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CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 6 **CX/CF 11/5/6**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON CONTAMINANTS IN FOODS

5th Session
The Hague, The Netherlands, 21 – 25 March 2011

PROPOSED DRAFT MAXIMUM LEVELS FOR DEOXYNIVALENOL (DON) AND ITS ACETYLATED DERIVATIVES IN CEREALS AND CEREAL-BASED PRODUCTS
(N10-2010)
(At Step 3)

Prepared by Electronic Working Group led by Canada

Codex Members and Observers wishing to submit comments at Step 3 on the above matter, including possible implications for their economic interests, should do so in conformity with the *Uniform Procedure for the Elaboration of Codex Standards and Related Texts* (Codex Alimentarius Commission Procedural Manual) before **4 March 2011**. Comments should be directed:	
to: Mrs Tanja Åkesson Codex Contact Point Ministry of Agriculture, Nature and Food Quality P.O. Box 20401 2500 EK The Hague The Netherlands Fax.: +31 70 378.6134 E-mail: info@codexalimentarius.nl- ***preferably*** -	with a copy to: Secretariat, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Viale delle Terme di Caracalla, 00153 Rome, Italy Fax: +39 (06) 5705 4593 E-mail: codex@fao.org - ***preferably*** -

BACKGROUND

1. The 1st Session of the Codex Committee on Contaminants in Food (CCCF) agreed to discontinue consideration of maximum levels (MLs) for deoxynivalenol (DON) until more information became available. The information being sought included: the toxicity of the 3-acetyl and the 15-acetyl DON that occur along with DON and a new overview of exposure data, including more regional data on incidences and levels of DON in cereals over a period of several years and consumption patterns for various countries[1].

2. The 4th Session of the CCCF agreed to restart work on MLs for DON and its acetylated derivatives in cereals and cereal based-products in view of the availability of sufficient occurrence data and the 2010 evaluation by the Joint FAO/WHO Expert Committee on Food Additives at its 72nd meeting (FAO/WHO)[2].

3. At the 4th Session of the CCCF it was clarified that this work on DON would apply to cereals and cereal-based products for human consumption and was not relevant to animal feed. While the possible

[1] ALINORM 07/30/41, para. 108

[2] ALINORM 10/33/41, para. 108 – 110

preparation of a discussion paper on DON transfer from animal feed to food for human consumption was considered, no decision was taken on this matter.

4. The 4th CCCF agreed that the Delegation of Canada would prepare a project document for submission through the Secretariat to the 63rd Executive Committee for consideration. Subject to approval by the Commission, the proposed draft MLs for DON and its acetylated derivatives in cereals and cereal-based products would be prepared by an electronic Working Group led by Canada for comments and consideration at the 5th CCCF session.

5. This new work was approved by the 33rd Session of the Codex Alimentarius Commission in July, 2010[3]. The preparation of this document was led by Canada with contributions from the FAO, European Commission, Argentina, China, Japan, Norway, South Africa, Sweden, Switzerland, the Confederation of the Food and Drink Industries of the EU (CIAA) and the Grocery Manufacturers Association.

6. The Electronic Working Group could not reach consensus on the appropriateness of establishing MLs for DON in cereals and cereal-based products and concluded that CCCF may wish to consider as one option elaborating MLs for DON only. The following MLs are proposed based on a review of mean occurrence levels (rather than a review of complete data sets, which were not available and of current nationally enforced MLs

a) raw wheat, maize and barley, to be subjected to sorting or physical treatment before human consumption or use in as an ingredient in foodstuffs: 2mg/kg

b) all foods derived from wheat, barley and/or corn, including those intended for direct human consumption, except cereal-based foods for infants and young children: 1mg/kg

c) cereal-based foods for infants (up to 12 months) and young children (12 to 36 months): 0.5mg/kg..

7. If MLs are elaborated, then a request to the Codex Committee on Methods of Analysis and Sampling should be requested that a suitable sampling plan be developed. Consideration could also be given for developing validated analytical methods for 3AcDON, 15AcDON and DON-3-glucoside.

8. The CCCF may also consider that further collection of data is necessary before DON MLs are elaborated, in which case, it is recommended that:

- Codex members continue to monitor, or implement monitoring of DON and DON derivative occurrence in wheat, maize and other cereals to provide a more complete picture of seasonal and regional differences.
- Members should continue to be encouraged to submit complete data sets that include individual sample results rather than only aggregate data.
- The CCCF consider requesting that an assessment of the impact on dietary exposures of different MLs be undertaken by JECFA.
- The CCCF consider requesting that distribution curves be generated by JECFA for the DON levels in wheat, maize and barley and foods derived from these cereals to evaluate the potential impact of proposed MLs on the availability of these staple foods and to permit consideration of whether MLs could be established based on the lowest achievable levels of DON on a global basis.

9. Codex Members and Observers are invited to submit comments at Step 3 on the above proposals of the Electronic Working Group.

10. The full report is presented in Appendix I.

[3] ALINORM 10/33/REP, Appendix VI

APPENDIX I

PROPOSED DRAFT MAXIMUM LEVELS FOR DEOXYNIVALENOL IN CEREALS AND CEREAL-BASED PRODUCTS

(AT STEP 3 OF THE PROCEDURE)

INTRODUCTION

1. Deoxynivalenol (DON; vomitoxin) is a member of the trichothecene family, an important class of mycotoxins that share the same basic chemical structure, a tetracyclic 12,13-epoxy – trichothecene skeleton. The trichothecenes are subdivided into four groups according to their chemical structure and producing fungi (Ueno, 1983). DON, its derivatives, 3-acetyldeoxynivalenol (3AcDON), 15-acetyldeoxynivalenol (15AcDON) and DON-3-glucoside, and nivalenol (NIV) are members of the Type B trichothecenes. Type B, together with Type A trichothecenes, which include T-2 toxin and HT-2 toxin, are the predominant trichothecenes found as natural contaminants in cereals grains

2. The Fusarium genus is a large and chemically diverse group of plant-associated fungi and includes species that can produce trichothecenes or fumonisins. The most economically important DON-producing species are *F. graminearum* and *F. culmorum* (Foroud and Eudes, 2009). *F. graminearum* occurs on cereal grains such as barley, maize, oats, rice and wheat, causing ear rot in maize and Fusarium head blight (FHB) in wheat and barley grown in temperate climates such as those found in North America, China and Europe (Desjardins, 2006). FHB severity is dependent on weather conditions, with high humidity during and after flowering being conducive to head blight epidemics and mycotoxin production (Edwards, 2009).

3. *F. culmorum*, while widespread, is more abundant in temperate to cold climates such as those in eastern Australia, northern United States, Canada and Europe. It causes root and stem rot in numerous plant species and is a major component of FHB in cereal crops (Desjardins, 2006). *F. pseudograminearum*, formally described as a subgroup of *F. graminearum*, causes root and crown rot of wheat and other small grain cereals, particularly in warm, semi-arid regions, but it is rarely isolated from the heads (Desjardins, 2006).

4. *F. graminearum* is considered a species complex, consisting of at least nine phylogenetically distinct species some of which are localized on particular continents or geographical regions (Goswami and Kistler, 2004). *F. graminearum* species complex and *F. culmorum* produce one of three strain-specific profiles (chemotype) of Type B-trichothecene metabolites: NIV and acetylated derivatives; DON and primarily 3AcDON (3AcDON chemotype); and DON and primarily 15AcDON (15AcDON chemotype) (Miller et al. 1991). A survey in the 1980s indicated that the 3AcDON chemotype of *F. graminearum* predominated in warmer climates such as Europe, China, Australia and New Zealand and the 15AcDON chemotype was predominant in cooler regions including North America (Mirocha etal 1989). Both DON and nivalenol-producing strains of *F. graminearum* have been found in surveys in regions of China, Japan, Korea and Nepal (Yoshizawa and Jin, 1995, Desjardins, 2006).

5. There are indications that globalization of trade in horticultural and agricultural plants has resulted in changes in regional profiles of FHB pathogens (Starkey et al. 2007). Recent surveys indicate that the 3AcDON chemotype of *F. graminearum* is replacing the 15AcDON chemotype in parts of North America (Guo et al, 2008, Ward et al., 2008, von der Ohe et al., 2010). Surveys in the United Kingdom (UK) have indicated that a shift is occurring in the *Fusarium* population associated with FHB, traditionally dominated by *F. culmorum*, towards a higher proportion of *F. graminearum* (Jennings et al. 2004). Similar trends have been reported in Germany and the Netherlands (Jennings et al. 2004).

6. DON-3-glucoside has recently been detected in wheat, corn and barley (Berthiller et al., 2009). Research suggests that plants metabolize DON to the glucoside conjugate as a detoxification mechanism. There is concern that DON-3-glucoside, "masked" to some analytical methods, may be metabolized by humans and animals to release the parent DON (Sasanya et al., 2008). Consequently, the occurrence data for cereals and finished foods may underestimate DON exposures.

Toxicology

7. At its 72nd Meeting, JECFA considered previously reviewed toxicological data and new toxicity and toxicokinetics studies giving greater emphasis to studies in which pure DON or acetylated DON derivatives were added to defined diets in mammalian species. The committee concluded that the NOEL based on

reduced body weight in the mouse cancer bioassay and used to establish a provisional maximum tolerable daily intake (PMTDI) of 1 µg/kg bw at the 56th Meeting, remained appropriate. Since metabolic studies indicated that 3AcDON is rapidly and extensively deactylated to DON and therefore contributes to the total DON-induced toxicity, the PMTDI for DON was converted to a group PMTDI of 1 µg/kg bw for DON and its acetylated derivatives, 3AcDON and 15AcDON (FAO/WHO, 2010). The Committee also concluded that there was insufficient information to include DON-3-glucoside in the group PMTDI.

8. JECFA (FAO/WHO, 2010) also derived a group acute reference dose (ARfD) of 8 µg/kg bw/day for DON and its acetylated derivatives using a $BMDL_{10}$ of 0.21 mg/kg bw/day for emesis in pigs and applying an uncertainty factor of 25. The Committee also noted that limited data from human case reports indicated that dietary exposures to DON up to 50 µg/kg bw/day are not likely to induce emesis.

9. DON was nominated by the National Institute for Environmental Health Sciences (NIEHS) for chronic toxicity and carcinogenicity studies and reproductive studies based on a lack of definite long-term studies and the widespread contamination of human foods (NTP 2009).

Sampling

10. The nature of fungal infection and mycotoxin contamination necessitates that care be taken to obtain representative samples of the commodity being analysed in order that the mycotoxin levels can be accurately and precisely determined. Sampling steps include: (1) the collection of an aggregate (bulk) sample, (2) homogenization and division of the aggregate sample to obtain the laboratory sample, (3) the laboratory sample is comminuted to reduce its particle size, and (4) the comminuted sample is homogenized and a sub-sample taken for the analysis of mycotoxin content (CX/CF 07/1/17, Köppen et al., 2010). Sampling typically represents the largest source of variability in the analysis of mycotoxins (Whitaker 2003).

11. In general, a sampling plan describes how to physically select a sample taking into consideration the mycotoxin and product being analyzed. Commodities with a small particle size, such as cereal grains, can be expected to have a smaller variance associated with sampling than those with a larger particle size, such as nuts (Coker et al., 1995). DON was found to be distributed fairly evenly throughout a lot of wheat, unlike ochratoxin A (OTA) which was more heterogeneously distributed in random hot spots (Rivas Casado et al., 2009). Finished products sold at retail often have lower variability due to processing (Macarthur et al., 2006). Variance also increases in proportion to the level of contamination of the lot (Whitaker, 2006).

12. To be representative of a lot, the sample should be an aggregate of many incremental samples taken throughout the lot, and this is more difficult to obtain from a static lot than from a moving stream of product (Whitaker, 2006). The number of incremental samples taken and the aggregate sample weight depend on the total weight of the lot in question. For example, the sampling parameters required by EC Regulation 401/2006 for mycotoxins in foodstuff are shown in Table 1 below. Studies involving a 26-ton static lot of wheat found that the variability associated with taking different numbers of incremental samples was relatively low for DON (Biselli et al., 2008). The size of the incremental samples, which can be influenced by the choice of sampling probe, also affects the variability of results (Park et al., 2000).

13. The aggregate sample may be ground in order to reduce particle size and evenly distribute the mycotoxin in the sample before sub-samples are taken for analysis. It has been demonstrated that fine grinding the entire aggregate sample and further grinding individual sub-samples of wheat prior to analysis reduces the variability in DON and OTA results (Biselli et al., 2008). Slurry mixing techniques were found to produce smaller particles and more homogeneous samples (Spanjer et al., 2006) although approaches to reducing the variability associated with dry milling techniques are being investigated (Nowicki et al., 2010).

Table 1. Sampling parameters for cereal and cereal products based on lot weight as specified under EC Regulation 401/2006.

Lot weight (tonnes)	Weight or number of sublots	Number of incremental samples	Aggregate sample weight (kg)
≥ 1 500	500 tonnes	100	10
> 300 and < 1 500	3 sublots	100	10
≥ 50 and ≤ 300	100 tonnes	100	10
> 20 and < 50	—	100	10
> 10 and ≤ 20	—	60	6
> 3 and ≤ 10	—	40	4
> 1 and ≤ 3	—	20	2
> 0.5 and ≤ 1	—	10	1
> 0.05 and ≤ 0.5	—	5	1
≤ 0.05	—	3	1

Adapted from EC Regulation 401/2006 Tables 1 and 2.

14. The variability in DON quantification due to sampling in cereal grains and cereal-based foods can be expected to be less than for other mycotoxin-food matrices, such as aflatoxin in nuts or OTA in cereals. As with any mycotoxin quantification, sampling variability can be minimized by obtaining a representative sample, increasing the number of incremental samples and consequently the size of the aggregate sample, as well as ensuring that the bulk sample is adequately homogenized prior to sub-sampling. However, in developing a sampling plan for mycotoxins with the desired operating characteristics, reducing sampling variability must be weighed against the cost associated with handling and processing more and/or larger-sized samples as well as against the risks to fair trade practices, that is, the probability of inappropriate rejection or acceptance of product lots that are actually below or above, respectively, any proposed MLs.

Analytical Methods

15. Considerable research has been conducted on analytical methods for the determination of DON in the last decade. More recently, methods have been investigated for the determination of DON's acetylated derivatives and DON-3-glucoside. In its review of analytical methods, JEFCA (2010) considered the use of mass spectrometry (MS) or tandem mass spectrometry (MS/MS) coupled with high performance liquid chromatography (LC-MS/MS) for DON to be the most important development. Reviews have been published on analytical methods discussing trichothecene determination (Koch, 2009, Lattanzio et al., 2009) and the more general aspects of mycotoxin determination (Krska et al., 2005, 2008, Cigic and Prosen, 2009, Turner et al. 2009, Köppen et al. 2010).

16. The variety of different methods developed for detection and quantification of DON can be generally categorized as screening tests for rapid cost-effective analysis and quantitative methods with low limits of detection. Screening tests that tend to be qualitative or semi-quantitative in nature, are based on various analytical techniques including thin-layer chromatography (TLC), infrared spectroscopy and immunochemical-based assays. TLC enables the screening of large numbers of samples with low operating cost as well as identification of target compounds, using UV-Vis spectral analysis (Köppen et al., 2010). The most common format of immunoassay is the microtiter plate enzyme-linked immunosorbent assay (ELISA) but two more recently developed immunoassay formats for DON analysis are based on fluorescence polarization and surface plasmon resonance (Schneider et al., 2004, Zheng et al., 2006). Non-instrumental immunochemical-based assays include lateral flow, dipstick and flow-through tests in which antigens or antibodies are immobilized on carrier membranes instead of microtiter plates (Köppen et al. 2010). Many immunoassay kits are commercially available for DON, but they should only be used for the food matrices and in the test ranges for which they were designed (Schneider et al. 2004). The development of array

biosensors permits rapid simultaneous analysis of multiple samples or analytes (Ngundi et al., 2006, Sapsford et al., 2006). Several non-immunochemical methods also exist for DON detection (Köppen et al., 2010).

17. Quantification of DON in cereals generally involves extraction, clean-up, chromatographic separation and detection. TLC procedures for detection and analysis of DON are reliable and cost-effective for use in laboratories with a restricted budget. Other classical quantitative methods include high-performance liquid chromatography (HPLC) coupled with diode array, fluorescence, MS or MS/MS and gas chromatography coupled with electron capture, flame ionisation or MS detection (Köppen et al., 2010). As indicated by JECFA (FAO/WHO, 2010), currently, analytical method development is focussing largely on the use of LC-MS/MS methods. Not only does this method offer high sensitivity and accuracy, it permits the detection of multiple mycotoxins in a single run. The detection limits of multi-mycotoxin methods vary significantly, in part due to differences in equipment, challenges of clean-up, and the significantly different structures of certain toxins. Limits of detection can be reduced by using methods specific to trichothecenes (Dall'Asta et al., 2004, Buttinger and Krska, 2003, Tanaka et al., 2009), or by using the most appropriate matrix-matched ^{13}C-labelled standards (Häubl et al., 2006, Asam and Rychlik, 2007).

18. Compared to the research on analytical methods for DON, relatively little work has focussed on the detection of the acetylated derivatives, 3AcDON and 15AcDON, and DON-3-glucoside. Acetylated DON can be determined by GC or MS methods used for DON analysis although selection of the GC column is critical for separation (JECFA, 2010). An LC/APCI-MS analytical method has been reported useful for the determination of DON and acetylated DON (Tanaka et al., 2006). LC-MS/MS is ideal for the identification and analysis of DON-3-glucoside. Alternate methods to measure DON-3-glucoside involve their hydrolysis to increase the level of free DON prior to quantification (Zhou et al., 2007). Acetylated DON derivatives can exhibit cross-reactivity with certain DON-specific antibodies, leading many immunochemical assays to overestimate the DON content if their presence is not accounted for (Zachariasova et al., 2008). Recent research demonstrated that anti-DON antibody recognized 3-Ac-DON and DON-3-glucocide by surface plasmon resonance immunoassay (Kadota et al., 2010)

19. Validated methods, such as those adopted by the International Organization for Standardization (ISO), the Association of Analytical Communities (AOAC), or the European Organization for Standardisation (CEN), are required for enforcement purposes. For DON in cereal grains and grain products, there exists validated TLC (AOAC method 986.17), GC (AOAC method 986.18) and HPLC-UV (EN 15891:2010) methods and several AOAC performance-tested ELISA kits which are commercially available. There is a CEN standard (EN 15891:2010) for HPLC with UV detection of DON in cereal and cereal products. Commercial ^{13}C-labelled standards are available for DON and 3-AcDON (Bretz et al., 2006).

DON in Cereal Grains

20. The worldwide occurrence of DON in cereal grains has been well documented over the last two decades (Tanaka et al., 1988, Scott, 1990, Placinta et al., 1999, Desjardins, 2006 and Binder et al., 2007). Wheat, barley and corn, the crops accounting for two-thirds of the world's cereal product, are most susceptible to *Fusarium* disease and trichothecene contamination (Abramson, 1998). The types of wheat affected by DON include both winter and spring varieties and hard and soft cultivars. DON is also found to contaminate other cereal grains, including oats, rye, rice, and triticale (JECFA, 2001). Although other trichothecenes and zearalenone do occur concomitantly with DON, it is usually the most predominant toxin.

21. *Fusarium* species can produce DON in the field and also during storage if the moisture content of the grain kernels is high. Local temperatures, rainfall and humidity are major factors for infections that occur at the time of flowering. It is the timing of rainfall rather than the amount that is the critical factor for infection. For these reasons, the incidence of high concentrations can vary greatly from year to year and from region to region.

22. In 2001, the 56th meeting of JECFA assessed the levels and patterns of contamination of cereals by DON on the basis of occurrence data submitted by Argentina, Brazil, Canada, China, Finland, Germany, Italy, the Netherlands, Norway, Sweden, the United Kingdom, Uruguay and the USA and taken from the published literature for 1990 through 2000. DON was found to be a frequent contaminant of cereal grains with 57% of wheat, 43% of maize, 68% of oats, 59% of barley, 49% of rye and 29% of rice samples being positive. It was also detected in buckwheat, popcorn, sorghum and triticale. Most of the data available were for the Latin American and European diets in the Global Environmental Monitoring System – Food

Contamination Monitoring and Assessment Programme (GEMS/Food) with only limited data for the Far Eastern and African diets. A summary of the DON concentrations used in JECFA's 2001 GEMS/Food-based exposure assessment is presented in Table 2.

23. In 2010, the 72nd meeting of JECFA considered occurrence data submitted by Austria, Belgium, Brazil, China, Finland, France, Hungary, Japan, the Netherlands, Norway, Singapore and the United Kingdom as well as surveys published in the open literature between 2001 and 2009. As in JECFA's 2001 assessment, DON was frequently detected in cereal grains, with 73% of wheat, 92% of maize, 50% of oat, 68% of barley, 30% of rye, 74% of rice samples being positive. The highest levels of DON were detected in wheat, maize and barley grains. Wheat was the only commodity for which data were reported from each of the ten cluster diets. The majority of the data were from countries in the E and F GEMS/Food cluster diets (Western and Northern Europe respectively). Occurrence data for the Americas (GEMS/Food cluster M) relied largely on the limited data available in published literature. A summary of the DON concentrations used in JECFA's 2010 GEMS/Food based exposure assessment is presented in Table 2.

Table 2. Summary of occurrence data used in GEMS/Food based exposure assessment.

Commodity	JECFA 2001			JECFA 2010		
	No of samples	Weighted mean[a] conc. µg/kg	Max value[b] µg/kg	No. of Samples	Weighted mean conc. µg/kg	Max value µg/kg
Barley	1 778	720	34 000	1 353	442	10 000
Maize	5 719	180	19 000	2 643	625	17 500
Oats	834	89	2 600	238	79	5 000
Rice	203	150	9 500	462	12	320
Rye	295	65	1 300	909	63	1 095
Wheat	14 200	390	30 000	9 997	367	14 000

[a] Weighted mean of all samples combined.

[b] Maximum analytical value reported.

24. DON was detected in 47% of 538 durum wheat, 36% of 1226 hard wheat and 54% of 194 soft wheat samples collected in Canada between 1994 and 2009. The mean and maximum DON levels were 150 and 3150 µg/kg for durum wheat, 210 and 2790 µg/kg for hard wheat and 330 and 2150 µg/kg for soft wheat, respectively. Twenty percent of 303 barley samples were found positive for DON with the mean and maximum levels being 210 and 4460 µg/kg respectively. Of 169 oat samples analysed during the same period, 35% were positive for DON with the mean and maximum levels being 100 and 940 µg/kg (Canadian Grain Commission, 2010).

25. The occurrence of DON derivatives 3AcDON and 15AcDON in wheat, maize, barley, oats rye and their products were considered by JECFA for the first time in 2010. Data were available on 3AcDON from 6980 samples (92% from Europe and 8% from Asia) and on 15AcDON from 4300 samples (81% from Europe, 16% from Asia and 3% from the USA). These derivatives were infrequently detected and their levels when detected were generally 10% of those reported for DON. The highest reported mean levels of 3AcDON in wheat, maize and barley were 193, 17 and 19 µg/kg, respectively. The highest levels of 3AcDON reported were for maize from China (368 µg/kg) and France (520 and 1320 µg/kg) and for oats from Finland (438 µg/kg). For 15AcDON, the highest reported mean levels in wheat, maize and barley were 365, 236 and 0.3 µg/kg, respectively with the highest levels reported as 1800 µg/kg and 1734 µg/kg for wheat and maize from China.

26. Data on DON-3-glucoside in cereals were reviewed by JECFA in 2010 but considered too limited for dietary exposure assessment. Mean levels of DON-3-glucoside in wheat ranged from 26 to 393 µg/kg and the highest level reported as 5400 µg/kg in wheat from the USA.

Effects of Milling and Food Processing

27. The initial cleaning of grain, the milling of the whole cereal and the processing of different milling fractions to manufacture foods can all change the level of DON relative to that in the raw harvested crop

(Scudamore, 2008). The effects of processing on DON levels are relevant because it is through the finished food products that most human exposure to DON occurs. Comprehensive reviews of the influence of these processes on mycotoxin levels have been published (Bullerman and Biachini, 2007, Hazel and Patel, 2004, Kushiro, 2008, Scudamore, 2008, and Trigo-Stockli, 2002).

28. Harvested cereals intended for food consumption are generally cleaned to remove any impurities prior to milling, a step that can be used to remove broken or damaged grains. Wheat and barley kernels infected by *Fusarium* become shrivelled and lower in weight than healthy ones and can be separated on the basis of specific gravity, size and shape by the use of gravity separators (Hazel and Patel, 2004). Delwiche et al. (2005) reported that high-speed optical sorting could reduce DON concentration in the sorted wheat to an average of 51% of the original concentration with one-pass sorting, with further reductions occurring with additional passes. While sorting of grossly contaminated samples have been reported to significantly reduce DON levels, the effect of cleaning is extremely variable (Scudamore, 2008).

29. The effect that milling has on the levels of DON in the resulting food products depends on several factors including the grain, the level of contamination and the milling process. Dry milling is a process by which grains are ground and their components separated into fractions based on particle size. Studies have shown that in milled wheat, higher concentrations of DON are found in the bran and shorts fractions than in the original wheat with lower concentrations in white flour (Samar et al., 2003, Trigo-Stocki et al., 1996, Seitz et al. 1985, Young et al., 1984.) Milling techniques can reduce DON levels in flour by approximately 50% (Lancova et al. 2008a, Nisho et al. 2010). However, the early studies by Sietz et al. (1985) and Young et al. (1984) and more recent studies (Pinson-Gadais et al., 2007, Rios et al., 2009) indicate that the effectiveness of the milling process in reducing the level of DON in flour depends on the extent to which the fungi has penetrated the kernel. Higher levels of DON contamination are generally associated with a lower percent reduction during milling (Trigo-Stocki, 2002). Recent study shows that distribution of DON in milling Japanese wheat could be influenced by contamination level of the original grain and the milling process is not always effective for removal of toxins from wheat grains (Thanmawong et al., 2010)

30. Milling of oats involves de-hulling to remove the husk from the grain, conditioning (kilning) with heat and/or steam to inactivate lipase, separating the groats according to size and rolling to produce the flakes used in food products. Grinding of the flaked oat or groat and separation are used to produce oat bran and oat flour. De-hulling oats results in a large reduction in the level of DON compared to the covered grain (Scudamore et al. 2007) and the kilning process further reduces the levels (Tekauz et al., 2004). Scudamore et al. (2007) reported that the concentration of DON in oat flakes were 5-10% that of the intake oats.

31. Maize can be subjected to either dry milling to produce flour and grits or wet milling to product starch and glucose syrups. In the wet milling of maize, DON being a water-soluble mycotoxin, is found to transfer to the steep water and gluten fractions with low carryover to the starch and subsequent syrup fractions (Lauren and Ringrose, 1997, Hazel and Patel 2004). For dry-milled maize, the highest levels of DON are found in the germ and bran fractions with lower levels in the grits and flour which are used in the production of breakfast cereals, snacks and polenta (Scudamore and Patel, 2009, Schollenberger et al., 2008, Schaafsma et al. 2004).

32. The fermentation and baking conditions for making bread and non-yeast products vary considerably throughout the world, resulting in different effects on DON levels in final baked goods (Hazel and Patel, 2004). Bread-baking has been reported by some to reduce DON levels (Abbas et al., 1985, Samar et al. 2001, Pacin et al, 2010, Valle-Algara et al., 2009) while others have found DON to be highly stable during the process (Scott et al, 1984, Neira et al., 1997, Sugita-Konishi et al., 2006, Lancova et al., 2008a). While Samar et al. (2001) and Neira et al. (1997) reported reductions in DON levels during fermentation, Valle-Algarra et al. (2009) observed no change and Young et al. (1984) observed an increase in yeasted products. It has been suggested that the ingredients used (Boyacioğlu et al., 2003) and the baking technology (commercial vs handmade) (Scudamore etla. 2009, Bergamini et al. 2010) and fermentation and baking conditions (Valle-Algarra et al., 2009) impact the reduction in DON levels observed during bread making.

33. Reductions in DON levels in final non-yeast bakery products compared to the levels in flour were reported to be due to the dilution effect from other ingredients and not the processing (Scudamore et al., 2009). Extrusion processing, used extensively in the production of breakfast cereals, snack foods and textured food (Bullerman and Bianchini, 2007) is reported to have varying effects on DON stability. While Cazzaniga et al. (2001) reported that extrusion cooking of corn flour was effective in inactivating DON

particularly if sodium metabisulphite was added, Scudamore et al. reported DON in wholemeal flour (2008a) and maize flour (2008b) to be relatively stable. During the commercial production of breakfast cereals, the loss of DON was significantly greater in the product from which excess cooker effluent was drained (Scudamore and Patel, 2008).

34. Traditional home frying of Argentine empanadas (stuffed pastry) resulted in reductions in DON to levels of 20 to 28% of that in the raw dough depending on frying temperature (Samar et al., 2007). Boiling of pasta or noodles results in loss of DON to the cooking water (Visconti et al., 2004, Hazel and Patel, 2004, Sugita-Konishi et al., 2006, Scudamore, 2008). Tortilla fabrication, which involves first boiling maize in a calcium hydroxide solution, resulted in DON levels being reduced 18-28% of that in the maize (Abbas et al., 1988)

35. The effects of malting and brewing on mycotoxin levels including DON have been reviewed by Wolf-Hall and Schwarz (2002), Hazel and Patel (2004) and Wolf-Hall (2007). During the malting process, significant increases in DON levels compared to the intake barley can occur, mainly during the germination step, along with the formation of high-levels of DON-3-glucoside (Lancova et al. 2008b). Further increases in this DON conjugate have been shown to occur during the brewing process (Lancova et al. 2008b).

DON in Cereal-based Foods

36. The levels of DON in cereals intended for direct human consumption, cereal flour and cereal-based finished foods, like the levels in the unprocessed grains, can vary widely. While the cleaning and milling processes can substantially reduce the levels of DON in some grains, DON is relatively stable to the high-temperature and high-pressure conditions used in food processing.

37. Published surveys conducted around the world which included analysis of from 3 to 272 wheat flour samples, reported mean levels of DON ranging from 19 to 1309 ppb (µg/kg) with maximum levels ranging from 95 to 9000 ppb (Appendix A, Table 1). Several surveys of bread have been conducted which found DON at mean levels ranging from 20 to 264 ppb. The highest level of DON reported was 1130 ppb for a bread sample purchased in Thailand (Poapolathep et al., 2008). Levels of DON in pasta and/or noodles have been reported to range from not detectable to 1670 ppb. Surveys of wheat-based breakfast cereals in Europe and North America have found mean levels of DON ranging from 75 to 110 ppb with the highest levels ranging from 238 to 940 ppb. Levels in other wheat-based foods tend to be lower, probably reflecting the proportion of wheat in the product (Appendix A, Table 1).

38. Mean and maximum levels of DON reported in surveys of processed maize- and oat-based foods tend to be lower than those for wheat-based foods (Appendix A, Table 2), possibly because milling/cleaning processes result in greater DON reductions in these grains as compared to wheat. Ok et al. (2009) detected no DON above the limit of detection (2.2 ppb) in 25 samples of canned corn purchased in Korea. Mean levels of DON in other maize-based foods surveyed worldwide ranged from 8 ppb (breakfast cereal) to 153 ppb (snack foods) with maximum reported levels ranging from 36 ppb (breakfast cereal) to 807 ppb (dried corn). Three surveys of oats and oat-based products reported means from 20 to 48 ppb with the highest level of 148 ppb detected in oat flakes (Appendix A, Table 2).

39. Schellenberger et al. (1999), Lombaert et al. (2003) and Tanaka et al. (2010) reported mean levels of DON in infant foods ranging from 17 ppb for biscuits to 150 ppb for barley-based infant cereal. The maximum levels of DON reported in these surveys ranged from 90 (oat-based infant cereal) to 980 ppb (barley-based infant cereal).

40. The use of DON-contaminated grain for brewing can result in its transfer to beer (Scott, 1996) and several surveys have examined DON occurrence in beer. Scott et al. (1993) detected DON in 29 of 50 samples of domestic and imported beer in Canada with levels in positive samples ranging from 0.3 to 50.3 ng/mL. In a Korean study, 14 of 54 domestic and imported beer samples were found to contain DON at levels ranging from 1.0 to 23 ng/mL (Shim et al., 1997). A total of 75 samples of lager beer samples brewed in Kenya were found to contain a mean of 3.42 ng/mL DON with the maximum level reported as 6.40 ng/mL (Mbugua and Gathumbi, 2004). Papadopoulou-Bouraoui et al. (2004) reported results of a survey which included 296 samples of European beers from 19 countries and 17 samples of beer imported from 11 countries. For both European and imported beers, approximately 88% of the samples were positive for DON. The mean and median levels for the positive samples were 13.5 and 11.2 ng/mL, respectively, with levels ranging from 4.0 to 56.7 ng/mL (Papadopoulou-Bouraoui et al., 2004). A survey of European and North

American beers found DON-3-glucoside to be ubiquitously present in beer, sometimes at levels exceeding free DON (Kostelanska et al., 2009).

Dietary Exposure

41. In 2001, JECFA assessed dietary exposure at the international level according to the WHO *Guidelines for the Study of Dietary Intakes of Chemical Contaminants* (WHO, 1985) on the basis of mean DON levels for ten commodities and mean food consumption from the five GEMS/Food regional diets. Contaminant levels for ten commodities were submitted by countries from four of the five regional diets. The contaminant levels were pooled, means calculated and the same means were applied to each regional diet.

42. Total intakes of DON (Table 3) ranged from 0.78 µg/kg bw/day in the African diet to 2.4 µg/kg bw/day in the Middle Eastern diet. Wheat was found to be a major contributor to DON exposures in all regions, contributing from 24 to 88% of the total DON exposure. Maize and rice are the next highest contributors, though their contribution varied significantly between regions, from 2 to 44% of total exposure. Contributions from barley were less significant, ranging from 1 to 16% of the total DON exposure, while oats and rye contributed less than 1% to DON exposure for any of the regional diets.

43. The 2001 JECFA assessment indicated that dietary exposures to DON exceeded the PMTDI for four of the five regional diets. However, they noted that there were considerable uncertainties in the estimates and that food processing would be expected to reduce DON levels, resulting in lower intakes.

44. At the recent 2010 JECFA meeting, occurrence data for wheat, maize, rice, barley, oats, rye, and beer made available between 2001 and 2009 were considered. Food consumption data was based on the thirteen newer GEMS/Food cluster diets, for which occurrence data was available for all but cluster diets A (Africa), H (Central America) and J (Africa). DON intakes for each of these 10 diets were estimated using occurrence data from that cluster exclusively, rather than a pool of the worldwide data (FAO/WHO, 2010).

Table 3. Estimates of total DON exposure and the percent contribution of select commodities from the 2001 and 2010 JECFA assessments.

Regional Diet	**Est. DON Exp.**	**Primary Sources of DON (% Contribution)**						
(JECFA 2001)	**(µg/kg bw/day)**	**Wheat**	**Maize**	**Rice**	**Barley**	**Oats**	**Rye**	**Beer**
African	0.78	24	40	33	3	< 1	0	--
European	1.4	79	2	2	16	< 1	< 1	--
Far Eastern	1.6	47	6	44	3	0	< 1	--
Latin American	1.2	64	10	18	7	< 1	0	--
Middle Eastern	2.4	88	6	5	1	0	0	--

Cluster Diet	**Est. DON Exp.**	**Primary Sources of DON (% Contribution)**						
(JECFA 2010)	**(µg/kg bw/day)**	**Wheat**	**Maize**	**Rice**	**Barley**	**Oats**	**Rye**	**Beer**
B - S.Europe	14.52	37	63	--	--	--	--	0
C - N.Africa	0.19	100	--	--	--	--	--	--
D - E.Eur/Rus	0.54	56	20	--	24	--	0	--
E - W.Eur	1.61	75	19	0	1	0	2	2
F - N.Eur	0.81	85	2	0	5	2	1	4
G - E.Asia	1.32	87	13	0	0	0	0	--
I - S.Africa	4.37	20	80	--	--	--	--	--
K - NE S.Amer	0.65	89	--	11	--	--	--	--
L - FarE.Asia/Pac	0.25	40	40	--	16	--	--	0
M - Can/US/Aus NZ/Arg/Chile/Uru	11.04	83	--	--	10	--	--	8

45. Total dietary exposure (Table 3) was estimated to range from 0.19 µg/kg bw/day for cluster diet C to 14.52 µg/kg bw/day for cluster diet B. JECFA noted that the two extremely high exposures in clusters B and M derived from high DON levels in commodities from single countries within these clusters and that these data might not be representative of chronic dietary exposures.

46. Wheat was found to be a major contributor to DON exposure in all regions, contributing from 20 to 89% of total exposure in the regions where data on multiple commodities were available. Maize was the next highest contributor to DON exposure, although intakes from maize varied significantly between regions, contributing from 2 to 80%. Rice was not found to be a major contributor to total exposure. Barley and beer contributed from 0 to 24% and from 0 to 8% of total DON exposures, respectively, their contributions varying significantly between regions. Oats and rye each contributed less than 2% to total DON exposures (FAO/WHO, 2010).

47. JEFCA (FAO/WHO, 2010) also considered national evaluations of dietary exposure to DON available in the published literature. Some of these reports contained overall dietary exposure assessments from a variety of cereals, whereas others assessed single commodities. After considering both national evaluations and the GEMS/Food-derived exposure estimates, a dietary exposure of 0.5 µg/kg bw/day for an average exposure and 1.0 µg/kg bw/day for a high exposure, based on national estimates, was chosen by JECFA for the risk characterization.

48. Some national evaluations of dietary exposure estimates, highlighting the potential exposure of young children and high percentile consumers, are presented in Table 4.

Table 4. Mean exposure estimates from national assessments selected to highlight exposures among young children and high percentile (90^{th} or 95^{th}) consumers.

National Assessment	Commodities Assessed	Age Group	Est. DON Exp. (µg/kg bw/day)		Reference
			Mean	High	
Austria	Cereal grains	all	0.294	1.037	Scoop Report 2003
Belgium	Bread, pasta, bran	13-18 yr	0.245	0.84	Scoop Report 2003
Canada	Comprehensive	31-50 yr M	0.341	0.827	Unpublished data
Denmark	Bread, flour	all	0.171	0.743	Scoop Report 2003
Finland	Wheat, rye, oats, barley	24 - 64	0.144	--	Scoop Report 2003
France	Comprehensive	adults	0.461	1.667	Scoop Report 2003
Germany	Bread, pasta, baby food	adults	0.274	0.548	Scoop Report 2003
Japan	Wheat	1-6	0.69	--	Watari 2011
Japan	Wheat	7-14	0.49	--	Watari 2011
Japan	Wheat	Adults	0.24	--	Watari 2011
Lebanon	Comprehensive	8 - 13 yr	0.545	0.975	Soubra et al. 2009
Lebanon	Comprehensive	14 - 18 yr	0.409	0.664	Soubra et al. 2009
Netherlands	Comprehensive	all	0.338	--	Scoop Report 2003
Norway†	Wheat, rye, oats, barley	all male	0.343	0.628	Scoop Report 2003
Norway†	Wheat, rye, oats, barley	all female	0.3	0.53	Scoop Report 2003
Portugal	Wheat, flour, bran, bfc	adults	0.363	--	Scoop Report 2003
South Africa	Maize meal, wheat flour	1 - 5 yr (R)	3.80*	--	Shephard et al. 2010
South Africa	Maize meal, wheat flour	6 - 9 yr (R)	2.73*	--	Shephard et al. 2010
South Africa	Maize meal, wheat flour	10+ yr (R)	1.77*	--	Shephard et al. 2010
South Korea	Comprehensive	3 - 6 yr F	0.144	0.302	Ok et al. 2009b
South Korea	Comprehensive	7 - 13 yr F	0.096	0.2	Ok et al. 2009b
South Korea	Comprehensive	30 - 49 yr M	0.068	0.143	Ok et al. 2009b
Sweden	Wheat, rye, oats	18 - 74	0.078	0.155	Scoop Report 2003
UK	Comprehensive	16 - 64 M	0.176	--	Scoop Report 2003
UK	Comprehensive	16 - 64 F	0.142	--	Scoop Report 2003

* Values shown are based on rural consumption data, with estimates for urban consumers being approximately 25-30% lower.

† The Norwegian Scientific Committee for Food Safety has upon request from the Norwegian Food Safety Authority started to work on an updated exposure assessment from mycotoxins (including DON) in the Norwegian diet. This work will be finished during fall 2011.

Risk Management Considerations

49. DON contamination of cereal grains occurs worldwide with the incidence and levels varying considerably depending on factors such as environmental conditions, cultivar of cereal planted, and traditional agronomic practices employed in different countries. Managing the risk associated with DON contaminated cereals requires an integrated risk management system approach which takes into consideration pre-harvest management (Good Agricultural Practices), harvest management and post-harvest management (Good Manufacturing Practices, decontamination and diversion strategies). The *Code of Practice for The Prevention and Reduction of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Trichothecenes* (CAC/RCP 51-2003) provides guidance on such an approach.

Pre-harvest Control

50. Prevention and control practices for the pre-harvest management of DON contamination of cereal grains were discussed in the 2003 Discussion Paper on Deoxynivalenol (CX/FAC 03/35). These strategies include the timing and application rate of fungicides and insecticides to control the presence of DON and the use of cultivars that may be highly resistant to *Fusarium*. Also discussed are strategies related to agricultural practices such as crop rotation and ploughing under or removing infected post-harvest debris.

51. These control strategies and the use of biological and chemical agents to prevent growth of DON-producing fungi during pre-harvest have been discussed more recently in comprehensive reviews by Kabak et al., (2006) and Yuen and Schoneweis (2007).

52. The use of microorganisms to control the growth of *Fusarium* species and the levels of DON has shown promising results. For instance, several bacterial strains, under greenhouse conditions, were able to reduce the growth of *F. graminearum* and the production of DON on irradiated wheat grains by 60 -100%, whereas the disease severity was reduced by 49-71%. Two bacterial strains of the *Brevibacillus* sp. and *Streptomyces* sp. were selected as biocontrol agents for further greenhouse and field studies (Palazzini *et al*., 2007).

53. The ability of fluorescent pseudomonad bacteria to control FHB and to reduce DON contamination of wheat and barley was shown under greenhouse and field conditions. These bacteria were more effective in controlling the disease when applied 24 h pre- instead of 24 h post-pathogen inoculation (Khan & Doohan, 2009a). Chitosan, a crabshell-derived chemical, was also effective in controlling FHB and DON contamination when applied before pathogen inoculation (Khan & Doohan, 2009b).

54. The use of antagonistic microorganisms to control FHB, to reduce the severity of disease and minimize DON contamination has been recently reviewed in detail (Kabak & Dobson 2009). It was also discussed that biological agents should be used at the pre-harvest management level to counteract more effectively the effects of DON and other mycotoxins.

55. Computer models to predict the occurrence of FHB and/or DON levels in wheat have been developed in several countries including Argentina (Moschini and Fortugno, 1996), Belgium (Detrixhe et al., 2003), Canada (Hooker and Schaafsma, 2003), Italy (Rossi et al., 2003), the Netherlands (Van Der Fels-Klerx et al., 2010), Switzerland (Musa et al., 2007) and the United States (De Wolf et al., 2004). These forecasting systems are principally based on host susceptibility, inoculum strength and meteorological conditions. In a review, Pradini et al. (2009) indicate that almost all the models developed to date are descriptive models outlining the system and showing the existence of relations between elements without explaining these relationships. Generally these models can be developed relatively quickly with limited amounts of information and have been shown to be reliable in the geographic area of develop or other very similar locations (Pradini et al., 2009). Explanatory models, such as that developed in Italy, are based on a large amount of data, collected over several years and consequently take more time to develop and validate (Pradini et al., 2009).

Post-harvest Control and Decontamination

56. DON contamination occurs in the field prior to harvesting and consequently post-harvest management strategies can only limit further *Fusarium* growth and minimize the entry of DON into the food and feed chain (Magan and Aldred, 2007). However, poor post-harvest drying and storage management of wheat may exacerbate DON contamination already present at pre-harvest (Magan et al., 2010). Chulze

(2010) reviews strategies to minimize further *Fusarium* contamination during the drying and storage of maize.

57. Several physical methods have been used to decontaminate cereal grains including removal of the damaged grains, washing procedures and extraction with organic solvents. Automated methods for removing *Fusarium*-damaged kernels include screening and aspiration techniques, which rely on general seed size and weight differences, specific gravity tables, which rely on density differences and optical sorting which rely on differences in kernel morphology and colour characteristics (Delwiche, 2005). Hand-sorting by subsistence farming communities has also been examined as a means to reduce levels of mycotoxins in wheat and maize (Desjardins et al., 2000, van der Westhuizen et al., 2010). Sorting techniques are only partly effective in reducing DON levels largely because the appearance and weight of a particular kernel does not necessarily indicate the level of DON present (Awad et al., 2010). While rinsing grain with water or an aqueous sodium carbonate solution can lower DON levels in wheat and maize, the cost of drying the grain limits the use of this approach to before wet milling and brewing (Awad et al. 2010).

58. The use of several chemicals including sodium bisulphate, hypochlorite bleach, natural and modified clay minerals, ozone, and ammonia to decontaminate DON-contaminated grain or feed were reviewed by JEFCA in 2001. Despite the great potential of chemical treatment in DON decontamination, their widespread use is limited because some chemical agents reduce the nutritional value of the feed/food while others leave toxic residues (Kabak *et al*. 2006).

59. The use of microbial additives has also been proposed as a post-harvest strategy since microorganisms commonly found in the ruminal and intestinal microflora have the potential to detoxify DON by metabolism or degradation prior to their absorption from the gastrointestinal tract. However, the practicality and economic feasibility of this approach needs validation (Awad *et al*. 2010).

Risk Management Strategies in Various Countries

60. While many countries around the world have established maximum levels (MLs) for DON in various raw cereals and/or cereal-based foods, most focus on wheat and wheat-based foods (Appendix B). For unprocessed wheat, MLs range from 0.7 mg/kg (ppm) in Armenia, Belarus and the Russian Federation to 2 mg/kg for soft wheat intended for non-staple foods in Canada (the latter ML is currently under review). The EU and Ukraine permit higher levels of DON in unprocessed hard varieties of wheat than in soft varieties. The MLs for wheat flour range from 0.5 mg/kg for soft wheat flour (Ukraine) to 1.0 mg/kg for wheat flour and products in Uruguay.

61. Some countries have also established MLs for other unprocessed cereals, notably maize, barley and oats. MLs for maize have been established by China, the EU, and Iran at levels of 1, 1.25 and 1 mg/kg, respectively. Armenia, Belarus, China, Iran, and the Russian Federation have established MLs for barley at 1 mg/kg. The EU has established an ML of 1.75 mg/kg for unprocessed oats. The FAO report on worldwide mycotoxin regulations, published in 2003, indicates that Cuba has an ML of 0.3 mg/kg for imported cereals. However it is unclear if this applies to unprocessed or processed cereals.

62. While several countries have a general ML for wheat, wheat flour and wheat-based foods, the EU has established separate MLs for a variety of finished foods: 0.75 mg/kg for DON in cereals intended for direct human consumption and dried pasta and 0.5 mg/kg for DON in bread, pastries, biscuits, cereal snacks and breakfast cereals.

63. The EU and the Ukraine have established an ML of 0.2 mg/kg for processed cereal-based foods and baby foods for infants and young children. Canada is currently reviewing its ML of 1.0 mg/kg for DON in uncleaned soft wheat destined for use in infant food.

64. To date, no country has established MLs for the acetylated derivatives of DON or DON-3-glucoside.

Conclusions and Recommendations

65. DON contamination of cereal grains is a potential problem worldwide. DON levels in cereal grains vary from year to year and from region to region depending on weather conditions. Tools are being developed to forecast the likelihood of contamination and/or to assist in the timing of fungicide application. However, DON contamination of cereal grains cannot be prevented and no practical methods for decontaminating affected grain are currently available.

66. At its 72nd meeting in 2010, JECFA reported that exposures for five of the ten GEMS/Food cluster diets exceeded the group PMTDI for DON but concluded that mean estimates of national exposures to DON were below the group PMTDI of 1 µg/kg bw with exposures exceeding this value only for children at upper percentiles in a few cases. An acute dietary exposure estimate of 9 µg/kg bw per day was also calculated based on a high consumption of bread and a regulatory limit for DON of 1 µg/kg in bread. The acute dietary exposure estimate is close to the ARfD of 8 ug/kg bw. Populations whose diets rely primarily on regional staple foods with limited food choices might be expected to not only exceed the PMTDI, but could also exceed the ARfD with some frequency.

67. DON exposure assessments conducted by JECFA in 2010 indicated that the largest contributors to dietary exposure are wheat and maize which contributed greater than 10% of the PMTDI in 10 and 5 of the GEMS/Food Consumption Cluster Diets, respectively. Wheat and maize are staple foods for a large proportion of the world population and are also important commodities for international trade. Many countries have established MLs for DON in unprocessed wheat while fewer have established MLs for maize. High levels of DON can occur in barley and exposures through barley consumption contribute 10% or more of the PMTDI for DON in GEMS/Food European diet (2001) and cluster diets D (Eastern Europe/Russia) and M (North America/South America/Australia/New Zealand). MLs for barley have been established by Armenia, Belarus, China, the EU, Iran, and the Russian Federation.

68. High levels of DON can occur in oats but according to JECFA's 2001 and 2010 assessments, consumption of oats contributes less that 10% of the PMTDI for DON in any of the diets. JECFA's 2001 finding that rice was a significant contributor to DON exposure in the Far Eastern diet was the result of a few reports of high DON levels. Rice was found to contribute to less than 10% of the PMTDI in the K cluster diet in JECFA's 2010 assessment. Only a few countries have established MLs for oats or rice.

69. DON levels in cereal-based foods tend to be lower than those in the raw grain, the reduction depending on the commodity, level of contamination and processing method. The available DON occurrence data for wheat flour and wheat-based foods suggest that they can contribute to high DON intakes. While exposure to DON from processed corn products is likely to be low, people consuming whole maize as a regular part of their diet can also be exposed to high levels of DON.

70. The available information, considered against the Codex General Standard for Contaminants and Toxins in Food and Feed and the criteria contained in paragraph 11 of the Policy of the Codex Committee on Contaminants in Foods for Exposure Assessment of Contaminants and Toxins in Foods or Food Groups, suggests that it would be appropriate to limit the establishment of MLs to wheat, maize and barley and their products as they can contribute significantly to DON dietary exposure.

71. The CCCF may wish to consider, as one option, elaborating MLs for DON. According to Codex criteria for establishing MLs, MLs should be set at levels necessary to protect the consumer and as low as reasonably achievable but at a level that is (slightly) higher than the normal range of variation in levels in food that are produced with current adequate technological methods, in order to avoid undue disruptions of food production and trade. However, the variability in DON contamination of cereal grains from year to year and region to region, and differences in countries' capabilities to forecast and control FHB occurrence, and the nature of the occurrence data that were provided make it challenging to determine DON and its derivative's normal range of variation in food on a global scale and thereby apply the ALARA principle in establishing MLs.

72. It is suggested that, at this time, any proposed MLs would apply to DON only. While the original intent was that the proposed MLs be applicable to the sum of DON, 3Ac DON and 15Ac DON, which are considered toxicologically equivalent and included in the current JECFA group PMTDI, at this time, the lack of occurrence data and a validated interlaboratory analytical method suggest that this would be premature and should only be considered as a priority for future work. Currently available data suggest that the frequency of occurrence and levels of acetylated DON in cereals are generally lower than for DON and consequently, it may be considered that exposure to the DON derivatives would be controlled through the establishment of MLs for DON.

73. In elaborating MLs for foods derived from wheat, maize and barley, the possibility of considering the occurrence data for raw commodities and appropriate processing factors was considered. However, given the wide variety of cereal-based foods consumed, the differences in food processing and preparation

methods employed worldwide and the variability in the results of studies examining processing factors, such an approach is not currently feasible.

74. The CCCF could consider the following MLs, which have been proposed based on a review of mean occurrence levels (rather than a review of complete data sets, which were not available) and of current nationally enforced MLs:

a) raw wheat, maize and barley, to be subjected to sorting or other physical treatment before human consumption or use in as an ingredient in foodstuffs: 2 mg/kg

b) all foods derived from wheat, barley and/or corn, including those intended for direct human consumption, except cereal-based foods for infants and young children: 1 mg/kg

c) cereal-based foods for infants (up to 12 months) and young children (12 to 36 months): 0.5 mg/kg

75. Setting and implementing a 2 mg/kg maximum level of DON in wheat, maize and barley, in conjunction with good agricultural practices, should contribute to the reduction of mean and higher percentile DON exposure levels by preventing the marketing of highly contaminated grains for food uses. Harmonised maximum levels for unprocessed wheat, barley and maize would provide clear guidance and transparency for international trade. However based on the form and manner (i.e., aggregate data rather than distributions) in which the occurrence data was available, the working group could not assess the percentage of these crops that would exceed the proposed MLs.

76. A 2 mg/kg ML for raw wheat, maize and barley would not, on its own, be a measure that would ensure that products derived from raw cereals containing 2 mg/kg DON would meet the proposed ML of 1 mg/kg. Differences in processing factors among cereal types and processes, and the nature of the final food, i.e., whether a composite, multi-ingredient food or a single ingredient (e.g. wheat flour), would influence the DON concentration in the final processed cereal-derived product.

77. Tables 5(a) to 5(c) demonstrate the estimated DON exposures using the 13 GEMS/Food Cluster diet consumption figures for certain, more heavily consumed cereal-derived products assumed to always contain 1 mg/kg DON. The calculations also assume that people will generally tend to consume either barley-, maize-, or wheat-based products (as opposed to a combination of more than one) in a given day. For barley products, the estimates suggest that the proposed ML would not lead to exposures in excess of the PMTDI for any GEMS/Food region. Estimated DON exposures from the consumption of maize products are below or approximate the PMTDI for all but two GEMS/Food regions: H (Central America) and I (Southern Africa). For wheat-based products, consumption figures lead to the estimation that if all such products contained 1 mg/kg DON, then exposures would exceed the PMTDI in the majority of GEMS/Food regions.

Tables 5(a) – 5(c). Estimated cereal product intake (g/person/day); DON intake (µg/kg bw/day) assuming 1 mg/kg (µg/g) in the specified cereal products and assuming a 60 kg body weight; and percent contribution of the estimated DON intakes to the WHO PMTDI of 1 µg/kg bw/day for the general, global population using the 13 GEMS/Food regional diets.

Table 5(a). Based on pot barley, pearled barley, barley flour and grits.

GEMS/Food regional diet	A	B	C	D	E	F	G	H	I	J	K	L	M
Barley product consumption (g/person/day)	29	0.7	50.6	4.7	2.9	14.3	1.6	0.1	0.1	0.7	4.1	4.9	0.1
Estimated DON intake (µg/kg bw/day)	0.48	0.012	0.84	0.078	0.048	0.24	0.027	0.0017	0.0017	0.012	0.068	0.082	0.0017

% contribution to PMTDI	48.3	1.2	84.3	7.8	4.8	23.8	2.7	0.2	0.2	1.2	6.8	8.2	0.2

Table 5(b). Based on maize flour and germ maize.

GEMS/Food regional diet	A	B	C	D	E	F	G	H	I	J	K	L	M
Maize product consumption (g/person/day)	69.1	24.3	56.3	17.8	16.7	2.4	29.3	250.0	210.6	47.8	48.4	14.0	25.5
Estimated DON intake (µg/kg bw/day)	1.15	0.41	0.94	0.30	0.28	0.04	0.49	4.2	3.5	0.80	0.81	0.23	0.43
% contribution to PMTDI	115.2	40.5	93.8	29.7	27.8	4.0	48.8	416.7	351.0	79.7	80.7	23.3	42.5

Table 5(c). Based on wheat germ, wheat bulgur wholemeal, wheat flour, wheat macaroni, wheat pastry, wheat bread, and wholemeal bread.

GEMS/Food regional diet	A	B	C	D	E	F	G	H	I	J	K	L	M
Wheat product consumption (g/person/day)	70.1	310.7	330.3	306.4	189.8	183.9	135.5	119.6	56.8	32.8	88.5	82.2	184.7
Estimated DON intake (µg/kg bw/day)	1.17	5.18	5.51	5.11	3.16	3.07	2.26	1.99	0.95	0.55	1.48	1.37	3.08
% contribution to PMTDI	116.8	517.8	550.5	510.7	316.3	306.5	225.8	199.3	94.7	54.7	147.5	137.0	307.8

78. The proposed ML of 1 mg/kg for DON in all foods derived from wheat, barley and maize, except cereal-based foods for infants and young children, should reduce DON exposures but may not be protective against the toxicological endpoint (reduced growth) for certain foods and in certain regions in years where DON levels may be elevated, although national estimates suggest that generally, exposures are within the PMTDI. Also, the form and manner in which the available occurrence data was provided did not permit an assessment of what percentage of food samples derived from wheat, barley, and maize that would exceed the proposed ML, which could have implications for food security for certain countries. The mean concentrations presented in Appendix A suggest that this level should be achievable, on average, in finished foods based on data received; however, in the case of wheat flours in particular, the maximum values reported often exceed the proposed ML.

79. One of the most consistent effects observed in most species during short- or long-term toxicology studies has been reduced growth, suggesting that infants and young children may be a vulnerable group. For

this reason it is appropriate to set a lower level for cereal-based food for infants and young children. If cereals to be used in the manufacture of infant food are carefully selected, this level should be achievable.

80. If the CCCF considers that MLs should be elaborated, then a request to the Codex Committee on Methods of Analysis and Sampling should be made requesting that a suitable sampling plan be developed. Consideration could also be given for developing validated analytical methods for 3AcDON, 15AcDON and DON-3-glucoside.

81. Rather than consider MLs at this time, the CCCF may consider that further collection of data is necessary and that further examination of available and additional data is necessary before DON MLs are elaborated, in which case, it would be recommended that:

- Codex member states continue to monitor, or implement monitoring of, DON and DON derivative occurrence in wheat, maize and other cereals to provide a more complete picture of seasonal and regional differences.
- Member states should continue to be encouraged to submit complete data sets that include individual sample results rather than only aggregate data.
- The CCCF consider requesting that an assessment of the impact on dietary exposures of different MLs be undertaken by JECFA.
- The CCCF consider requesting that distribution curves be generated by JECFA for the DON levels in wheat, maize and barley and foods derived from these cereals to evaluate the potential impact of proposed MLs on the availability of these staple foods and to permit consideration of whether MLs could be established based on the lowest achievable levels of DON on a global basis.

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Appendix A: Occurrence of DON in cereal-based foods

Table 1: Occurrence of DON in wheat flour and wheat-based foods.

Commodity	Region of Purchase	# of Samples	Mean µg/kg	Median µg/kg	Max level µg/kg	Reference
Flour						
	Asia	37	19		173	Ok et al. (2009)
	Europe	3	237			Vendl et al. (2010)
Semolina	Europe	3	<100			Vendl et al. (2010)
	Europe 1999	16	175	167	527	Rasmussen et al. (2003)
	Europe 2001	30	32	10	204	Rasmussen et al. (2003)
Durum flour	Europe 2000	23	1157	1242	2591	Rasmussen et al. (2003)
Durum flour	Europe 2001	10	1153	1224	1619	Rasmussen et al. (2003)
Bulgur	Middle East	26	132		289	Antonios et al. (2010)
	South America	55	72.1	53	317	Pacin et al. (2010)
	South America	61	1309	950	9000	Pacin et al. (1997)
White	North America	272	450		2630	Trucksess et al. (1997)
Whole	North America	90	540		3800	Trucksess et al. (1997)
Germ	Europe	5	50	40	95	Schollenberger et al. (2005)
Bran	Europe	5	360	365	389	Schollenberger et al. (2005)
Bran	North America	163	670		2920	Trucksess et al. (1997)
Bread						
	Asia	8	20		78	Ok et al. (2009)
	Asia	30	62		1130	Poapolathep et al. (2008)
	Europe	4	<100			Vendl et al. (2010)
	Europe	41	246	242	739	Cano-Sancho et al. (2010)
	Europe	75			147	González et al. (2011)
French	South America	12	263	294	436	Pacin et al. (1997)
French	South America	66	41.6	35.5	271	Pacin et al (2010)
Vienna	South America	45	30.1	22	149	Pacin et al (2010)
	North America	3			400	Trucksess et al. (2010)
	Middle East	40	176		700	Scoubra et al. (2009)
Pasta or Noodles						
	Asia	30	4.3		350	Poapolathep et la. (2008)
	Europe	4	nd			Vendl et al. (2010)
	Europe	75			623	González et al. (2011)
	Europe	29	158	62	1670	Schollenberger et al. (1999)
	North America	2			100	Trucksess et al. (2010)
Wheat-based products						
Breakfast cereal	Europe	32	75	53	238	Schollenberger et al. (1999)
Breakfast cereal	Europe	27	130	157	437	Cano-Sancho et al. (2010)
Breakfast cereal	North America	4			400	Trucksess et al. (2010)
Breakfast cereal	North America	29	110		940	Roscoe et al. (2008)
Biscuits	Middle East	20	31		70	Scoubra et al. (2009)
Cakes	Middle East	20	60		100	Scoubra et al. (2009)
Crackers	North America	4			400	Trucksess et al. (2010)
Pretzels	North America	7			1200	Trucksess et al. (2010)
Biscuits	Asia	8	9		35	Ok et al. (2009)
Biscuits	Asia	70	23		791	Tanaka et al. (2010)

Table 2. Occurrence of DON in maize-based and oat-based products.

	Region of Purchase	# of Samples	Mean µg/kg	Median µg/kg	Max level µg/kg	Reference
Maize-based products						
Semolina	Europe	6	40	31	84	Schollengerger et al. (2005)
Flour	Europe	8	51	45	98	Schollengerger et al. (2005)
Breakfast cereal	Europe	6	70	52	142	Schollengerger et al. (2005)
Breakfast cereal	Europe	65	109	93	580	Cano-Sancho et al. (2010)
Breakfast cereal	Europe	55		45*	121	Castillo et al. (2008)
Breakfast cereal	Middle East	20	58		100	Scoubra et al. (2009)
Breakfast cereal	North America	34	30		420	Roscoe et al. (2008)
Breakfast cereal	Asia	18	8		36	Ok et al. (2009)
Dried corn	Africa	29	59		273	Njobeh et al. (2010)
Dried corn	Asia	82	130		807	Ok et al. (2009)
Sweet corn	Europe	72	114	114	139	Cano-Sancho et al. (2010)
Canned	Asia	25	nd			Ok et al. (2009)
Baked snacks	Europe	57		63*	132	Castillo et al. (2008)
Fried snacks	Europe	63		56*	80	Castillo et al. (2008)
Snacks	Europe	71	153	143	304	Cano-Sancho et al. (2010)
Oat-based Products						
Flakes	Europe	9	48	32	148	Schollenberger et al. (2005)
Bran	Europe	7	46	28	97	Schollenberger et al. (2005)
Breakfast cereal	North America	27	20		80	Roscoe et al. (2008)

Table 3. Occurrence of DON in infant foods.

Infant Food	Region of Purchase	# of Samples	Mean µg/kg	Median µg/kg	Max level µg/kg	Reference
Various	Europe	25	61	23	314	Schollenberger et al. (1999)
Oat based cereal	North America	53	32		90	Lombaert et al. (2003)
Barley based cereal	North America	50	150		980	Lombaert et al. (2003)
Biscuits	North America	24	45		120	Lombaert et al. (2003)
Biscuits	Asia	110	17		177	Tanaka et al. (2010)

Appendix B

Maximum levels for deoxynivalenol in cereal grains for various countries around the world

Country	Regulatory Authorities	Maximum Level
Armenia*	Supervision Service of Haypetstandard and Authorities of Health Sphere	• 0.7 ppm in wheat • 1 ppm in barley
Belarus*	Ministry of Public Health	• 1 ppm in barley • 0.7 ppm in wheat • in infant food not allowed
Canada	Health Canada	• 2 ppm uncleaned soft wheat intended for use in non-staple foods (under review) • 1ppm in uncleaned soft wheat for use in baby foods (under review)
China	Ministry of Health	• 1 ppm in wheat and wheat flour, maize and maize flour* • 1 ppm in barley, oatmeal and flour
Cuba*	Ministry of Public Health/ Instituto de Nutricion e Higiene de los Alimentos	• 0.3 ppm in imported cereals
European Union	European Commission	• 1.25 ppm in unprocessed cereals other than durum wheat, oats and maize • 1.75 ppm in unprocessed durum wheat, oats and maize • 0.75 ppm in cereals intended for direct human consumption, cereal flour (including maize flour, maize meal and maize grits, semolina), bran as end product marketed for direct human consumption and germ • 0.75 ppm in pasta (dry) • 0.5 ppm in bread (including small bakery wares), pastries, biscuits, cereal snacks and breakfast cereals • 0.2 ppm in processed cereal-based foods and baby foods for infants and young children
Iran, Islamic Republic of*	Institute of Standard and Industrial Research of the Islamic Republic of Iran; Ministry of Health and Medical Evaluation	• 1 ppm in barley, maize, rice and wheat
Japan	Ministry of Health, Labour and Welfare	• 1.1 ppm in unprocessed wheat
Norway	Norwegian Food Safety Authority	• Same as applied in the European Union
Russian Federation, The*	Ministry of Health	• 0.7 ppm in wheat • 1 ppm in barley
Singapore*	Agri-Food and Veterinary Authority	• Cereal and grain products (specific ML not given)
Switzerland*		• 1 ppm in cereal grains
Ukraine*	Ministry of Health Protection; State Department of Veterinary Medicine (Ministry of Agricultural Policy)	• 0.2 ppm grain-based baby food products; fruit-vegetable – dairy mixes for baby food • 0.5 ppm in wheat of other than hard strong varieties, flour, bread • 1 ppm in wheat of hard strong varieties; all seeds to be used for immediate human consumption and for processing into the products for human consumption; wheat middlings
United States of America	U.S. Food and Drug Administration (U.S. FDA)	• 1 ppm in finished wheat products (e.g. flour, bran and germ) for human consumption
Uruguay*	Ministerio de Salud Pública; Technological Laboratory of Uruguay; Ministerio de Ganaderiá Agricultura y Pesca	• 1 ppm in wheat flour and by-products

* As reported in Worldwide regulations for mycotoxins in food and feed in 2003 (FAO, 2004)