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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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DISCUSSION PAPER ON FUMONISINS

Prepared by the Electronic Working Group led by Brazil

BACKGROUND

1. The 2nd Session of the Codex Committee on Contaminants in Food (CCCF) agreed to establish an electronic working group led by Brazil, open to all members to prepare a discussion paper on fumonisins (ALINORM 08/31/41 paragraph 177). The paper should include an overview of available data and scope of the problem of fumonisin contamination, taking into consideration the position paper presented at the 32nd Session of the CCFAC. The electronic working group included Costa Rica, European Community, France, Iran, Japan, Korea, Romania, South Africa, Thailand, The Netherlands, United States, United Kingdom and FAO.

2. The position paper presented at the 32nd Session revised the available data on fumonisins concerning the toxicological aspects, sampling plans, analytical and residue data, levels of intake, agricultural, technological and commercial aspects, risk management consideration and public health aspects.

3. Based on the information presented, the position paper recommended that additional research was still needed on (a) methods to prevent and/or reduce fungal contamination of maize in the field, during storage and processing; (b) *Fusarium*-maize interactions in asymptomatic and symptomatic infections in maize in the field; and (c) development of genetically engineered maize that resists *Fusarium* growth or degrade fumonisins *in planta.*

4. The position paper also recommended that Codex should elaborate a Code of Practice and a sampling plan for fumonisin in maize. It further recommended that in order to develop an appropriate and fair international standard, Codex Member States be encouraged to submit data from surveys of maize and maize based products, taking into consideration geographical locations and regional differences in food consumption patterns. The Committee should defer the development of international standards until JECFA performs a risk assessment.

5. JECFA evaluated extensive technical, biochemical and toxicological data, as well as data on human dietary exposure to fumonisins at its 56th meeting in 2001 (FAO/WHO, 2001). A Provisional Maximum Tolerable Daily Intake was established and JECFA conducted a risk assessment based on occurrence data provided by member countries. JECFA also reviewed analytical methods and published sampling plans for fumonisin in maize. Furthermore, JECFA provided recommendations on further research on the modes of action and possible influence of dietary and other factors on adverse effects of fumonisins in humans.

6. The present paper presents the conclusions of the JECFA evaluation in 2001 and includes more recent relevant literature on fumonisins not considered previously, including those that will answer some of the questions raised by the position paper and the JECFA.

7. The 26th Session of the Codex Alimentarius Commission approved in 2003 the Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals, including of fumonisins in maize, which will also be considered in the present paper.

8. This paper was prepared by Brazil with contributions from the FAO, Japan, South Africa, Korea, Costa Rica, Romania, United States, United Kingdom and the Netherlands.

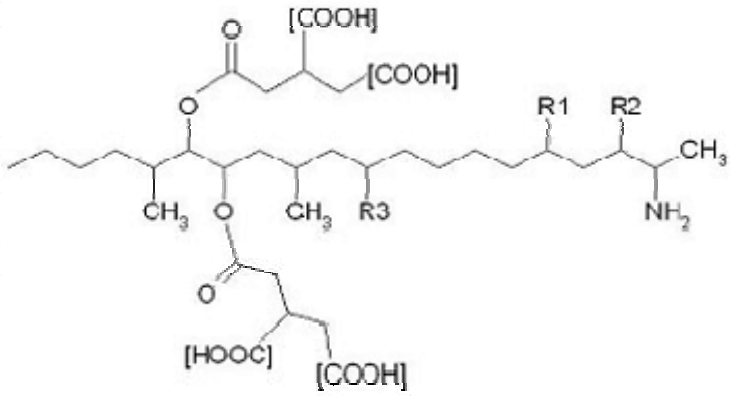
INTRODUCTION

9. Fumonisins are mycotoxins produced mainly by *Fusarium verticillioides* (Sacc.) Nirenberg (synonym *F. moniliforme* Sheldon) (teleomorph, *Gibberella moniliformis*) and *Fusarium proliferatum* (Matsushima) in maize. Other species are *Fusarium nygamai*, *F. napiforme, F. thapsinum, F. anthophilum, and F. dlaminii,* as well as *Alternaria alternata f. sp. lycopersici* in millet, sorghum, wheat and rice (Marasas et al., 2001; Rheeder et al., 2002; Frisvad et al., 2006).

10. Biological interactions between the crop plant, maize maize (Zea mays L, referred to as corn in some countries) and the fungus are complex and may have diametrically opposing results (Yates and Spaks, 2008). *F. verticillioides* grows within the maize plant as an endophyte (Bacon and Hinton, 1996), an interaction of benefit to plant growth in other members of the Gramineae (Clay, 1990; Yates et al., 2005). However, under plant stress growth conditions, the symptomless endophytic relationship may convert to a disease- and/or mycotoxin-producing interaction (Bacon and Nelson, 1994; Abbas et al., 2006).

11. Mechanisms that trigger the conversion between *F. verticillioides* and the maize plant from that of a symptomless to a disease and mycotoxin-producing interaction have not yet been identified (Yates and Sparks, 2008). It is possible that water stress and insect predation, factors that have been related to the onset of the deleterious aspects of this fungal plant interaction (Dowd, 2003), might be involved in the conversion from a symptomless to a symptomatic metabolic lifestyle.

12. Fumonisins are a structurally related group of diesters of propane-1, 2, 3-tricarboxylic acid and various 2-amino-12, 16-dimethylpolyhydroxyeicosanes in which the C14 and C15 hydroxyl groups are esterified with the terminal carboxyl group of tricarboxylic acid (Bezuidenhout, 1988) (Figure 1). There are at least 18 fumonisin analogues that have been identified and these have been classified into series A, B, C and P based on their chemical structure (Plattner et al., 1996, Sewram et al., 2005, Torres et al., 2007, Kumar et al, 2008). The B series, consisting mainly of fumonisin B_1 (FB_1), and fumonisin B_2 (FB_2), are believed to be the most abundant and most toxic naturally occurring analogues (Sydenham et al., 1992a,b Thiel et al., 1992).



Fumonisin B_1: R1= OH; R2= OH; R3= OH

Fumonisin B_2: R1= OH; R2= OH; R3= H

Fumonisin B_3: R1= H; R2= OH; R3= OH

Fumonisin B_4: R1= H; R2= OH; R3= H

Figure 1. Chemical structure of fumonisin B_1 (FB_1). FB_2 differs from FB_1 only by the absence of the hydroxyl group at C10, FB_3 differs from FB_1 by the absence of the hydroxyl group at C5, and FB_4 lacks both the C5 and the C10 hydroxyl groups (Voss et al., 2006).

13. The ratio of FB_1/FB_2 is approximately 3:1 in naturally contaminated maize (Ross et al., 1992) and FB1 accounts for approximately 70% of total fumonisins found in nature (Nelson et al., 1993 Marasas, 2001; Wang et al. 2008a,b). Fumonisin B_3 (FB_3) can be found at low incidence, with the ratio between FB_3 and FB_1 varying from 0.34 to 0.87 (Bacon et al., 1992; Sydenham et al., 1991; Chulze et al., 1999). When they were quantified in the same sample, the ratio of fumonisin B_1:B_2:B_3 is estimated to be 10:3:1 (JECFA, 2001). Little is known about the natural occurrence of fumonisin B_4. It is produced by strains of *F. verticillioides*, generally at lower concentrations than fumonisin B_1, B_2, or B_3 (Seo & Lee, 1999).

14. The extent of maize contamination with fumonisins varies with geographical location, agricultural practices, and the maize genotype which determines the susceptibility of the maize plants to fungal and insect invasion during the growing phase of the maize in the field (Jackson and Jablonski, 2004). The levels of fumonisins produced in maize are also influenced by environmental factors such as temperature, humidity, drought stress and the extent of rainfall during the pre-harvest and harvesting periods; storage of the harvested maize kernels under improper moisture conditions can result in additional accumulation of fumonisins (Bacon and Nelson, 1994). Higher levels of fumonisins are usually found in maize kernels produced in the warmer regions of the world (Shelby et al., 1994; Miller, 1999).

BIOLOGICAL ASPECTS

15. In 2001, JECFA at its 56th meeting evaluated an extensive technical, biochemical and toxicological data on fumonisins as well as data on human dietary exposure to fumonisins. Laboratory animal and in vitro studies have shown disruption of lipid metabolism as the initial site of action of fumonisin. The proposed lipid-based mechanism involves inhibition of ceramide synthase, a key enzyme in the biosynthesis of sphingolipids, and changes in the polyunsaturated fatty acid and phospholipid pools. Both lead ultimately to lipid-mediated alterations in signaling and metabolic pathways crucial to cell growth, death and differentiation (FAO/WHO, 2001).

16. In all animal species studies revised by JECFA, the liver was a target for fumonisin B_1; the kidney was also a target in many species. In the kidney, the effects seen included increased in free sphingoid bases, renal tubule-cell apoptosis, and cell regeneration. In the liver, apoptotic and oncotic necrosis, oval-cell proliferation, bile-duct hyperplasia, and regeneration are early signs of toxicity. In rodents, the toxicity of fumonisin B_1 was strain- and sex-dependent; in mice, the liver is more sensitive than the kidney. The non-observable-effect-level (NOEL) for renal cancer in Fischer 344N rats was 0.67 mg/kg bw per day, and the NOEL for renal toxicity was 0.2 mg/kg bw per day. The NOEL for liver cancer in male BD IX rats was 0.8 mg/kg bw per day, and the NOEL in feed-restricted female $B6C3F_1$ mice was 1.9 mg/kg bw per day.

17. A Provisional Maximum Tolerable Daily Intake (PMTDI) of 2 µg/kg body weight per day was allocated by the JECFA to FB_1, FB_2 and FB_3 alone or in combination, on the basis of a NOEL of 0.2 mg/kg body weight per day from short-term and long-term renal toxicity studies in rodents and a safety factor of 100 (FAO/WHO, 2001).

18. Human epidemiological studies revised by the JECFA have indicated an association between the occurrence of *Fusarium verticillioides* on maize and the incidence of oesophageal cancer in various regions of the world. Geographical differences in demography, ethnic groups, genetic susceptibility, culture, economy and nutritional status all affect the rates of disease; however, some common risk factors are emerging, such as having maize as the main dietary staple and, to some extent, a low socioeconomic status. Thus, high incidences of oesophageal cancer have been associated with limited diets consisting mainly of wheat or maize and low contents of certain minerals and vitamins.

19. The JECFA evaluation included reports on higher rates of neural tube defects (NTD) in areas of South Africa, China and USA when the maize based foods contained relatively high levels of fumonisins. As folate metabolism has been related to the development of NTD, the blockage of folate uptake by fumonisins may have been a factor in this regard

20. The International Agency for Research on Cancer (IARC) has classified FB_1 as possibly carcinogenic to humans (Group 2B) (IARC, 2002).

21. In its evaluation, JECFA identified some areas of research that needs to be investigated to bring a better understanding of the biological/toxicological profile of fumonisins in humans. These areas are: (a) the biochemical and physiological mechanism(s) underlying the fumonisin-induced renal tubular carcinomas in Fischer 344N rats and the apparently different sensitivity compared with BDIX rats; (b) whether dietary factors such as folate, vitamin E, and choline modify renal or hepatic toxicity induced by fumonisin B_1 and

its ability to alter the folate transport at the cellular level and from the placenta to the fetus; (c) the role of inhibition by fumonisins of ceramide biosynthesis in protection of cells from ceramide-mediated apoptosis induced by mitochondrial dysfunction; (d) the relationship between the intake of fumonisin and human disease in areas where nixtamalized maize-products comprise a large portion of the diet and; the ability of fumonisins to modify the expression of receptors for microbial pathogens and toxins that are associated with renal and hepatic disease in humans should be investigated.

22. In a recent study conducted in China, the status of FB1 contamination in food samples in areas of high and low incidences of oesophageal and liver cancer was investigated (Sun et al., 2007). Higher fumonisin levels were found in the high cancer incidence areas, suggesting a possible contributing role of FB1 in human esophageal- and hepato-carcinogenesis

23. In a review of the toxicological profile of fumonisins in laboratory animals and epidemiological studies in humans, Marasas et al (2004) have indicated that fumonisins are potential risk factors for NTD, craniofacial anomalies, and other birth defects arising from neural crest. This was later supported by a study conducted by Missmer et al. (2006) with Mexican-American women, finding an association between increasing maternal serum sphinganine:shingosine ratio (Sa:So) with increase risk of NTD in the offspring.

24. Theumer et al (2002) demonstrated that subchronic FB_1 intake could affect the small intestine and alter the interleukin profile and some main functions of macrophages in antitumor activity in rats. Posterior *in vitro* studies showed that the co-exposure to fumonisins and aflatoxin B_1 (AFB_1) produced a higher liver toxicity, with respect to their individual administration, inducing apoptosis and mitotic hepatocytes. There was an inversion of the typical Sa:So ratio in rats (Theumer et al. 2003). Therefore, the mixture of fumonisins and AFB1 induced toxic responses which could not be considered the sum of the effects caused individually by these mycotoxins (Theumer et al. 2007). Although FB_1 is poorly absorbed and metabolized in the intestine, some studies have shown that it induces intestinal disturbances (abdominal pain or diarrhea) (Bouhet and Oswald, 2007).

SAMPLING PLANS

25. A study conducted by Whitaker et al (1998) describing the sampling variance associated with the testing of shelled maize for fumonisin was evaluated by the JECFA in 2001. In this study, a bulk sample of about 45 kg was taken from each of 24 batches of shelled maize which had been harvested from 24 fields in North Carolina, USA. Each bulk sample was riffle-divided into 32 1.1 kg test samples, and these were comminuted in a Romer mill. A nested design used to determine the variation was: selection of 10 batches with a wide range of fumonisin concentrations; from each batch, 10 comminuted test samples were taken randomly, and two 25-g portions were taken from each by riffle division. Fumonisins B_1, B_2, and B_3 were determined by AOAC official method 995.15. At a batch contamination concentration of 2 mg/kg, the coefficient of variation associated with sampling was 17%, that associated with sample preparation was 9.1%, and that for analysis was 9.7%. These values were independent of the fumonisin type. The coefficient of variation associated with the total test procedure was 45%, which was of the same order of magnitude as that for measuring aflatoxin in shelled maize by a similar test procedure.

26. The sampling plan for fumonisin analysis in various commodities included in the report JECFA is shown on Table 1. This plan assumes that a minimum of 30 batches of food should be sampled from each country or region; the coefficient of variation of the sampling plan should be no more than 30% and the coefficient of variation of the complete analytical method should be no more than 10%.

Table 1 - Proposed sampling plans for fumonisins analysis (FAO/WHO, 2001)

Commodity	Increments (n x y grams)	Subsample size (kg)	Notes
Whole maize	50 x 100	5.0	Whitaker et al. (1998): Sampling variation for fumonisins in maize similar to that reported for aflatoxins
Corn-on-the-cob	50 cobs	7.5	Assuming that core of cob contributes about 30% of total weight of cob and that a cob yields about 100 g of kernels
Maize flour, maize meal, maize grits, processed maize foods (e.g. cornflakes, tortilla chips, popcorn, muffin mix, starch)	10 x 100	1.0	Assumed that sampling variance for these commodities was similar to that associated with aflatoxin in comminuted feeds; suggested sampling plan associated with sampling precision of 12.5% for aflatoxin in comminuted feeds

27. In a work conducted in Nigeria by Whitaker et al (2007) using the same test procedure described by Whitaker et al. (1998), a total of 86 maize lots intended for human consumption sampled in 2002 were analyzed. In average, 17 test samples were taken from each lot. Sample preparation and analytical variances were assumed to be negligible and not considered for the estimation of total variability. Variance (S^2_t) appeared to be linearly related to fumonisin concentration (F) when plotted on the full-log scale through the relationship (r^2=0.91) - $S^2_t = 0.63F^{1.584}$ (Eq. 1). The variance, standard deviation and CV among 100 g samples at a 2.0 µg/g fumonisin level are 1.91, 1.36 and 69 %, respectively. The authors found that the variance expressed by Eq. 1 was similar to the one found in the previous work done in USA (Whitaker et al., 1998), which indicates that the variability associated with a specific test procedure (primarily reflecting uncertainty on the sampling step) maybe similar in other global markets. The performances of several sampling plan designs using 100 g, 500 g or 2000 g samples were determined by using the negative binomial distribution to compute the operating characteristic curves (OC) considering an accept/reject limit of 1, 2 or 3 µg/g. Two of these curves are shown on Figure 2.

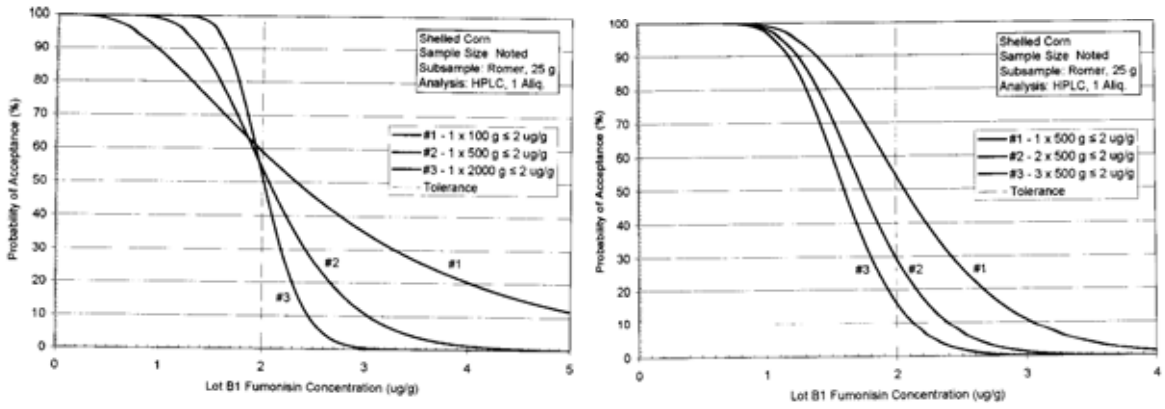


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Figure 2. Operating characteristic curves for sampling plan designs for fumonisin in shelled maize. All sampling plans use a Romer mill, 25 g analytical subsample and HPLC method

28. Fumonisins are polar molecules, soluble in water and in polar solvents and thus ideally suited for determination by reversed-phase HPLC. As they lack a significant UV chromophopore, low levels of fumonisins can be detected after derivatization of sample extracts with OPA (*o*-phthaldialdehyde), NDA (naphthalene-2,3 dicarboxaldehyde) or NBD-F(4 - Fluoro - 7 - nitrobenzofurazan) followed by fluorescence detection. In general, fumonisin can be extracted from maize or maize based products using methanol-water

or acetonitrile-water. Clean up using C18 cartridges, SAX (strong anion exchange) or immunoaffinity columns are normally used (Sydenham et al., 1996; Caldas and Silva, 2007). Solfrizzo et al (2001) extracted FB1 and FB2 with acetonitrile(ACN):methanol (MeOH):water(H_2O), followed by immunoaffinity colum clean up and derivatization with OPA/mercaptoethanol. The LOQ of the HPLC/fluorescent methods are the range of 0.02 to 0.5µg/kg.

29. A reversed-phase HPLC method for the analysis of fluorescence OPA derivatized FB_1 and FB_2 and FB_3 is the official AOAC-IUPAC method [995.15] for maize kernels at concentrations of 0.5 - 8 µg FB_1/g or 0.8 -12.8 µg total fumonisins/g (Sydenham et al., 1996c).

30. In addition to HPLC/fluorescence methods, fumonisins can be analyzed by thin-layer chromatography (TLC), capillary electrophoresis and various immunochemical methods (ELISA). ELISA methods have received a lot of attention lately because they can be used for rapid screening purposes under field conditions or in the laboratory (Castells et al., 2008). Maragos et al. (2001) detected FB1 using Fluorescence Polarization detection, with a LOD of 0.5µg/kg. Wang et al. (2008b) extracted FB_1, FB_2, FB_3 and FB_4 with ACN:water and analysed them by HPLC coupled with an evaporative light scattering detector.

31. LC/MS or LC/MS-MS methods have been extensively used n the last years as they provide quantitative analysis, as well as fumonisins identity confirmation; additionally, no clean-up step is necessary before the analysis (Plattner, 1996; D´Arco et al., 2008). However, it is recognized that these instruments are of high cost, what might make it difficult to be used in developing countries for monitoring programs.

32. Fumonisins bound to starch and proteins found in food subject to heat during processing, such as cereal breakfast and tortillas, cannot be detected by conventional analysis. In a method described by Kim et al (2003), the protein-bound FB_1 was extracted with 1% sodium dodecylsulfate (SDS), the bound fumonisin hydrolyzed with 2 M KOH, the extract cleaned-up on an OASIS polymeric SPE and fumonisins determined by HPLC as HFB_1 (hydrolyzed FB_1). This method was further improved by Park et al (2004) by complexing the SDS with methylene blue, and eliminating its interference in the HPLC analysis.

OCCURRENCE IN FOOD

33. The worldwide occurrence of fumonisins in food has been well documented and reviewed in the literature (Doko and Visconti, 1994; Marasas, 1996; Bullerman, 1996; Pohland, 1996; Shephard et al., 1996; Patel et al., 1997; Castelo et al., 1998; De Nijs et al., 1998a; Solovey et al., 1999). Although fumonisins are found mainly in maize and maize-based products, the sporadic natural occurrence of fumonisins in sorghum, rice and navy beans has been reported (Bhat et al., 1997; Tseng et al., 1995; Patel et al., 1996; Munibazi and Bullerman, 1996; Abbas et al., 1998). Because of their water solubility, fumonisins are unlikely to bioaccumulate in animal tissues, hence, they have either not been detected or are detected at extremely low levels in milk, eggs and meat (Prelusky et al., 1996; Miller et al., 1996). Low levels of fumonisins have been detected in commercial beer, probably as a result of the use of maize grits as an adjunct in replacement of, or in addition to the traditional use of barley in the brewing process (Scott and Lawrence, 1995; Hlywka and Bullerman, 1999).

34. Lower contamination levels of FBs detected in heat treated food, such as pre cooked corn flour, snack and corn flake samples found in many studies can be explained by the bound fumonisins formed during processing and which cannot be detected by the usual analytical methods (Seefelder et al., 2003; Lu et al., 2002). Kim et al. (2003) found an average of 2.6 times more FB_1 present in bound form in corn flakes compared to conventional analysis. Park et al (2004) found about 1.3 times more FB1 in the bound form compared with extractable FB_1 in the 15 samples of alkali-processed corn-based foods, such as tortilla chips and maize chips analyzed.

35. The JECFA (2001) evaluated extensive data on fumonisin contamination on maize and maize products produced and or consumed in various countries in South, Central and North America, Asia, Africa and Europe. Tables 2 to 4 show the FB_1 and FB_2 levels detected in products for human consumption in various countries from some studies reported latter than the year 2000.

Table 2. Levels of fumonisins (FB_1 and FB_2) in maize, maize-based products and other grains and foods for human consumption in European countries

Country	Sample	Positive samples/ analysed samples	Range of FB_1 mg kg^{-1}	Mean FB_1 mg kg^{-1}	Range of FB_2 mg kg^{-1}	Mean FB_2 mg kg^{-1}	Reference
France	Breakfast cereals (maize, oat, rice)	30/32	<0.001-1.113	NR	NR	NR	Molinie et al., 2005
	Maize (transgenic)	5/5	0.05-0.3	NR	NR	NR	Bakan et al, 2002
Italy	Maize hybrids	40/40	0.368-64.15	15.5	0.193-37.09	6.74	Cavaliere et al., 2007
Portugal	Yellow maize	6/9	<0.020-0.871	0.322	< 0.015-0.272	0.099	Lino et al., 2006
	White maize	2 /2	<0.020-0.725	0.363	0.113-0.437	0.275	
	Maize flour	2/3	< 0.020-1.569	0.822	< 0.015-0.457	0.173	
	Maize semolina	2/3	<0.020-0.183	0.118	<0.015	NR	
	Maize starch	0/3	< 0.020	NR	< 0.015	NR	
	Sweet maize	2/11	<0.020-0.523	0.064	< 0.015	NR	
	Portuguese maize bread	25/30	< 0.020-0.448	0.197	<0.020-0.207	0.077	Lino et al 2007
	Sweet maize	36/49	<0.10-0.400	0.154	< 0.10	NR	Martins et al., 2008
	Maize meal	41/41	<0.10-1.30	0.474	0.050-0.450	0.177	
	Corn flakes	0/15	<0.05-	NR	<0.10	NR	
Spain	Maize	92/92	0.337-10.61*	2.61*	NR	NR	Castells et al., 2008
	Maize meal	90/90	0.144-2.00*	0.761*	NR	NR	
	Maize flour	90/90	0.892-6.31*	2.64*	NR	NR	
	Flaking grits	78/78	0.073-1.05*	0.366*	NR	NR	
	Cooked grits	13/47	< 0.025-0.258*	0.140*	NR	NR	
	Corn flakes	21/47	<0.025-0.067*	0.042*	NR	NR	
	Conventional Maize	4/30	<0.025- 0.354	0.043	<0.025-0.120	0.022	Ariño et al., 2007
	Organic Maize	3/30	<0.025 - 0.359	0.035	< 0.025-0.153	0.019	

NR = not reported; *Total fumonisins

Table 3. Levels of fumonisins (FB_1 and FB_2) in maize, maize-based products and other grains and foods for human consumption in American countries

Country	Sample	Positive samples/ analysed samples	Range of FB_1 mg kg^{-1}	Mean FB_1 mg kg^{-1}	Range of FB_2 mg kg^{-1}	Mean FB_2 mg kg^{-1}	Reference
Argentina	Maize flour	8/23	1.0 - 2.6	NR	< 0.10- 0.5	NR	Lerda et al., 2005
	Rice	3/29	0.8-0.9	NR	0.8	NR	
	Maize Maize flour Maize meal			1.54 0.358 0.148		0.716 0.122 0.052	Broggi et al., 2002
Brazil	Maize	23/26	<0.09 - 10.87	NR	<0.05 - 0.52	NR	Almeida et al., 2002
	Maize	90/90	<0.02-18.74*	2.89*	NR	NR	Westhuizen et al., 2003
	Maize Base Products	70/74	<0.02-8.60	NR	NR	NR	Kawashima and Soares,2006
	Maize meal	30/30	1.1 - 15.3	5.2	0.2 - 3.9	1.0	Bittencourt et al., 2005
	Maize flour	30/30	0.5-7.2	2.1	0.11	1.8	
	Maize Meal I	62/62	0.16 - 4.74	1.24	0.11 - 1.57	0.439	Caldas and Silva, 2007
	Maize meal II	11/11	0.593-2.56	1.43	0.251-1.09	0.617	
	Pré-cooked food I	21/21	0.035 - 1.96	0.449	<0.02-0.534	0.204	
	Pré-cooked food II	21/21	0.188-1.36	0.696	0.149-1.02	0.397	
	Snacks	17/20	<0.02–0.330	0.115	<0.02-0.260	0.064	
	Corn flakes	8/20	<0.02-0.784	0.108	<0.02-0.122	0.019	
	Popcorn	22/24	<0.02-1.24	0.398	<0.02-0.858	0.266	
	Sweet corn, on the cob	0/6	<0.02	NR	<0.02	NR	
	Sweet corn, frozen	3/8	<0.02-1.31	0.352	<0.02	0.02	
	Sweet corn, frozen	3/15	<0.02-1.44	0.190	<0.02	NR	
USA	tortilla and masa flour	38/38	0.01-0.729 0.028-1.863*	NR	NR	NR	Dvorak et al., 2008

NR = not reported. *Total fumonisins

Table 4. Levels of fumonisins (FB_1 and FB_2) in maize, maize-based products and other grains and foods for human consumption in some African, Asian and ME countries

Country	Sample	Positive samples/ analyzed samples	Range of FB_1 mg kg^{-1}	Mean FB_1 mg kg^{-1}	Range of FB_2 mg kg^{-1}	Mean FB_2 mg kg^{-1}	Reference
Iran	Maize	48/49	1.19 - 12.95	6.14	NR	NR	Yazdanpanah et al., 2006
South África	Maize Beer	18/18	0.038 – 1.066	0.281	<0.005 - 0.255	0.069	Shephard et al., 2005
Nigeria	Maize	73%	0.01-0.76	0.117	NR	NR	Adejumo et al., 2007
Marocco	Maize	10/20	0.001-5.96	1.93	NR	NR	Zinedine et al.,2006
Benin	Maize	NR	ND-12.00*	NR	NR	NR	Fandohan et al,2005
China	Maize kernell	42/104	0.30-3.20	1.42	NR	NR	Wang et al, 2008[a]
	Maize	16/24	0.25-1.8	0.74	NR	NR	Wang et al, 2008b
	Maize	6/21	0.21-0.29	0.24	NR	NR	
	Maize	6/20	0.3-3.13	0.47	NR	NR	
	Maize	15/20	0.058-1.976	0.377	0.056-0.890	0.257	Li et al., 2001
Republic of Korea	Frozen maize	6/14	ND-0.05	0.01	ND-0.04	0.003	Chung, et al, 2008
	Whole kernel maize	36/39	ND-9.98	1.21	ND-2.49	0.26	
	Maize flour	10/10	0.01-0.79	0.23	ND-0.21	0.04	
	Maize grits	7/8	ND-0.65	0.29	ND-0.15	0.05	
Japan	Canned or frozen corn	2/51	0.016-0.036	0.026	0.014	0.014	Sugita-Konishi et al., 2006
	Popcorn grain	15/15	0.005-0.354	0.057	0.002-0.094	0.016	
	Cornflake	9/30	0.013-0.059	0.027	NR	NR	
	Corn grits	10/10	0.017-0.073	0.051	0.017-0.029	0.021	

NR = not reported *Total fumonisins

AGRICULTURAL, TECHNOLOGICAL AND COMMERCIAL ASPECTS

Agricultural Approaches

36. According to the Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CAC/RCP 51-2003), it is important for producers to realize that good agricultural practices (GAP) represent the primary line of defense against contamination of cereals with mycotoxins, followed by the implementation of good manufacturing practices (GMP) during the handling, storage, processing, and distribution of cereals for human food and animal feed (Codex Alimentarius, 2003).

37. In Annex 2 concerning fumonisins, the Code recommends that the time of harvest for maize should be carefully planned, as it has been shown that maize grown and harvested during warm months may have fumonisin levels significantly higher than maize grown and harvested during cooler months of the year. Post-harvest practice cannot be expected to eliminate such problems, as mycotoxin formation is already occurring when the harvest is taking place. This distinction between preharvest and postharvest cannot be overstressed.

38. *F. verticillioides* appears to be a true commensal, found in association with the crop wherever maize is grown, being benign under good growth conditions. While maize is very sensitive to water loss and go into drought stress at about 0.98 water activity (aw), *Fusarium* species grow well down to about 0.90 aw. Hence, under drought stress, the fungus grows very well and fumonisin control in crops where fungus infection occurred pre-harvest is extremely difficult (Pitt JI, personal communication, 2009).

39. According to Cavaliere *et al* (2007) irrigation can be used to minimize the effect of drought stress.

Similarly, fertilization can be used to minimize nutrition stress and optimal planting and weed control methods can be used to minimize population stress. Heat is considered a major uncontrolled source of stress, although additional unrecognized sources may have been present. The adequate supplementation of minerals, both macro and micronutrients to the maize culture protect against fungal attacks and fumonisins production in maize samples (Hassegawa et al., 2008).

40. The presence of *F. verticillioides* suggests a permanent risk of fumonisin contamination in maize. Fandohan et al. (2005) found no significant differences in presence of Fusarium from one season to another (1999-2003) in Benin, Africa, but the levels decreased significantly throughout the storage period every season. Most of the isolates were very high fumonisin producers (FB1, FB2 and FB3), with total fumonisin levels ranging from 8240 to 16,690 mg/kg. This would suggest that adequate postharvest management procedures should be adopted in order to assure good quality of stored maize. Moreover, fumonisin contamination was higher in pre-harvest maize. One of the important measures to be recommended for farmers is to ensure adequate drying before storage and dry storage conditions (Fandohan et al, 2005Maize grains with 15% moisture content did not support mould growth even after 45 days of storage in modified atmosphere storage (MAS) systems and dry matter loss was also significantly reduced under 60% CO2-modified atmosphere in maize grains with 20% moisture content (Janardhana et al., 1998, Kumar et al., 2008)

42. The results from investigations on agronomic practices indicate that: (a) fungal infection rate are higher in crops planted in fields previously planted with maize, particularly when residues from those crops were left in the field, (b) the incidence of *Fusarium* kernel rot is higher in warm climates under drought conditions, and (c) freshly harvested maize should be dried to a suitable moisture level immediately and stored (Bacon and Nelson, 1994; Munkvold and Desjardins, 1997; Warfield and Gilchrist, 1999; Miller, 1994).

43. The feeding habits of several insect species have been associated with an increase in incidence and severity of Fusarium ear rot. Cry1Ab protein may reduce kernel feeding by corn earworm and indirectly reduce fumonisin concentration in grain under some conditions. Clements et al. (2004) studied the effects of Cry1Ab protein in kernels and silks on fumonisin concentration in grain and the severity of Fusarium ear rot. The results suggest that Bt hybrids can reduce fumonisin concentration in grain during seasons when European corn borer is favored, but not during seasons when corn earworm is favored. Hybrid genotype was an important factor in reducing fumonisin concentration in grain.

44. Fungal infection and mycotoxin production in organically and conventionally grown produce is still an extremely controversial issue (Magkos et al., 2006). According to Ariño et al (2007), there is no scientifically tenable evidence that the differences observed between conventional and organic foodstuffs would lead to any objectively measurable effect on consumer health.

Stability of fumonisin during processing

45. The fate of fumonisin during processing is affected by many factors, including the temperature, moisture of the product, the toxin concentration in the raw product and the presence of other ingredients in the processed food. Processing operations that maize is submitted include sorting, milling (dry and wet), heat, extrusion and nixtamalization

46. The position paper as well as the JECFA evaluation performed in 2001 summarized the available data concerning the impact of processing in the fumonisin levels in maize products. The main studies are summarized here, in addition to more recent studies reported in the literature.

47. Sorting and cleaning may lower fumonisin concentration by removal of contaminated material, but do not destroy the mycotoxins. Broken maize kernels contain near 10 times higher levels of fumonisins than intact ones and different studies have shown physical strategies to separate health from contaminated kernels. As contaminated maize has a low density, over 80 % of the toxin can be removed in the buoyant fraction after treatment with saturated sodium chloride solution (Shetty & Bhat, 1999). Sequentially passing stored maize kernels through cleaning equipment followed by a gravity table had proven to remove about 60 % of the fumonisin contamination (Malone et al., 1998). Afolabi et al. (2006) had proposed the visible sorting of maize grain as a technique to reduce fumonisin levels by subsistence farmers.

48. Wet-milling is used to obtain maize starch, germ and fibers. Bennett and Richard (1996) did not found any measurable FB1 in starch obtained from a laboratory scale wet milling of maize, while fiber and germ contained 10-40 % of the concentration found in maize.

49. Dry-milling of maize is a physical process by which the components of the grain are separated, giving rise to the bran (obtained from the removal of pericarp) and the germ, followed by the fractions obtained by decreasing particle size - grits, corn meal and flour (Alexander 1987). Fumonisins are not expected to be destroyed during this process and are found in all fractions, with higher concentration in bran and germ (Katta et al. 1997, Brera et al, 2004). In a recent study conducted in Argentina, germ and bran had fumonisins levels 29 fold higher than corn meal and corn grits, 13 fold higher than corn flour and 3 fold higher than whole maize (Resnik, 2006).

50. The effects of heating on the stability of fumonisins vary among the process, the temperature and is time-dependent. Many studies demonstrate that fumonisins are fairly stable to heat and that significant removal occurs only during processes that reach temperatures > 150 °C, such as those used for dry or moist maize meal production (Scott & Lawrence, 1995), frying maize chips (Jackson et al., 1997), baking, roasting and alkaline cooking (Castelo et al. 1998, Jackson et al. 1997, Katta et al. 1999). Flaking, cooking and toasting processes reduced fumonisin B_1 levels at 60 – 70%, 53.5 % and 48.7%, respectively. The addition of glucose increased the reduction percentage at 86% and 89 % during cooking and toasting processes, respectively (De Girolamo et al., 2001).

51. Extrusion processing is used extensively in the production of breakfast cereal, snack and textured foods. Bullerman et al. (2007) found that the greatest reduction of fumonisins occur at extrusion temperatures of 160 ^{o}C or higher and in the presence of glucose. Extrusion decreased fumonisin B1 by 21–37%, whereas the same process with added glucose further decreased fumonisin B1 by 77–87% (Bullerman et al., 2008). Analysis by LC-fluorescence and LC-MS indicated that 57–66% of the fumonisin B1 species detected in corn (spiked and fermented) extruded with glucose was *N*-(deoxy-D-fructos-1-yl) fumonisin B1. Fumonisins products such as hydrolyzed fumonisin B_1 and N-carboxymethyl fumonisin B_1 have been also obtained during extrusion process (Castelo et al. 2001, Bullerman et al., 2008).

52. In a study conducted by Seefelder et al (2003), FB_1 and HFB_1 were incubated with alpha-d-glucose and sucrose (mono- and disaccharide models), with methyl alpha-d-glucopyranoside (starch model), and with the amino acid derivatives N-alpha-acetyl-l-lysine methyl ester and BOC-l-cysteine methyl ester (protein models). The reaction products were analyzed by LC/MS-MS. These model experiments demonstrate that fumonisins are able to bind to polysaccharides and proteins via their two tricarballylic acid side chains.

53. Voss et al (2008) evaluated the toxicity of maize grits spiked with fumonisin B1 extruded with 10% glucose fed to rats. With one exception, the fumonisin B1-spiked and fermented extrusion products caused moderately severe kidney lesions and reduced kidney weights, effects typically found in fumonisin-exposed rats. Lesions in rats fed contaminated grits after extrusion with glucose were significantly less severe and not accompanied by kidney weight changes. The authors concluded that extrusion with glucose supplementation is potentially useful for safely reducing the toxicity of fumonisins in maize-based products. Lu et al (2002) had reached the same conclusion and shown that glucose bind to fumonisins via the amino group.

54. Nixtamalization is a process for making masa for tortillas and other maize products, highly consumed in American countries, involving boiling and soaking maize in a solution of calcium hydroxide. The process can reduce fumonisin concentration from 50 to 80 %, with 35 to 60 % of fumonisin being detected in its hydrolyzed form (Burns et al., 2008; Dombrink-Kurtzman et al., 2000). Modified nixtamalization procedure, incorporating various combinations of hydrogen peroxide and sodium bicarbonate in addition to calcium hydroxide, has been reported to give a 100% reduction of FB_1, however the masa product exhibited about 60% of the toxicity of the untreated maize using a brine shrimp assay procedure (Park et al., 1996). In a study conducted in rats, Burns et al. (2008) had suggested that mycotoxin-in-corn matrix interactions during nixtamalization reduce the bioavailability and toxicity of FB1.

55. Palencia et al (2003) found that tortillas prepared using the traditional nixtamalization method of mayan communities contained FB1, FB2 and FB3 and their hydrolyzed counterparts. There were equimolar amounts of FB1 and HFB1 in the tortillas, but the total fumonisins were reduced by 50%. They also found a reduced sphinganine elevation in cells treated with extracts of tortillas compared with cells treated with extracts of contaminated maize.

56. Ethanol fermentation of fumonisin contaminated maize results in very little degradation of the toxins; most of the toxins remain in the distiller's grains, thin stillage and distiller's soluble fraction (Bennett and Richard, 1996; Bothast et al., 1992). Fumonisins have also been found in beer, indicating that the toxins persist under the conditions (temperature, pH) prevailing during the brewing process (Scott & Lawrence,

1995; Scott et al., 1997; Hlywka & Bullerman, 1999).

57. The efficacy of gamma-irradiation as a method of decontamination of maize containing *Fusarium verticillioides* have been studies by many authors. Visconti et al. (1996) found that 15 kGY effectively sterilized the maize flour, but caused only about a 20% reduction in its fumonisin content. Ferreira-Castro et al (2007) found possible to decrease fumonisins levels by irradiating maize to 5 or 10 kGy; however, at 2 kGy, the survived fungi (36%) can produce more fumonisins than the fungi in the control unirradiated. Aziz et al. (2007) found that the viable counts of Fusarium in seeds decreased by increasing the radiation dose levels and the growth of *Fusarium spp*. was inhibited at 4.0 kGy for barley and 6.0 kGy for wheat and maize. Application of radiation dose at 5 kGy inactivated FB_1 by 96.6%, 87.1% and 100% for wheat, maize and barley, respectively, and a dose of 7 kGy was sufficient for complete destruction of FB_1 in wheat and maize.

HUMAN EXPOSURE AND RISK ASSESSMENT

58. Exposure to fumonisins is thought to occur mainly from the consumption of maize and maize-based products. The amount of intake may vary considerably, depending on fumonisin levels among maize samples from a particular crop, amount of maize/maize-products consumed by different individuals and crop variation from year to year.

59. The JECFA (2001) conducted an international intake estimate for FB1 using the Regional GEMS/Food diets. Nine countries, Argentina, Brazil, Canada, China, Denmark, Sweden, the United Kingdom, the United States, and Uruguay, submitted information on the concentrations of fumonisins in maize and maize-derived foods. Fumonisins were detected in over 60% of all food products tested. The rate of detection was much lower in sound maize than in moldy maize, and processed maize-containing foods generally contained lower concentrations of fumonisins than maize grain, flour, or grits.

60. A frequency distribution of the concentrations of fumonisins in maize was derived by the JECFA from available data in 1997 and published as part of an assessment of human intake of fumonisins in the Netherlands (de Nijs et al., 1998b). All maize consumed in the Netherlands is imported, and most was from Europe, South America, and the USA, with some imported from Asia and Africa. As the concentrations of fumonisins and the incidences of fumonisin contamination reflected those found in the submitted data, they were taken as representative of the maize available in trade throughout the world. Analysis of data available since 1997 showed little change in the patterns of incidence and concentration of fumonisins in maize and maize-based foods.

61. The concentrations of fumonisins were shown by the least-squares method to be distributed log-normally. The arithmetic mean concentration of FB1 in the 349 samples used in the distribution was 1.36 mg/kg, and this distribution was combined with appropriate food consumption for assessing intake. It is important to point out that this estimated FB1 level is higher than the levels found in most of the data presented in Tables 2-4. Food consumption data from the GEMS/Food regional diets are for Maize all (GC 645) and includes maize, maize flour, sweet maize (on-the-corn and kernels) and popcorn.

62. Three scenarios were examined. In the first scenario, the per-capita consumption of maize in the GEMS/Food diets was combined with the distribution of concentrations of fumonisins to yield a distribution of fumonisin intake. In the second scenario, a hypothetical distribution of maize consumption was estimated by assuming that it is log-normally distributed in each diet, with a standard deviation equal to 66% of the mean consumption. The third scenario was intended to mimic the worst case, in which the only grain that a person consumes is maize.

63. The mean intake of fumonisins in scenarios 1 and 2 ranged from 12µg/day per person in the European diet to 140µg/day per person in the African diet. This would correspond to 0.2 and 2.4 µg/kg bw/day, for a body weight of 60 kg. These estimates were based on the assumption that an individual consumes randomly contaminated maize over a lifetime and will consume maize at a daily rate equal to the per-capita disappearance of maize. The intake of fumonisins at the 97.5th percentile in scenario 2 ranges from 82 µg/day per person in the European diet to 980 µg/day per person in the African diet. Below this percentile, the predicted intakes in the two scenarios are not appreciably different.

64. The JECFA estimated that when they were quantified in the same sample, the ratio of fumonisin B_1:B_2:B_3 was approximately 10:3:1 and to estimate the intake of all three fumonisins, the intake for fumonisin B_1 in this evaluation should be increased by 40%. Furthermore, the intake of $FB_1 + FB_2 + FB_3$ would represent 14 % of PMTDI in Europe and 160% PMTDI in Africa. For the Latin American diet, this intake was 1.4 µg/kg bw/day, or 70 % PMTDI of 2 µg/kg bw/day.

65. The predicted intake of fumonisins in the third scenario, which describes the potential intake of fumonisins by persons who eat maize in place of all other grains, is appreciably higher than those in the first two scenarios. The JECFA emphasized that the number of individuals covered by this scenario is extremely small on a global basis and consists primarily of rural subsistence farmers, who are not representative of national or GEMS/Food regional populations. The mean intake in this scenario ranged from 310µg/day per person in the European diet to 610µg/day per person in the Far Eastern diet (in which the diet would typically be dominated by rice). The 95th percentile intake ranged from 1400 µg/day per person in the European diet to 2800 µg/day per person in the Far Eastern diet.

66. The dietary intake of fumonisin through the consumption of maize and maize products was calculated by the electronic group using the 13 GEMS/FOOD Consumption Cluster Diets (WHO, 2006) using the same fumonisin level in maize estimated previously by the JECFA (1.36 mg/kg FB1; i.e. 2.12 mg/kg FB1 + FB2 + FB3). The assessment was performed using consumption figures for maize (including flour, excl. oil and beer) (GC 0645). The results are shown on Table 5. The intake represented from 0 % of PMTDI for fumonisins in clusters E, F and L, that include countries in Europe and Asia, and exceeded the PMTDI in clusters A and I (Central, South and East of Africa) and H (South and Central America and Mexico). Even if we assume a 50 % reduction in fumonisin levels in nixtamalized maize based food consumed in Central America, the intake would still exceed the PMDI for this population.

Table 5. Intake estimates for fumonisins in Maize (incl. flour, excl. oil and beer) at levels of 2.12 mg/kg in the 13 Cluster Diets*

Cluster diet	A	B	C	D	E	F	G	H	I	J	K	L	M
Intake, µg/person)	175.3	3.1	109	97.4	0.5	0.3	74.6	633.0	526.0	121.7	133.8	0.0	41.1
Rounded % PMTDI	150%	3%	90%	60%	0%	0%	70%	530%	440%	100%	110%	0%	30%

* a body weight of 60 kg was used for all clusters, with exception of G and L (55 kg).

67. A chronic dietary exposure assessment of fumonisins (B_1+B_2) from the consumption of maize-based products was conducted in Brazil using a national household budget survey to estimate consumption data (Caldas and Silva, 2007). The intake represented 24.1% of the PMTDI for the total population and 355% PMTDI for consumers-only. The authors concluded that the high incidence of fumonisins in some maize-based products and the exposure levels found for specific sub-populations indicate the need for setting safe regulatory levels for fumonisins in food in Brazil.

68. The EU SCOOP Task estimated the dietary intake of FB_1 + FB_2 in Europe fumonisins using occurrence data of various foods provided by 9 countries and consumption data by 7 countries (EC, 2006). The average daily intake represented 0.8 to 13.2% PMTDI for the whole population and 22.3% PMTDI for infants. A total diet study performed in France estimated a total average intake of fumonisins of 14 ng/kg bw/day for adults and 46ng/kg bw/day for children of an age of 3 to 14 years. The 95th percentile exposure represented 3.2 % of the PMTDI for adults and 8.7 % PMTDI for children. For adults, alcoholic beverages contributed with over 50% of the intake; for children, breakfast cereals contributed with over 90 % of the intake (Leblanc et al., 2005). In the Netherlands, it was conservatively estimated that 97% of individuals with gluten intolerance had a daily intake of fumonisin B_1 of at least 1 µg, and 37% had an intake of at least 100 µg, while the proportions of the general population exposed to these concentrations of fumonisin B_1 were 49% and 1%, respectively (de Nijs et al., 1998b). In Denmark, an estimate for an 'eater' shows that the intake of fumonisins will not exceed 0.4 µg/kg bw/day (Petersen and Thorup, 2001).

69. A study conducted in the USA concluded that no human risk of renal toxicity would be expected at the maize contamination levels and consumption patterns for the consumers-only population in the United States. They also suggested that reducing maize consumption would have a greater impact in lowering human risk to kidney damage than lowering the level of FB permitted in maize by a similar factor (Humpreys et al., 2001).

70. In a study conducted in Guatemala, Torres et al (2007) found that the consumption of nixtamalized maize products made with maize with levels and incidence found in the markets in 2005, 50% of the maize

samples would result in exposures exceeding the PMTDI. The women intake in three different areas of the country was 3.5 to 15.6 µg/kg bw/day. Even when were consider that the nixtamalization process by the traditional Mayan method can reduce fumonisin by ~50 %, the intake still exceed the PMDI in central highlands and rural areas of Guatemala.

71. Yazdanpanah et al. (2006) estimated the exposure of individuals of two provinces of Iran to fumonisins B1 and B2 through the consumption of maize from 1998-2000. The mean intake ranged from 0.009 to 0.34 µg/kg bw/day, with a maximum at 0.71 µg/kg bw/day.

72. Fumonisin exposure (B_1+B_2) was estimated in two areas of South Africa by Shephard et al (2007). Assuming an individual adult body weight of 60 kg, fumonisin exposure in Bizana, an area of relatively low oesophageal cancer incidence, was 3.43 +/- 0.15 µg/kg bw/day, which was significantly lower ($p < 0.05$) than that in Centane (8.67 +/- 0.18 µg/kg bw/day), an area of high oesophageal cancer incidence. In both regions, the intake exceeded the PMTDI for fumonisins.

73. In Mexico, urinary FB_1 was compared with dietary intake after tortilla consumption (Gong et al., 2008). The geometric mean (95% confidence interval) of urinary FB_1 was 35.0, 63.1, and 147.4 pg/mL for the low, medium, and high consumer groups, respectively. Women with high intake had a 3-fold higher average FB_1 levels compared with the "low intake" group. Urinary FB_1 was correlated with maize intake, suggesting that measurement of urinary FB_1 is sufficiently sensitive for fumonisin exposure assessment in human populations and could be a valuable tool in investigating the associated health effects of exposure. It should be emphasized, however, that measurement of urinary fumonisin levels, as a potential biomarker of fumonisin intake, is only feasible for high level exposure populations. In Europe and USA urinary fumonisin levels are generally not detectable.

74. A survey for fumonisins(FB_1 + FB_2) on 131 maize and processed maize products commercialized in Korea, the mean and 95th percentile estimated daily intake of fumonisins was evaluated to be 0.03 µg/kg bw/day (1.5% PMTDI) and 0.08 µg/kg bw/day (4.0% PMTDI), respectively (Chung, et al, 2008).

75. In a study conducted in China, eight healthy adult volunteers consumed for 1 month a normal diet containing their homegrown maize potentially contaminated with FB_1. Immediately preceding the start of the test, morning urine samples for the determination of So and Sa from each person were collected before and after the test started, and the maize samples analyzed for FB_1. All the homegrown maize samples contained FB_1 ranging from 0.08 to 41.1 mg/kg, and the estimated daily FB_1 intakes ranged from 0.4 to 740 µg/kg bw/day. This study suggest that sphingolipid metabolism of humans could be affected by FB_1 intake, the urinary Sa:So ratio may be useful for evaluating FB_1 exposure when the contamination of FB_1 is high, and that males are more sensitive to FB_1 disruption of sphingolipid metabolism than females (Qiu and Liu, 2001).

76. Sphinganine and sphingosine were measured in urines of residents in Argentina and Brazil with high maize consumption and compared with urine samples collected in areas with very low or no maize consumption. Mean Sa:So ratio was 1.27 in urine of subjects with high maize consumption (n = 123) and 0.36 in controls (n = 66) and the difference was statistically significant ($p<0.001$). The mean fumonisin level in maize samples collected in Argentina and Brazil was 0.35 mg kg(-1) (n = 40). Although a similar maize and fumonisin intake was recorded for the two exposed populations, the mean Sa:So ratio in Brazil (1.57) was significantly higher ($p<0.05$) than that of Argentina (0.69), suggesting that the higher Sa:So values observed in Brazil cannot be associated with high fumonisin exposure. Further studies are necessary to provide convincing evidence for using the Sa:So ratio as a biomarker of human fumonisin exposure (Solfrizzo et al., 2004).

RISK MANAGEMENT CONSIDERATIONS AND PUBLIC HEALTH CONCERNS

77. Current technology cannot prevent fumonisin contamination of maize crops before harvest. The incidence and levels of fumonisins in maize crops around the world vary considerably depending on many factors including environmental conditions, extent of insect damage, hybrid of maize planted and agronomic practices employed.

78. Guideline levels of fumonisins (FB_1+FB_2+FB_3) in food in the United States include 2 mg/kg for degermed, dry-milled maize products (<2.5% fat content) and 3 mg/kg for popcorn grain (USFDA, 2001). In the European Community, the maximum limit (FB_1+FB_2) is 1 mg/kg for maize flour, grits, semolina, germ and oil; 0.4 mg/kg for maize-based products ready for consumption and 0.2 mg/kg for maize-based products for babies and children (EC, 2006)

79. In Republic of Korea, the Korea Food and Drug Administration (KFDA) had notified to WTO/SPS(G/SPS/N/KOR/283, 6 June 2008) to set maximum limits for fumonisins (FB_1+FB_2) as 4 mg/kg for maize, 2 mg/kg for maize grits and flour (excepted germ).

80. Table 6 shows the JECFA (2001) evaluation of the impact of various enforcement limits on the intake, using the Regional African diet, based on the fumonisin distribution in maize data from the Netherlands.

Table 6. Potential intake of fumonisins from maize and maize products (flour, sweet corn and popcorn) in the African diet when various limits are imposed and enforced (FAO/WHO, 2001)

Limit (mg/kg)	Intake of fumonisins (µg/day per person)						
	Mean	Minimum	Maximum	50th	90th	95th	% excluded
1	27	0.4	110	13	77	90	32
2	46	0.4	210	21	130	160	20
5	86	0.4	530	34	260	370	7.6
10	120	0.4	1100	42	400	580	1.6
None	140	0.4	2500	44	440	660	0

CONCLUSIONS & RECOMMENDATIONS

81. High consumers of maize and maize products might be exposed to unsafe levels of fumonisins, including populations in certain areas of Africa and Central and North America. While in Africa the maize is subject to very little processing and is mainly home-grown, in America there is a high consumption of nixtamalized maize products.

82. Bound fumonisins found in extruded maize products, such as breakfast cereal, are not detected by the usual extraction procedure and the exposure to fumonisins cannot be fully accessed. Efforts should be made to broaden the survey of bound fumonisins in these products and to better elucidate the potential release of FB1 from these bound species in the human gastrointestinal tract.

83. In certain communities where the staple foods are maize and maize based products, the co-occurrence of fumonisins, a strong cancer promoter, and aflatoxins, which are proven human carcinogens, is a cause for concern. Possible synergistic or combined effects of these mycotoxins on human health should be investigated.

84. Research should be encouraged into ways of reducing fumonisin contamination in maize, especially using appropriate technology in the developing world and in ways to reduce exposure in subsistence communities by culturally acceptable means.

85. Consumer protection in the developing world should be promoted by appropriate education and public awareness initiatives aimed at sensitizing the general population to the problems of fungal contamination of food supplies.

86. Members, especially those producing maize, are invited to present information on how they have implemented the Code of Practice, whether they succeeded in reducing fumonisin contamination, and how they monitor the effectiveness of the Code in reducing contamination level.

87. Maize is major trade commodity in the world and some countries and the European Community have already established maximum level for fumonisin in maize and maize products.

88. The Committee should consider establishing a maximum level for fumonisins in maize and in some maize products, such as maize flour, taking into account the need to decrease consumer exposure, especially in some critical areas, without a major impact on trade. According to the JECFA evaluation in 2001, a maximum level of 5 mg/kg would lead to a mean exposure of 72 % PMTDI in the Regional African diet (60 kg bw) with 7.6 % of world production rejected.

89. The Committee should also consider the adoption of a sampling plan for fumonisin in maize and maize products considering the JECFA recommendation and more recent studies.

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