Food and Agriculture Organization of the United Nations

Case study

Food safety considerations to achieve best health outcomes under limited food availability situations

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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
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ABBREVIATIONS AND ACRONYMS

BMDL	Benchmark dose level
bw	body weight
CCCF	Codex Committee on Contaminants in Foods
CSB	Super cereal corn-soya blend
DALY	Disability-adjusted life years
dL	decilitre
EC	European Commission
EED	Environmental enteric dysfunction
EFSA	European Food Safety Authority
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
FBF	Fortified blended foods
FDA	United States Food and Drug Administration
FERG	WHO Foodborne Disease Burden Epidemiology Reference Group
GAP	Good Agricultural Practices
GMP	Good Manufacturing Practices
HACCP	Hazard Analysis Critical Control Points
HBGV	Health-based guidance value
IQ	Intelligence Quotient
JECFA	Joint FAO/WHO Expert Committee on Food Additives
kg	kilogram
kPa	kilopascal
LNS	Lipid-based nutrient supplements
µg	microgram
ML	Maximum level
MNP	Micronutrient powders
mmHg	Millimetre of mercury
ng	nanogram
NOAEL	No observed adverse effect level
PMTDI	Provisional maximum tolerable daily intake
PTWI	Provisional tolerable weekly intake

RSB	Super cereal rice-soya blend
RUF	Ready-to-use foods
RUSF	Ready-to-use supplementary foods
RUTF	Ready-to-use therapeutic foods
SC+	Super cereal plus
TDS	total diet study
WFP	World Food Programme
WHO	World Health Organization
WSB	Super cereal wheat-soya blend

INTRODUCTION

Ensuring a safe food supply is a public health priority and is an essential step toward achieving food security. Food control systems designed to promote effective food safety and quality are key to safeguarding the health and well-being of people, and for ensuring fair access to trade.

The Codex Alimentarius Commission, operated jointly by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), is responsible for developing international standards, guidelines and for making any other recommendations related to food safety and quality. Codex has the dual mandate of protecting the health of consumers and ensuring fair practices in food trade.[1] While Codex standards are developed within a global context, they can also serve as the basis for national governments to develop their own food regulations. In addition to providing (jointly with WHO) the scientific advice that underpins the Codex standard setting process, FAO contributes to and supplements Codex work by supporting countries to apply risk-based food safety management along food chains that are appropriate for national and local food production systems. Ultimately, the goal of this work is to develop food control systems, including food safety policies and regulatory frameworks, that are both designed and suited for accessing international trade, and are applicable to the regional/national context with respect to food safety and food security.

SCOPE OF THE CASE STUDY

Food security occurs when "all people, at all times, have physical and economic access to sufficient, s afe and nutritious food to meet their dietary needs and food preferences for an active and healthy life" (World Food Summit, 1996). In contrast, the term food insecurity is used to describe situations where it is difficult to access sufficient amounts of safe and nutritious food to allow for normal human growth and development. Food insecurity correlates with malnutrition, hunger, impaired growth and other undesirable public health outcomes.[2]

This case study presents two scenarios to illustrate food safety considerations that might be helpful in situations where the impact of limited food availability is mitigated through food aid, which is meant to ensure acceptable health outcomes. Recommendations are provided as to how to address these food safety issues, recognizing that there are likely multiple contributing factors directly related to the food insecurity conditions described in the scenarios.

1 Codex Alimentarius International Food Standards, https://www.fao.org/fao-who-codexalimentarius/en
2 Hunger and food insecurity, https://www.fao.org/hunger/en

SCENARIO
LEAD IN MAIZE

BACKGROUND

Maize (*Zea mays* L.) is the third most important cereal grain worldwide, after wheat and rice (Golob *et al.*, 2004). Maize accounts for 40 percent of the cereal production in sub-Saharan Africa, where more than 80 percent is used as food (FAO, 2016). The crop provides at least 30 percent of the total calorie intake of people in sub-Saharan Africa (Nuss and Tanumihardjo, 2010). According to a report by the International Institute of Tropical Agriculture,[3] maize is the most important cereal crop in sub-Saharan Africa and is an important staple food for more than 1.2 billion people in the region and in Latin America. Consumption of maize can range from 52 g to 328 g/person/day in many African regions (Ranum, Peña-Rosas and Garcia-Casal, 2014). In several African countries, in particular Lesotho, Malawi, South Africa, Zambia and Zimbabwe, consumption can exceed 200 g/person/day. Overall, the consumption of maize is expected to increase mainly in developing countries, including those in sub- Saharan Africa, where populations are increasing quite rapidly (OECD and FAO, 2018).

As with most cereal grains, maize is susceptible to contamination by various mycotoxin-producing fungi and can also absorb toxic metals from the growing environment. Increasing heavy metal content in soils that have been polluted by wastewater irrigation results in an accumulation of various toxic metals, including lead, in maize (Lu *et al.*, 2015). The WHO Foodborne Disease Burden Epidemiology Reference Group (FERG) estimated that of the four main foodborne toxic metals (lead, methylmercury, arsenic and cadmium), lead accounted for almost 60 percent of the total disability-adjusted life years (DALYs) of all four metals combined (Gibb *et al.*, 2019).

Recognizing cereal grain consumption as a route of exposure to contaminants, Codex has developed a number of standards (including maximum levels [MLs]) to ensure the safety of cereals traded internationally. The Code of Practice for Source Directed Measures to Reduce Contamination of Foods with Chemicals (CXC 49-2001) provides general guidance on the major sources of environmental chemicals

[3] International Institute of Tropical Agriculture (IITA), https://www.iita.org

that could contaminate foods and constitute a hazard to human health while the Code of Practice for the Prevention and Reduction of Lead Contamination in Foods (CXC 56-2004) specifically deals with sources of lead and provides recommended Good Agricultural Practices (GAP) and Good Manufacturing Practices (GMP) to minimize the lead contamination of foods (FAO and WHO, 2001; FAO and WHO, 2004). The current Codex commodity standards for maize (CXS 153-1985) and products derived from maize (CXS 155-1985) specify that maize should be "free from heavy metals in amounts which may represent a hazard to human health" (FAO and WHO, 1985a, 1985b). The same provision appears in the World Food Programme (WFP) Technical Specifications for Maize (WFP, 2013). As totally eliminating lead from foods is unachievable due to its ubiquitous nature in the environment, Codex has developed more than 40 MLs for lead (CXS 193-1995) in a large number of foods to ensure that dietary exposure is as low as is reasonably achievable and does not represent a health risk to consumers (FAO and WHO, 1995a). While no ML has been developed to date that is specific to lead in maize, there is an ML for cereal grains of 0.2 mg/kg, which would be applicable. The same limit for milled maize products has been proposed by the East African Community while Sierra Leone has set a limit of 0.1 mg/kg for lead in fortified milled maize products.

STATE OF ZAMFARA IN NIGERIA: AN EXAMPLE OF LEAD POISONING

In March 2010, during the course of an annual meningitis immunization programme, excess childhood death and illness occurring primarily among children under five years of age in Zamfara State in Nigeria, was reported by *Médecins Sans Frontières* to the state health authorities. More than 400 children under the age of five died, and hundreds more were confirmed to be at risk of death or serious acute and long-term irreversible health effects due to extremely high levels of lead in their blood (WHO, 2011). Of the children tested in two villages, 100 percent exceeded 10 µg/dL lead in blood, with some levels measuring as high as 700 µg/dL. Investigations in the two most contaminated ore-processing villages revealed that 97 percent of the children (n=204) under the age of five years had blood lead levels greater than 45 µg/dL and soil-lead levels >400 mg/kg (Lo *et al.*, 2012; Getso *et al.*, 2014). The source of the lead was determined to be artisanal gold mining involving processing of gold ores containing up to 10 percent lead within the residential compounds. The main routes of lead exposure were incidental ingestion and inhalation of contaminated soil and dusts. Follow-up investigations demonstrated that most dietary lead exposure was associated with contamination of staple cereal grains and legumes during post-harvest processing and preparation in contaminated homes. Staple foods made from maize, guinea corn, millet and local rice prepared in home compounds were associated with most of the suspected dietary lead intake. Average post-harvest and processed cereal grain lead levels were 0.32 mg/kg and 0.85 mg/kg dry weight, respectively. Age-specific food lead intake ranged from 7 to 78 µg/day. Factors such as dusty environment, fasting between meals and nutritional deficiencies likely aggravated lead ingestion and absorption.

Contamination of staple cereal grains by highly bioavailable pulverized ores could account for as much as 11 to 34 percent of the lead level in the blood of children during the epidemic. This continued to be a major source even after residential soil remediation until stored grain inventories were exhausted (Tirima *et al.*, 2018).

EXPOSURE ASSESSMENT SCENARIO

> *This scenario presumes an emergency food security assessment has been conducted, a food insecure population has been identified and food aid is being provided.*

WFP provides a range of specialized nutritious foods meant to prevent or treat undernutrition. Specialized nutritious foods are often defined or categorized as follows: Ready-to-use foods (RUFs), including ready-to-use therapeutic foods (RUTFs) and ready-to-use supplementary foods (RUSFs), lipid-based nutrient supplements (LNS), fortified blended foods (FBFs), including super cereal corn-soya blend (CSB), super cereal plus-CSB, super cereal wheat-soya blend (WSB), super cereal plus-WSB, super cereal-rice soya blend (RSB), super cereal plus-RSB and micronutrient powders (MNPs) (WFP, 2012). Products such as super cereal plus (SC+) (children 6–23 months) and super cereal (intended for populations including pregnant and lactating women) are used both to prevent stunting and acute malnutrition, and to treat moderate acute malnutrition.

Super cereal plus-CSB is comprised of maize (54.8 percent), de-hulled soya beans (23.5 percent), dried skimmed milk powder (8 percent), sugar (9 percent), vegetable oil, vitamins and minerals premix. Super cereal plus provides a minimum of 400 kcal/100 g of dry product. When super cereal plus is consumed as a porridge or gruel, it should be prepared by mixing an appropriate proportion of flour and clean water (i.e. 50 g of super cereal plus with 250 g of water) followed by a cooking time at the simmering point of five to ten minutes. Super cereal plus is to be used as a complement to breast feeding and is not a breast-milk substitute. The daily ration is 100 to 200 g (200 g provides enough for sharing) (UNHCR, 2014).

This intake scenario assumes there is complementary breastfeeding and, therefore, consumption of 100 g of the product per day (54.8 g of maize). An average body weight used will be 5 kg; therefore, maize intake from SC+ will be 11 g/kg bw/day.

According to the WFP specification for maize, the maize used as an ingredient should conform to Codex STAN 153-1985 - “Maize (corn) shall be free from heavy metals in amounts which may represent a hazard to human health” (FAO and WHO, 1985a). As maize is considered a cereal, it should be subject to the 0.2 mg/kg lead ML (CXS 193-1995) (FAO and WHO, 1995a). The lead ML for infant formula (0.01 mg/kg) would not be applicable and there is no Codex lead ML for cereal-based foods for infants and young children. Therefore, at 0.2 mg/kg, with no loss of lead due to processing/cooking, the lead intake would be 2.2 µg/kg bw/day for consumption of 100 g per day of SC+ by infants (5 kg bw). Recent total diet study (TDS) lead intake estimates (mean) for sub-Saharan Africa range from 0.2 to 1.24 µg/kg bw/day, with the main sources of dietary exposure being sorghum, millet and cassava (Ingenbleek *et al.*, 2020).

RISK CHARACTERIZATION

At the thirtieth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA),[4] the health risks associated with the exposure of infants and children to lead was evaluated and a provisional tolerable weekly intake (PTWI) of 25 µg/kg bw was established for this population group, based on the information that a mean daily exposure to lead of 3 to 4 µg/kg bw for infants and children was not associated with an increase in blood lead levels (FAO and WHO, 1987). At its fifty-third meeting, JECFA concluded that current concentrations of lead in food would have very little impact on the neuro-behavioural development of infants and children but stressed that a full risk assessment of lead should take other sources of exposure into account (FAO and WHO, 2000). In comparison to the dietary intake estimate for children consuming SC+, no health risk have been identified (less than the JECFA PTWI originally established for infants and children).

At the seventy-third meeting of JECFA, the neurodevelopmental effects of lead were considered to be pivotal in its assessment for children. Based on the results of a meta-analysis of epidemiological data, the chronic dietary exposure corresponding to a decrease of 1 IQ point was estimated to be 0.6 µg/kg bw/day (5th to 95th percentiles: 0.2 to 7.2 µg/kg bw/day). Based on this analysis, the previously established PTWI of 25 µg/kg bw was estimated to be 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. JECFA concluded that the PTWI established at the thirtieth meeting could no longer be considered health protective, and it was withdrawn. Because the analyses did not indicate a threshold for the key effects of lead, JECFA concluded that it was not possible to establish a new PTWI that would be considered health protective (FAO and WHO, 2011a).

The mean dietary exposure estimates provided at the most recent JECFA meeting for children 1 to 4 years of age ranged from 0.03 to 9 µg/kg bw/day. The health impact at the lower end of this range was considered negligible by JECFA, because it is below the exposure level of 0.3 µg/kg bw/day calculated to be associated with a population decrease of 0.5 IQ points. The higher end of the exposure range is higher than the level of 1.9 µg/kg bw/day calculated to be associated with a population decrease of 3 IQ points, which is deemed by JECFA to be a concern (FAO and WHO, 2011b).

[4] Joint FAO/WHO Expert Committee on Food Additives, https://www.fao.org/food-safety/scientific-advice/jecfa/en

In applying the latest JECFA lead assessment to this scenario, a dietary intake of 2.2 µg/kg bw/day would be associated with a blood lead level of approximately 1.8 µg/dL and an IQ decrease of 2 points. While an IQ decrease of this range may not have significant impacts on individuals, at a population level, it can increase the proportion of children assigned to categories of concern with respect to central measures of intelligence. Research has also shown that increased blood lead in children has long term consequences regarding lower cognitive function in adults (Reuben *et al.*, 2017). While most lead risk assessments have reported that there is no low dose threshold for adverse developmental effects, it has also been suggested that limitations in epidemiologic datasets can make predictions of the low dose dose-response analysis of children with blood lead less than 5 µg/dL somewhat questionable (van Landingham, Fuller and Schoof, 2020).

> *Recognizing that lead pharmacokinetics in humans are variable and strongly influenced by a number of factors, including nutrition and maternal body burden, it is presumed that the duration of exposure of the children to lead in SC+ is sufficient to achieve steady-state blood levels It is also assumed that the exposure happened during a critical period of neurodevelopment. This is in line with the known relationship in children between adverse neurodevelopmental outcomes and blood lead.*

If SC+ were to represent the primary source of lead exposure and the ingredient of concern is maize, at a daily intake of 11 g maize/kg bw, the lead concentration in maize would need to be no greater than approximately 25 to 30 µg/kg in order not to exceed the daily lead intake associated with an IQ decrease of 0.5 points (0.3 µg/kg bw/day). Although unlikely, due to the ubiquitous nature of lead dietary exposure, the other main ingredients of SC+ are being considered to include a negligible amount of lead for the intake scenario. If additional components of SC+ were to be considered in this scenario, the maximum lead concentration in maize in order to not exceed the exposure level associated with a population decrease of 0.5 IQ points would likely decrease. For example, 8 percent w/w of SC+ is skimmed milk powder and 3 percent is refined soybean oil. While no specific reference to lead is found in the Codex standard for a blend of skimmed milk powder and vegetable fat in powdered form (CODEX STAN 251-2006) (FAO and WHO, 2006), it does state that "The milk used in the manufacture of the products covered by this Standard shall comply with the Maximum Levels for contaminants and toxins specified for milk by the General Standard for Contamina nts and Toxins in Food and Feed" (CODEX STAN 193-1995) (FAO and WHO, 1995a).

According to the latter standard, the maximum concentration of lead in skimmed milk powder would be 0.02 mg/kg (ML for milk) and 0.08 mg/kg for soybean oil (ML for edible fats and oils). Possible additional lead intake from these two components when applying the existing MLs would only increase the estimated lead exposure by 3.6 percent. No Codex lead ML is available for sugars although Commodity Standard CXS 212-1999 states that "Raw cane sugar shall be free from heavy metals in amounts which may represent a hazard to human health" (FAO and WHO, 1999). However, the WFP technical specification for white sugar (ICUMSA 45) lists a lead limit of 0.5 mg/kg (WFP, 2019). If a lead contribution to the intake estimates from SC+ were considered using the WFP specification as a maximum lead concentration, the exposure would increase by approximately 40 percent. Previously, JECFA reported that sugar and vegetable fats rarely contained detectable levels of lead. Vitamins, minerals and various essential elements used in SC+ may also be sources of lead, depending on their source and manufacturing. In a survey of the United States Food and Drug Administration (FDA) of pharmaceutical products and dietary supplements, the maximum detected lead concentration was 500 µg/kg (mean 48 µg/kg) (Kauffman *et al.*, 2007). In comparison, maximum limits for lead in food supplements and herbal drugs/extracts as established in the European Union range from 3 to 5 mg/kg. While lead is somewhat unique as a contaminant in that it can be found in almost all food products and/or ingredients, in this particular scenario the main source of lead was assumed to be from maize.

CONCLUSIONS

> Consumption of SC+ by infants and children at 100 g/day (54.8 g of maize) where maize conforms to the 0.2 mg/kg Codex ML for lead in cereal grains would result in a lead intake of approximately 2.2 µg/kg bw/day which is seven-fold higher than the intake described by JECFA as being associated with an IQ decrease of 0.5 points (0.3 µg/kg bw/day or a minimum effect dose).

> A potential IQ decrease associated with the intake of 2.2 µg/kg bw/day would be approximately 2 IQ points.

> For a scenario where children (5 kg bw) are consuming 100 g of SC+/day, the lead concentration in maize would need to be less than approximately 25 to 30 µg/kg in order not to exceed a minimum effect dose as described by JECFA (0.3 µg/kg bw/day). This would presume additional components of SC+ are making a negligible contribution to dietary exposure.

SCENARIO 2

FUMONISINS IN CEREAL GRAINS

BACKGROUND

Recent studies relying on up-to-date sampling and monitoring protocols, combined with sensitive analytical testing methods, suggest as much as 60 to 80 percent of the world's food crops are contaminated with mycotoxins (Eskola *et al.*, 2020). According to Wild and Gong (2009) and Wu *et al.* (2011), the mycotoxins of main concern to human health in sub-Saharan Africa are aflatoxins, fumonisins, ochratoxins, trichothecenes and zearalenone.

Fumonisins (FB1–FB4) are secondary metabolites/mycotoxins produced by various *Fusarium* species and *Aspergillus niger* and are common contaminants of maize. Food survey results from sub-Saharan Africa have demonstrated high levels of fumonisins, sometimes approaching those seen in maize, can also be detected in a variety of other cereal grains including sorghum (Chilaka *et al.*, 2017; Braun and Wink, 2018). Fumonisins are considered to be a major food contaminant for rural African populations (Alberts *et al.*, 2019).

It is hypothesized that mycotoxins, specifically fumonisins and aflatoxins, can contribute to childhood growth impairment through a process known as environmental enteric dysfunction (EED). Specifically, fumonisins inhibit ceramide synthase, which is an enzyme critical to sphingolipid metabolism, due to their structural similarity to sphinganine and sphingosine (Voss and Riley, 2013). Sphingolipids play a role in cellular stress response, cell signalling, membrane stability and apoptosis. Disturbances in the sphingolipid biosynthetic pathway could then affect intestinal epithelial cell viability and impair intestinal barrier function leading to a reduced absorptive capacity of the small intestine (Smith *et al.*, 2015; Crane, Jones and Berkley 2015). In experimental animal models, exposure to fumonisins has also been shown to increase the susceptibility and severity of pathogenic infections of the gastrointestinal tract, which can then affect gut function, nutrient absorption and physical development (Chen *et al.*, 2018a).

Stunting is characterized by poor linear growth and is directly associated with chronic malnutrition. Children are considered as stunted if their height-for-age is greater than two standard deviations below the WHO Child Growth Standards median.[5] Stunting leads to lifelong negative consequences such as cognitive impairment and an increased risk of nutrition-related chronic diseases in adult life. WHO estimates the prevalence of world-wide pediatric stunting at 171 million children, with 97.6 percent of the burden in developing countries (de Onis, Blossner and Borghi, 2011). While globally, the percentage of children classified as stunted continues to decrease, in Africa rates have remained stagnant at approximately 40 percent with little improvement expected.

Recognizing cereal grain consumption as a route of exposure to various contaminants, including mycotoxins, Codex has developed a number of standards (including MLs) to ensure the safety of cereals traded internationally. The Codex Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CXC 51-2003) provides general principles for the reduction of various mycotoxins in cereals and is applicable to all cereal grains and cereal products relevant to human dietary intake and health as well as international trade (FAO and WHO, 2003). This code recommends practices based on GAP and GMP, which are generally consistent with Hazard Analysis Critical Control Points (HACCP) principles. The Codex standard for processed cereal-based foods for infants and young children (CXS 74-1981) has no specific reference to mycotoxins but does state that these products should be "practically free from other contaminants, especially pharmacologically active substances" (FAO and WHO, 1981). This standard is applicable to those foods that are prepared mainly from the following cereals: wheat, rice, barley, oats, rye, maize, millet, sorghum and buckwheat. Various other Codex commodity standards state that the product should comply with those maximum mycotoxin limits established by the Codex Alimentarius Commission for the applicable commodity. An exception would be the Codex standard for wheat and durum wheat (CXS 199-1995), which indicates the product "shall not contain any substance originating from micro-organisms, including fungi, in amounts which may represent a hazard to health" (FAO and WHO, 1995b). Finally, Codex has developed approximately 20 maximum levels for mycotoxins (CXS 193-1995) in a large number of foods in order to ensure that dietary exposure does not represent a health risk. For fumonisins, these include raw maize grain: 4 000 µg/kg and maize flour and maize meal: 2 000 µg/kg (FAO and WHO, 1995a).

[5] The WHO Child Growth Standards, https://www.who.int/tools/child-growth-standards/standards

EXPOSURE ASSESSMENT SCENARIO

Cereal grains in most African countries represent an important source of daily calories consumed. Maize production in Africa is dominant compared to other cereal grains and accounts for approximately 40 percent of total cereal production (Taylor, 2016). Maize-based products are consumed by 67 to 83 percent of South Africans, and the mean consumption per day in rural areas is estimated between 476 to 690 g per person (Burger *et al.*, 2014). Similar high daily maize intakes (246 g) have also been reported for children 1 to 9 years from rural South Africa (Shephard *et al.*, 2007). Nearly 80 percent of the population in Uganda rely on maize, sorghum, millet and groundnut for their daily calories (Ssewanyana and Kasirye, 2010). The average daily intake for the grains in northern Uganda was: maize=106 g/day, sorghum=115 g/day, millet=0.18 g/day (Wokorach *et al.*, 2021). For Africans living in the Centane region of the Eastern Cape province of South Africa, the mean total dry weight maize intake of home-grown, commercial or combined (both maize sources) are 474, 344, 462 g/day, respectively (Burger *et al.*, 2010).

Grain samples (n=66–130) were collected between 2018 and 2019 from nine districts in northern Uganda and mycotoxins (aflatoxins, fumonisins, ochratoxins and deoxynivalenol) analysed by enzyme-linked immunosorbent assay (ELISA). Contamination with all four mycotoxins mainly occurred in sorghum grains (40.7 percent) while sorghum also resulted in the highest levels of fumonisins (mean 4.4 mg/kg, max. 37 mg/kg), which is significantly higher than the levels measured in groundnut, maize and millet. The estimated daily intake of fumonisins from sorghum consumption by children and adults was 46.0 and 8.2 µg/kg bw/day, respectively, while 71 percent of the sorghum samples (n=127) exceeded a regulatory value of 1 mg/kg.

Shephard (2004) calculated that, at a contamination level for fumonisins in maize of 2 000 µg/kg (current Codex ML for fumonisins in maize flour and meal) based on the consumption of 400 g/day, dietary exposure for a 60 kg adult would be 13 µg/kg body weight/day or 650 percent of the JECFA current provisional maximum tolerable daily intake (PMTDI). Previous surveys of maize flour samples from Kenya demonstrated mean fumonisin concentrations of 1.9 mg/kg, with 50 percent of samples (n=985) exceeding the Kenyan regulatory limit of 1 mg/kg (Mutiga *et al.*, 2015). In 101 samples of maize porridge collected from three agro-ecological zones of the United Republic of Tanzania, fumonisins were detected in 100 percent of the samples (Geary *et al.*, 2016). Mean FB_1+FB_2 ranged from 160-647 ng/g while 57 percent of samples exceeded the European Commission limit for fumonisins in food products intended for infant consumption ($FB_1+FB_2>200$ ng/g). At its eighty-third meeting, JECFA concluded that maize is the predominant source of exposure for total fumonisins in most cluster diets; however, these estimates did not include information on fumonisin levels in maize in countries in the African, Eastern Mediterranean and South-East Asia WHO regions (FAO and WHO, 2018).

For the current scenario, it is presumed that infants and young children (5 kg bw) are consuming 100 g of maize-based products per day while adults (60 kg bw) are consuming 400 g of maize-based products per day. For consistency with the previous scenario, the 100 g of maize-based products being consumed by infants/young children will contain 54.8 g of maize. Of the current Codex MLs, only one, 2 000 µg/kg for maize flour and maize meal, would apply to both intake groups. In comparison, the European Commission has expanded its food categories for fumonisins to include MLs for food products intended for infants (200 µg/kg) and maize-based breakfast cereals and maize-based snacks (800 µg/kg).

RISK CHARACTERIZATION

The current JECFA health-based guidance value (HBGV) for fumonisins is based on a sub chronic (90 day) study conducted in rats that were maintained on diets of up to 81 mg/kg fumonisin B_1 (FB_1), corresponding to intake levels of 0, 0.1, 0.2, 0.7 and 5.7 mg/kg bw/day (WHO, 2001). Indications of renal toxicity were observed in male rats at intakes greater than 0.2 mg/kg bw/day. Applying a safety factor of 100, the no observed adverse effect level (NOAEL) resulted in setting the HBGV, the PMTDI, of 2 µg/kg bw/day. Confidence in this NOAEL was increased because of results from a more recent six-month feeding study in cancer-prone mice with purified FB_1, which identified a lower 95 percent confidence limit on the benchmark dose for a 10 percent response ($BMDL_{10}$) of 0.165 mg/kg bw/day for increased incidence of karyocytomegalic hepatocytes and hepatocellular apoptosis (Bondy *et al.*, 2012). It is also noted that, compared to this minimal effect dose of 0.165 mg/kg bw/day, data from humans has indicated that biochemical effects, i.e. inhibition of ceramide synthase (based on changes in blood sphinganine-1-phosphate [Sa 1-P] levels), may occur at doses considerably lower (greater than approximately 1.67 µg FBs/kg bw/ day as estimated from urinary FB_1 concentrations) (Riley *et al.*, 2015). A significant correlation in a positive dose-dependent manner has been observed between dietary fumonisin exposure and the urinary fumonisin B_1 (UFB_1) levels in human populations (Riley *et al.*, 2012). While these intermediate intracellular "effect" biomarkers of ceramide synthase inhibition provide useful indications of exposure to fumonisins, progression/linkages to symptoms of overt toxicity in humans are not fully understood (Voss *et al.*, 2011).

Based on previous studies conducted in the United Republic of Tanzania (Kimayam *et al.*, 2010; Shirimi *et al.*, 2015), it was concluded that mycotoxin (aflatoxins and fumonisins) exposure can be a significant risk factor for growth impairment in young children. However, other risk factors such as micronutrient status or exposure to infectious agents were not generally taken into account in these studies. In a follow up prospective study conducted in a cohort of infants (n=114; <3 months old) from Haydom, in the United Republic of Tanzania, fumonisin exposure, as determined by UFB_1, was negatively associated with children being underweight at 24 and 36 months, but not with stunting or wasting.

No associations were found between aflatoxin exposures, as defined by plasma aflatoxin B1-lysine (AFB1-lys) adducts, and growth impairment as measured by stunting, underweight or wasting. At enrollment, a high percentage of children (61 percent) at 24 months of age were classified as stunted (height-for-age Z score [HAZ] of equal to or less than minus two standard deviations (-2 SD) below the median of the WHO reference standard), which increased to 75 percent by 36 months of age. Fumonisin intake (mean) was estimated at 13.8 µg/kg bw/day (8.4 to 19.2 µg/kg bw/day 95 percent CI) or approximately seven times greater than the current JECFA PMTDI (Chen *et al.*, 2018b). While numerous factors can contribute to impaired growth and development in children, the impact that individual mycotoxins have on linear growth remains an active concern.

Applying the default maize intakes of 54.8 g or 400 g/day to the current Codex ML for fumonisins in maize flour and maize meal (2 000 µg/kg) would result in intakes of approximately 22 µg/kg bw/day for children and 13 µg/kg bw/day for adults (approximately 7 to 10-fold greater than the current JECFA HBGV). This presumes no loss of fumonisins during food preparation and no additional dietary sources of fumonisins. In comparison, applying the EC MLs for either maize-based breakfast cereals (800 µg/kg) or food products intended for infants (200 µg/kg) to the same maize intakes would result in fumonisin exposures of 2.2 µg/kg bw/day for children and 5.3 µg/kg bw/day for adults.

CONCLUSIONS

> Consumption of maize-based foods that meet the current Codex ML for fumonisins by adults or children in regions of Africa associated with high daily maize intakes could result in fumonisin exposures that may exceed the current JECFA HBGV by up to 7 to 10-fold.

> The high fumonisin intake for children significantly exceeds the JECFA HBGV and is at an intake that has been associated with growth impairment.

> In both adults and children, indications of ceramide synthase inhibition may be detected following intakes that would still be almost an order of magnitude below the current experimental point of departure used to derive the JECFA HBGV.

> Applying a lower fumonisin ML specific to maize-based foods consumed by infants and children would result in intakes that would be considered health protective based on the current JECFA PMTDI. For example, an ML of 250 µg/kg for food products intended for infants/young children would result in fumonisin exposures not exceeding the JECFA PMTDI, if maize is being consumed at <8 g/kg bw/day.

RISK MANAGEMENT RECOMMENDATIONS

In the two previous scenarios designed to investigate possible health effects associated with the consumption of foods that met current and/or applicable international food safety standards, a health risk, as defined by exceeding health-based guidance values, was identified. The following sections will describe options that could be developed in order to mitigate the health risk.

SCENARIO 1 - LEAD IN MAIZE

This scenario considered consumption of SC+, a WFP product, by infants and children. The main ingredient of SC+ is maize (54.8 percent) and exposure to lead was considered relevant based on recently published total diet study results from sub-Saharan Africa indicating high lead exposure (Ingenbleek *et al.*, 2020). Considering maize as the main source of lead exposure from the consumption of SC+ and applying a worse-case scenario of lead in maize conforming to the current Codex standard for cereal grains (0.2 mg/kg), the estimated intake by infants/children (5 kg bw) would be approximately 2.2 µg/kg bw/day, which would be associated with a possible IQ decrease of 2 points. This intake is also approximately 73-fold greater than the lead intake described by JECFA to be associated with a negligible health risk (0.03 µg/kg bw/day) or 7.3-fold greater than an intake estimated to be associated with an IQ loss of 0.5 points (0.3 µg/kg bw/day).

RISK MITIGATION/MANAGEMENT OPTIONS:

1. Applying the current Codex ML for cereals (CXS 193-1995) to the maize content of SC+ can result in an exposure to lead associated with possible adverse health effects (FAO and WHO, 1995a). Decreasing the current Codex lead ML for cereal grains to no greater than 30 µg/kg would result in lead exposure from consumption of SC+ at <0.3 µg/kg bw/day. This lead exposure may be considered by risk mangers to be "tolerable" as the IQ decrease would be only 0.5 points. At the seventy-third meeting of JECFA (its most recent meeting) in which lead exposure was considered, the weighted mean lead concentration in cereals was reported as 9 µg/kg, with the range of national mean concentrations <LOD–0.029 µg/kg. This would suggest a further data review to support a possible revision of the current Codex ML for cereals to a value less than 0.2 mg/kg (FAO and WHO, 2011a).

2. The current Codex commodity standard for maize (Codex STAN 153-1985) states that maize (corn) shall be free from heavy metals in amounts that may represent a hazard to human health (FAO and WHO, 1985a). Any revision to the current cereal ML for lead (CXS 193-1995) should also consider modifying the current maize commodity standard by removing this generic wording and referencing the contaminant standard with "shall comply with the Maximum Levels of the General Standard for Contaminants and Toxins in Food and Feed (CXS 193-1995)" (FAO and WHO, 1995a).
3. Recognizing that early post natal exposure to certain contaminants can have long term negative health consequences, Codex could consider developing lead MLs for main foods consumed by infants/young children. While a Codex commodity standard exists for processed cereal-based foods for infants and young children (CXS 74-1981), its reference to contaminant limits is that "The product shall be free from residues of hormones, antibiotics as determined by means of agreed methods of analysis and practically free from other contaminants, especially pharmacologically active substances" (FAO and WHO, 1981). To compliment this standard, the Codex Committee on Contaminants in Foods (CCCF), as part of its review of existing lead MLs, could consider prioritizing work to identify new foods for ML development. From a risk perspective, processed cereal-based foods consumed by infants and young children should be included.
4. WFP provides technical specifications for their specialized foods, including SC+, which state that the "product shall be free from contaminants in amounts that may represent a hazard to health. The product shall comply with those maximum contaminant limits established by the Codex Alimentarius Commission for this commodity (e.g. following the latest version of CODEX STAN 193-1995)" (FAO and WHO, 1995a). As WFP has recently updated the specifications for SC+ to include numerical limits for tropane alkaloids and certain mycotoxins, consideration could be made to include a numerical limit for lead in the absence of a Codex ML for cereal-based foods consumed by infants and young children. Any lead ML proposed for SC+ would need to consider not only the potential risk but also recent monitoring data applicable to cereal-based foods for infants. For example, when the European Food Safety Authority (EFSA) reviewed lead exposure from food, the mean concentration in all cereals and cereal products was 28 µg/kg (lower bound) (EFSA CONTAM, 2010). Similarly, the CCCF, at its fourteenth session, discussed setting an ML for cereal-based products for infants/young children (FAO and WHO, 2021). The reported mean lead concentration for cereals as consumed was 10 µg/kg with a 95th percentile of 40 µg/kg.

SCENARIO 2 – FUMONISINS IN CEREAL GRAINS

This scenario considered exposure to fumonisin mycotoxins from consumption of cereal grains. The analysis in the scenario was supported by studies reporting that cereal grains, in particular maize, are important sources of daily calories in many African countries and that fumonisins are considered to be a major food contaminant for rural African populations. Dietary surveys from African countries have reported high daily consumption of maize-based foods by both young children (>200 g/day) and adults (>400 g/day). The exposure scenario considered maize to contain the maximum fumonisin concentration of 2 mg/kg, based on the Codex ML for fumonisins in maize flour and meal, and an intake of 54.8 g maize/day by children of 5 kg bw and 400 g/day by adults of 60 kg bw. Based on this, the estimated fumonisin exposure from maize would be 22 µg/kg bw/day by children and 13 µg/kg bw/day by adults; this would mean a level of exposure 6.5 to 11-fold greater than the current JECFA PMTDI of 2 µg/kg bw/day.

RISK MITIGATION/MANAGEMENT OPTIONS:

1. The current Codex fumonisin ML for maize-derived products (flour and meal) is specific to ingredients that may be consumed as components of other foods or separately. As current scientific research has identified early life exposure to mycotoxins as being implicated in growth impairment in infants and young children, Codex could consider (as it did with deoxynivalenol) expanding the ML categories for fumonisins to specifically include foods being consumed by this age category. For instance, the European Commission (EC) has included MLs for fumonisins in listings for breakfast cereals and for food products intended for infants. The latter is an order of magnitude lower than the Codex ML for fumonisins in maize flour and meal. This would acknowledge that for certain mycotoxins, including fumonisins, early life stage is a critical time to apply prevention and control methods.
2. While maize is typically regarded as the main source of dietary exposure to fumonisins (62 to 96 percent for Global Environment Monitoring System (GEMS) cluster diets (G01-17), other cereal grains, such as wheat and sorghum, can also be significant sources. Therefore, total dietary exposure to fumonisins could be reduced by expanding the Codex ML category to include other cereal grains.
3. At the eighty-third (and most recent) JECFA meeting, which re-evaluated fumonisins, it was reported that due to the lack of data for fumonisins in maize from countries belonging to the African (cluster A) and the South-East Asia (cluster G) WHO regions, some national exposures may have been underestimated, as well as the current international estimates for the clusters that represent these regions (G01, G03, G04 and G13) (FAO and WHO, 2018). Updating exposure estimations using more recently available data may identify the need for additional exposure control methods related to diet.

Decreasing exposure would require an integrated approach to mycotoxin reduction, part of which would involve establishing regulatory limits that are both achievable and enforceable. At the same time, as maize is an important crop, any regulatory limit applied should be carefully evaluated for its impact on food availability so that food insecurity is not increased unintentionally.

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