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Summary of Comments Received as part of Health Canada's 2010 Call for Data on Ochratoxin A

October 2012

Bureau of Chemical Safety
Food Directorate
Health Products and Food Branch

Canada

Table of Contents

Background

Ochratoxin A (OTA) is a toxic fungal metabolite that causes nephrotoxic, teratogenic, immunosuppressive and carcinogenic effects in a number of animal species. It has also been implicated in the development of a chronic kidney disease in humans known as Balkan Endemic Nephropathy. OTA occurs naturally in low concentrations in many foods, such as cereal-derived staples as well as other food commodities including grapes, raisins, wine, coffee and beer.

On August 29, 2008, the Bureau of Chemical Safety, within Health Canada's Food Directorate, sent pre-consultation letters to targeted stakeholder groups requesting input on Health Canada's proposed maximum levels for ochratoxin A (OTA) in foods. On March 2, 2009, the Food Directorate's Bureau of Chemical Safety published its *Information Document on Health Canada's proposed Maximum Limits (Standards) for the Presence of the Mycotoxin Ochratoxin A in Foods* on the Health Canada website, requesting further comments on this proposal from the larger stakeholder community. Comments were accepted until 12:00 a.m. EDT on June 1st, 2009. A Summary of the comments received on Health Canada's proposed maximum limits for OTA in certain foods, as well as Health Canada's responses, were posted on Health Canada's website in August 2010.

On December 9, 2009 the Bureau of Chemical Safety's Health risk assessment of ochratoxin A for all age-sex strata in a market economy was published on-line in the journal *Food Additives and Contaminants* (Volume 27, Issue 2, February 2010, pages 212-240). The article was made publicly available by Health Canada through a link on Health Canada's Natural Toxins web page in April 2010.

Following the closure of the online OTA consultation, Health Canada was made aware of more recent OTA occurrence data for cereal grains and cereal-derived products that would have been of relevance to the proposed maximum levels (MLs) for certain cereal commodities. As a result of the availability of such additional data, Health Canada initiated a 2010 Call for Data on Ochratoxin A, in which published and unpublished data on the occurrence of OTA in cereal grains and grain-based foods, as well as information on sampling plans and analytical methodologies to detect OTA in food and other matrices, were actively sought. The main goal of this Call for Data was to obtain information to assist in identifying priorities for the development of risk management strategies. The Call for Data opened on August 6, 2010 and comments were accepted until December 31, 2010.

Summary of Comments

Health Canada received input from various stakeholders representing the food industry and professional organizations, including:

- Canadian National Millers Association
- Canadian Wheat Board
- Grain Growers of Ontario

- Grain Millers, Inc.
- H.J. Heinz Company of Canada LP
- NeoVentures Biotechnology Inc.
- PepsiCo Foods/Quaker Oats Canada
- ProChem Consulting Services

The submission from NeoVentures Biotechnology Inc. informed Health Canada of a new commercially available analytical methodology for detecting OTA in a variety of food matrices that the company described as being simple and cost-effective.

No information on sampling plans was provided.

The Canadian National Millers Association, Canadian Wheat Board and the Grain Farmers of Ontario sponsored Cantox Health Sciences International to conduct a technical review of Health Canada's Health risk assessment of ochratoxin A for all age-sex strata in a market economy. While this technical review did not provide new occurrence data, the principal comments provided in the Cantox document are presented herein.

All other comments and data submitted were in relation to the proposed OTA MLs in unprocessed cereal grains and grain-based foods. Overall, the proposed MLs for unprocessed cereal grains and grain-based foods were generally not supported by those who submitted comments. Some new data was provided in summary format for unprocessed oats and various cereal flours that suggest higher concentrations of OTA than the data used by Health Canada in its Health risk assessment of ochratoxin A for all age-sex strata in a market economy. Data illustrating the variability in analytical results for OTA within and between analytical test methodologies was also submitted. It was requested that Health Canada, with industry involvement, update its human health risk assessment for OTA and ensure that contemporary research on OTA formation, occurrence and prevention is considered before adopting MLs for OTA.

Comments and questions concerning compliance monitoring and enforcement of MLs should be forwarded to the Canadian Food Inspection Agency (CFIA).

Key comments and information that were submitted as part of the 2010 Call for Data on OTA are summarized below. Although many of the comments received were not a direct response to Health Canada's Call for Data on OTA, they have nonetheless been responded to below.

1) Data submitted in response to the Call for Data on OTA

The submitted data, as described below, is being taken into consideration. Although the 2010 Call for Data on OTA is closed, new information and data can be submitted at any time to the Food Directorate's Bureau of Chemical Safety at bcs-bipc@hc-sc.gc.ca.

Question / Comment	Health Canada's Response
Summary data collected by Canadian milling establishments between 2007 and 2010 on the OTA levels in unprocessed oats and oat flour were submitted. On average, 26% of oat flour (range 6 to 43%) would not be in compliance with the proposed ML of 3 ng/g. Twenty-four percent (24%) of the unprocessed oat samples would not be in compliance with the proposed ML of 5 ng/g. Furthermore, the data submitted for unprocessed oats delivered to Canadian milling establishments had a 5-fold higher incidence of containing OTA in excess of 5 ng/g compared to data for unprocessed oats from export cargoes collected by the Canadian Grain Commission between 1994/5 and 2008/9.	The data submitted in response to Health Canada's Call for Data on OTA suggests higher concentrations of OTA in unprocessed oats and oat-based products than those identified in Health Canada's Health Risk Assessment (HRA), where 15% of the unprocessed oat samples exceeded 3 ng/g OTA and < 6% were greater than 5 ng/g. Additionally, < 2% of the oat-based breakfast cereals exceeded the proposed ML of 3 ng/g. Health Canada has reviewed other datasets for OTA in oats and oat-based foods that have become available since Health Canada's HRA was completed. In a dataset for OTA in rolled oats, oatmeal and oat bran purchased at retail from several locations in central and eastern Canada, 5% of the samples had an OTA concentration greater than the proposed ML of 3 ng/g.
The OTA concentrations in oat, wheat, rice, barley, rye and some other types of flour destined for use in infant cereals were submitted. Approximately 50% of the flour results were greater than the proposed 0.5 ng/g ML for OTA in infant cereals, whose main ingredient is flour. Oat and durum wheat flours accounted for the majority of samples exceeding the proposed ML.	In a dataset for oat flour destined for use in infant cereals that was submitted as part of the Call for Data, the mean OTA concentration was 1.7 ng/g. This data would suggest that infant cereals that contain large amounts of oat or durum wheat flours may have difficulty consistently meeting the proposed ML for infant cereals of 0.5 ng/g. In Health Canada's HRA, < 9% of samples from commercially available infant cereals exceeded the proposed ML of 0.5 ng/g, and most of these were "mixed" cereals, which typically contain significant amounts of oat and wheat flours. In a dataset made available after Health Canada's HRA, 28% of oat-based infant cereal samples exceeded the proposed ML of 0.5 ng/g for cereal-based infant foods. Health Canada will re-examine the available datasets and further consider whether the proposed MLs are still appropriate.

2) Health Canada's Health risk assessment of ochratoxin A for all age-sex strata in a market economy (hereafter referred to as "HRA")

2a) Hazard Identification and Characterization

Question/Comment	Health Canada's Response
The discussion of Balkan Endemic Nephropathy (BEN) was limited and did not include recent research regarding the potential role of aristolochic acid in this condition.	At the time the HRA was drafted, most literature supported a possible link between OTA and BEN. A reassessment of the aetiology of BEN has been conducted, taking into consideration all recent research on aristolochic acid. While a strong case can be made for aristolochic acid exposure being a risk factor in the development of BEN, there is no unanimous agreement that it is the only risk factor, therefore, a role for OTA in the aetiology of BEN cannot be entirely ruled out at this time.
Health Canada has not been able to provide any evidence of a link between OTA and human health issues in Canada nor is the department aware of health improvements in countries that have implemented OTA regulations or controls.	The Food Directorate's Bureau of Chemical Safety is fulfilling its mandate to manage the health-related risks posed by contaminants in the Canadian food supply. It is difficult to demonstrate measurable health improvements as a result of controls on a single environmental contaminant such as OTA, since there are various risk factors for kidney disease and kidney cancer. However, 1995 to 2005 survey data on blood OTA levels in humans, mainly from Europe, demonstrate a possible decrease in blood OTA values compared to earlier surveys: mean blood OTA ranged from 0.1 ng/ml to 40 ng/ml in surveys conducted between 1977 and 1995 and from 0.15 ng/ml to 0.56 ng/ml for those conducted between 1995 and 2005. EFSA (2006)† also commented that a tendency for a decline in plasma concentrations in recent years can be observed which they attributed "most likely to an increased awareness of the potential adverse health effects from mycotoxins, and to the preventive measures (establishing of maximal permissible levels in food commodities) taken by various countries." Several European countries introduced MLs for OTA in foods in the 1990's, while the European Union established MLs for OTA in raw cereal grains, cereal-derived products, directly consumed cereal grains and dried vine fruit in 2002 and for baby foods and cereal-based foods for infants and young children in 2004.
All available toxicological data was not considered, particularly data regarding genotoxicity and gender and species differences in sensitivity, related to OTA's mode of action. The adoption of the "default" position that OTA be regulated as a non-threshold carcinogen is overly conservative and cannot be scientifically justified.	While the HRA did not discuss all available data regarding OTA's mode of action, it summarised the information considered pertinent to the assessment at the time it was drafted. The Food Directorate's Bureau of Chemical Safety has reviewed a number of recent research studies including those mentioned in the Cantox Health Sciences International report. To date, there is no evidence that resolves whether OTA causes cancer strictly through a genotoxic or non-genotoxic mechanism. Studies examining the sensitivity of the

Question/Comment	Health Canada's Response
	male rat to OTA's carcinogenic effects have not identified a species and sex specific mechanism of action that would not be applicable to human risk assessment. Since 1993, the International Agency for Research on Cancer has classified OTA as possibly carcinogenic to humans (Group 2B)*. In addition, the US National Toxicology Program, in its latest *Report on Carcinogens*ŧ, reiterates its 1991 conclusion that OTA is reasonably anticipated to be a human carcinogen based on the results of animal studies.
The decision to regulate OTA as a non-threshold carcinogen is not consistent with the approach taken by the European Food Safety Authority (EFSA) and the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA).	EFSA (2006)† and JECFA (2008)‡, while recognizing there remained some uncertainty regarding OTA's mode of action, both adopted a threshold-based approach and derived toxicological references values for OTA. Health Canada considered that the uncertainty regarding OTA's mode of action was sufficient to adopt the more conservative, precautionary approach of treating OTA as a non-threshold (genotoxic) carcinogen. Currently, there is insufficient information to discount the possibility that OTA operates through a genotoxic mechanism and therefore applying the precautionary approach remains valid.
The use of the dose at which 5% of male rats would have renal tumours (TD_{05}) and the negligible cancer risk intake (NCRI) appears to be a Health Canada-specific methodology.	The TD_{05} was derived using a multi-stage dose-response model in a process similar to that used to derive a benchmark dose. The TD_{05} was used as a point of departure to derive margins of exposure (MOEs) and to determine the NCRI, the exposure associated with a 1 in 100,000 cancer risk. The TD_{05} value of 19.6 µg/kg body weight-day used in the assessment is comparable to the benchmark dose ($BMDL_{05}$) value of 15 µg/kg body weight-day determined using the more conventional benchmark dose modelling approach. MOEs calculated using the TD_{05} or $BMDL_{05}$ would be comparable.

*International Agency for Research on Cancer (IARC). 1993. Ochratoxin A. *IARC Monographs Volume* 56:489-521.

ŧNational Toxicology Program. 2011. *Report on Carcinogens*. Twelfth Edition. US Department of Health and Human Services, Public Health Service, National Toxicology Program. pp 335-337.

†European Food Safety Authority (EFSA). 2006. Opinion of the Scientific Panel on Contaminants in the Food Chain on a Request from the Commission Related to Ochratoxin A in Food. *EFSA J*. 365:1-56.

‡JECFA. 2008. Ochratoxin A (Addendum). In: *Safety Evaluation of Certain Food Additives and Contaminants*. (Sixty-eighth meeting of the Joint FAO/WHO Expert Committee on Food Additives.) WHO Food Additive Series No. 59. pp.357-429.

2 b) Exposure Assessment

Question/Comment	Health Canada's Response
There is limited historical and contemporary data available on the incidence of OTA in unprocessed cereal grains that are further processed in Canada (as opposed to unprocessed grain that is exported from Canada). Therefore, the OTA levels in Canadian-processed grains that can be achieved under usual industry operating conditions using best practices and commercially available technologies and that are As Low As Reasonably Achievable (ALARA) are unknown.	Any new occurrence data for OTA in unprocessed cereal grains delivered to Canadian processing facilities can be submitted to the Food Directorate's Bureau of Chemical Safety and will be assessed for its relevance to the risk assessment and risk management strategy for OTA.
The processing factor of 1.0 that was applied to unprocessed oats is incorrect. A processing factor of 0.3 for groats (bran, endosperm, germ) is more realistic as oats are the only cereal grain under consideration that arrive at the processing mill with their hull on. The removal of the oat hull can significantly reduce mycotoxin levels at the initial processing stage.	Health Canada recognizes that applying a processing factor of 1.0 to unprocessed oats in its HRA may not accurately reflect the potential removal of OTA as a result of the dehulling process. Nonetheless, modifying the processing factor for unprocessed oats in the HRA would not result in a change to the risk management strategy for OTA in oats or oat-based products.
The processing factors used for the different wheat fractions were criticised for being overly conservative in some cases (i.e. durum wheat) and in other instances not conservative enough (i.e. wheat bran).	Upper and lower bound processing factors were employed in Health Canada's HRA in order to estimate the most likely range of OTA concentrations in milled cereal grain products. Any new information available on processing factors that was obtained since the HRA was conducted can be submitted to Health Canada for evaluation to determine whether it impacts the results of the HRA. It should be noted that no new information specific to processing factors for wheat was submitted to Health Canada as part of its Call for Data on OTA.
The OTA occurrence data used in the HRA for oats was based on oats grown, stored and exported from Western Canada while most consumed domestically are sourced almost exclusively from Ontario and Québec.	The HRA also employed Health Canada data for oat-based breakfast cereals collected from retail locations throughout Canada. Data for OTA in rolled oats, oatmeal and oat bran from several locations in central and eastern Canada that became available after the HRA was completed was comparable to the datasets employed in the HRA.
The broad range of food products influenced by the proposed MLs does not appear to have been fully considered by Health Canada in its HRA.	Thirty-seven food commodities were included in the HRA. Many of these commodities were used on an ingredient basis (e.g. hard wheat, barley) and combined with recipe information to enable the estimation of total exposure to OTA in a wide variety of foods (e.g. beer-battered fish, beef barley soup).
The OTA data for cereal-based foods was collected between 1997 and 2006. This data does not reflect that the formulation of packaged foods, including those intended	The inclusion of more whole and multi-grain ingredients in foods would potentially increase exposure to OTA. However, in the 83 samples of multi-grain breakfast cereal

Question/Comment	Health Canada's Response
for infants and toddlers, has changed significantly in the past decade to include more whole grain and multi-grain ingredients.	utilized in the Food Directorate's HRA, none exceeded the proposed ML of 3 ng/g and the average OTA concentration over all samples was 0.25 ng/g.
Recognizing that Health Canada will be bringing forward proposals for other mycotoxins in the future, national dietary intake surveys that collect information relevant to the risk assessment of mycotoxins should be completed every few years. Regular food consumption surveys would provide further information on the increasing trend towards whole and multi-grain food consumption in Canada	The most recent comprehensive survey cataloguing the detailed food consumption habits of Canadians is the Canadian Community Health Survey (CCHS) - Cycle 2.2 on Nutrition (Statistics Canada, 2004)‡. This survey contains a more than sufficient level of detail for health risk assessments involving mycotoxins. Since Cycle 2.2 was completed in 2004, detailed food consumption information suitable for use in quantitative health risk assessments has not been collected through the CCHS or any other survey known to Health Canada. Comprehensive national food consumption surveys are highly complex and take years to complete. Evidence of this lies in the fact that other than the CCHS, only two prior comprehensive Canadian food consumption surveys exist, one conducted in the 1990's and the other in the 1970's. The expertise for designing, executing and analyzing the data associated with a national dietary survey does not reside in Health Canada, but rather with Statistics Canada. Until the next national food consumption survey is conducted by Statistics Canada, Health Canada will continue to rely on the CCHS – Cycle 2.2 on Nutrition.
Dietary intake surveys should be made publicly accessible so as to inform future industry-government consultations.	Statistics Canada should be contacted for any questions relating to the Canadian Community Health Survey (CCHS) - Cycle 2.2 on Nutrition (Statistics Canada, 2004)‡, including how to access dietary intake information. A formal agreement between Statistics Canada and Health Canada enables those Health Canada employees with the necessary approvals access to the raw data files from the CCHS – Cycle 2.2 on Nutrition.

‡Statistics Canada, 2004. Canadian Community Health Survey--Nutrition (CCHS). Detailed information for 2004 (Cycle 2.2). Ottawa (ON): Statistics Canada.

2 c) Risk Characterization

Question/Comment	Health Canada's Response
Lifetime cancer risk rather than life stage cancer risk would have indicated that an increased risk of adverse effects from OTA is unsubstantiated.	While not presented in Health Canada's published health risk assessment, lifetime (0 to 71+ years of age) average OTA intakes were determined using the full probabilistic exposure model. The OTA intakes for consumers whose food consumption patterns result in high exposures (90^{th} percentile) exceed the NCRI. Based on the Margins of exposures (MOEs), which are less than 5000, risk reduction strategies are considered appropriate.
The HRA clearly states that applying European Commission (EC) MLs was of little or no benefit in reducing OTA exposure to the population sub-group Health Canada concluded to be at risk of adverse health outcomes, children < 4 years. Therefore, there appears to be no merit in proceeding to adopt the proposed MLs for OTA.	The probabilistic exposure modeling indicated that average OTA exposures for children from 1 to 4 years of age approximated the NCRI of 4 ng/kg body weight per day, with higher percentile exposures exceeding the NCRI. While the HRA noted that the higher exposures in children could be attributed to higher food intake relative to their body weight, there was also concern that short-term exposure to higher levels of OTA during childhood could have long-term adverse health effects. This approach is consistent with the US Environmental Protection Agency's (EPA) *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens**, which proposes adjustment factors to account for greater susceptibility for development of tumours following early life exposures. In addition, acute studies in rats have demonstrated that the neonate is more sensitive to high doses of OTA (Skaug et al., 2001)†. The EC MLs, while leading to higher MOEs in general, would not result in MOEs greater than 5000 in young children who regularly consume products known to frequently contain high levels of OTA. While recognizing that it may not be possible to totally eliminate OTA from the diet, the proposed MLs would be expected, over time, to lower OTA exposures in most, if not all, young children to levels posing less of a health concern.

*US Environmental Protection Agency. (EPA). 2005. *Supplemental guidance for assessing susceptibility from early-life exposure to carcinogens.* US Environmental Protection Agency, Washington DC. EPA /630/R-03/003F.

†Skuag MA, Helland I, Sovoll K, Saugstad OD. 2001. Presence of ochratoxin A in human milk in relation to dietary intake. *Food Additives and Contaminants* 18:321-327.,

3) Revision/Update of Health Canada's Health Risk Assessment for OTA

Question/Comment	Health Canada's Response
Will Health Canada, with industry involvement, use the information and data that has been submitted as part of the Call for Data on OTA, along with forthcoming data from planned research projects, to update its human health risk assessment for OTA?	As part of its ongoing activities, the Food Directorate's Bureau of Chemical Safety, evaluates new data and information as it becomes available to determine its relevance to risk assessments and any related risk management strategies. Health Canada welcomes data and information from external stakeholders that can assist in ensuring that all relevant information is taken into consideration. In this regard, Health Canada has considered all data and information submitted as part of the Call for Data, as well as new research available in the published literature. At this time, Health Canada does not consider this new information to be sufficient to modify its entire HRA. However, new data and information will be considered prior to the formal implementation of MLs for OTA in foods (see the Next Steps section).

4) Risk Management Approach

Question/Comment	Health Canada's Response
Why was such a conservative risk management approach taken for OTA, a natural contaminant that cannot be entirely eradicated? It contrasts the approach used to establish the drinking water guideline for arsenic, which is higher than a strictly health-based guideline would be due to the prohibitively high treatment costs and the small additional health protection associated with implementing the strictly health-based guideline.	The principle fungi that produce OTA are not usually significant in the growing plant. Rather, the fungi can grow and produce OTA under storage conditions. The principles of good storage practices such as preventing the infection of the cereal by OTA-producing fungi and avoiding conditions that are conducive to mould growth can reduce the formation of OTA in cereals. In comparison, the occurrence of arsenic in drinking water resulting from its natural presence in mineral deposits and rocks cannot be prevented. Health Canada's risk management decision to establish a maximum acceptable concentration for arsenic above the health-based guideline value was consistent with international guidelines for arsenic in drinking water.
A risk management strategy for OTA, DON and other mycotoxins in food that is proportionate to the demonstrated risk, can be achieved under usual industry operating conditions using best practices and commercially available technologies and imposes the least possible cost upon the grain industry is required. These principles are outlined in the Government of Canada's 2007 publication, *Cabinet Directive on Streamlining Regulation*.	The 2010 Call for Data on OTA was intended to encourage industry to provide data that addresses the question of what is technologically achievable based on current industry practices. The *Cabinet Directive on Streamlining Regulation* applies to the development, implementation, evaluation and review of regulations. In its web-based consultation on the proposed MLs for OTA in foods, Health Canada did not propose setting out regulatory tolerances for OTA in Division 15 of the *Food and Drug Regulations*.

Question/Comment	Health Canada's Response
Management of OTA to a precise numeric level should not be the regulatory approach taken because of the high degree of variability introduced during sampling, sample preparation and sample analysis of OTA in cereal grains and grain-based commodities. The business risk imposed by numeric MLs is unacceptable when compared to the potential health benefits of reducing exposure to OTA through the introduction of the proposed MLs.	The importance of appropriate sampling procedures when analysing mycotoxins is recognised. The establishment of any MLs for OTA may also require the concurrent establishment of an appropriate sampling plan, depending on the commodity. The development of the proposed MLs involved consideration of both the health objective as well as the ability of industry to achieve those levels.
There is support to implement voluntary reference values for OTA in raw cereal grains and include standards for finished food products in the *Food and Drug Regulations*, if such standards are necessary.	As the intent of the proposed MLs is to reduce overall food-based exposure to OTA, following further consultation with stakeholders, Health Canada is now recommending that the previous ML suggested for raw cereal commodities not be formally adopted but would be used as an industry guidance value (see Next Steps).

5) Comments on the Proposed MLs

Questions/Comments	Health Canada's Response
The proposed ML of 5 ng/g for unprocessed ('covered') oats is too low; a ML of 10 ng/g would be more realistic. Oats are the only cereal grain under consideration that arrive at the processing mill in raw/unprocessed form with their hull on ('covered' oats). If OTA behaves like other mycotoxins, the majority (70-90%) of OTA is contained in the oat hull.	In Health Canada's HRA, < 6% of the unprocessed oat samples exceeded the proposed ML for unprocessed cereal grains of 5 ng/g. However, Health Canada is now recommending that the ML suggested for raw cereal commodities be used as an industry guidance value and not formally adopted. .
The proposed ML for wheat bran should also apply to all other derived cereal brans, including oat brans, corn brans, etc.	Health Canada is considering which cereal brans should be included in the proposed ML for wheat bran of 7 ng/g. To address this issue, Health Canada is working with the CFIA to conduct a targeted survey of cereal brans. No data for cereal brans was submitted as part of Health Canada's Call for Data on OTA.
The proposed guideline value of 5 ng/g OTA in unprocessed cereal grains and the proposed ML of 7 ng/g wheat bran are incompatible with, and not enabling of, the proposed MLs for whole and multi-grain cereal-derived products intended for the general population (3 ng/g) and infants (0.5 ng/g).	Health Canada agrees that if unprocessed cereal grains and wheat bran consistently contain OTA levels at the proposed guideline value of 5 ng/g and proposed ML of 7 ng/g, respectively, whole and multi-grain foods may have difficulty meeting the proposed MLs for cereal-derived products. However, this notion was not supported based on the occurrence data used in Health Canada's HRA. In the data used in the HRA, the average OTA concentrations in unprocessed cereal grains and cereal-based finished foods are several-fold lower than the proposed MLs and only a small proportion of the samples (<9% in all cases) contained OTA concentrations above the proposed MLs.

Questions/Comments	Health Canada's Response
In order for products based on whole or multi-grain ingredients, particularly those intended for infants and young children, to comply with Health Canada's proposed MLs, buyers in the cereal grain supply chain will impose lower MLs into product procurement specifications.	The majority of the lower MLs that buyers may incorporate into product procurement specifications are still higher than the typical OTA concentrations in unprocessed cereal grains and grain-based products based on the data utilized in the HRA. Buyers in the cereal grain supply chain are free to take the actions that they feel most appropriate to meet any proposed MLs for OTA in cereal-based foods and food ingredients, based on their own product recipes.

6) Legal Implications of MLs listed inside and outside of the *Food and Drug Regulations*

Question/Comment	Health Canada's Response
Industry stakeholders affected by the proposed MLs need to better understand the difference between regulatory and non-regulatory MLs in terms of legal implication and compliance and enforcement powers.	In Canada, limits on the levels of contaminants in retail foods can be established as regulatory tolerances, which are found the *Food and Drug Regulations*, or as standards or MLs, which are available on Health Canada's website. Tolerances set out in Division 15 of the *Food and Drug Regulations* are introduced through regulatory amendments which must be approved by the Governor in Council and, as regulations, they are a form of law. Under the *Food and Drugs Act*, noncompliance with the regulations would be considered a criminal offense. Similar to tolerances, standards and MLs represent a maximum tolerable concentration of a contaminant in food established by the Food Directorate's Bureau of Chemical Safety, on the basis of a health risk assessment. While not set out in law, standards and MLs can provide a basis for interpreting Part I, Section 4(1)(a) of the *Food and Drugs Act*, for compliance and enforcement purposes. In general, when CFIA detects food contaminant levels in excess of any regulatory tolerances, standards or MLs, Health Canada would be requested to conduct a health risk assessment specific to that food and the contaminant level detected. The results of the assessment are considered by the CFIA when it determines the most appropriate risk management approach to be taken.
Part I, Section 4(1)(a) of the *Food and Drugs Act* states that "no person shall sell an article of food that has in or on it any poisonous or harmful substance". It is unfair to apply Section 4(1)(a) of the *Act* to OTA in cereal-based foods and food ingredients because OTA is naturally occurring and it is not removable through processing.	Part 1, Section 4(1)(a) of the *Food and Drugs Act* provides the basis for taking enforcement actions when foods contain a poisonous or harmful substance whether intentionally added or present from anthropogenic or natural sources at a level that would pose a safety concern to human health. The Food Directorate's approach to establishing MLs for contaminants from natural sources is not new or unique to OTA. MLs currently exist for several naturally-occurring substances such as mercury, glycoalkaloids and various seafood toxins. In these cases, stakeholders in the food

Question/Comment	Health Canada's Response
	supply chain have no control over the occurrence of these potentially hazardous substances in their products, although in the case of glycoalkaloids, poor storage conditions can increase levels. With respect to OTA, although research demonstrates that it is not removable through processing, there is data to support that its formation can be minimized and its contamination of grain controlled through a variety of best practices.

7) Implementation and enforcement of the proposed MLs

Question/Comment	Health Canada's Response
What level of compliance with a proposed ML does Health Canada consider acceptable? If not 100%, then what?	Standards or MLs are developed to address whether or not a product may be potentially hazardous/harmful to the consumer. In this sense, the ML will provide the CFIA with a level below which HC has already determined that no hazard exists. If the ML is exceeded, the CFIA will request a safety assessment to be conducted by Health Canada in order to determine whether the product poses a health risk to the consumer. If a safety concern is identified, appropriate action will be taken by the CFIA to protect the consumer. If no safety concern is identified, the product will be considered to be compliant with the *Act*. The objective is that 100% of the products on the market meet their respective ML. However, Health Canada realises that this is not always practical, therefore when products are found to contain contaminant levels higher than an existing ML, they are assessed on a case-by-case basis giving consideration to various factors that may impact exposure to the contaminant.
Will Health Canada provide clear, detailed guidance on sample collection that includes information on sample quantity, blending, grinding, compositing, etc. and is practically achievable by industry based on cost and the current functioning of the cereal value chain?	The extent of testing activities carried out by industry is a business decision left to the industry sector. The CFIA's sampling and testing protocol used to test and monitor cereal-based products are based on the applicable CODEX Alimentarius codes of practice for the prevention and reduction of OTA in foodstuffs. It is important to note that the CFIA does not test whole or unprocessed grains and that the Agency has limited it's testing activities to milled or manufactured products. The CFIA is aware of the ongoing collaborative efforts between the various partners in the grain sector, the Canadian Grain Commission and Agriculture and Agri-Food Canada. The CFIA will consider the results of this collaborative work and adapt their sampling and testing protocols if required.

Question/Comment	Health Canada's Response
Industry members have expressed concerns that no rapid, accurate, reliable and affordable analytical methods for OTA are available to the grain industry.	There are many official and validated methods for OTA analysis in foods. Most of them use liquid chromatography and fluorescence detection (LC-FD) and immunoaffinity columns (IAC) for sample clean-up. This methodology is precise, accurate, reliable and affordable. Furthermore, automation capabilities will significantly improve the cost-effectiveness. Other less sophisticated techniques are sensitive but require confirmation by LC-FD. Novel technologies, allowing for rapid, portable detection, are not currently available. Health Canada understands that there is active research in this area and that new analytical technologies that meet the needs of industry may be forthcoming.
The proposed MLs will necessitate changes to grain production and storage practices as well as handling practices for milled grain ingredients throughout the food supply chain which will add significantly to the cost incurred by cereal processors and manufacturers of cereal-based foods.	Health Canada identified a potential safety concern based on the presence of OTA in cereal-based foods available in Canada and subsequently proposed MLs in order to manage the associated health risk. In order to further reduce the levels of OTA in unprocessed cereal grains and cereal-based foods, Health Canada recognizes that costs may be incurred by stakeholders throughout the cereal value chain. Health Canada's 2010 Call for Data on OTA was intended to help gather a larger database of OTA occurrence data so that levels that are currently technologically feasible could be identified.
Regulatory misalignment with our most important trading partner of processed foods, the United States, could have serious financial consequences to the Canadian food industry.	Significant amounts of unprocessed cereal grains are also exported from Canada to the European Union (EU) annually. The OTA MLs that Health Canada has proposed align with the OTA MLs of the EU. The United States Food and Drug Administration is currently monitoring levels of OTA in domestic and imported food supplies for the purpose of determining whether the risk posed by OTA warrants implementation of regulatory control measures.

8) New and ongoing research on OTA

Question/Comment	Health Canada's Response
The risk management strategy would require changes in the grain production and storage practices of Canadian grain producers and marketers and a significant amount of research is needed to determine best practices in this regard. To date, there is little evidence to support the assumption that changes in grain storage practices would be effective in reducing OTA contamination.	Some research is available indicating which conditions favour the growth of OTA-producing fungi and their production of this mycotoxin and consequently on how contamination of cereal grains can be minimizing. Industry has communicated that all available best practices, particularly those relating to on-farm storage, are not being consistently applied throughout Canada at the present time. As such, Health Canada is of the opinion that there is still potential for the OTA contamination of cereal grains to be reduced given the current state of knowledge.

Question/Comment	Health Canada's Response
There are a number of industry-led research projects that are being conducted through collaborative efforts of industry, academia and several federal government partners who are researching various aspects of OTA formation, occurrence, detection and prevention. These projects are planned for the period of time spanning December 2010 to mid-2014.	Health Canada is supportive of the ongoing research efforts relating to minimizing OTA in cereal grains and cereal-derived foods and would evaluate any new data and information for its relevance to the risk assessment and risk management strategy for OTA in foods.

9) Public Communication

Question/Comment	Health Canada's Response
Public communication regarding the health concerns presented by OTA and other mycotoxins should not create confusion or erode hard won and still growing consumer preference for whole and multi-grain foods.	Health Canada will work to ensure that any written or verbal communication regarding OTA and other mycotoxins accurately and clearly communicates health-related information to Canadians, within the context of the health benefits of eating a balanced diet, as per advice in *Eating Well with Canada's Food Guide*.

Next Steps

Health Canada has reviewed the comments, information and data submitted as part of the 2010 Call for Data on OTA. This work also involved the review of the Cantox Health Sciences International report submitted under the 2010 Call for Data on OTA, as well as additional toxicological studies published since the preparation of Health Canada's HRA. Research indicates that OTA has both genotoxic and non-genotoxic effects at the cellular level. However, the mechanism by which OTA causes cancer has not been fully elucidated. There is currently insufficient evidence to discount that OTA may induce cancer through a genotoxic (non-threshold) mechanism. Consequently, applying the precautionary approach of characterizing OTA as a genotoxic carcinogen remains valid. While the male rat used in these toxicological studies appears particularly sensitive to OTA's carcinogenic effect, to date research has not identified a gender or species-specific mechanism to account for this sensitivity. Therefore, it remains appropriate to use the male rat data when characterizing the hazard to humans caused by OTA. Based on its review of the recent toxicological data, Health Canada does not consider that a revision of the hazard identification and hazard characterisation components of its HRA is warranted at this time.

Although standards or MLs are still considered to be an appropriate risk management approach for OTA in foods, due to questions about the achievability of some of the proposed MLs in certain commodities, specifically raw oats and oat-based infant cereals, Health Canada will not formally implement any of the proposed MLs for OTA in foods at this time. Instead, Health Canada's next steps with respect to the risk management of OTA are:

- Evaluate data from more recent surveillance work by Health Canada, the CFIA, and the Canadian Grain Commission;

- Consider results from the on-going research being conducted by the Canada Industry-Government Working Group on Mycotoxins on OTA occurrence and management, as well as any additional OTA occurrence data submitted by stakeholders; and
- Conduct HRAs on a case-by-case basis for any elevated or unexpected surveillance results.

Upon the review of additional OTA occurrence data and other relevant information, Health Canada will finalize a decision regarding the risk management approach for OTA in foods. However, until such time, the MLs for OTA in foods will remain in "proposed" status.

Health Canada is also considering that the proposed ML for OTA in unprocessed cereal grains of 5ng/g would be put forth as a guidance value to industry and not as a tolerance in the *Food and Drug Regulations.*

Appendix 1-
Proposed Guidance Value and Maximum Levels for OTA in Foods

Health Canada's proposed guidance value for OTA in raw/unprocessed cereal grains and proposed MLs for OTA in foods are provided below.

Proposed Guidance Value for OTA in Foods

Food	Proposed guidance value for OTA
Raw/unprocessed cereal grains (i.e., wheat[1], barley, oats, rice)	5 ng/g

Proposed Standards/Maximum Levels (ML) for OTA in Foods

Food	Proposed standard/maximum level for OTA
Wheat bran[2]	7 ng/g
Directly consumed cereal grains (e.g. bulgur wheat, rice, oats, pearled barley) and cereal-derived products (e.g. flour; finished foods such as bread and breakfast cereals)	3 ng/g
Grape juice	2 ng/g
Dried vine fruit (e.g., raisins)	10 ng/g
Infant formulas	0.5 ng/g
Cereal-based foods for infants and young children	0.5 ng/g

[1]The ML for raw wheat is intended to cover all common varieties of wheat, including kamut, spelt, and triticale.
[2]The initial focus is on wheat bran but bran fractions of other cereal grains are being considered by Health Canada.