Article

The MYCOTOX CHARTER: Increased Awareness for Harmonized Research on and Regulation of Mycotoxins Worldwide

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**Abstract:** Mycotoxins are major food contaminants affecting global food security, especially in low and middle income countries. The EU funded project, MycoKey, focuses on “Integrated and innovative key actions for mycotoxin management in the food and feed chains” and the right to food safety through mycotoxin management and regulation, which is fundamental to minimizing the differential access to safe and sufficient food worldwide. As part of the MycoKey project, a Mycotoxin Charter (charter.mycokey.eu) was launched to share the need for global harmonization of mycotoxin legislation and policies and to minimize human and animal exposure worldwide with particular attention to less developed countries with little effective regulation. All suppliers, participants and beneficiaries of the food supply chain, *e.g.*, farmers, consumers, stakeholders, researchers, members of civil society, and government, *etc.*, are invited to sign this charter and to support this initiative.

**Keywords:** Consumers, Education and Outreach, Food safety, Food production, Food security, Health risks, Sustainable Development Goals, Trade

**Key** **Contribution:** The Mycotox Charter provides a globally applicable statement for food suppliers and consumers on mycotoxin management that enhances food and feed safety along the supply and consumption chains.

1. Introduction

Food safety is a concern of the general public and governments worldwide. Despite this, the serious problem of mycotoxin contamination of staple foods is a generally overlooked. Fungi that damage crops in the field or in storage produce a number of very poisonous compounds that are regulated in food and feed. Mycotoxins regulated –and most commonly reported- in most countries include aflatoxin, fumonisin, deoxynivalenol, ochratoxin and zearalenone (Lee & Ryu 2017; Pitt et al. 2012). A number of other compounds that are regulated in some jurisdictions including ergot alkaloids, patulin and T-2 /HT-2 toxins (Miller 2016; van Egmond et al. 2007).

In the fully developed market economies, these problems are generally invisible but their management adds a considerable economic burden to agriculture and consumer alike. These costs include sampling and analytical costs but also the larger costs of embargoed shipments of grain as the purchase of replacement grain. Destroying non-compliant product, particularly when facing a recall is very expensive not least because positive impressions of the brand can be lost. A less obvious cost can be that a grain-producing region to be seen as an unreliable supplier of quality grain. This forces food companies to create a new supply chain from a different region (Miller et al. 2014). Most information is available for the USA but it is reasonable to anticipate that the information is broadly similar to many other agricultural economies. The cost of mycotoxin contamination in the U.S. economy was estimated to be between $2 and $3 billion per year (Vardon et al. 2018). Based on data from 2016-2017, the estimated cost of mycotoxins sampling and analysis in the USA and Canada including for large scale ethanol plants was $US200-500 million depending on the year (Miller, unpublished data). The majority of this cost is visited on farmers. Although mycotoxin exposures are believed not to affect directly health in western Europe, Canada and the USA, increased costs of food, especially for the most economically disadvantaged can prevent people from purchasing health grain based products to cheaper fast food.

Aflatoxin B1, is commonly found in maize and groundnuts grown in tropical and subtropical regions. Under conditions of exposure, aflatoxin B1 causes acute, often fatal, toxicosis mainly in children, is associated with child stunting and is a potent liver carcinogen (JECFA 2017; McMillan et al. 2018; Wild et al. 2015). In countries with chronic aflatoxin contamination of maize, animal production, notably poultry is severely reduced. This results in less available protein as well as reduced milk production (and lower milk qualityy in the diet (JECFA 2017; Pitt et al. 2012).

For more than six decades, aflatoxin contamination has been studied in Africa. Despite this, more than 500 million Africans are exposed at multiples of acceptable limits (Wild et al. 2015) and progress remains slow. Poor awareness about aflatoxins, appropriate control measures to control contamination in the field and in storage, and the negative health effects of aflatoxin consumption are reported in most African countries. In Africa, grains contribute about 46% of the total energy intake, this figure may even be higher in rural Sub-Saharan Africa (SSA), where maize and tubers and roots are virtually the sources of nutrition. This over dependence on a few crops in rural Africa is a major reason for the high AF exposure for many the continent (Wild et al. 2015).

When corn is grown under warm and dry conditions or under conditions of insect stress, the mycotoxin fumonisin is commonly present in maize and maize products. With sufficient exposure, fumonisin B1 causes equine leukoencephalomalacia, a typically fatal brain disease in horses and other equines. At very high exposures, pulmonary edema can occur in swine. Fumonisin causes liver or kidney cancer in multiple rodent species and strains (JECFA 2017; Wild et al. 2015). The role of fumonisins in human disease remains unresolved. From studies conducted in the 1950-1990, the consumption of corn highly contaminated by fumonisin has been associated with high rates of esophageal cancer in Italy and the former Transkei in South Africa (IARC 1993). Based on animal studies, fumonisin exposure may result in neural tube defects (JECFA 2017). There is now good evidence that fumonisin exposure can result in childhood stunting (Chen et al. 2018; JECFA 2017; Kimanya et al. 2010; Shirima et al. 2015).

In much of Africa as well as parts of Central America, co-exposure to both aflatoxin and fumonisin is common (JECFA 2017; Wild et al. 2015). In laboratory animals, co-exposure suggests an additive or synergistic effect of fumonisin and aflatoxin co-exposure in the development of hepatocellular carcinoma (JECFA 2017; Qian et al. 2017). There are no data demonstrating and interaction between aflatoxin and fumonisin in humans. However, as noted by the 83rd JECFA “the interaction between AFB1, a compound with known genotoxic properties, and fumonisins, which have the potential to induce regenerative cell proliferation (particularly at exposures above the PMTDI), remains a concern.”

Trichothecenes [10] are a large group of mycotoxins, frequently found in maize and small grains such as wheat and barley in temperate regions worldwide. Of these, the most important by far is deoxynivalenol produced by the cereal disease *Fusarium graminearum* and related species. First reported from grain that had resulted in human toxicosis in Japan. Up until the early 1990s, incidents of acute human toxicosis were seen in China, Japan, Russia, and India (Pitt & Miller 2017). The PMTDI of deoxynivalenol is based on its impressive neurotoxicity and impact on various appetite suppression mechanisms i.e. feed refusal in a two-year mouse bioassay (Maresca 2014; Pestka 2010). Exposure is typically below the PMTI for adults in Europe, Canada, the USA, parts of South America and China (e.g. Bianchini et al. 2015; Han et al. 2014; Pacin et al. 2011; Silva et al. 2017). However, based on urinary biomarkers, exposure especially to children in some European countries may be above the PMTDI (e.g. Heyndrickx et al. 2015; Solfrizzo et al. 2014). Swine are the most affected domestic animal with losses in production resulting from feed refusal of grain at concentrations much greater than 1 mg/kg (Pitt et al. 2012).

*F. graminearum* and related species also produce zearalenone particularly in maize but also small grains albeit under different environmental conditions. Zearalenone is a potent estrogen analogue. Female pigs are the most sensitive domestic animal. Zearalenone exposure at ~0.5 mg/kg results in hyperestrogenism and reproductive effects at lower exposures (EFSA 2004; Gromadzkal et al. 2008; Pitt et al. 2012). In young women, zearalenone was associated with visible estrogenic effects in a number of case reports noting that the reporting was incomplete (JECFA 2000; Kuiper-Goodman et al. 1987).

Although apparently higher in the past (Kuiper-Goodman et al. 1987), current levels of exposure for humans in the fully developed market economies is generally modest (e.g. EFSA 2004; Gromadzkal et al. 2008). However, there is limited evidence of an association of zearalenone with idiopathic precotious puberty in populations in Italy, China and possibly the USA (Deng et al. 2012; Bandera et al. 2012; Massart & Saggese 2010). Zearlaleone is not uncommon in highland corn-producing areas of Africa (e.g. Chilaka et al. 2017; Ngoko et al. 2001). Human exposures in women and girls in these areas should be examined more critically.

The remaining agriculturally-important mycotoxin, ochratoxin A, is a common contaminant in cereal based foods in temperate climates. (EFSA 2006; 2010; Lee & Ryu 2017). Ochratoxin can also be found in many diverse foods such as raisins and wine (e.g. Battilani et al. 2006; Fanelli et al. 2017). First described from a laboratory culture, ochratoxin A was not reported as a natural contaminant until some years later. The early focus was as the cause of a serious renal disease in swine notably in Denmark. When first measured more broadly from the 1970s, it was very common in cereals sometimes at high levels (Pitt & Miller 2017). Based on the well-understood renal toxicity, regulation of ochratoxin in Europe in 2006 has been very successful at lowering overall exposure (EFSA 2010).

**2. Need for stronger action.**

At the third FAO/UNEP/WHO of three decanal meeting on mycotoxins (Nairobi 1977; Bangkok 1987; Tunisia 1999), some 50 countries met to consider the serious problem. There was general agreement that mycotoxins posed a substantial threat to human health in some countries and to world trade in grains and some other food products. Recommendations were made on the need for better exposure assessments, studies of the effect of mycotoxin exposure on human health in highly-affected regions, linking stringent international tolerances of mycotoxins in commodities to genuine public health gains and more focus on the planting of appropriate crops and crop genotypes to avoid the problem. The United Nations Environment Programme (UNEP) and the World Health Organization (WHO) International Programme on Chemical Safety (IPCS) – have declared that humans have a right to food free from mycotoxins that could cause significant health risk. Nonetheless, mycotoxins in staple crops remain the most significant foodborne risk for human health, animal health, and market access (Pitt et al. 2012, p.105). Further, an analysis by the United Nations Education Program notes that climate variability is increasing the risk for mycotoxins in some regions (UNEP 2016).

Much attention has been paid by the EU commission and institutions of the government of the People’s Republic of China to mycotoxin issues. In Horizon 2020, both MycoKey and MyToolBox were funded with to generate innovative solutions for sustainable mycotoxin management. During the first 18 months of the MycoKey project, the idea of a Mycotox Charter was discussed and a draft document developed. More recently, a web site was established to enable people and institutions worldwide to contribute to the discussion about increased equity in the availability of safe food.

3. Mycotox Charter structure

The Charter is structured in sections that delineate the commitments of its supporters. The major sections are:

2.1. Preamble

The primary purpose of the Charter is to provide a globally applicable statement for food suppliers and consumers on mycotoxin management that enhances food and feed safety along the supply and consumption chains. Sharing and spreading common intentions and behaviours can sustain and boost collective action towards this goal.

2.2. Rights

All people have the right to access a sufficient quantity of safe, healthy and nutritious food (with mycotoxin content below regulatory limits)*.*

2.3. Awareness

Mycotoxin contamination is a longstanding problem in public health and represents a great challenge for at least the next decade. Stakeholders and subscribers are aware of the economic and health risks arising from mycotoxin contamination in field crops and other food products. Consumers also need to be made more aware of the health risks posed by exposure to mycotoxin-contaminated food and empowered to demand safe, quality food.

2.4. Commitments

Both stakeholders and subscribers accept responsibility for leaving a healthier, fairer, more sustainable world to future generations, and commit to increasing food safety, fostering responsible and sustainable consumer behaviour, and providing recommendations for mycotoxin regulation. They embrace the principles and practices outlined below in the Mycotox Charter, which will reduce mycotoxin contamination in food and associated health hazards and contribute to the achievement of United Nations Sustainable Development Goal no. 2 UN (2018). Any intervention to reduce mycotoxin contamination and the consumption of contaminated food and feed will require a better understanding markets.

3. Mycotox Charter declaration

We, the undersigned endorse this Mycotox Charter and make a clear commitment to the right to food safety and mycotoxin management and regulation. This commitment is fundamental to minimizing the differences in access to sufficient safe food for all humanity

We believe that only our collective action as citizens, together with businesses and local, national and international institutions, will enable us to overcome the major challenges posed by mycotoxin contamination and to improve food safety at a global level. These challenges include:

* Insufficient knowledge of mycotoxin occurrence, accumulation, and transformation;
* Lack of suitable facilities at farmer level for post harvest handling and storage (especially in low income countries);
* Slow and often expensive methods for detecting mycotoxins at regulatory concentrations;
* Combating undernutrition and malnutrition related to mycotoxin exposure of humans and animals;
* Reducing waste of contaminated food and feed;
* Ensuring sustainable management of food and feed production processes.

3.1. In signing the Mycotox Charter:

* We affirm our collective responsibility to implement practices and choices that lead to the reduction of mycotoxins in food and to increased food safety for future generations;
* We commit to advocate for political decisions that will realize the fundamental goal of harmonizing mycotoxin regulations at the global level, thereby enable a more equitable access to safe food, and feed worldwide.

3.2. We believe that:

* Mycotoxins are major food contaminants that reduce global food security, especially in low and middle income countries;
* Everyone has the right to access a sufficient quantity of safe, healthy and nutritious food, with mycotoxin content as low as reasonably achievable;
* Mycotoxinsremain a “largely ignored global health issue” (Wild and Gong 2010);
* “There is a lack of action to address the problem of mycotoxins mostly in low-income countries and the reasons for it are undoubtedly complex and incompletely researched” (Wild and Gong 2010) and that this has been the feeling for decades (e.g. Boutrif 1995);
* Food spoilage caused by serious mycotoxin contamination results in perhaps 25% of the world’s food supply which increases food insecurity;
* Mycotoxin contamination is a major non-tariff trade barrier for agricultural products, which negatively impacts international trade and the world economy;
* The need to adopt a greater diet diversification strategy and less dependency on specific crops is crucial for food staples export especially for African Countries . The contaminated produce is often rejected by major buyers, processors and traders and by international regulatory agencies before entry in key export markets. High consumption of aflatoxin-susceptible commodities in Africa is compounded because rejected produce that does not meet international standards enters African food and feed value chains, leading to increased risk of exposure to the toxins;
* GAP (Good Agricultural Practices) and GMP (Good Manufacturing Practices) are important strategic measures to address mycotoxin problems;
* Early warning of contamination problems can limit the extent of damage and more readily enable remediation;
* Improvement facilities at the farmer level will reduce and prevent entry point of fungal contamination.
* We accept that the challenges are greater in food insecure countries (Wild et al. 2015).

3.3. We consider it unacceptable that:

* Where food production is sufficient, many countries do not regulate mycotoxin levels in food and feed even while recognizing that enforceable safety standards are needed;
* Informal and dispersed markets lack controls, which can result in increased risks of mycotoxin exposure;
* Inspection and enforcement capabilities are often inadequate, especially in developing countries;
* Best quality food commonly is sometimes exported; whereas poorer quality food is consumed domestically;
* Developed countries apply regulations to enforce mycotoxin standards and protect their population while not supporting resource-poor countries to meet these standards;
* People that suffer chronic hunger, are malnourished and have stunted growth are more highly exposed to mycotoxins;
* Each year, thousands of tonnes of food produced for human consumption is wasted due to mycotoxin contamination;
* Detection strategies are not applied uniformly.

3.4. We are aware that:

* Although most exposure is from staple crops, for some mycotoxins exposure can come from serveral different foods with high levels of contamination. Food safety risks need to be addressed using a dietary rather than a commodity perspective;
* The economic and health hazards of mycotoxin contamination in crops and food products present a huge challenge;
* Climate change could have an important impact on mycotoxin contamination of food and feed, and these changes could disproportionally affect economically-disadvantaged people;
* Children are particularly susceptible to the effects of mycotoxins;
* Improved dietary diversity can reduce mycotoxin exposure;
* All people are all inter-related and all are responsible for promoting conditions to improve access to adequate healthy food;
* Improvements in knowledge of and practical experience with mycotoxin management in both traditional and advanced production systems is critical in developed and developing countries;
* The lack of biomarkers for assessing exposure of humans and animals to many mycotoxins may limits our understanding of the health effects of mycotoxin exposure*.*

4. Mycotox Charter commitment

4.1. Since we are responsible for leaving a healthier, fairer, more sustainable world to future generations, as citizens, we commit to:

* Improve the safety of available food, particularly by reducing its mycotoxin content;
* Provide recommendations for mycotoxin regulations developed by academic and governmental experts and key industrial partners;
* Promote dietary and environmental education in the family context to reduce mycotoxin exposure;
* Provide farmers with information that enables rational decisions/solutions for addressing potential mycotoxin problems;
* Respect and protect the environment through responsible behavior and sound practices, such as recycling or remediation, to reduce mycotoxins in food;
* Play an active role in building a sustainably safe food supply, with lower mycotoxin content, including innovative solutions, based on our collective work, creativity and skills.

4.2. As members of civil society, we commit to:

* Making our voices heard at all decision-making levels relevant to mycotoxin issues;
* Representing civil society bodies in debates and processes for shaping public policy and public opinion on mycotoxin risk management;
* Increasing the interest of the scientific community in developing countries and their research on mycotoxins;
* Building human resource capacity in mycotoxicology;
* Strengthening and supplementing an international network of projects, actions and initiatives on mycotoxins and food safety;
* Identifying and reporting critical issues in international regulation of mycotoxins;
* Sharing new technologies with developing countries to enable them to meet global regulations.

4.3. As businesses, we commit to:

* Increase access to quality food for all by considering the limitations of producers and designing strategies to minimize mycotoxin exposure based on sound research;
* Develop new strategies to monitor and predict mycotoxin contamination in specific foods/feeds and in particular geographic regions;
* Sustain the systematic development of research centers that work on mycotoxins;
* Promote the establishment of national and regional hubs of excellence for coordination of response;
* Investing in research, promoting a wider sharing of results and their implications for the collective good, without distinction between the public and the private sector;
* Build a database on health-related risks caused by mycotoxins;
* Translate existing monitoring technologies into on-site/storage-specific application tools for growers to record data and communicate with ICT systems;
* Improve production, storage, processing and logistics, to reduce (or eliminate) mycotoxin contamination;
* Produce and market healthy, safe food, informing consumers about the mycotoxin risk;
* Contribute to achieving the UN Sustainable Development Goals, by using innovative processes, products and services, and by adopting and practicing codes of social responsibility.

4.4. Through our signing of the Mycotox Charter, we strongly urge governments, institutions and international organizations to commit to:

* Include mycotoxin control in national strategies and plans, and in relevant long-term development projects;
* Harmonize mycotoxin regulations to increase food safety and food security, and make them effective;
* Strengthen legislation to promote the implementation of equitable mycotoxin regulations;
* Promote the theme of nutrition/malnutrition in relation to mycotoxin contamination in international government forums, ensuring effective implementation at the national level and coordination among specialized international organizations;
* Formulate and implement rules and regulations regarding mycotoxins in food and environmental safety that are easy to understand and effective when applied;
* Promote the culture of a safe, healthy diet with low mycotoxin risk as a global health tool;
* Increase resources for research and the dissemination of its results, especially in areas where populations have a significant mycotoxin exposure risk;
* Develop national health service measures and policies that promote a healthy, sustainable diet that is free of or low in mycotoxin for people with special nutritional requirements;
* Improve facilities for good agricultural practices as well as good manufacturing practices at farmer levels and small-scale industries.

We believe in the possibility of a world with reduced risk of mycotoxin contamination. We commit to adopting the principles and practices outlined in the Mycotox Charter as a strategy that the member states of the United Nations should follow to reduce the problem of mycotoxins in food and related health hazards. The importance of the reduction of mycotoxin exposure is evident from the number of interdisciplinary EU and International projects funded on mycotoxin research.

By signing the Mycotox Charter, we declare our concrete and active support for the Sustainable Development Goals promoted by the United Nations (2018). We encourage readers to go to the web site for the Charter ( ) and to add their support to ours.

5. Conclusions

Considering the high risk associated with the consumption of food with material concentrations of mycotoxins, it is essential to strengthen food safety measures. We believe this can be done by increasing the supply of safe food and promoting cultural awareness of mycotoxins to policy makers and business to support and adopt the current best practices. Strengthening an international network of projects, actions and initiatives on mycotoxins and food safety, harmonizing mycotoxin regulations worldwide and supporting more equitable access to safe food, are fundamental goals to be pursued by producers, researchers, stakeholders, politicians, and governments, and are all captured by the spirit of the Mycotox Charter.

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