established Maximum Levels for OTA

CODEX				
Raw material/ Commodity	**Maximum Level (ML) µg//kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (CODEX/JECFA 1990/95 & 2001/2007)**
Wheat	5	Whole commodity	The ML applies to raw common wheat, raw durum wheat, raw spelt and raw emmer.	PTWI (Provisional Tolerable Weekly Intake): 0.0001 mg/kg bw/week (2001)
Barley	5	Whole commodity	The ML applies to raw barley.	
Rye	5	Whole commodity	The ML applies to raw rye	
EU REGULATION (EC) No 1881/2006				
Raw material/ Commodity	**Maximum Level (ML) µg/kg**	**Portion of the Commodity/Product to which the ML applies**	**Notes/Remarks**	**Toxicological guidance value (EU 1998/2006)**
All products derived from unprocessed cereals, including processed cereal products and cereals intended for direct human consumption	3.0	n.a		Tolerable weekly intake (TWI): 120 ng/kg bw/ week (corresponding to 0.00012 mg /kg bw/day)
Unprocessed cereals	5.0	n.a		
U.S. FDA				
Not listed				

5. Conclusion and recommendation

Conclusion and considerations of the validity of the MLs for identified contaminants in RUTF and its target group

When it comes to setting of maximum levels it must be noted that they are only set for those foods in which the contaminant may be found in amounts that are significant for the total exposure of the consumer. The human exposure to a contaminant is affected by the concentration of the chemical found in food and the amount of the food consumed. Therefore, both the concentration and the amount of food normally consumed must be considered when developing an ML. Integrated toxicological expert advice regarding the acceptability and safety of intake levels of contaminants (toxicological guidance value), including information on population groups which are especially vulnerable are usually included when ML are set. In general, also dietary exposure assessments which cover the general population, would also include critical groups that are vulnerable or are expected to have significantly different dietary exposures than the general population (e.g. infants, children, pregnant women or elderly).

Whether the established MLs in food commodities are applicable also for the target group of RUTF products, it needs to be emphasized that both within WHO and EU context, the MLs and the associated toxicological guidance values are in general considered applicable for the whole population except for infants below 12 weeks (WHO) and 16 weeks (EU). This age group is considered a particularly sensitive subgroup due to physiological immaturity

of many of the organ systems in the first weeks after birth and hence an enhanced vulnerability, nutrition habits up to that age (i.e. mother's milk or infant formulae intended for use as the sole source of nutrition) and since the standard animal testing currently used to assess the toxicity of chemicals do not address this specific age group, (8, 9 ,10 & 11).

The toxicological guidance values are essential when decisions about maximum levels in foods are considered (1). Traditionally the toxicological guidance values such as ADI (Acceptable Daily Intake for food additives and pesticides) and TDI (Tolerable Daily Intake for contaminants) or similar incorporates a high safety margin. A toxicological guidance value is the amount of a chemical that can be consumed daily over a lifetime and which is likely to be without appreciable human health risk (including subgroups). Usually the toxicological guidance value is established applying a safety factor (a.k.a. uncertainty factor) of 100 from the highest dose tested without toxicological adverse effects. The safety factor includes and inter-species factor of 10 to extrapolate from animal data to humans and an intra-species factor of 10 to consider the increased vulnerability of sensitive human populations such as infants and children. The intra-species factor of 10 is generally accepted as being adequate.

A recent literature search was carried out by EFSA identifying publications in the areas of toxicokinetics (TK), the physiology of the gut, the nervous system, the immune system, the male and female reproductive systems and the endocrine system in the developing infant and young children (8). The outcome of available evidence indicates that the differences in these areas between infants above the age of 16 weeks and young children and adults are rather limited in comparison with adults. In addition, it was noted that on a body weight basis, therapeutic doses of pharmaceuticals used in infants and young children do not differ significantly from those used in adults. Based on these findings, it was concluded that the toxicological guidance values were applicable to infants above 16 weeks of age and young children, and that an additional assessment factor is not necessary for these age groups (8).

RUTF are primarily intended for children with uncomplicated SAM (implies the absence of symptoms for infection) from the age of 6-59 months (6). Recommended dosage regimen is 100-135 kcal/kg/day per child for an average period of 4 to 8 weeks (7). It is assumed that the RUTF products constitute the sole nutrition in the given period.

As infants and children intended to undergo RUTF treatment are above the age of 12 weeks - and hence do not differ significantly from adults in the physiological areas described above - and considering the large safety margin provided in the toxicological guidance values the established Codex MLs should provide sufficient safety for the users of RUTF

Specific and lower MLs for some contaminants (e.g. DON and lead) have been set for special commercially products such as processed cereal-based foods and baby foods for infants, infant formula and follow-up formula both in EU and in Codex (these MLs are not listed in this report). These products are also intended to be used by infants below 12-16 weeks (up to 12 months) when they are weaned and by young children as supplement to

their diet. The ML applies to the whole commodity/product. Infants and children have a higher food and drink intake than adults on a body weight basis and especially the first weeks after birth is the time with the highest relative food consumption on a body weight basis (9). The main differences between these baby products and RUTFs are that baby food is also intended for infants below the age of 12 weeks where the general toxicological guidance value does not apply. Secondly, infants and young children also have relatively high food consumption per body weight basis (highest being the first weeks after birth) and are exposed to the same kind of food for a longer period than children receiving RUTF treatment which should not exceed 8 weeks.

Whether malnutrition in general and especially for infants/young children is a factor which could have a critical impact on the sensitivity to contaminants (due to e.g. different uptake or metabolism/elimination) cannot be elucidated or concluded upon. Limited data seems to be available in the open literature and several scientific articles and references (e.g. WHO Environmental Health Criteria 237) highlights the need for elucidating nutrition status and exposure to environmental chemicals as well as xenobiotic in general. Whether the large margin of safety, generally provided when establishing toxicological reference values and the margin of exposure, also covers a potential effect on sensitivity to chemicals caused by malnutrition is a question where JECFA could be asked for scientific advice. However, based on the current knowledge and with the risk assessment approach used when developing Codex MLs - such as taken into account lifetime exposure and extra safety factor for the toxicological guidance value- it is assumed that the Codex MLs provides sufficient margin of safety for the target group for RUTF.

Finally, the benefit of RUTF treatment of SAM children should also be weighed against the potential risk from contaminant exposure. Even minor exceeds of ML`s for a short period of time are not expected to cause health effects as it's the lifetime exposure to contaminants that causes adverse health effects. Furthermore, it should be noted that a normal diet also can have high concentrations of the same contaminants considered for RUTF products.

Recommendations

All the mentioned contaminants in this report can in principle occur in raw ingredients used for RUTF products. The contaminants identified and which can occur in raw ingredients used in RUTF products are listed in the table below.

Contaminants in raw ingredients used in RUTF
aflatoxins (B1, B2, G1, G2 and M1)
DON
arsenic
lead
cadmium
mercury
glycidol
Dioxin and PCBs
PAH
zearalenone

fumonisins
T-2 and HT-2 toxin
erucic acid
ochratoxin A

For some of these contaminants no Codex MLs have been established due to low dietary exposure levels, or because Codex has developed a Code of Practice that when followed will reduce the level of contaminants in food. Furthermore, some contaminants where health concerns have been substantiated, JECFA has either been requested to provide scientific advice or are currently reviewed by Codex for the most appropriate risk management measures. Finally, for the contaminant erucic acid which might occur in RUTF products neither JECFA or Codex activities have been initiated. For this contaminant EU has established a ML for vegetable oils and fats. The most appropriate place for guidance on proper risk management measures for this contaminant would be to use the EU Regulation (EC) No 1881/2006 and as a starting point.

- In general, it is recommended that all Codex MLs for contaminants and all relevant Code of practice for reducing contaminants in food should be applied for raw ingredients that are or can be used in RUTF products. MLs set by Codex are in general considered to best reflect global dietary patterns[11] and food chemical contamination. It's important to note that ML is only set for raw ingredients in which the contaminant may be found in amounts that are significant for the total exposure of the consumer.

- Furthermore, it is recommended for aflatoxin (total) to apply the ML proposal for ready-to-eat peanuts of 10 µg/kg for peanuts used in RUTF products when adopted. Also, the Codex ML of 0.5 µg/kg for aflatoxin M1 for milks should be applied since milk and other dairy products (milk and whey powder) are raw ingredients in RUTF products. As JECFA (2016) highlighted a need for future risk management activities for aflatoxins in cereals, it is expected that further measures will be proposed to reduce aflatoxin in cereals. When available this will need to be considered for RUTF.

- Glycidol is a contaminant that can be found in refined fats and oils and which is relevant as refined oils are used in RUTF products. JECFA has recommended that measures to reduce glycidyl esters (glycidol) in fats and oils continue, particularly when used in infant formula. This will need to be taken into account when a decision is made by Codex.

- It is proposed to ask JECFA for scientific advice when it comes to erucic acid. Erucic acid occurs in common food commodity as vegetable oil. Such a request scientific advice is not especially related to RUTF products, but to food in general. However, if a JECFA evaluation identifies a need for further risk management measures and Codex establish such measures it would also have to apply to RUTF.

- To reduce the risk of exposure to a single contaminant it could be considered to use two or more RUTF products (containing different raw materials) in the same treatment as food diversity will minimize the exposure to a single contaminant.

[11] While EU MLs uses food chemical concentration data from EU and a European dietary pattern.

- If meat is included as raw ingredients in future RUTF products, contaminants that often occur in meat products such as metals, dioxin and PCB should be considered in the guideline.

Consideration of listing MLs for contaminants in raw ingredients used in RUTF products in the guideline

Including specific MLs in the RUTF guideline for contaminants in raw ingredients used in RUTF products would have both advantages and disadvantages. An immediate advantage would be that it makes it easy for RUTF producers and suppliers to find relevant information about existing ML for contaminants that can occur in raw ingredients used in RUTF products. This will especially be relevant for smaller producers of RUTF products with limited resources and where it could be anticipated that they find it difficult to collect information about established ML and code of practices from various Codex standards and guidelines.

In the current draft guideline for RUTF products only mycotoxins and especially aflatoxins are highlighted in the section on contaminants. Aflatoxins are especially a problem in peanuts-based food products but can also occur in other raw ingredients used in RUTF products such as in cereals and milk. Considering that many raw ingredients other than peanuts will be used in future RUTF products it can be misleading to highlight only one food contaminant in the RUTF guideline. There is a risk that it would give the impression that other food contaminants are of less importance and therefor no measures are needed to manage other contaminants. As this project has clarified there are clearly other food contaminants in various raw ingredients that are relevant to control and manage in RUTF products. Therefore, it is either recommended to list all contaminants (including their ML) that can occur in raw ingredients used in RUTF products in the guideline or a very clear reference is made saying that all ML/Code of Practices for contaminants listed in CODEX STAN 193-1995 applies to the raw ingredients used in RUTF products. If a choice between the two options would have to be made the best option would be to refer to CODEX STAN 193-1995 in the RUTF guideline. This will ensure up to date information about relevant contaminants to control and manage in ingredients used in RUTF products.

It is stated in the general Codex standard for contaminants (193-1995) that the Codex maximum level (ML) for a contaminant in a food is the maximum concentration of that substance recommended by the Codex Alimentarius Commission to be legally permitted in that commodity. It means that the ingredients used in RUTF products needs to be controlled at the level of the raw material**.**

A proposal for a text to be used in the RUTF guideline under the header contaminants could be:

The products should be prepared with special care and under good manufacturing practices. The products should not contain contaminants or other undesirable substances (e.g. biologically active substances) in amounts which may represent a hazard to the health of SAM children or other users of RUTF products. The raw ingredients in these products covered by the provisions of this Guideline shall comply with those maximum levels established by the Codex Alimentarius Commission and which is listed in CODEX STAN 193-1995 and follow relevant Codex code of practices for prevention and reduction of food contaminants in food. Future scientific advice provided by JECFA and decisions by Codex regarding risk management measures of aflatoxin (in cereals and the ML proposal for ready-to-eat peanuts), glycidol and erucic should be implemented as necessary.

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Annex I