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### Keeping Mycotoxins Away from the Food: Does the Existence of Regulations Have any Impact in Africa?

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## Keeping Mycotoxins Away from the Food: Does the Existence of Regulations Have any Impact in Africa?

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*Following the discovery of aflatoxins in the early 1960s, there have been many studies leading to the uncovering of many mycotoxins and the understanding of associated health effects in animals and humans. Consequently, there has been a global increase in the number of countries with mycotoxin regulations in foods. However, many African countries have only regulations for aflatoxins (or a few other mycotoxins) in specific foods or no regulations at all. This article critically reviews the challenges thwarting the establishment of mycotoxin regulations and their impacts on human dietary mycotoxin exposure in Africa. Mycotoxin regulatory limits for different countries are compared with mycotoxin tolerable daily intakes established by international food safety bodies taking into account consumption patterns. The agrarian setup, food insecurity and mycotoxin analytical challenges in African countries are discussed; and more feasible mycotoxin dietary exposure reduction strategies proposed.*

**Keywords:** Mycotoxin regulation, agrarian, food safety, food security

## 1. Introduction

Fungi are ubiquitous in nature and are capable of colonizing a wide range of substrates including food crops. Under favourable conditions, some of the fungi produce low molecular weight secondary metabolites called mycotoxins. Mycotoxins have been proven under laboratory experiments not to be necessary for the fungi' growth and have been thought to aid in competition against other organisms in habitat (Shwab and Keller, 2008).

Mycotoxins are generally heat stable and are not destroyed during most normal cooking processes (Bullerman and Bianchini, 2007; Raters and Matissek, 2008). They can potentially lead to carcinogenicity, mutagenicity, teratogenicity, oestrogenicity, neurotoxicity and immunotoxicity based on the kind of toxins, dose, sex, health, age and nutritional status of the exposed individual (Hussein and Brasel, 2001; Ready et al., 2010). Acute exposures to mycotoxins can potentially lead to sudden death (Lewis et al., 2005).

Mycotoxins have probably existed since the origin of mankind and have an extremely ancient history (Dugan, 2008) but were not identified and fully characterized until the early 1960s when aflatoxin was first discovered (Lancaster et al., 1961; Nesbit et al., 1962). A comprehensive review of time line for key events in the discovery, toxicological evaluation, molecular epidemiology, and regulation of aflatoxins has been provided by Kensler et al., (2011). The discovery of aflatoxins has led to the discovery of about 400 more mycotoxins (Miller 1994; Hussein and Brasel, 2001; Bennett and Klich, 2003; Miller, 2008), but there

probably do exist thousands. However to date only a few mycotoxins are considered to be of toxicological relevance either because they have been proven so or due to insufficient toxicological data.

Mycotoxins have been classified in many ways by chemists, biologists, biochemists and clinicians based on chemical structure, fungal species that produce them, biosynthetic origins and affected organ respectively (Bennett and Klich, 2003). Some of the most studied mycotoxins (classes) include aflatoxins, fumonisins, zearalenone, trichothecenes, citrinin, ergot alkaloids, ochratoxin and patulin. Recently, the so called ‘emerging *Fusarium*-mycotoxins’ which include fusaproliferin, beauvericin, enniatins, and moniliformin have received much attention (Jestoi, 2008). To date, there exist many reviews that cover biosynthesis, the chemistry and toxicokinetics of mycotoxins (Hussein and Brasel, 2001; Pohland, 1993; Betina, 1989; Bennett and Klich, 2003; Santin and Diaz, 2005; Bräse et al., 2012). Likewise there are hundreds and thousands of reviews and articles respectively on occurrence of mycotoxins in several food commodities on regional and global levels.

## 2. Production of mycotoxins in food

The formation of mycotoxins depends on the interaction of several factors such as nutritional composition of the substrate (Luchese and Harrigan, 1993; Abbas et al., 2009), genetic susceptibility of the host plant or commodity to fungi infestation (Brown et al., 1999; Munkvold, 2003; Somers et al., 2003), moisture content, humidity, water activity ( $a_w$ ), aeration, temperature, pH value (Marin et al., 1995; Dorner et al., 1989), fungal populations (Cotty and Mellon, 2006),

physical damage of grain due to insect pests and other stress factors (Widstrom, 1979; Schatzki and Ong, 2001). Climate is thought to be the most critical driving factor for fungal colonization and mycotoxin production as it has influence on most of the factors listed above (Paterson and Lima, 2010; Magan et al., 2011). Mycotoxin contamination in food may occur while crops are in the fields, during storage or processing or maybe carried-over into milk, meat or eggs, when farm animals are fed on mycotoxins contaminated feed (Gareis and Wolff, 1999; MacLachlan, 2011).

### 3. Prevention and control of mycotoxin contamination in food

There are many pre- and post- harvest prevention strategies for of mycotoxins for several crops (Bruns, 2003; Magan and Aldred, 2007; Guo et al., 2009; Choudhary and Kumari, 2010; Chulze, 2010; Lehoczki-Krsjak et al., 2010). These strategies are based on good agricultural practices (GAP) which represent the primary line of defense against contamination of food commodities with mycotoxins while in the field, followed by the implementation of good manufacturing practices (GMP) during the handling, storage, and distribution of the food commodities. Complementary to this management system is Hazard Analysis and Critical Control Point (HACCP), a preventive system based on the systematic identification of hazards, establishing controls and monitoring these controls (Park et al., 1999). To this effect, the Codex Alimentarius Commission (CAC), an intergovernmental body established to implement the Joint FAO/WHO Food Standards Programme, has developed several codes of practice for reduction of mycotoxins in a range of food commodities (CAC, 2003, 2004, 2009, 2013). However, it is impractical to totally preclude mycotoxin contamination as already highlighted that most critical factors for mycotoxin production are extrinsic beyond man's control and such there are

continued reports of incidences of mycotoxin contamination in various food commodities particularly in the tropics where high ambient humidity make the control of commodity moisture difficult (Chulze, 2010). Besides in some parts of the tropics such as Africa, there are additional compounding social factors such as theft of food commodities while still standing in the fields (McCall, 1985) which may compel farmers to harvest and store produce before adequate drying thus increasing the risk of fungal colonization and mycotoxin contamination.

#### 4. Managing mycotoxin contaminated commodities in a food chain

Although mycotoxins can never be completely removed from the food supply, it is possible to keep the levels low. This could be achieved by physical, chemical and microbiological decontamination strategies which have been extensively explained (Park, 1993; Charmley et al., 1994; Bata and Lásztity, 1999; Galvez et al., 2002; Galvez et al., 2003; Siwela et al., 2005; Van der Westhuizen, 2011; Grenier et al., 2014)

The other way of achieving this is through institutionalisation of mycotoxin regulations. By 2003, about 100 countries, including fifteen African countries, had mycotoxin regulations for at least the aflatoxins (FAO, 2004). By early 2007, the European Union (EU) had implemented the most extensive and detailed regulations for food mycotoxins worldwide that encompassed 13 different mycotoxins or groups and for 40 different food combinations (Van Egmond et al., 2007). Due to complexity of obtaining similar data for Africa, the exact state of affairs remains unknown. However, in several recent publications, authors report the inexistence of specific mycotoxins (eg fumonisins, zearalenone, ochratoxin, deoxynivalenol) regulations in their

countries and they made reference to maximum tolerable guidelines set by international food safety bodies or regulations set by other states (Adetunji et al., 2014; Mohale et al., 2013; Kimanya et al., 2010; Warth et al., 2012; Matumba et al., 2014a, Ediage et al. 2014), an indication of little or no improvement at all as regards to the mycotoxin regulatory situation reported in 2003. Perhaps what is also interesting is the absence of fumonisin regulations in South Africa, a country where fumonisin research was pioneered and where there is a clear evidence of high dietary exposures from maize (Dutton, 2003; Shephard et al., 2007; Shephard, 2013; Leroux, 2014). What could be the reasons?

Scientific as well as socio-economic factors are considered when establishing mycotoxin regulation and these include 1) toxicological data, 2) exposure data, 3) availability of analytical facilities and methods, 4) distribution of mycotoxin within a lot, 5) food sufficiency, and 6) legislation in other countries with which trade contacts exist (FAO, 2004). Equally important is the influence of societal set-up (industrial or agrarian) and food supply system. Subsequent sections critically analyse these factors to understand the disparity between Europe's and Africa's scenarios as regards to institutionalization of mycotoxin regulations and further examine the impact of existing regulation in Africa.

#### *4.1. Toxicological data on mycotoxins*

Regulations are primarily made on the basis of toxicity of a particular mycotoxin as different mycotoxins exhibit different toxicities and at varying doses. All over the world toxicologists are actively trying to understand risks associated with various mycotoxins *in vitro* or using animal

models. The majority of animal *in vivo* data on toxicity of mycotoxins are limited to studies of laboratory animals such as mice, rats and guinea pigs. These animal studies principally aim at determining the 1) kinds of adverse effects (hazard identification); the potency or sensitivity of effects (dose–response assessment); 3) the no observed adverse effect level (NOAEL) and the lowest observed adverse effect level (LOAEL) (Faustman and Omenn, 2001; Boermans and Leung, 2007). Data from such studies are pooled together and scientifically evaluated by national or international scientific teams of experts. For a toxin, where the effect shows a threshold, tolerable daily intake (TDI) (measure of the amount of a contaminant that can be ingested on a daily basis over a lifetime without an appreciable health risk) is established (WHO, 1987). On a global level, these evaluations are carried out by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) where as in the EU, these evaluations are performed by the European Food Safety Authority (EFSA). Most of the time the TDIs established by JECFA and EFSA are the same or comparable. For instance provisional maximum tolerable daily intake (PMTDI) or TDI for zearalenone, deoxynivalenol and fumonisins are universally 0.5, 1.0 and 2.0 µg/kg body weight (bw)/day respectively (JECFA 2000, 2002; SCF, 2003).

However, the TDIs are not applicable for toxins where carcinogenicity is the basis for concern, as is the case with aflatoxins. In 1993, the International Agency for Research on Cancer (IARC) assessed and classified naturally occurring mixtures of aflatoxins as class 1 human carcinogens (IARC, 1993). For aflatoxin B1, exposure of as little as < 1 ng/kg bw/day can contribute to a risk of liver cancer (SCF, 1994) and because of this JECFA failed to establish a numerical TDI for aflatoxins (JECFA, 1999). Therefore it is recommended that levels of aflatoxins should be as low



as technologically feasible or as low as reasonably achievable (ALARA). Nevertheless, TDIs of  $< 1$  ng/kg bw/day have been used in risk assessments elsewhere (Kuiper-Goodman, 1995; Leblanc et al., 2004; Sekiyama et al., 2005; Ediage et al., 2014)

#### *4.2. Exposure data, availability of analytical facilities and sampling criteria*

Also critical in risk assessment of mycotoxins is exposure estimation. For this reliable and sufficient data on the occurrence of mycotoxins in various food commodities and consumption data are needed to estimate the probable daily intake (PDI). Usually mycotoxin occurrence data are never sufficient, however for most developing parts of the world including Africa it is almost non-existent (FAO, 2004). Unlike in the EU where there are regular surveys of occurrence of multi mycotoxins, until now there are several countries in Africa where there has hardly been any survey carried out to investigate the incidence of mycotoxins on a national basis. Literature search revealed that for Africa with exception of Morocco (Zinedine and Mañes, 2009) even in cases where there is at least a record of mycotoxin survey, it is often a limited survey (few samples) and mostly only focusing on aflatoxins in food commodities on a market (Daniel, et al., 2011; Elshafie et al., 2011; Kamika et al., 2011; Babana et al., 2013; Chala et al., 2013; Asiki et al., 2014; Matumba et al 2014b).

Recently the use of biomarkers in assessing mycotoxin exposure is rapidly becoming a complimentary approach to traditional food analysis (Lattanzio et al., 2011; Solfrizzo et al., 2011; Turner et al., 2011; Ediage et al., 2012; Warth et al., 2013). However, with the exception of fumonisins biomarker research work that has been carried out in South Africa,

comprehensive mycotoxin biomarker exposure assessments in Africa have involved exportation of urine or blood samples to advanced laboratories overseas (Wild et al., 1992; Gong et al., 2004; Ediage et al., 2012; Shephard et al., 2007a, 2013). The exportation of specimens may be constrained by ethical challenges and may also not be sustainable in a long-term.

The lack of mycotoxin surveys in Africa is undoubtedly linked to the limitations in analytical capabilities. Typically mycotoxin analysis involves a sequence of five discrete steps and these are sampling, sample preparation, extraction, clean-up, separation and determination. Sample preparation involves grinding, homogenisation or slurry preparation and this requires laboratory mills, blenders and homogenizers. Sample extraction usually involves mixtures of water and polar organic solvents and mechanical shaking or high speed blending. Sample clean-up involves removal of non-mycotoxin "interfering" compounds through liquid extraction, solid-phase extraction (SPE), immunoaffinity-column (IAC), molecular imprinted polymers (MIP) or aptamers (Razzazi-fezeri and Reiter, 2011). Mostly mycotoxin quantitation involves chromatographic technique such as thin-layer chromatography (TLC), gas chromatography (GC) or high-performance liquid chromatography (HPLC) coupled to a photo diode array, UV-Vis or fluorescent detector, or liquid chromatography with mass spectrometry (LC-MS) or tandem mass spectrometry (LC-MS/MS) (Shephard, 2011; Spanjer, 2011). Exception to the above analytical scheme are 'dilute and shoot' methods that bypass sample clean-up but require the use of more sensitive LC-MS/MS equipment (Sulyok et al., 2007; Razzazi-fezeri and Reiter, 2011).

The realization of the fact about mycotoxins synergism in humans and animals (Speijers and Speijers, 2004; Pedrosa and Borutova, 2011) coupled with technological advancement has caused a rapid shift from single mycotoxin targeted analysis to LC-MS/MS based multi-mycotoxin analysis (Sulyok et al., 2006; Garon et al., 2006; Sulyok et al., 2007; Spanjer et al., 2008; Vishwanath et al., 2009; Rasmussen et al., 2010; Monbaliu et al., 2010; Ediage et al., 2011; Spanjer, 2011; Streit et al., 2013). In spite of all these developments at global level, Africa remains constrained with lack of mycotoxin laboratory infrastructure and overall shortage of trained mycotoxicologists and analytical chemists to support the laboratory services. Recently there has been some technological advancement of relatively cheaper, easy-to-use rapid mycotoxins screening kits for use in the field, point of delivery to storage or processing facilities (Ediage et al., 2012; Berthiller et al., 2014; Burmistrova et al., 2014; Dzantiev et al., 2014; Li et al., 2014). However, due to logistical problems (eg transportation) and social-economical factors, such tests are not readily available for use in this part of the world. Moreover it is generally argued that food safety programmes are not fully appreciated by most African governments as such they are not given priority and hence have reduced budgets (WHO Regional Office for Africa, 2004).

It is therefore not surprising that until now there are hardly any mycotoxin sampling plans tailored for African setting. The distribution of mycotoxins in food is highly heterogeneous as such statistically based sampling plans are required to obtain a representative laboratory-sized sample (Whitaker, 2006). Mycotoxin sampling criteria depend on the type of mycotoxin, food type, volume and nature of a lot (i.e. field, truck, warehouse, pack, ...) (Whitaker, 2006; Cheli et al.,

2009). The EU has laid down the most detailed statistically-based sampling plans for a wide range of mycotoxins in different foods and in different scenarios for official control/enforcement purposes (EC, 2006). Unfortunately the EU sampling plans can not just be exported to Africa as they may not represent the African setting where small lots dominate and besides there are differences in food types and probably in the spectra of mycotoxins in these two regions.

#### *4.3. Food sufficiency or food safety? The Africa dilemma*

According to the World Summit on Food Security held in 2008, food security is defined as all people, at all times, have physical, social and economic access to sufficient, safe and nutritious food to meet their dietary needs and food preferences for an active and healthy life (World Food Summit, 2009). Ironically FAO experts estimate that 25% of the world food crops are affected by mycotoxins annually (CAST, 1989). This is even more complex in Africa, particularly sub-Saharan Africa which faces perennial food shortage (Clover, 2003; Baro and Deubel, 2006; Smith et al., 2006; FAO, IFAD and WFP, 2013). Although there has been a gradual improvement, sub-Saharan Africa has been persistently ranked highest in human undernourishment worldwide with rates estimated between 31% in 2000-2002 and 25% in 2011-2013 (FAO, IFAD and WFP, 2013). Given the clear evidence of food shortage and high incidence of mycotoxin in food in Africa (Matumba et al., 2014; Adetunji, et al., 2014; Ediage et al., 2014; Mohale et al., 2013; Matumba et al., 2013; Lewis et al., 1995), is there any room for reaching a compromise between achieving food sufficiency and food safety in Africa?

#### *4.4. Trade clusters*

Most African countries rely heavily on exports of agricultural commodities for a large share of their export revenues (Diao et al., 2007). Exports may include food commodities even in situations where millions of citizens are going hungry (Clover, 2003). Given the challenges, faced by African countries in developing and enforcing mycotoxin regulations it is more likely that the establishment of some of the existing regulations could have been influenced by existence of regulations in trade partnering countries. A typical example is a case of Malawi which during the 2003 FAO mycotoxin regulation survey was reported to have aflatoxin B1 regulation for peanuts (5 µg/kg) specified for 'exports' and had none for the local market (FAO, 2004). The 5 µg/kg aflatoxin B1 regulation for peanuts matched that of long time Malawi's peanut importer and former colonial master, Great Britain. Wu and Guclu (2012) recently offered a detailed account of the existence of maize trade clusters among countries with similar aflatoxin regulations. However, in the process of meeting importers' regulations, agricultural countries tend to concentrate mycotoxins in food for the locals (FAO, 2004).

#### *4.5. Societal set-up: Agrarian vs industrial*

In industrialized societies a vast majority of the population live in urban settings (UNFPA 2007) and heavily rely on supermarkets for their food supply (Hawkes, 2008). In case of the EU, most of the food commodities are imported from elsewhere (WTO, 2013) and usually undergo thorough safety inspection at the European border (Otsuki, et al., 2001; Kleter et al., 2009). Within the EU, there are also regular food safety inspections at manufacturing and retail level by government food agencies and recently this system is increasingly being complemented by private food safety regulations by supermarkets (Havinga, 2006).

In contrast, in spite of sub-Saharan Africa's unprecedented urban growth rate estimates at 3% and the highest in the world (White et al., 2008; UNFPA, 2007) about 63% of sub-Saharan Africa's population still lived in the rural setting by 2012 (World Bank, 2012). In this region, almost all rural dwellers and a significant proportion of the urban dwellers rely on subsistence farming for their livelihoods (Arku et al., 2012). While there has been significant supermarket expansion due to the rapid urbanization in sub-Saharan Africa, informal food sources such as street trades, vendors, and spazas remain vital as supermarket shelves are unaffordable for the vast urban dwellers (Crush and Frayne, 2011).

From the above one can clearly see the relevance of food safety regulations in the EU and the ease with which the regulations would be established and enforced. This further explains the reasons behind existence of detailed and efficient mycotoxin regulations in the EU (Van Egmond et al., 2007) and the converse hold for Africa.

#### 5. Are the existing or borrowed regulatory standards protective enough?

There have been suggestions to harmonize regulatory limits for mycotoxins across the world (Berg, 2003; Whitaker, 2003). Proponents argue that standardized mycotoxin regulation may facilitate international trade and offer improved consumer protection. While standardization of regulatory limits for mycotoxins may indeed work in that way for countries with similar food consumption patterns and food security status such as the EU countries, it remains impractical to achieve the same legal framework while maintaining universal food safety due to differences in

food consumptions patterns across the world. None the less the Codex Alimentarius Commission has international standards laid down for different mycotoxins for different products (CAC, 2013).

Dietary aflatoxin B1 exposure is known to increase hepatocellular carcinoma (HCC) risk particularly among hepatitis B virus positive (HBV+) carriers (McGlynn et al., 1995). Recognising this, Wu et al., 2013, recently examined the level of protection offered in reducing HCC risk by existing aflatoxin regulation for maize and peanuts (mostly between 4 and 20µg/kg) around the globe taking into consideration the prevailing HBV+ rates. They found most existing regulatory standards do not adequately protect even if enforced, particularly in countries where large amounts of maize and peanuts are consumed which include sub-Saharan Africa.

Surprisingly, Kenya a country within sub-Saharan Africa with a record of acute aflatoxicosis and probably with the high HBV+ prevalence rate (11-15%) in the world (Liu and Wu, 2010) maintains the aflatoxin regulatory limit at 20µg/kg for maize and groundnuts despite the high dietary consumption rate associated. Could it be that the decision for setting the regulatory limit was heavily influenced by Kenya's food insecurity situation (FAO, IFAD and WFP, 2013) or that it was just borrowed from elsewhere without performing risk assessment? This question holds for all existing regulations in Africa. If these regulations are borrowed, say from the EU, or just adopted from the CAC recommendations, do they serve the purpose (i.e. are they protective)?

Given the high maize consumption in sub-Saharan Africa where daily average intake for an adult can be as high as 500g (Shephard et al., 2013; Dowsell et al., 1996) the borrowing of *Fusarium* mycotoxin regulatory limits from anywhere would not suffice. For instance the EU regulatory limits for fumonisins, deoxynivalenol and zearalenone for raw unprocessed maize are 4000, 1750 and 200 µg/kg respectively (EC, 2007, 2010). Assuming an average weight to 60 kg and a daily intake of 400g of maize for an adult, the consumption of maize containing these mycotoxins at the maximum limits would result in exposure roughly 13, 12 and 3 times JECFA's guided TDIs for fumonisins (2 µg/kg bw/day or 120 µg per 60 kg-person/day), deoxynivalenol (60µg per 60kg-person/day) and zearalenone (30 µg per 60 kg-person/day) respectively (JECFA 2000, 2002) (Figure 1).

Conversely, using the TDI approach only maximum limits of less than 300, 150 and 75µg/kg for fumonisins, deoxynivalenol and zearalenone respectively could adequately protect 60kg adults of consumers with daily intake of 400g (Figure 1). As regards to nivalenol which still has not been assigned a regulatory limit by the EU but has a TDI of 72 µg per 60 kg-person/day (EFSA, 2013), an average intake of 400g would require an maximum limit of less than 180 µg/kg (Figure 1).

Based on available occurrence data on these mycotoxins (Doko et al., 1996; Bankole et al., 2013; Mohale et al., 2013; Shephard et al., 2013; Adetunji et al., 2014 ; Ediage et al., 2014; Matumba et al, 2014a), the above calculated maximum limit would seriously exacerbate starvation in sub-Saharan Africa if enforced. Perhaps what would make it more complicated is that the climate in



sub-Saharan Africa favours co-occurrence of multiple mycotoxins and considering the mycotoxin synergism, a wide margin of safety may be required (Egmond et al., 2007).

### **Conclusions and perspectives**

From the above it can be clearly seen that the existence of mycotoxin regulations in an agrarian setting of Africa would have very little impact. In as much as governments need to establish and enforce regulations in order to protect the minority that rely on supermarkets, prevent the influx of contaminated foodstuffs from elsewhere and facilitate exports (Wu et al, 2013), there is need for much more to be done in order to protect citizens from high dietary mycotoxin exposures. The subsistence nature of food production in sub-Saharan Africa offers huge opportunities to a consumer in ensuring food safety as he/she has almost full control over intrinsic pre-and post-harvest management factors. In that regard, governments in agrarian countries need to invest a lot of effort in augmenting farmers' knowledge about the health hazards and prevention strategies highlighted earlier in this paper. As opposed to the approach followed by most governments by emphasizing only on achieving quality of exports as means of survival strategy, augmenting farmers knowledge about the health hazards would more likely improve the quality of exports as producers (and at the same time consumers) would be more careful than when the ultimate goal of food safety would be to export.

Perhaps the biggest opportunity in an agrarian setting is the application of mycotoxin decontamination strategies. Physical decontamination methods which include hand sorting, washing, dehulling, screening, density separation and fractionation would certainly work better

on raw food products than processed food due to their complexity (Matumba, under review). In this sense, an agrarian consumer has an advantage. However most mycotoxin decontamination methods require optimization before wide dissemination and usage. The other important thing is the need to explore feasible ways of diverting contaminated food fractions, otherwise contaminated food will still find its way onto the table of an agrarian consumer.

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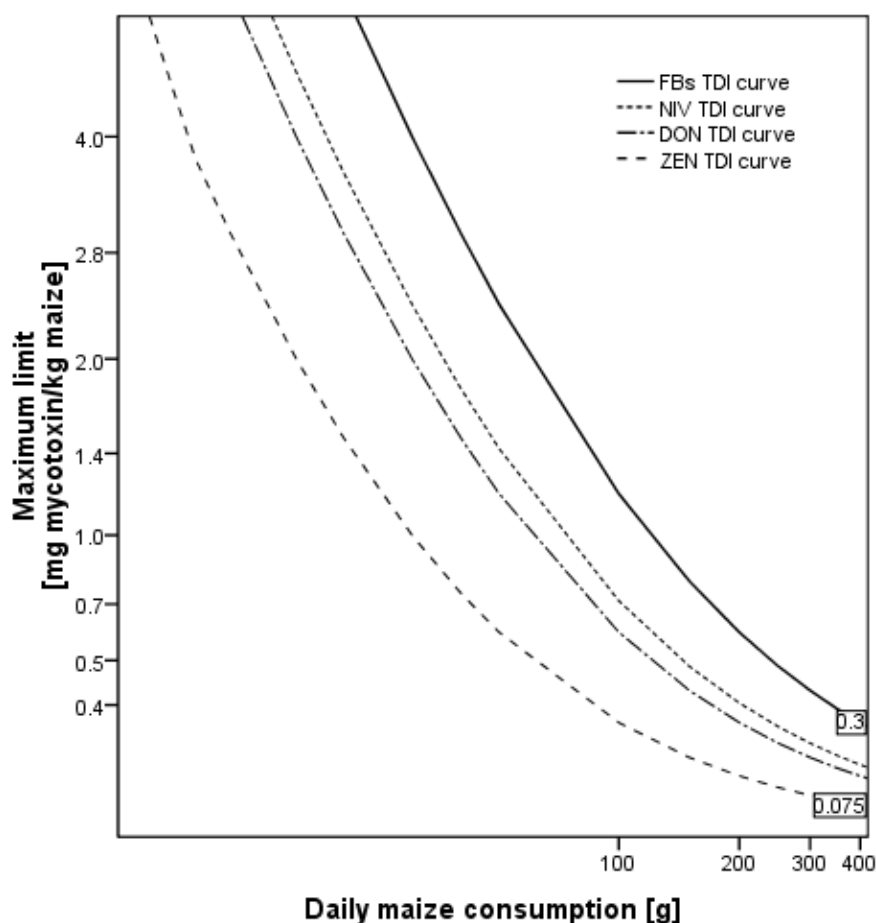


Figure 1: TDI curves for fumonisins (FBs), deoxynivalenol (DON), nivalenol (NIV) and zearalenone (ZEN) for a 60kg adult based on JECFA's guided PMTDIs or TDIs for fumonisins (2.0  $\mu$ g/kg body weight (bw)/day), deoxynivalenol (1.0  $\mu$ g/kg bw/day), nivalenol (1.2  $\mu$ g/kg bw/day) and zearalenone (0.5  $\mu$ g/kg b.w./day). Area under each curve represent "safe area", in contrast area above the curve represent the "unsafe area". The numbered points in small white boxes (0.3 and 0.075) illustrate maximum limits in mg/kg level for fumonisins and zearalenone respectively that could be set for to protect a 60kg adult with an average maize intake of 400g.