Mycotoxins –

The Hidden Danger in Food and Feed

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THE HIDDEN DANGER IN FOOD AND FEED

BY

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Mycotoxins – the Hidden Danger in Food and Feed

- ✓ Concerted action needed to stem growing threat from mycotoxins in agriculture
- ✓ When consumed, mycotoxins cause illness in both humans and in animals
- ✓ Mycotoxin contamination impacts on farm businesses as well as human health
- ✓ An estimated 3.2 million cases of illness and 50,000 hospitalisations per year are due to mycotoxins in the EU alone
- ✓ Costs include hospital stays, lost working days and reduced productivity
- ✓ Fungi that cause mycotoxins reduce both crop yields and quality
- ✓ Mycotoxins in animal feed can reduce livestock output and fertility
- ✓ Mycotoxins are extremely difficult to remove from the food and feed chain
- ✓ Focus is therefore on preventing them entering food and feed in the first place
- ✓ Good agricultural practice has a key role to play – and so too do fungicides

SUMMARY: Prevention is better than cure when it comes to mycotoxins: they are extremely difficult or costly to remove from food and feed – so it is best to keep them out in the first place.

Mycotoxins are toxins made by fungi. The fungus itself can be simply eliminated using heat or chemicals – but it is much more difficult to remove or denature the mycotoxins, so the best control method is to suppress the fungi in the first place.

Found wherever fungi grow, including on grain, mycotoxins have been around a long time. The first records of mycotoxin-related foodborne disease are from ancient China some 5,000 years ago. But more mycotoxins have been discovered since the 1960s and their number continues to rise.

Some scientists suggest mycotoxins are one of the most underestimated sources for foodborne illnesses. At the same time, researchers have warned that the importance of mycotoxins is increasing in relation to other substances that are potentially hazardous to human health.

Recent years have seen mycotoxins regularly in the top three causes for food and feed safety alerts. And evidence suggests that mycotoxins are occurring increasingly in agricultural products – including in grain destined for human and animal consumption.

Studies suggest an increasing occurrence of fungi-based toxins in world agriculture, with positive samples rising for a number of reasons. Products from outside Europe are more often contaminated than EU products, which demonstrates EU member states are trying to keep the mycotoxin problem below critical thresholds.

Unlike bacterial toxins, fungal toxins are not proteins. Usually barely detectable by the immune systems of humans and animals, most illnesses caused by mycotoxins are not referred to a doctor. But above very low threshold levels, they can be dangerous to human health.

It is estimated that at least 3.2 million cases and 50,000 hospitalisations per year are due to mycotoxins in the EU alone. It is therefore the vendor's responsibility to guarantee that grain is safe for human consumption.

Even if grain is not rejected for human or animal consumption, farmers face additional costs due to extra testing requirements unless the problem of mycotoxins is mitigated. Mycotoxins thus have an economic cost for the producer, as well as a health cost for the consumer.

Contamination can cost a UK farmer with an 8 t/ha wheat crop as much as £200/ha in lost milling premiums – and often more if it impacts on yield too. In Germany, a grower can lose as much as €450/ha in revenue on a maize crop rejected for food and feed production.

In pigs, mycotoxins can severely affect growth, reproduction and immunity to disease, causing lower feed consumption and reduced weight gain. Mycotoxins are also bad for poultry, slowing the rate of fat absorption, reducing egg production as well as shell thickness.

Ruminants are less affected because of their digestive system. But mycotoxin residues have been found in milk – and the presence of mycotoxins in animal feed can have a major impact on dairy farming profitability.

Farmers who fail to ensure their grain is free from contamination face a hefty penalty. This means that good post-harvest storage – as well as the application of fungicides to combat fungi in the fields – is crucial for preventing further mycotoxins along the value chain.

If most mycotoxins are kept out of the crops, they are unlikely to become a problem later along the supply chain – and consumers and livestock will remain unaffected. Most methods of managing mycotoxins are therefore preventative.

Good agricultural management to combat mycotoxins is seen as key to feeding the world's population in the years and decades to come. Control should begin as early as possible, starting at the farm level with primary agricultural production.

Effective tools include integrated crop management – a mix of appropriate crop rotation, soil preparations, choosing less susceptible varieties, quality control, and agronomy. And on a practical level, sensibly applied fungicides have a fundamental role to play too.

Fusarium, for example, can shrivel grain causing yield losses of up to 30%. But a fungicide application can lower the risk of a fusarium contamination – helping to manage the health and economic risks that mycotoxins pose.

Fusarium mycotoxins are the most frequently identified mycotoxins in grain and animal feed and it is imperative for farmers to manage fusarium accordingly. Good farming practice, including fungicides, is the primary way to reduce mycotoxins in cereals and cereal products.

Changes in farming practices have contributed to the increasing presence of mycotoxins. These changes include fewer break crops, a move from ploughing towards minimum tillage systems, and an increase in the area of mycotoxin-susceptible crops such as maize.

Together, this has led to fewer opportunities to “clean” fields between crops, fewer opportunities to bury fungal spores after harvest, and a gradual increase in mycotoxin build-up. Forecasts suggest climate change will further contribute to the risk of mycotoxins in maize and wheat.

This makes it even more important to prevent mycotoxins from entering food in the first place. Fungicides have a key role in this – as has been said – and they are on average at least 100-1000 times less toxic than the mycotoxins that they control.

It is uncertain how fast mycotoxins will develop in the future. But it is certain that they are here to stay and need careful management. Mycotoxins should be considered an emerging concern – so all available tools should be used to combat them and keep them under control.

Suppressing the fungi that cause mycotoxins is the safest, most reliable and low-cost way to control the what threatens to be a growing problem – for producers as well as consumers.

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LIST OF ABBREVATIONS

AD	–	Anaerobic Digestion
AF	–	Aflatoxins
AHDB	–	Agricultural and Horticultural Development Board
AGES	–	Agentur für Gesundheit und Ernährungssicherung
BfR	–	Bundesinstitut für Risikobewertung
BSE	–	Bovine Spongiform Encephalopathy
CAST	–	Council for Agricultural Science and Technology
CDC	–	Centres for Disease Control and Prevention
CSL	–	Central Science Laboratories
DDGS	–	Distillers Dried Grains with Solubles
DEFRA	–	Department for Environment, Food & Rural Affairs
DON	–	Deoxynivalenol
EFSA	–	European Food Safety Authority
EHEC	–	Entero-Haemorrhagic Escherichia Coli
EPA	–	(United States) Environmental Protection Agency
EU	–	European Union
FDA	–	Food and Drug Administration of the U.S.
FAO	–	Food and Agriculture Organization
FSA	–	Food Standards Agency
FUM	–	Fumonisins
GDP	–	Gross Domestic Product
KTBL	–	Kuratorium für Technik und Bauwesen in der Landwirtschaft
NABIM	–	National Association of British and Irish Millers
OECD	–	Organization for Economic Cooperation and Development
OT	–	Ochratoxins
PPB	–	Parts Per Billion (i.e. micrograms (µg) per kilogram)
RASFF	–	Rapid Alert System for Food and Feed
TCT	–	Trichothecenes
UK	–	United Kingdom
USA	–	United States of America
USDA	–	United States Department of Agriculture
WHO	–	World Health Organization
ZEA	–	Zearaleone

1 INTRODUCTORY REMARKS

Food is one of the most emotive topics in the world. It is at the base of the hierarchy of needs as described by Maslow (1954), it has spiritual connotations, appearing in scriptures of all major religions, it is a social activity shared daily amongst friends and family and of course, passing into, and becoming part of the body, it is also a topic of heated debate regarding health and safety. People around the world face many dangers related to the food they eat daily. The actions people take regarding such risks and hazards are often highly emotive and irrational; often different to what science tells us. Perceptions guide various debates whereas scientific facts are frequently overlooked. In contrast, real hazards are often neglected in private decision-making.

A series of food safety crises since the 1990's, including Bovine Spongiform Encephalopathy (BSE), dioxin contamination in food chains, the debate about the effects of acrylamides, and the identification of emerging pathogens such as E. coli have evoked broad public concern about the safety of the food and feed chains. In this context, mycotoxins, i.e. toxic fungal metabolites, are considered one of the most underestimated and ignored sources for foodborne and feedborne diseases (Wild and Gong, 2010). Indeed, they are widely neglected (Bhat et al., 2010) and insufficiently recognised (Peraica et al., 1999).

This paper aims to provide clear, understandable and science-based evidence on the importance of mycotoxins versus other causes of foodborne and feedborne diseases in the past, present and future. Moreover, it is an objective of this research to provide a sound analysis of the potential economic and health effects of an increasing mycotoxin problem. This includes the farmer as well as other market stakeholders and society at large.

The objectives are challenging. Answering the associated questions needs a thorough analysis which is reflected by the structure of this report. Following these introductory remarks in chapter 1, the causes of foodborne and feedborne diseases are discussed in general but also with respect to mycotoxins in chapter 2. The discussion particularly looks at the past, present and future of such foodborne and feedborne illnesses thus highlighting their complexity and dynamics. Chapter 3 explores a variety of impacts of mycotoxins on farming, the agricultural value chain and the society at large; a wide spectrum of effects is discussed starting with economic impacts for arable farmers and finishing with an analysis of possible health issues on consumers. A comparison of the risks and hazards associated with mycotoxins versus other food-related issues is provided with chapter 4 before chapter 5 draws some conclusions and recommends actions for the various decision-makers.
Throughout the report, the British, German and partially the French perspective is foremost used. However, the European Union (EU) and global dimensions are also integrated.

2 GENERAL AND SPECIFIC CAUSES OF FOODBORNE AND FEEDBORNE DISEASES

2.1 ANALYSIS OF MAJOR DRIVERS AND SOURCES AT PRESENT AND IN THE PAST

2.1.1 Initial Definitions and Figures

Human foodborne and animal feedborne diseases as understood by the World Health Organization (WHO) are diseases that spread by food and feed consumption as well as beverages and drinking water (Sockett, 1993). There are about 200 known diseases that are transmitted via food (Kruse, 2015; Pavia de Sousa, 2008) which is usually contaminated with a pathogen or toxicant. These can be bacteria, viruses, chemicals, poisonous plants, fungi, and other natural toxicants (Aidoo, 2009). Accordingly, related illnesses are classified into infections and intoxications (Sharma et al., 2009):

- Foodborne and feedborne infections are caused by the entrance of pathogenic microorganisms contaminating food or feed into the body, and the reaction of the body tissues to their presence. Major pathogens can be bacterial, viral, or parasitic. Typical infectious diseases are, among others, salmonellosis, campylobacteriosis, E. coli infection, bacillary dysentery, cholera, listeria monocytogenes infection and hepatitis A.
- Foodborne and feedborne intoxications are caused by consumption of food or feed containing bio-toxicants found in tissues of certain plants and animals, metabolic products, i.e. toxins, formed and excreted by micro-organisms, and poisonous substances and chemicals which may be added to food during production, storage, processing, transporting etc. Often, intoxications are caused by Staphylococcus aureus, Bacillus cereus, Clostridium perfringens, Clostridium botulinum, toxic fishes and fungi. The latter may cause various forms of mycotoxicoses, for example aflatoxicosis.

The agents which cause foodborne and feedborne diseases are numerous. Sharma et al. (2009) list 65 groups of agents. Their importance changes over time and location and can lead to severe health consequences. Indeed, foodborne diseases are considered a serious health problem (van de Venter, 2000) particularly targeting vulnerable groups (such as children, pregnant women, the elderly, or persons who have a weakened immune system) causing kidney and liver failure, brain and neural disorders, reactive arthritis, cancer, septicaemia, and even death (Kruse, 2015; Sockett, 1993). Kruse (2015) quoting WHO (2015) provides figures on how foodborne diseases currently affect humans:

- Globally, approximately one in ten people fall ill every year from contaminated food. This is more than 600 million people. Around 420,000 of them die of which one third are children under five.
- The burden varies considerably around the world: Africa and South-East Asia have the highest incidences and death rates, and Europe is comparatively "safe". Nevertheless, **over 23 million people in Europe fall ill from contaminated food every year, with 5,000 reported deaths.**

Comparable data are seldom reported on a country basis. However, such information is at least available for some developed countries. For example, figures for the United Kingdom (UK) published by FSA (2011) reveal that each year around one million people suffer from foodborne diseases of which around 20,000 receive hospital treatment and 500 die. In the United States of America (USA), 4 percent of all foodborne illnesses lead to hospitalisation and 0.1 percent of all monitored cases are fatal (CDC, 2015).

Globally, diarrhoeal diseases cause the majority of the burden:

- On average, almost 550 million cases and over 230,000 deaths are registered annually (Kruse, 2015; WHO, 2015):
- The Norovirus (causing 124 million cases and 35,000 deaths) and bacteria such as Campylobacter spp. (95 million cases and 21,000 deaths) and E. coli (111 million cases and 63,000 deaths) are the most frequently reported causes for diarrhoeal diseases.
- Other globally important pathogens are Salmonella bacteria, the Hepatitis A virus, Toxoplasma gondii, nematodes, and
- mycotoxins such as aflatoxins.

Aflatoxins are particularly interesting: These specific mycotoxins **have globally caused only 22,000 reported cases of illness and more than 19,000 deaths**, according to WHO (2015 p75). Obviously, it has a high mortality rate, i.e. people having been contaminated with aflatoxins are heavily endangered. This concerns first of all the North and West Africa region, the South-East Asian region, including China, and India as well as neighbouring countries. Interesting to note is also that WHO (2015) considers its own coverage of the specific problem as only "tipping the iceberg".

In Europe, the situation is different (WHO, 2015). Here, diarrhoea accounts for about 96 percent of all registered foodborne illnesses: **Approximately 15 million people fall ill from the Norovirus and close to 5 million from Campylobacter spp. These two pathogens and Salmonella cause almost all of the 5,000 deaths per year**. Less often noticed but still important in terms of obvious illnesses in

Europe are, among others, pathogens such as Toxoplasma gondii, Giardia spp., Cryptosporidium spp., E. coli, Listeria monocytogenes, the hepatitis A virus, and dioxin.

These figures however, point at a remarkable uncertainty, because for the years 2013 and 2014, EFSA (2015a; 2015b) reported not millions (as the WHO) but only around 45,000 human cases of foodborne diseases in the EU leading to more than 5,000 hospitalisations and well below 100 deaths per annum. Evaluating numbers in regards to foodborne diseases is evidently an imperfect undertaking. Indeed, it is argued that the numbers of cases that come to the attention of the healthcare services is extremely low, with even fewer cases investigated (van de Venter, 2000). Käferstein et al. (1997) also call the existing data collection as merely the "the tip of the iceberg".

Real cases of foodborne diseases might thus be 300 to 350 times higher than reported cases (WHO, 1997). Even in a highly developed country such as the USA, non-reporting of foodborne illnesses is a problem. According to Andrews (2014), approximately 30 cases of Salmonella, E.coli and Campylobacter go unreported for every diagnosed case; a Vibro cholerae infection is reported just once in 150 cases; and although it is estimated that the Norovirus infects 5 million people, it is almost never detected. McMillen (2011) states that foodborne disease outbreaks caused 23,152 cases of illness in the USA in 2008; however, at the same time it is estimated that contaminated food has caused as many as 48 million illnesses. That is one reported case per more than 2,000 illnesses!

Reasons for the many unreported cases are complex: Often, patients with weak symptoms do not seek a doctor's advice – and if they do, such cases might not be reported to the food control agencies (van de Venter, 2000). As a result, it is impossible to develop perfect global or European information and thus develop a precise understanding of the impacts of foodborne (and feedborne) diseases and their costs to human society (OECD and WHO, 2003). This high level of uncertainty should be borne in mind with regard to the following analysis of the importance of major foodborne and feedborne diseases.

2.1.2 The Importance and Causes of Major Foodborne Diseases Over Time

Major diseases have collectively always been a part of human history and influenced social development in various ways. Some interesting findings, in chronological order, are depicted in Figure 1. It is therefore apparent: Each historical period had major foodborne diseases.

Figure 1 ~ Major Foodborne Diseases in Human History: A Snapshot

Time horizon	Finding
Stone Ages	Before fire and cooking food was adopted, our ancestors probably experienced more fatalities than us from microbial and toxic exposures; with primitive cultivation and storage of crops, they would have been more frequently exposed to spoilage molds too.
Ancient Times	Evidence suggests Ancient Egyptian and Greek societies suffered a lot from parasites, plant toxins, and maybe also fungal toxins. The death of several archaeologists visiting ancient graves and caves is related to a particular mycotoxin, the so-called Ochratoxin A.
Biblical Times	The exodus of the Israelites from Egypt was seemingly triggered by a food poisoning incident – probably ergotism.
Etruscan Times	The Etruscan civilisation has been ascribed as suffering from what is known today as toxins produced by Fusaria.
Roman Times to Middle Ages	From the Roman times until the Medieval period, lead was used to cover cooking pots and "lead sugar" was used to sweeten wine. Consequently, epidemic colic caused severe illness and death of many people including some Roman emperors.
Middle Ages to 20th Century	Ergotism was a very common illness in the Middle Ages. Cereals were contaminated with ergot alkaloids caused by fungi. When eaten and digested, they caused what was called St. Anthony's Fire at this time. More than 100 major outbreaks of this "sacred fire" were recorded between the 8th and 16th century with as many as 40,000 deaths per incident. Still in the 20th century, some outbreaks of ergotism were observed in Europe and Africa, especially in times of famine, causing numerous deaths.
16th to 19th Century	Mold poisoning, in general, has most probably contributed to a large extent to the population growth suppression in Europe between the 16th and 19th century. The "Sun King" Louis XIV and his courtiers verifiably suffered from roundworms and liver fluke, two pathogenic organisms.
19th Century	During the Industrial Revolution in the 19th century, canning of food for preservation became more and more popular. Unfortunately, cans at this time were often made from heavy metal, such as lead, causing similar problems as in Roman times.
Modern Times	In modern times and with increasing food processing, errors in food processing became a new driver and were responsible for the widespread appearance of, e.g., E. Coli and Norwalk-like infections.

Source: Own figure based on Ashiq (2015), Peraica et al. (1999), Pittet (1998), Satin (2014a; b; c; d) and Schoental (1984).

The impact of specific pathogens changes over time, even in the short run. In the USA, for example, bacteria caused the majority of foodborne disease outbreaks between 1998 and 2002, whereas between 2004 and 2006 viruses triggered the highest number of such illnesses (Nyachuba, 2010). Several drivers are behind such short-term and/or long-term changes of importance (Newell et al., 2010; Rocourt, 2003; van de Venter, 2000) with multiple factors having interacted, leading to fast-developing illnesses (Peraica et al., 1999). They can be grouped into "nature-made" and "man-made" causes:

- Important nature-made triggers are, for example, changes in pathogens, changes in wildlife habits, and consequences of climate change.
- Man-made changes are more numerous: poverty, changing dietary and cooking habits, health sector performance, demographic changes, increasing travel and migration, accelerating trade in food, changing feeding and agronomic practices, and lifestyle are examples.

All factors that have contributed to foodborne (and feedborne) diseases in the past still exist (van de Venter, 2000). Consequently, **such illnesses will remain a major global health problem for people and animals, with implications for both, economic welfare and human well-bei**ng (Newell et al., 2010).

It is beyond the scope of this paper to deal with this complexity of causes, drivers and effects. In the following, the particular importance of one group of pathogens – mycotoxins – is explored. While mycotoxins are hitherto a "hidden" subject in scientific debate and public discussion, the following demonstrates that foodborne (and feedborne) intoxications from mycotoxins have not only played a pronounced role in the past, but may become more important in coming years.

2.2 The Particular Importance of Mycotoxins for Illnesses

2.2.1 Mycotoxins, What Are They?

Mycotoxins are toxic secondary fungal metabolites (Walker, 2015). This means they are made by fungi as a by-product (consequence) of metabolism (living). It is these by-products and not the fungi themselves that are poisonous. **There is much about mycotoxins that society does not yet know, such as how toxic they are at very low levels or how to remove or denature them. Indeed, once grain or other agricultural products are contaminated, there are today in most cases no cost-effective methods of reducing them.** Yet society is learning fast. For example, it is well understood that Fusaria, a common field fungi, produce common mycotoxins such as Deoxynivalenol (DON) and that Aspergilli and Penicillia, major grain store fungi, produce, Aflatoxin (AF) and Ochratoxin (OT) (Ashiq, 2015). Other important mycotoxins are Fumonisins (FUM), some Trichothecenes (TCT), Zearaleone (ZEA), Ergot alkaloids and Patulin. The most important mycotoxins for humans and animals are listed and discussed in more detail within Annex A.

Over the past two decades, other, previously unknown types of mycotoxins have been identified by scientists such as the T2 toxin and the HT2 toxin (e.g. Stancic et al., 2012). It is not clear whether this is because of the improvements in analytical techniques that mean that previously present mycotoxins are now identifiable or through mutations or other changes to the environment. In any case, **new mycotoxins are now known about that were unknown before, and the story continues.**

It is also noteworthy that not only "parent" mycotoxins but also "modified" mycotoxins are increasingly considered as a concern. Such "modified" (or masked or bounded) mycotoxins are found in plants and result from plant defence reactions after fungal infections or can also be produced by the fungus itself (EFSA, 2014b). Literature data shows that such modified forms of mycotoxins may add substantially to the overall mycotoxin burden, in particular for ZEA and FUM (EFSA, 2014b): The joint exposure to "parent" and "modified" mycotoxins is considered to be much higher than the exposure of "parent" mycotoxins alone. Consequently, the risk for human and animal health related to their (combined) presence should not be neglected and poses a need for further research.

2.2.2 Mycotoxins' Place in History

Throughout history, fungi have been major causes of food contamination through the production of mycotoxins (Ashiq, 2015). **First records of mycotoxin-related foodborne diseases are from ancient China 5,000 years ago** (Angsubhakorn, 1992). Mycotoxicoses – diseases which are caused by mycotoxins – have had several revivals since then, especially since medieval times. They have been responsible for major human and livestock epidemics (Pitt, 1992). In the 1920s, for instance, many people died in Japan from the so-called "yellow rice disease" (Udagawa and Tatsuno, 2004), while in Russia alimentary toxic aleukia led to the death of many – over 100,000 people – with mortality rates as high as 60 percent (Peraica et al., 1999; WHO, 2011).

These and many other outbreaks among humans (and animals) had not hitherto gained much attention in scientific and medical literature, probably due to language problems and a poor understanding of the biochemical background. This changed in the 1930s. Again in Russia, many horses fed with hay contaminated with a black mold, died (USDA, 2006). Due to the crucial economic and military relevance of horses in Russia at that time, political measures as well as veterinarian research were introduced to combat the illness. The latter led to the discovery of stachybotryotoxicosis – the first well-understood mycotoxicosis.

However, a structured observation of mycotoxins and its relevance for foodborne as well as feedborne diseases did not happen before the outbreak of the so-called "turkey X disease" in the UK and USA in the 1960s (Ciegler and Bennett, 1980; FAO, 2001). The investigation of this disease led to the discovery of AF, a group of mycotoxins, lethal to humans (see also Annex A). **Since then, many mycotoxins have been discovered. The exact number is not known and continues to**

rise (CAST, 2003) but while at least 300 have been counted (Aidoo, 2009; Bhat et al., 2010; Milicevic 2009; Schatzmayr and Streit, 2013; Streit *et al.*, 2012, WHO, 2011), only those which are carcinogenic and/or very toxic have been focussed on in detail by scientific research (Zain, 2011). It is the carcinogenic nature in particular which has led to much greater research in recent years.

2.2.3 Mycotoxins: The Neglected Danger is Pervasive

Mycotoxins are toxic to humans and animals, even in low concentration (Zain, 2011). They arise when environmental and social conditions combine to favour the growth of molds and can be fatal (Peraica et al., 1999). **Unlike bacterial toxins, fungal toxins are not proteins and therefore barely detectable by the immune systems of humans and animals** (Aidoo, 2009). **Mycotoxins exhibit a number of effects** due to their very diverse structures (Streit et al., 2012) including acute and chronic toxicity, **specifically: carcinogenic, mutagenic, genotoxic, and immunotoxic effects** (Ashiq, 2015; Shepard, 2006).

The broad spectrum of mycotoxins and widespread relevance for foodborne (and feedborne) diseases, have so far not led to much attention from stakeholders of the food value chain, medics or the broader public. In fact, as mentioned in the introductory remarks, **mycotoxins are considered one of the most underestimated and ignored sources for illnesses** (Wild and Gong, 2010), widely neglected (Bhat et al., 2010), and insufficiently recognised (Peraica et al., 1999). Etzel (2006) calls it the "great masquerade" of the 21st century, because of the complexity of mycotoxicoses in terms of pathogens and related diseases.

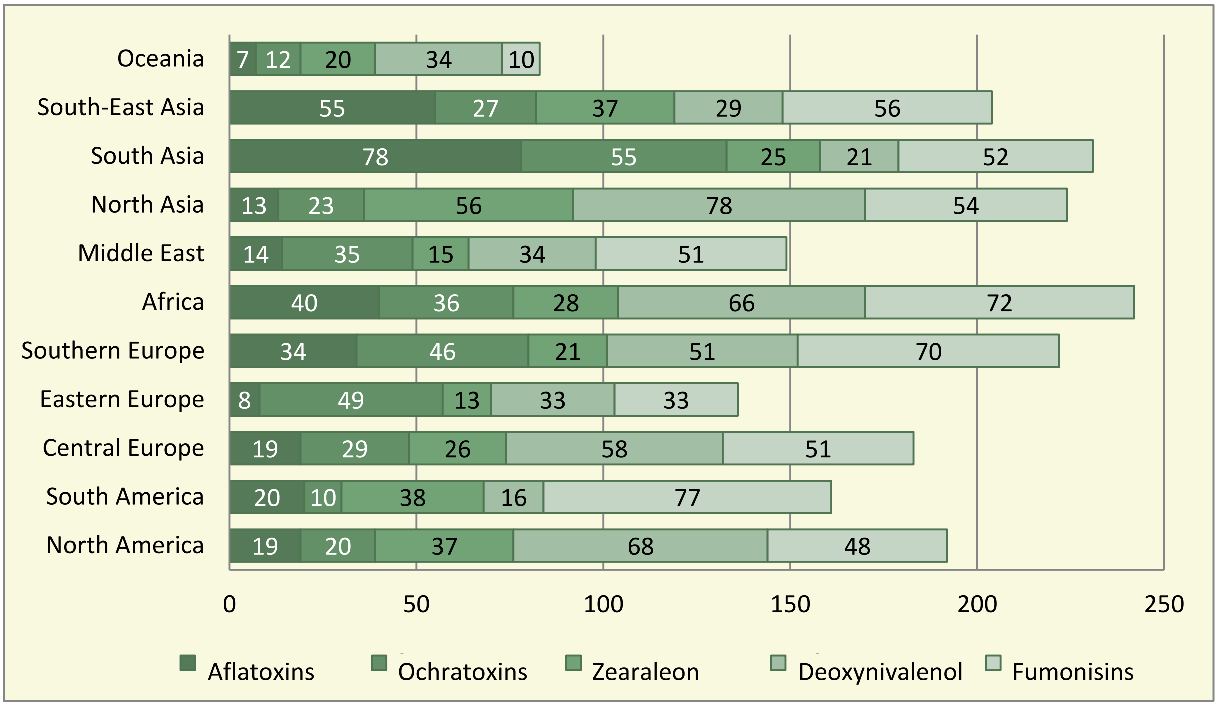
What are the main reasons for such public unawareness of mycotoxins? Mycotoxicoses often present as uncertain, sub-acute or chronic health conditions. Mycotoxin-related illnesses are systemized in different ways depending on different occupational groups (Zain, 2011). One way of systemization is to focus on the illness caused by mycotoxins itself (through physicians). However, other options are to focus on the organ they affect (through clinicians), on the generic groups (through biologists), on the chemical structures (through chemists), or on the biosynthetic origins (through biochemists).

These conceptual differences hamper communication and information exchange between disciplines. To make things worse, typical mycotoxin intoxication symptoms, such as abdominal cramps, vomiting, headache, and nausea, can also be linked to Staphylococcus aureus, Bacillus cereus, and heavy metals (WHO, 2011) and are, hence, often wrongly diagnosed. Finally, contemporary mycotoxin-related outbreaks are comparatively rare in developed countries where most mycotoxin research is located.

This limits media awareness and consequently public debates and policy reflections despite the fact that mycotoxins are a major danger and even killer of human life, especially in developing countries.

The subsequent ignorance, however, is far from justified. Mycotoxins can be produced on a wide range of agricultural commodities and under a diverse range of situations worldwide. A global monitoring project lasting more than ten years analysed over 70,000 samples of primary crop products (Schatzmayr and Streit, 2013): It concluded that 72 percent of all samples contained at least one mycotoxin, and almost 40 percent of samples were co-contaminated with two or more mycotoxins. Figure 2 shows the main finding of this study per surveyed world region and mycotoxin.

Figure 2 ~ Prevalence of Mycotoxins in World Regions (accumulation of percent values per mycotoxin with regard to analysed samples)



Source: Own figures based on Schatzmayr and Streit (2013).

The figure highlights at least three interesting aspects pointing at the facts that **mycotoxins are everywhere and often do not come alone**:

- First, mycotoxin contamination is a global issue.
- Second, co-occurrence is the rule, not the exception (see also Wild et al., 2015). In all but one world region (Oceania) the accumulated percentages are well above 100. This indicates that very often more than one mycotoxin has been found in a sample when tested. Most recently, this has been described comprehensively – using a French example – in Orlando and Leblanc (2016).

- And third, the mycotoxins tested are ubiquitously present in agricultural products. Although percentage values in more developed world regions are often lower than in less developed regions, they are still considerable. However, the importance of particular mycotoxins is different from continent to continent. Respective findings of Bhat et al. (2010) are supportive.

Taking the global perspective, it is very interesting that the Schatzmayr and Streit (2013) data almost perfectly correspond to information provided by Rodrigues and Naehrer (2012) who have also analysed 10,000 samples of primary products in the Americas, Europe and Asia over several years (2009-2011). This is shown with Figure 3.

Figure 3 ~ Prevalence of Mycotoxins Globally (percent of analysed samples)

Study	Aflatoxin	Ochratoxins	Zearaleone	Deoxynivalenol	Fumonisins
Schatzmayr and Streit (2013)	29	28	44	63	62
Rodriguez and Naehrer (2012)	33	28	45	59	64

Source: Own figure based on Schatzmayr and Streit (2013) as well as Rodrigues and Naehrer (2012).

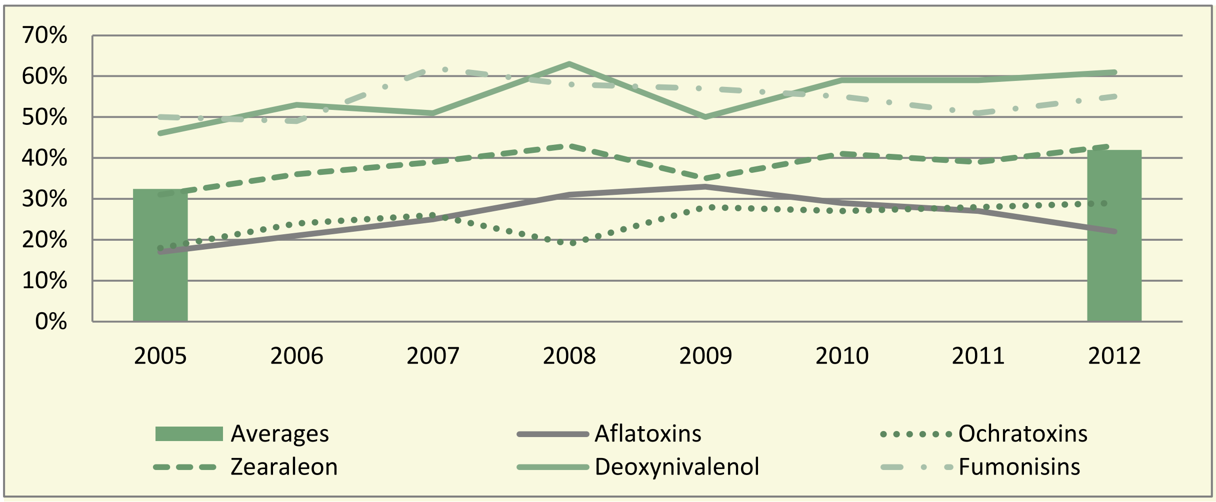
Comparing the percentage of samples that contain mycotoxin from the two studies supports the following assumptions:

- Regardless of the methodological approach, mycotoxins can be detected everywhere and frequently.
- The associated problems might exist at large scale and are a global phenomenon.

Furthermore, studying the Schatzmayr and Streit (2013) data over time reveals the percentage of samples containing mycotoxins over time, especially between 2005 and 2012, the most recent years the data was available (see Figure 4).

The figure indicates an increasing occurrence of fungi-based toxins in world agriculture. Combining the five groups of mycotoxins in Figure 4, the ratio of positive samples when tested for mycotoxins has increased by about a third: In 2005, 32 percent of all samples had mycotoxin contamination, but by 2012, the rate had risen to 42 percent. The same is true in Europe: According to Streit et al. (2013), 20 percent of analysed agricultural samples of that region in 2005 have been tested positive for ZEA and 40 percent for DON; six years later, 30 percent of samples were contaminated with ZEA and 60 percent with DON.

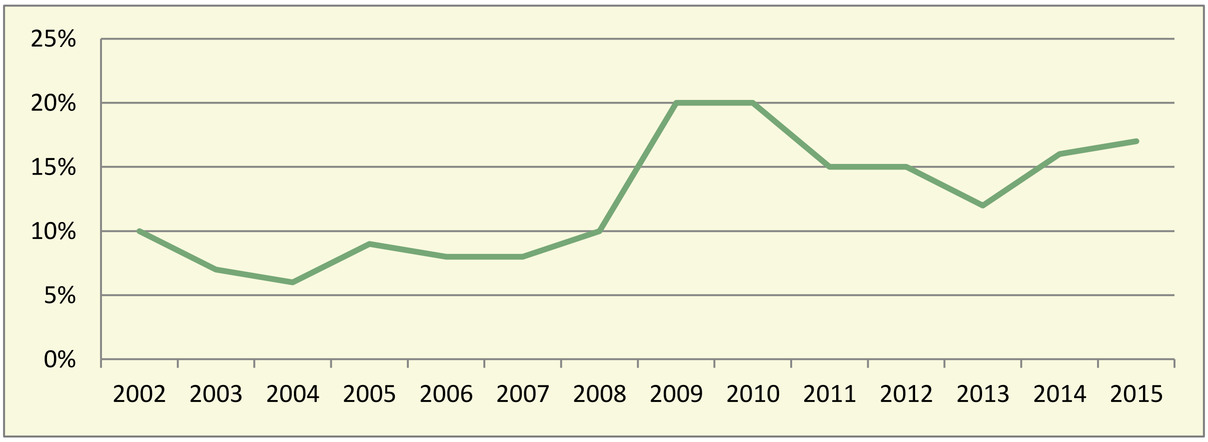
Figure 4 ~ Development of Percentage of Positive Samples Contaminated with Mycotoxins, 2005-2012



Source: Own figure based on Schatzmayr and Streit (2013).

Since 2002, the European Rapid Alert System for Food and Feed (RASFF) has reported annually on notifications by hazard category in the EU, including mycotoxins (see RASFF, various years). Accordingly, it concludes that **the importance of mycotoxins has increased over time in relation to other categories of potentially hazardous substances** – such as allergens, bio-contaminants, heavy metals, pathogenic microorganisms, residues of veterinary products, etc. – as Figure 5 visualises.

Figure 5 ~ Share of Mycotoxin-Related Notifications Among All Notifications within the Rapid Alert System for Food and Feed *)



Source: Own figure based on RASFF (various years);
**) since 2006 change of lower maximum limits and increased border control (e.g. as regards pistachios and hazelnuts.*

While on average only 7.7 percent of all hazard notification of food and feed in the EU were caused by mycotoxins in the three first years covered by the RASFF data base (2002-2004), this percentage has almost doubled for the past three years (average value for 2013-2015: 15.0 percent).

Although the trend is obvious, the two years 2009 and 2010 need some additional interpretation. In these two years, the number of notifications of other than mycotoxin-contaminated samples were lower than normal. Yet, a closer look into the data of the RASFF reveals two additional interesting facts indicating an increasing importance of mycotoxins' in feed and food chains:

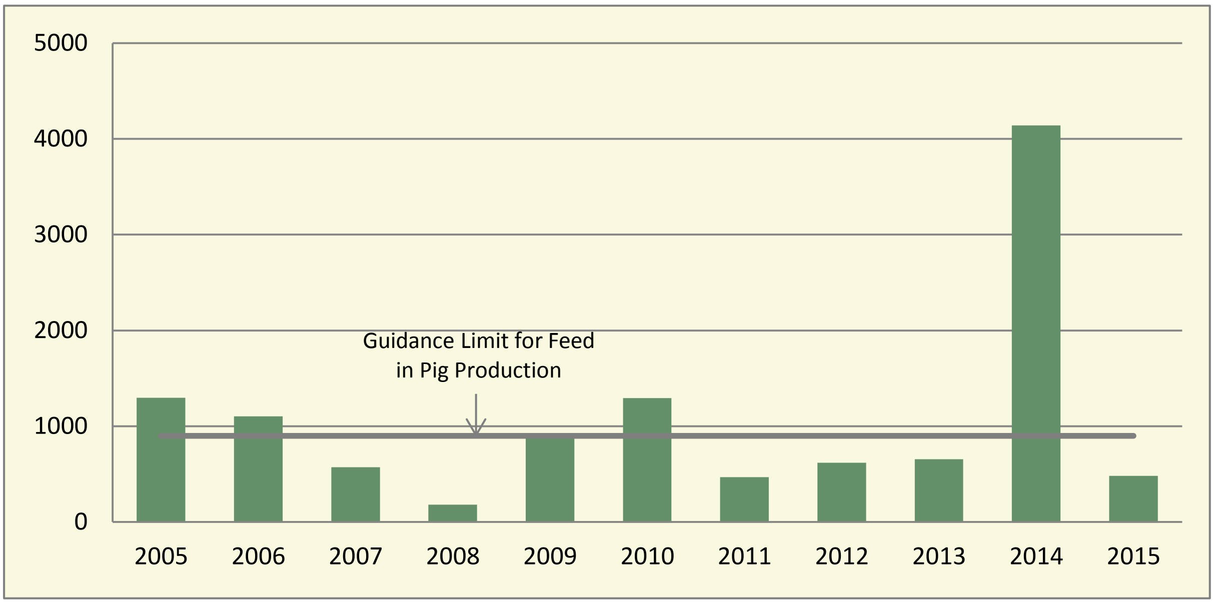
- In recent years, mycotoxins have regularly been in the "top three" causes for RASFF notifications. They were in third place in 2004, 2008, 2013, and 2014, rose to second place in 2012 and most recently in 2015, and were the very top causes in 2006, 2009, 2010, and 2011. Only in some of the early years of monitoring, namely 2002, 2003, 2005, and 2007, mycotoxins were fourth place of notifications.
- Most border trade rejections are currently related to notifications for mycotoxin-contaminated food and feed (see also Marin et al., 2013). Food and feed from third countries is more frequently contaminated than EU food and feed, which demonstrates EU member states can still combat the mycotoxin problem to a large extent.

The word "still" in the sentence above indicates that the EU and its member states are not free of emerging challenges. **Variations from year to year occur and "high-mycotoxin" years are common**. This is exemplified using maize as a potentially "high-mycotoxin" agricultural crop. Figure 6, for example, depicts average DON concentration in maize samples in Austria in the past decade.

DON concentration was particularly high in 2014, reaching, on average, more than 4,000 parts per billion (PPB, i.e. µg per kg). According to EU guidelines described e.g. in Swiss Granum (2015), piglets and sows should not be fed with feed containing more than 900 PPB DON in feed (at 88 percent dry matter). That means, that average Austrian maize that year could not be fed unblended. Blending maize-based feed was a European-wide problem in 2014 since almost all regions in middle and central Europe had a "high-DON" year: Caballero (2014) stated that 30 percent of all tested maize in Europe had DON levels of 3,000 PPB or more (see also Noleppa, 2015; Swiss Granum, 2015).

In 2013, EFSA (2014a) reported that France even requested a temporary derogation to the maximum levels of mycotoxins in maize and maize products. It did so because French 2013 occurrence data of DON, FUM and ZEA in harvested maize significantly increased. According to EFSA (2014a), this has contributed to a situation, where some consumer groups faced an exposure close to what is considered an unsafe level. France seems to be slightly more vulnerable to some mycotoxins. Indeed, Meleard (2013) has shown that high DON concentration in wheat was found quite often in the following years: 2003, 2006, 2007, 2008 and 2012. These are five years within a decade.

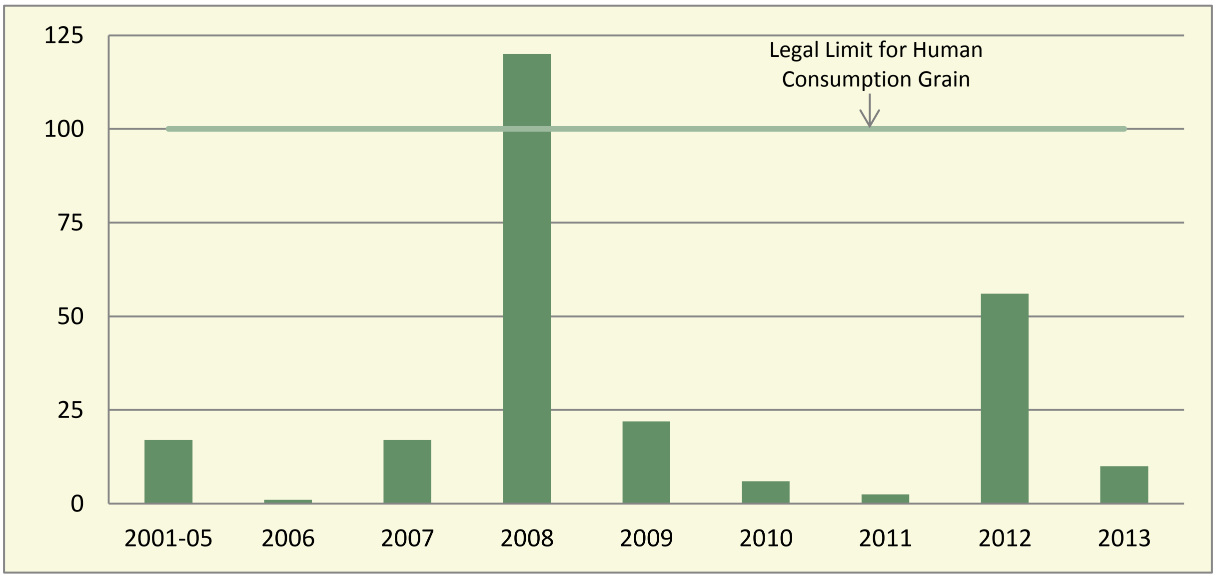
Figure 6 ~ Average Deoxynivalenol Concentration in Maize in Austria, 2005-2015 (in PPB)



Source: Own figure based on AGES (2016).

Another year with high DON and other mycotoxin levels in certain EU member states was 2009 (Channaiah, 2014; Kanora and Maes, 2009); and in the UK, 2008 was a problem year with respect to ZEA concentration as demonstrated by Figure 7. It becomes apparent: **Mycotoxins are clearly a problem across the EU, and decision-makers should be aware about the associated challenges, especially since the importance of mycotoxins is forecasted to increase.**

Figure 7 ~ Average Zearaleone Concentration in Wheat in UK, 2005-2013 (in PPB)



Source: Own figure based on data kindly privately supplied by Edwards S.

Following the link https://haccpeuropa.wordpress.com/tag/mycotoxins/, proves that product recalls due to excessive mycotoxin concentrations are more and more often reported. Accordingly, it may be stated that in 2014 alone, several products were recalled. Among others:

- Auchan BIO Galettes de Maïs (corn cakes) from France, were recalled because the product has been detected to be contaminated with mycotoxins.
- Kauratyyny Oat Rolls (frozen oat rolls) from Moilas Ltd located in Finland, had to be recalled because some of the batches may be contaminated with DON.
- An elevated level of OT A was detected in one batch of Girolomoni pasta from Ireland.
- Bio Village chez Leclerc Son de Blé from France was recalled because of DON contamination.
- AF was found in sunflower seeds from France also leading to a recall.

Also in 2015, such re-calls happened. An example is the withdrawal of cornflakes from Hahne, a German breakfast cereal company, due to a high DON contamination (see also Noleppa, 2015).

2.3 The Emerging Importance of Mycotoxins: Causes and Scale of the Problem

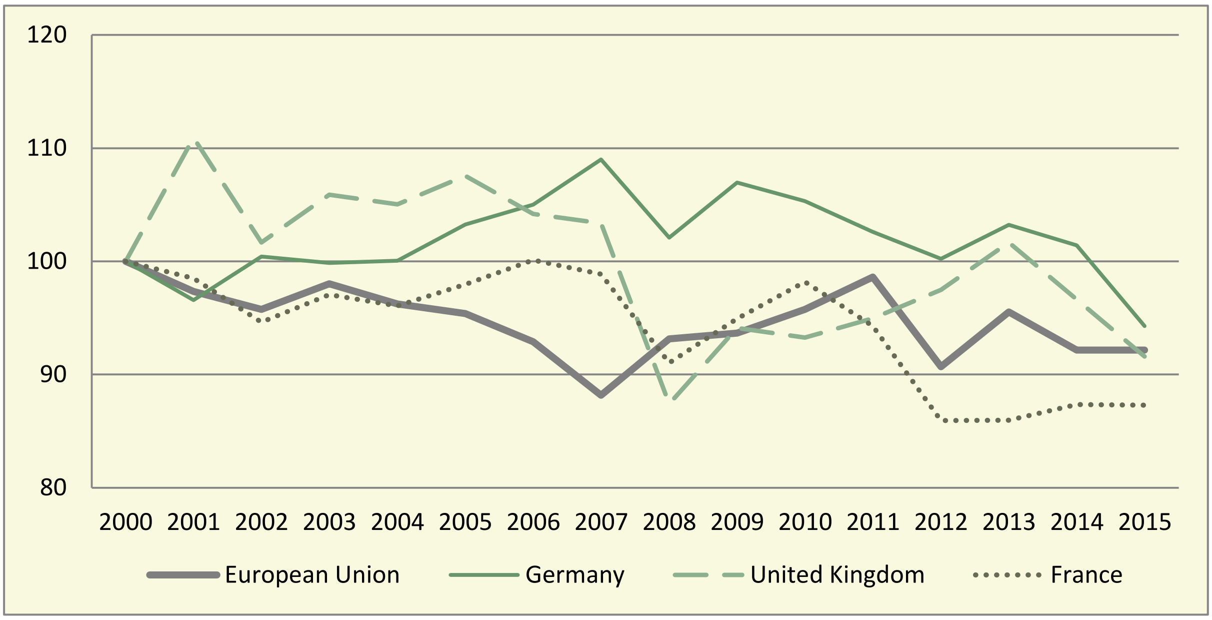
There are good reasons to believe that the presence of mycotoxins in many agricultural products for direct human consumption and animal nutrition may increase. A few key reasons are discussed here.

2.3.1 Declining Break Crop Area

A break crop is a broadleaf crop incorporated into a cereal rotation designed to separate cereals between years, allowing the soil to remove any built up spores that infect cereals. In particular, they help clean soils of fungal spores including fusarium. Break crops include all oilseed crops and pulses as well as non-combinable arable crops such as roots, field vegetables and rotational grass.

All UK agricultural costings books (see, e.g., Agro Business Consultants, 2015; Redman 2015) as well as standard calculation tables for Germany (e.g. KTBL, 2014) have wheat as the highest combinable crop gross margin over a long time series; wheat therefore occupies the greatest area in the arable rotation, as in many other EU member states such as France and Italy. In parallel, the area planted to break crops in the EU as a whole and also in individual member states such as Germany, France and the UK is gradually declining as is shown by Figure 8. This decline is set to continue, largely because the long term rise of oilseed rape (which peaked in 2012/2013) has come to a standstill and is now decreasing following the banning of neonicotinoids (HFFA Research, 2016).

Figure 8 ~ Change of Broadleaf (Break Crops) Arable Area in the European Union, Germany, France, and the United Kingdom (Indexed; 2000 =100)



Source: Own figure based on Eurostat (2016).

This means that the **cereal crops are moving closer together in the rotation**, with fewer break crop years between them. There is currently no evidence that this trend will stop, and **it implies that the pressure of managing cereal-based plant fungi producing mycotoxins is increasing**. Even the impact of the implementation of Ecological Focus Areas as part of the Greening regulations could turn out to be small. Certainly, it was not noticeable in 2015, the first year of the policy (as can be seen in Figure 8 with very low break crop areas).

The EU is adept at producing combinable cereals and importing vegetable proteins. Other countries compete at producing proteins and oils with crops such as soybeans. Indeed, EU agricultural policy is historically cereal-focussed, and lax on protein production. Hence, most protein crops are not subject to import tariffs into the EU, although wheat is exposed to tariff rate quotas and bound tariffs to limit its import (Nightingale, 2014). This policy discourages break crops, thereby increasing cereals. There is little evidence from economics or policy change that the farm rotation and therefore break crop popularity will undergo a renaissance in the UK, Germany or the EU as a whole in the medium term. **This will therefore present a factor encouraging mycotoxins to flourish.**

2.3.2 Rising Levels of Minimum and Zero Tillage

The benefits of deep cultivating are well rehearsed and long established. Ploughing buries crop residues, hides weed seed, lifts compacted soils and cleans the seedbed in preparation for the seed drill. Nevertheless, reduced and **minimum tillage techniques are an increasing practice throughout the EU** for two reasons:

- Ploughing is costly. It costs over EUR 100 to plough a hectare of arable land (KTBL, 2014). Shallow harrowing costs EUR 35. The difference of EUR 65 is equivalent to about 400 kg feed wheat at current prices, meaning ploughing would have to increase yield or reduce other costs by that much to be economic.
- The environmental benefit of low or no tilling is also important. Unploughed soil retains organic matter and micro-fauna. Both have fallen to low levels in ploughed fields across the EU. Farmers are increasingly aware of the benefits of organic matter and of micro-fauna such as worms in the soil. Organic matter slows erosion, increases water and nutrient retention and raises mineral availability for the crop (Bot and Benites, 2005). Micro-fauna helps build that organic matter as well as facilitate the drainage and general health of the soil.

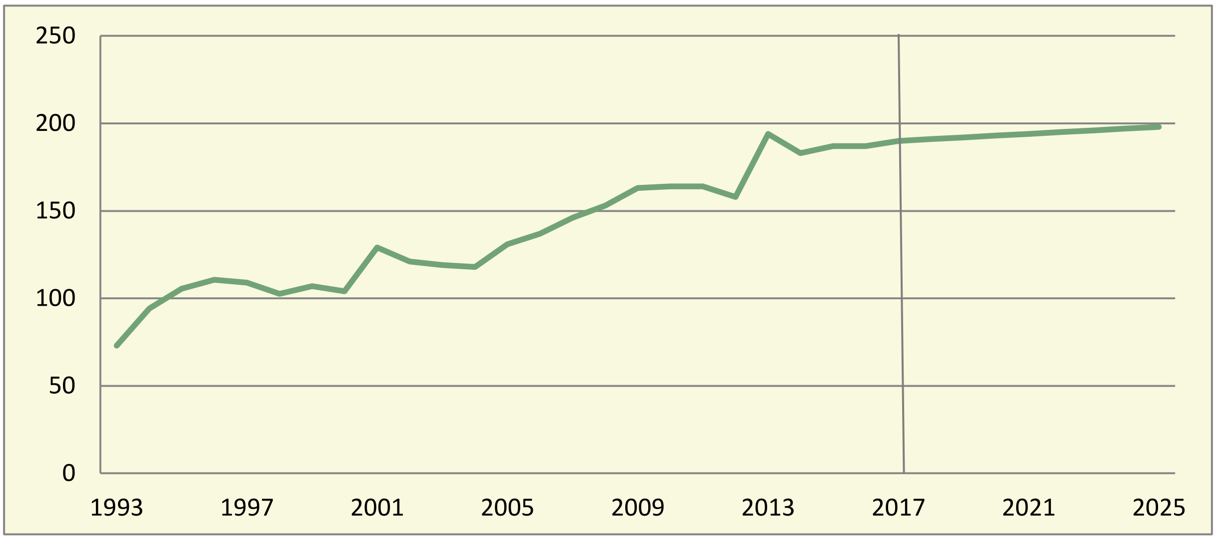
Yet ploughing buries crop debris and with it, fungal spores. **Minimal or untilled land carries a higher chance of spreading fungi that colonise crop residues and consequently facilitating mycotoxins**, as the debris remains on the surface of the soil for a longer time. Minimum tillage cultivation techniques were carried out on 37 percent of UK cereals farms in 2008 (Lang, 2010). The average size of farm using minimum tillage was 280 hectares compared with 175 hectares for those without minimum tillage. There is little empirical evidence to hand but this suggests minimum-tilled land is currently on the increase. If so, it will only add to the mycotoxin burden placed on agriculture.

2.3.3 Mycotoxins from Plant Residues, Particularly Maize

Fungal spores are prevalent on crop residues from previous crops, particularly maize. Growing wheat after maize encourages mycotoxin build up in the wheat. Most North European maize is grown for livestock feed as silage, usually within a "closed" grass and forage rotation, often only maize and grass. This means the lion's share of maize grown in many regions will not precede wheat. But not all.

The UK grows 180,000 hectares of maize, roughly a quarter of which is thought to be as a feedstock for anaerobic digestion (AD). This is often in substantial sized blocks of maize, potentially several hundreds of hectares at a time leaving potential "hot spots" of fusarium-based mycotoxin risks in areas of the UK where farming is dominated by the arable combinable crop rotation. Figure 9 demonstrates that the area of maize in the UK has doubled in the past 20 years.

Figure 9 ~ Development and Forecast of Maize Area in the United Kingdom, 1993-2025 (in 1,000 hectares)



Source: Own figure based on DEFRA data and Andersons own projection.

Maize is an efficient way of harvesting calories from land, so – regardless of the purpose of the energy – it is likely to remain a key component of agriculture and forecasters (The Andersons Centre undertakes regular short and long-term crop area projections) predict its continued growth.

Government incentives to produce renewable energy has for the time being subsided. However, climate change and human impact on it is not going to go away in the long term. Climate change and renewable energy policies may therefore look more towards agriculture in the long term. **Energy per hectare will remain a driver of the arable rotation in the long term and maize is therefore very likely to be included. This would add to the burden on mycotoxins on farm and therefore in food supply chains**. The situation may become even worse since by-product feeds of bio-energy production such as distillers dried grain with solubles (DDGS) often concentrate mycotoxins of the original substrate (Schatzmayr and Streit, 2013).

Analysis of factors affecting the incidence of DON in French arable rotations identified a high-risk previous crop coupled with a non-ploughing cultivation system leads to the highest DON levels in following crops with a median value of 1,220 PPB very close to the legal limit for food grains (Barrier-Guillot et al., 2004). Indeed, 52 percent of the samples in this study exceeded the legal 1,250 PPB limit. France is the largest producer of wheat, barley and maize in Europe (Coceral, 2016) so for the arable rotation, this is crucial. In some parts of France, cereals account for most of the cropping.

2.3.4 Climate Change and Mycotoxins

Most scientists agree that climate change is likely to affect the yield and ripening of crops globally (see e.g. Battilani et al., 2012; Miraglia et al., 2009; Paterson, 2010). They are also aware that this could place stress on crops, facilitating entry of fungal pathogens (Marroquin-Cardona et al., 2014). Indeed, in southern Europe and Hungary, changes to Fusarium and Aspergillus fungi in maize have already been identified (Paterson, 2010), leading to a rise in AF over DON, an observation supported by Farkas and Becxner (2011). AF is considerably more toxic than DON. Production of mycotoxins on crops varies depending on climatic factors such as temperature and relative humidity (Fernando, 2014). That's why a changing climate has a direct impact on mycotoxin production. **Mycotoxins are among the major foodborne risks that are most susceptible to climatic change.**

In line with this, a study by Battilani et al. (2012) is predicting AF contamination in maize and wheat will rise under a "+2°C" as well as a "+5°C" scenario. More particularly, the paper concludes that AF contamination is the main emerging issue related to maize grown in Europe due to climate change. It even suggests some current maize production areas might decline as contaminated crops will have a much lower economic value, making the production process uneconomical in certain locations.

Recent predictions have suggested fungal pathogens across the globe are migrating at 5 to 6 km per year on average from the equator towards the poles (Magan and Medina, 2016). The diversity of pests and diseases is seen increasing, impacting on food production. The migration of the mycotoxin-producing fungi is therefore increasingly encroaching on the traditional "bread baskets" for food production, including EU member states. This will be linked to increased mycotoxin contamination of cereal crops, which could cause new or greater problems to manage them in coming years. Newly identified mycotoxins occurring for the first time are also considered likely by the scientists, facilitated by climate change, having "profound impacts on food sustainability in many regions of the world" (Magan and Medina, 2016).

2.3.5 Emerging Importance of Mycotoxins is Mirrored by Regulators Awareness

Regulators are mostly aware of the emerging importance mycotoxins have and regulate accordingly. Since the late 1960s, most countries have developed such regulations, now covering the majority of countries and almost everybody and developed into harmonized international mycotoxin regulations in trading blocs such as the EU and Mercosur. However, despite these efforts, sources of mycotoxin-related diseases are still increasing (Milicevic, 2009).

Mycotoxins can be detected today at miniscule levels. Regulations can therefore legislate at such levels if necessary. Maximum legal levels of mycotoxins in food are set at EU level. Since their introduction in 2001, they have been updated regularly and are now amongst the most comprehensive mycotoxin regulations in the world (Siegel and Babuscio, 2011; Wu, 2008).

The principal piece of EU legislation regarding mycotoxins in food is Commission Regulation (EC) No. 1881/2006 as amended. As the presence of mycotoxins in samples of grain is heterogeneous, clear regulations have also been laid out on how to sample them. This is detailed in Commission Regulation (EC) No. 401/2006 as amended. Moreover, the Commission Recommendation (EC) No. 576/2006 on the presence of DON, ZEA, FUM and other mycotoxins in products intended for animal feeding applies. The legal and the advisory limits of the main mycotoxins in EU grain are laid out in Figure 10 and Figure 11.

Figure 10 ~ Legal Limits for Mycotoxins in Grain for Human Consumption in the European Union (in PPB)

	Deoxynivalenol	Zearaleone	Ochratoxins	Fumonisins
Unprocessed Wheat and Barley	1,250	100	5.0	-
Unprocessed Maize	1,750	350	-	4,000
Unprocessed Oats	1,750	100	5.0	-
Flour	750	75	3.0	-
Finished Products	500	50	3.0	800
Maize for Human Consumption	-	-	-	1,000
Infant Food	200	20	0.5	200

Source: Own figure based on Commission Regulation (EC) No. 1881/2006.

Figure 11 ~ Guidance Values for Mycotoxins in Grain for Animal Feedstuffs in the European Union (in PPB)

	Deoxynivalenol	Zearaleone	Ochratoxins	Fumonisins
Cereals and Cereal Products	8,000	2,000	250	-
Maize By-Products	12,000	3,000	-	60,000
Most Complete Feedstuffs	5,000	500	-	-
Complete Pig Feedstuffs	900	100 (sow) 250 (fattener)	50	5,000
Complete Poultry Feedstuffs	5,000	-	100	20,000
Complete Ruminant Youngstock Feedstuffs	3,000	500	-	50,000

Source: Own figure based on Commission Recommendation (EC) No. 576/2006.

The legal limits in the EU are different for food and feed: With respect to feed, only AF B1 is regulated while other mycotoxins have non-binding guidance values.

According to Article 17 (1) of the Regulation (EC) No. 178/2002 of the European Parliament and Council, the supplier must ensure that foods and feeds satisfy the relevant regulations. However, the precise processes, including methods of sampling and analysing, are not rooted in EU legislation.

Despite regulation 401/2006 as amended, Siegel and Babuscio (2011) argue that testing is almost arbitrary, at least very complex and often not conclusive. Sampling methods are increasing the chances of error since mycotoxins develop in localised areas and hot spots. Thus, a single highly contaminated kernel in a ten kg lot of 20,000 otherwise healthy peanuts can determine the test result and can lead to the violation of EU law – making sampling more of a lottery than a profound analytical analysis. The same may apply to DON and ZEA measurement using a 1 kg sample of grain in a huge truck carrying several tonnes. Since the costs of a rejection in an unrepresentative sample is borne by the producer or seller, they are often forced to rely on costly secondary analyses by external laboratories (Siegel and Babuscio, 2011).

Excursus: What is a Part Per Billion?
Several times above, the term PPB for "parts per billion" has been used. Demonstrating what a single PPB actually is, is difficult. Nevertheless, it can be equated to 1 second in nearly 32 years and is equivalent of a square centimetre – or approximately a 1-EUR-coin – in a 10-hectare field.

3 THE EFFECTS OF MYCOTOXINS AT PRESENT AND IN THE FUTURE

It becomes clear: Fungi and their metabolites – mycotoxins – are becoming more of a problem throughout the EU (and elsewhere). DON and ZEA in particular, the major fusarium mycotoxins, but also AF and other mycotoxins such as FUM are on the rise (Leslie et al., 2008; Gilchrist and Dublin, 2002). **But what does it mean for agriculture, food consumption and the society at large**?

3.1 ANALYSIS OF CURRENT AND POTENTIAL EFFECTS ON AGRICULTURE

Agriculture is the first point at which mycotoxins are able to enter the food supply chain. **If most mycotoxins are kept out of the crop before harvest (DON and ZEA for examples), they are unlikely to become a problem along the value chain** (Leslie and Logrieco, 2014). However, once mycotoxins are present, they remain in the food or feed product and are very difficult to remove. Hence, **the control of mycotoxins must begin as early as possible, i.e. with primary agricultural production.**

Most methods of managing mycotoxins are preventive. These include plant breeding strategies to develop host resistance as well as antifungal genes by genetic engineering, the use of bio-control agents, and the targeting of regulatory genes in mycotoxin development. However, such technologies have not yet solved the problem or even reduced it notably (Atanda et al., 2012). Against this background, the UK's Food Standards Agency (FSA) points out that **the primary mechanism to reduce mycotoxins in cereals and cereals products is through "good agricultural practice"** (FSA, 2007). **Suitable plant protection measures, namely the application of proper fungicides combating fungi in the fields, are one of these practices. At the same time, the relevance of good manufacturing practices, like post-harvest storage, is crucial for preventing further mycotoxins along the value chain** (Atanda et al., 2012). Difficulties – administrative, agronomic and economic ones – start at the farm level.

3.1.1 Farmer Paperwork and its Lack of Reliability

The farmer must ensure all grain sold into the human food supply chain is within the legal limits of mycotoxin contamination levels. The following UK-based example provides some background information on that and resulting challenges.

The UK grain supply chain has a mandatory mycotoxin risk-assessment for all farmers to complete for grain sales. It is a self-assessment so relies on trust. It covers geographic region, the previous crop, the cultivation ahead of drilling, the wheat variety used, the fungicide(s) used at flowering and rainfall at flowering and pre-harvest. This indicates the mycotoxin risks that the growing and stored crops have been exposed to. Some people are interested in detail, others not. The weather criteria affect the risk score more than any others. It is difficult to disprove any individual's claims.

However, the risk assessment, even when correctly completed, is not a guarantee of test results. In fact, the most diligently completed forms showing low risk of mycotoxins can still have pockets of mycotoxins in the grain, for example near to field edges, where the grain is damaged or damp and so on. **As mycotoxins become more of an issue, trust will remain the dominant tool for maintaining acceptable low levels of mycotoxins in food.** Still, it does not mitigate the potential problem of mycotoxins; **additional testing and paperwork might be a costly future outcome** if mycotoxins continue to rise. Paperwork itself does not reduce mycotoxins.

3.1.2 Agronomic Issues on an Arable Rotation

Fusarium molds are found in low levels in almost all samples of cereals and produce 70 different mycotoxins. Some strains can produce up to 17 mycotoxins simultaneously (North Carolina Cooperative Extension Service, 2007). **Fusarium mycotoxins are therefore the most frequently identified mycotoxins in grains and animal feed and is imperative for the farmer to manage fusarium accordingly.**

The farmer and his agronomist advisor have to maximise the commercial output of each hectare whilst also minimising the risks of diseases like fusarium. **The central tools for a farmer to control mycotoxins are the application of "good agricultural practice" as well as "integrated crop management" (combining crop rotation, soil preparation, choice of less susceptible varieties, the use of forecasting models, crop protection and quality control)** and thus the care-taking of soil fauna and related ecosystem services (Schrader et al., 2013). If diseases were not a consideration, the combinable crop farmer might be tempted to grow continuous wheat that generally offers the highest gross margin. However, this is not practical for crop health reasons. Instead, a rotation is used which will usually involve wheat, possibly barley or oats and a non-cereal such as oilseed rape or beans. With potentially increasing mycotoxin problems, fusarium could become a greater consideration when deciding on the rotation.

On a practical level, the only measure growers can take to reduce the risk of fusarium or other fungi once the crop is planted is to apply a fungicide programme (Edwards, 2009). Cereals farmers apply fungicides at set stages of the wheat (or other small grains) crop development: The flowering stage is when fusarium is best controlled. Indeed, the use of fungicides (e.g. representatives of the azole family) at flowering makes a considerable difference to fusarium levels, depending on different factors like region, climate and number of treatments (Giraud et al., 2011). Most farmers apply a fungicide programme as standard at that stage of plant development, primarily because it contributes more to yield development than many other costs on the farm.

Data from the Central Science Laboratories (CSL) suggest that fusarium can shrivel grain causing yield losses of up to 30 percent (Abraham, 2008). Most farmers are aware a fungicide application at flowering lowers the risk of a fusarium contamination although it is managed as part of a general ear disease control strategy. However, Abraham (2008) argues that **it may require specific targeting in the future as infections with fusaria become a more important disease. This might increase plant protection costs as the application of more sophisticated products is necessary**. If the weather has been very dry, many growers will skip this application, but if it has been particularly wet, or the forecast is for rain, more growers will use full-rate applications at this point. The need for provision of additional advice and knowledge transfer to farmers to achieve this might therefore increase.

Prediction and forecast models help to predict mycotoxin contamination. One of the available tools is the DONcast® approach (see www.doncast.eu), a tool designed for wheat producers to provide a means of predicting DON concentration in wheat at maturity. The calculator behind the tool uses actual, forecasted and historical weather data along with field-specific agronometric data to accurately predict DON concentrations. Producers can use this tool to make informed management decisions on whether or not to apply a fungicide at heading for reducing potential DON concentrations in mature grain. In addition, this and other similar tools – some more information on forecast models is provided by Coceral (2014) – help to decide which fields with an elevated mycotoxin potential should be harvested first. Furthermore, such tools provide an advance warning of mycotoxin concentrations.

3.1.3 The Costs of Mycotoxins to an Arable Farmer

The value of a milling wheat premium can be substantial. It can soon disappear though if mycotoxin concentrations are high as the following examples illustrate.

The average price premium for milling wheat over feed wheat over the five years to spring 2016 was GBP 25 per tonne (according to data from AHDB). Thus the financial benefit to the farmer to keeping the crop clean and suitable for human consumption is on average GBP 25 per tonne. The average yield of milling wheat in the UK is GBP 8 tonnes per hectare making the cost to a farmer of mycotoxin contaminated wheat GBP 200 per hectare disregarding the impact fusarium has on yield. A relatively small UK arable farmer with 200 hectares of combinable crops would probably have 100 hectares of wheat, thereby the benefit of keeping the crop clean and suitable for human consumption is potentially worth GBP 20,000 per year. Many farmers would be financially crippled if they could not protect their wheat in the field.

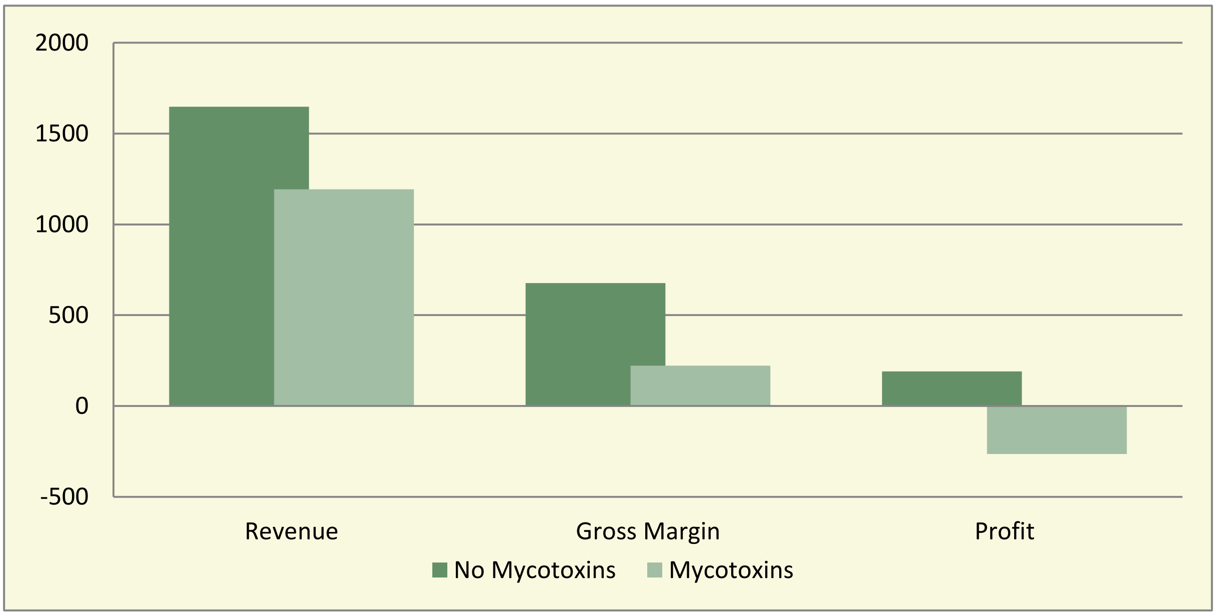
The situation could easily worsen: **If a load of grain at a mill is rejected for being above the legal mycotoxin limit, it is not food-worthy and it is rejected. The farmer instantly loses the milling premium.** If on the day, the premium is higher than the price the farmer sold at, say a GBP 40 premium per tonne, then that higher cost will be passed to the farmer, as the merchant has to replace that load on the day it is rejected in the spot market. It doesn't stop there either, because the nearest feed mill able to accept the consignment might be a GBP 8 per tonne haul away, and being a consumer of lower specification grain, the base price of wheat might also be lower. The farmer incurs all these costs. The cost of a rejection to the farmer could thus easily amount to over GBP 40 per tonne in the lorry making GBP 1,200 per lorry for a relatively small oversight.

The following German example (see Noleppa, 2015) accentuates the discussion. It refers to corn rejected for food and feed production because of a too high DON and/or ZEA concentration in maize. The farmer would need to take the grain to a bioethanol facility, which bids lower prices accumulating to a total of EUR 450 per hectare (using market data at time of publication in 2015). The market revenue and gross margin would decrease accordingly leaving the farmer in a net loss position. Its profit would become negative (still having not taken additional transport costs into account) as Figure 12 depicts.

Other costs that specifically affect small-scale farmers have to be taken into account; in particular, the cost of extension services. Partly because of the strict EU mycotoxin regulations, farmers depend on professional advice to secure their yields and the successful selling of their products. For example, in a 2009 survey, 60 percent of traders stated that they advise their contractual farmers on mycotoxin management, leading to a reduction of the mycotoxin problem in 80 percent of these cases. This stresses the importance of advisory services, prognostic models, new varieties, fungicides and much more innovative technologies in agriculture in reducing mycotoxin risks (Siegel and Babuscio, 2011).

Figure 12 ~ Economics of Maize Production in Germany with, and without Mycotoxins (in EUR per hectare)

Greater levels of mycotoxins simply mean less profit on the arable farm



Source: Own figure based on Noleppa (2015).

3.1.4 Fusarium Mycotoxins in an Intensive Pig Unit

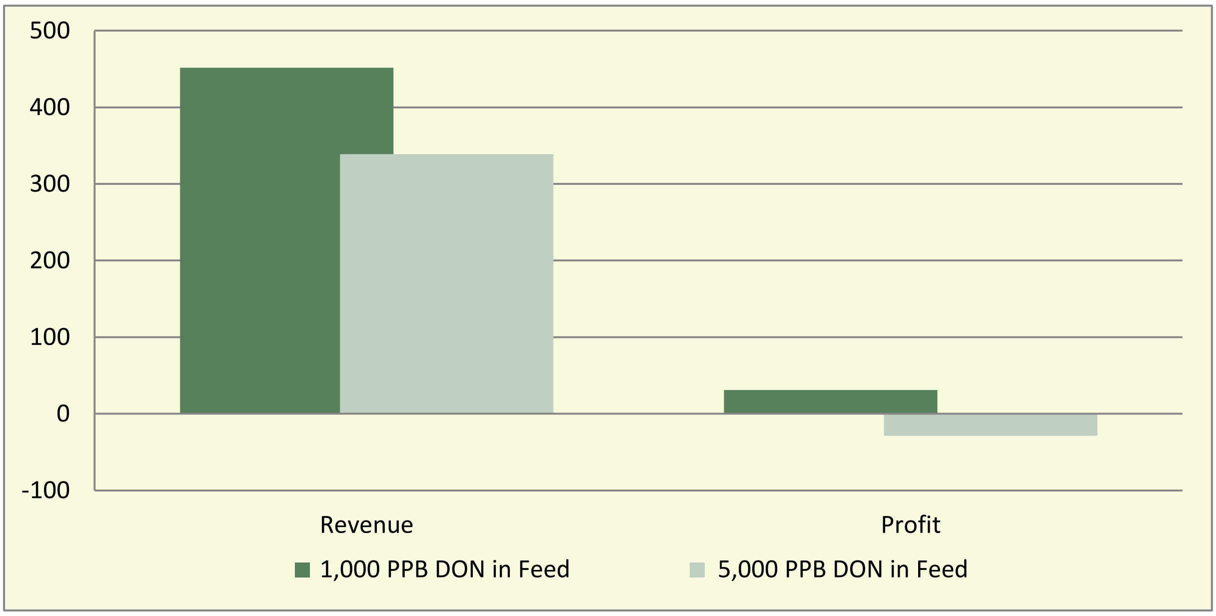
Pigs are very sensitive to DON and ZEA contamination. Both severely affect growth, reproduction and immunity to other diseases in pigs, especially young ones, decrease feed consumption and lower weight gain (Mok et al., 2013; North Carolina Cooperative Extension Service, 2007; Weaver et al., 2014, Friend et al., 1982; Overnes et al., 1997; Bergsjö et al., 1993 Young et al., 1983). More explicitly, the following should be noted:

- Low doses of mycotoxins cause impacts as above. At higher levels, more severe illnesses and bodily malfunctions also occur.
- At levels 20 times lower than the maximum EU guidance limit of DON in feed grains, feed intake and therefore weight gain falls meaning higher age of slaughter, costing more for the grower and poorer health of the pigs (EFSA, 2004).
- Feed intake falls and body weight falls 13 percent when DON is at half the European maximum guidance (Rotter et al., 1994 cited in EFSA, 2004). Feed intake continues falling as mycotoxin levels rise further.

Figure 13 displays the impacts of a DON concentration of 1,000 PPB and a DON concentration of 5,000 PPB of feed on market revenue and profit assuming a price for pork at farm-gate of EUR 1.70 per kg slaughter weight (as used by Noleppa, 2015). This pig farmer, having 1,000 places and 2.85 farrowings per year, would generate a profit of over EUR 30,000 per year with low DON levels but a loss of almost EUR 30,000 when DON is at the higher level. Since pork prices are currently much lower than the figures used in the chart at around EUR 1.30 per kg: With a DON concentration of more than 5,000 PPB, the example farm would lose more than EUR 100,000 in a year.

Figure 13 ~ Economics of Pork Production in Germany, with and without Mycotoxins (in EUR per pig place)

Greater levels of mycotoxins simply mean less profit on the pig farm



Source: Own figure based on Noleppa (2015).

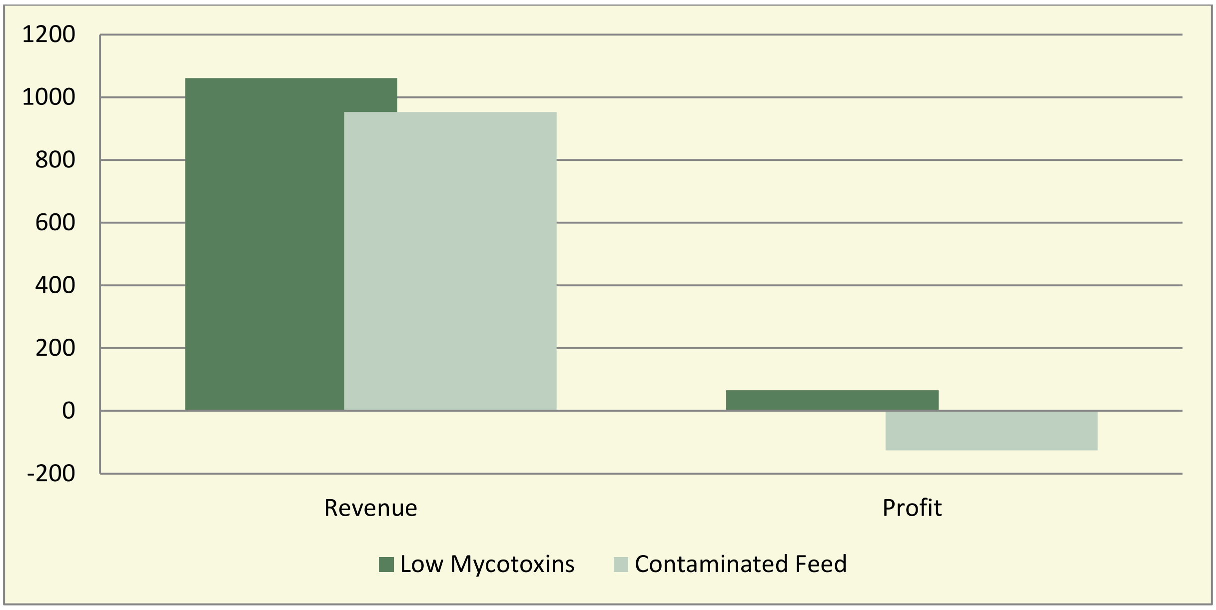
ZEA demonstrates a similar pattern as DON. A third of all EU maize samples contain 500 PPB (Caballero, 2014). Acceptable levels, according to the EU, are 100 PPB in feed for piglets and gilts, 250 PPB in feed for sows and fattening pigs, and 2,000 PPB in entire feed grains. Maize can account for up to half of the pig feed ration; therefore, **even when the mycotoxin levels in the cereals seem acceptable, precautions need to be taken to protect the health of the pigs**.

High DON and ZEA doses are problematic for piglet and weaner production. Apart from feed intake and bodyweight impacts, academic reports cite several other effects from high mycotoxins. Accordingly, mycotoxins have the potential to change the feed conversion ratio, sow and boar mortality, the sow and boar replacement rate, and thus the ratio of sows per boar; moreover, the litters per year, the piglets per litter and the piglet mortality, the weaner price and the sow and boar cull price are affected as well.

Noleppa (2015) has analysed the economic impact of too much ZEA and DON in piglet production. While referring to fewer litters per year, fewer piglets per litter, lower birthweight of piglets and higher mortality rates of piglets starting with 500 PPB of ZEA in the feed, data from a study of Humboldt University at Berlin quoted in Josera (2015) is used. Adding just 200 PPB ZEA and 2,500 PPB DON to a kg of non-contaminated feed leads to 30 instead of 16 percent of sows to be inseminated twice, furthermore to 8.7 instead of 10.0 piglets per realised litter and piglets weighting 8.2 instead of 8.7 kg when sold as a weaner. The combined economic impact is devastating: A profitable business becomes unprofitable as Figure 14 shows. Aggregating the results for a typical German producer with 750 sows, the loss accumulates EUR 95,000 or almost EUR 130 per sow.

Figure 14 ~ Economics of Piglet Production in Germany, with and without Mycotoxins (in EUR per sow)

Profits of a piglet farm are reduced by mycotoxins



Source: Own figure based on Noleppa (2015).

3.1.5 Mycotoxins in an Intensive Poultry Unit

Poultry has a lower sensitivity to DON than pigs, but feed refusal and reduced weight gain are found when concentrations reach 16,000 to 20,000 PPB DON in feed (Kubena et al., 1989; EFSA, 2004). Indeed, as with many other sectors of the (animal) product supply chain, it is the low-level symptoms that are often more of problem as they can go undetected for a long time.

In a recent commercial trial from Nutriad quoted in The Poultry Side (2015), chickens kept on feed contaminated with mycotoxins for 20 to 50 days produced eggs 22 percent smaller than the control group (43.7 g per day as opposed to 56.1 g per day). Not only is the yolk affected by the presence of mycotoxins, but shell strength is weakened thereby more breakages occurred. In a similar manner, the animals themselves experienced lower health and more brittle bones, so a higher mortality is observed. The impacts become cumulative to the overall costs to the farmer.

Mycotoxins particularly slow the rate of fat absorption in the poultry gut meaning fat-soluble nutrients are absorbed more slowly such as carotenoids. Carotenoids affect the colour of an egg yolk, deeper, yellower yolks being richer in them. Consumers naturally prefer deeper coloured egg yolk; this is reasonable as it is an indicator of healthy eggs and animals. Thus the value of eggs affected by mycotoxins can be lower (The Poultry Site, 2015). It is therefore not only the number of eggs that are laid, but their size and price.

Mycotoxins, ZEA and FUM in particular, also reduce feed intake, lower growth rates, decrease egg production, reduce shell thickness and have been linked with increased infertility and damaged carcass (Chi and Broomhead, 2008; Jewers, 2000; Tardieu et al., 2007). Mycotoxins increase the susceptibility of other diseases, again meaning the presence of mycotoxins can go undetected for several weeks (or longer) whilst other animal health avenues are explored.

Academic literature (CAST, 2003) suggests that performance changes of 1 percent are often caused by mycotoxin levels well below the EU guidance levels and are almost impossible to detect (even at laboratory level). It has been estimated that to detect a 1 percent fall of growth rate, it would take 400 sets of 10 broilers. Yet a 1 percent change of growth rate would have a considerable economic impact because margins are usually small anyway (North Carolina Cooperative Extension Service, 2007). If more mycotoxins become more commonplace, the challenge to keep them out of feed will increase.

Evidence is available to state impacts on various aspects of commercial poultry production, although little quantitative work has been identified that demonstrates how much impact is created from a known rise in mycotoxins. Thus, to demonstrate this, very small changes (1 percent) have been applied to the physical performance of a flock of laying chickens (smaller than the impacts stated in academic literature whenever they are quantified such as (CAST, 2003)) to understand the impact to the gross margin for the laying hens. Figure 15 presents the details.

Figure 15 ~ Economic Effect of 1 Percent Changes to Variables Due to Mycotoxins on an Egg Farm

Per Bird	No Mycotoxin Problems	Low Level Mycotoxin Issues
Eggs per Year and Bird	310	307
Egg Price (Pence per Dozen)	78	77
Undamaged Eggs (Percent)	98	97
Bird Mortality (Percent)	2	3
Egg Returns (GBP)	19.35	18.59
(less) Livestock Depreciation (GBP)	3.57	3.57
Output (GBP)	**15.79**	**15.01**
(less) Variable Costs (GBP)		
Feed	10.14	9.94
Other Costs	0.41	0.41
Gross Margin (GBP)	**5.23**	**4.66**

Source: Own calculations based data from Redman (2015).

The economic impact is calculated as losing 57 pence per bird. At first glance, this is a small cost. However, in order to make these farm systems work, a large number of birds is required. A small shed would have 20,000 birds in it. For the single shed, with very small (almost undetectable) changes to the bird this leads to a GBP 11,400 fall in output. The costs in Figure 15 still have overheads to take from the margin, meaning again, this fall could result in the difference between profit and loss. A 5 percent fall in these variables at today's prices would constitute a drop in output of GBP 3.40 per bird or GBP 68,000 for the shed. **So, if the number of mycotoxins that affects poultry growth and development has any chance of increasing, the management of the poultry food supply chain will have to tighten.**

3.1.6 Mycotoxins in Milk

Ruminants are less affected by mycotoxins because their digestion system (rumen) renders some metabolites harmless (Korosteleva et al., 2007; Weaver, 2014). Yet different effects on various organs and animal productivity and health are observed (Fink-Gremmels, 2008). BIOMIN (2016) lists a range of mycotoxicoses in ruminants:

- AF is carcinogenic. AF supresses immunity. AF also decreases feed intake and lowers milk production. It also causes liver damage and impairs rumen function.
- Mycotoxin residues have been found in milk.
- ZEA increases infertility, decreases conception rates and increases abortions. A decreased performance in milk production is also associated to ZEA.
- Ergot alkaloids cause neurotoxic effects and anorexia leading to lower milk production and reduced growth. Abortions, decreased pregnancy and calving rates are also reported along with low sperm production, necrosis and diarrhoea.

These findings are also supported by Dänicke (2001) as well as Whitlow and Hagler (2010). Much attention has also been paid to DON in milk production. According to Korosteleva et al. (2007), reductions in milk yield start at 3,300 PPB DON in feed; and Winkler et al. (2014) have analysed that an extra 4,900 PPB of DON (and 500 PPB ZEA) in feed causes a reduction in feed intake of 8 percent as well as a reduction in milk production of 7 percent. If DON concentration increases to 7,000 PPB, milk yield decreases by 13 percent (Gutzweiler, 2010; Richardt, 2008, Whitlow and Hagler, 2010).

Using a calculation approach described in Noleppa (2015), the associated economic costs for French milk producers can be assessed. Using the scientific findings just discussed, it is assumed in the following that 5,000 PPB DON in the feed decreases feed intake by 8 percent and milk yield by 7 percent and that 7,000 PPB DON decreases feed intake as well as milk yield by 13 percent. Using recent market revenue and production cost data provided by Raso and Rippe-Lascout (2015), the profit of a specialised milk farm and a mountain milk farm in France will shrink considerably as Figure 16 visualises.

Figure 16 ~ Profit of Milk Production in France, with and without Mycotoxins (in EUR per 1,000 litres)

	Without Deoxynivalenol		**With 5,000 PPB Deoxynivalenol**		**With 7,000 PPB Deoxynivalenol**	
	2013	2014	2013	2014	2013	2014
Specialised milk farm	–41	11	–230	–181	–388	–332
Mountain milk farm	–159	–83	–350	–273	–499	–430

Source: Own figure based on Noleppa (2015) as well as Raso and Rippe-Lascout (2015).

All numbers refer to 2013 and 2014. In these two years when milk price was good, a mycotoxin contamination in feed for dairy cows would have been lossmaking for average producers without additional policy subsidies; if one occurred now, whilst milk price is lower, profitable milk production, especially in the mountainous areas would probably be unfeasible. **The contamination of animal feed by mycotoxins has a major impact on the profitability of dairy farming.**

3.2 CURRENT AND POTENTIAL EFFECTS OF MYCOTOXINS ALONG THE VALUE CHAIN

So far impacts to agriculture of high and increasing concentrations of mycotoxins have been analysed on the basis of case studies covering arable and livestock farming. **Once mycotoxins are embedded in primary products they are almost impossible to remove and often affect other stakeholders along the value chain, including the final consumer.** Some examples are provided in the following of which the first one has been compiled thanks to the support of the National Association of British and Irish Millers (NABIM).

3.2.1 The Millers and Processors Dilemma

The UK milling industry recognises the importance of keeping mycotoxins to a low level. It appreciates if a mistake was made, it could be dangerous to human health and expensive to solve. It complies with regulations and (sometimes separately) works to minimise the risks of mycotoxins entering their supply chain. Millers know that the risk assessments have been performed early in the season, the grain will have been tested for mycotoxins and it is the vendor’s responsibility (and therefore liability) to guarantee the grain is safe for human consumption. Yet no level of vendor liability will retain the reputation of a major miller if errors are made that allowed mycotoxins through their mill and end up in a finished branded product.

In the EU, food supply businesses are legally required to report any food exceeding the statutory mycotoxin levels to the relevant authority (e.g. the FSA in the UK) under Article 19 of Regulation (EC) No 178/2002. Regulations forbid blending grains or flour destined for human consumption to reduce illegally high mycotoxin concentrations in food; if mycotoxins in a delivery of wheat or other grains are above the legislated limits, the cereals must be rejected from the human food supply chain. If a batch of flour has an excessive level, it too must be rejected. (Incidentally, grains can be blended to lower mycotoxin levels in grains for animal feed as these levels are only advisory, not legislative.) Rejecting a batch of flour is more expensive than rejecting a load of wheat for several reasons:

- It has been processed from grain so it is intrinsically more valuable.
- It might be blended with other flour or ingredients to make a grist, meaning it is greater in volume and value and non-affected ingredients also need to be discarded.
- The tanks holding the flour are not designed to deal with rejections and take longer to empty.
- Cleaning the system from milled flour takes longer than cleaning a grain tank.
- Milled wheat is often divided into more than one good; flour and bran for example – if mycotoxins are found in one, the other would have to be tested and probably discarded.
- Mills are sometimes used around the clock so closing a mill to empty it of flour will hold up an entire process.
- Milled flour (especially when mixed with ingredients) might not be suitable to feed to livestock and might incur a high cost of disposal instead.

This magnifies the importance of managing mycotoxins at the farm level and keeping them to a minimum. **All forms of good agricultural practice that reduce mycotoxins including the sensible use of fungicides are** therefore **critical to the millers' work**.

Whilst the chances of mycotoxin contamination in flour are low, the impacts could be devastating. The milling industry recognises that the years that have a mycotoxin-peak are higher risk years for this to occur. Nevertheless, from time to time, high mycotoxin concentrations do lead to a very costly removal of products from stores as the following example taken from Noleppa (2015) and referring to recalls of products due to too high mycotoxin concentrations mentioned in sub-chapter 2.2.3 above describes. In 2015, an important German breakfast cereals company had to remove cornflakes worth EUR 34,000 due to a high DON concentration. However, the maize that contained the mycotoxin was worth only 2,300 EUR. If this primary product was managed properly, costs would have been considerably lower (only 7 percent of the losses which have occurred in reality) as Figure 17 depicts.

Figure 17 ~ Cost of Mycotoxins Detected Very Early vs. Very Late in the Value Chain

Source: Own figure based on Noleppa (2015).

3.2.2 The Breakfast Cereal Manufacturer: Fighting with Moisture

Figure 17 focusses on a breakfast cereals manufacturer. Indeed, good mycotoxin management at farm level is critical for breakfast cereal manufacturers as this example demonstrates. Weetabix, a breakfast cereal, is manufactured to 5 percent moisture. The producing company – also called Weetabix and located in the UK – buys wheat with a maximum moisture specification of 15 percent. More water therefore comes out of the manufacturing process than goes into it. Wheat accounts for 95 percent of the ingredients. This means that food contaminants such as mycotoxins indirectly become concentrated in the process. The legal EU limit on DON in unprocessed wheat sold for feed consumption is 1,250 PPB, but the legal limit for breakfast cereals (as well as most other wheat-based food products) is only 500 PPB. Removing water increases the concentration of mycotoxins but regulation requires their reduction.

In 2010, Weetabix set up a growers' club of wheat farmers close to its factory as suppliers. As part of the contract it stipulates a maximum DON level of 500 PPB in the wheat it procures (see comment from Trevor Gates in Farmers Weekly, 2014). Why is this done? Weetabix is located in Northamptonshire, as far from a port as any part of the UK. Thus, it is highly dependent on the success of the UK wheat harvest to remain in operation. Without good quality, low mycotoxin, locally grown wheat, manufacturing at this plant would become uncompetitive. Indeed, only in 2013 the firm had to stop production of two of its cereal lines (Bakery and Snacks, 2013). Accordingly, the firm stated it was not only the small crop but the quality of the wheat caused by the extreme wet and cold weather during the growing season. The term "quality" will refer to various specifications that Weetabix requires from its raw materials, including the guarantee of mycotoxins below 500 PPB.

Weetabix is patriotic out of necessity (being inland) and so its success depends on the success of the UK wheat crop. A few anaerobic digestion plants using maize as a feedstock have emerged in the last three years within a short distance to their factory and wheat is the major crop in the area. If mycotoxins become more of a problem in future years when wheat is closer in the rotation, maize is more abundant and weather conditions increasingly unpredictable, the firm might be forced again to make decisions of stopping production in the future or impose tighter regulations on crop management practices on farm.

3.3 Current and Potential Effects of Mycotoxins for the Broader Society

Mycotoxicology as a science is only about 50 years old (CAST, 2003); the awareness of mycotoxins has emerged solely throughout the period of two generations despite them having been around for ever as chapter 2 discusses. This demonstrates, just how long the symptoms of these toxins can go undetected and how long they can be undiagnosed, even today. Thus, estimates of the costs of mycotoxins will be either too low (as it calculates only part of the costs) or a very vague estimate. Nevertheless, **it is well-accepted that mycotoxins incur a high cost on society** for a variety of reasons:

1. The fungi that cause mycotoxins also reduce crop yields;
2. The reduction of the value of the grain as it is downgraded to feed or then to other uses;
3. Food waste from discarded food;
4. The cost of managing the food supply chain including testing, auditing mitigation and litigation;
5. The reduction in productivity of the livestock that might consume the mycotoxins; and
6. The reduction of health of the people that consume mycotoxins, the health care costs, labour productivity losses as well as occasional mortalities.

Together, these costs are considerable. One study (Vardon et al., 2003) identified the costs to the USA alone as being between USD 629 million and USD 2,500 million per year with a mean estimate of USD 1400 million. However, this did not include costs associated to the human health system.

3.3.1 Human Health Impacts

It should have become apparent from the above that mycotoxins are much more wide-spread and of much more concern for human food consumption than expected at first glance. High levels of AF, OT, FUM and other mycotoxins are frequently found in food (see, e.g., Lerda, 2011; Pitt, 2000) and **may cause severe illnesses**. Resanovic et al (2013) provide a summary on mycotoxins and their effects on human health. Accordingly, it can be stated that, among others:

- **AF contamination contributes to a number of health disorders**. They are responsible for developing hepatocellular carcinoma, one of the most malignant diseases. In addition, acute toxic hepatitis and lymphocyte deficiency are associated with AF.
- **OT are hazardous to human health as well**. Among others, chronic interstitial nephropathy as well as renal adenomas and carcinomas are linked to OT as are urinary tract tumours.
- Due to its estrogenic structure, **ZEA is considered to cause praecox puberty, oestrogenisation and pseudo-pregnancy in woman as well as prostate cancer in men**.

In addition, mycotoxins such as AF, FUM and TCT are immunosuppressive which has wide implications for the ability of human populations to resist diseases (Pitt, 2000). The subsequent assumption of Pitt (2000) is that foodborne bacteria are rightly a major cause for concern to human health. Nevertheless, it is difficult to escape the conclusion that mycotoxins in foods might be responsible for much higher numbers of human health problems and even deaths than foodborne bacteria through secondary infections and diseases. This cannot be categorically proven due to the wide disparity between real and reported cases. Yet the argument itself is alarming.

The hazard of mycotoxins for human health becomes additionally obvious by looking at the following Figure 18, which displays the classification of the International Agency for Research on Cancer (IARC) related to some important mycotoxins.

Figure 18 ~ IARC Classification for Important Mycotoxins

Mycotoxin (in alphabetic order)	Classification
Aflatoxin B1	Carcinogenic
Aflatoxin B2	Carcinogenic
Aflatoxin G1	Carcinogenic
Aflatoxin G2	Carcinogenic
Aflatoxin M1	Possibly carcinogenic
Deoxynivalenol	Not classifiable
Fumonisin B1	Possibly carcinogenic
Fumonisin B2	Possibly carcinogenic
Ochratoxin A	Possibly carcinogenic
Patulin	Not classifiable

Source: Own figure based on Lerda (2011).

In this context, it must be repeated what has already been highlighted in chapter 2.1.1: **Most illnesses caused by mycotoxins are not referred to a doctor.** Those that do lead to a medical appointment, are often either not identified as mycotoxin related or officially recorded as such. In other words, these cases might be noticed by the individual but not identified as what caused it or collected as a statistic. **Mycotoxin illnesses are therefore woefully under-reported on a global scale.**

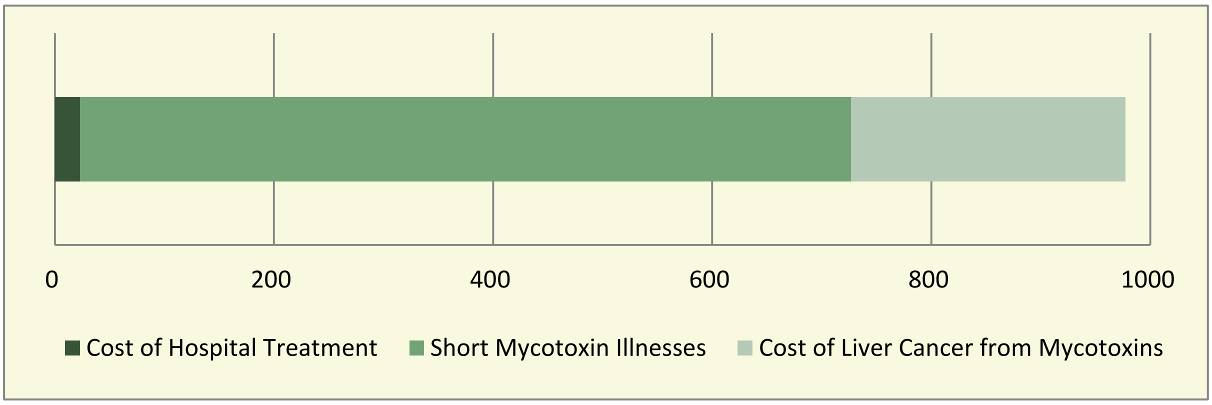
This makes it very difficult to calculate the truly societal (monetary) impact of mycotoxin-related human health problems. If Pitt (2000) is right when arguing that mycotoxin-related foodborne diseases are more important than foodborne bacteria illnesses, the costs to society become calculable. Tam et al. (2014) estimated the costs associated to foodborne disease in the UK (interestingly neglecting mycotoxins as a cause), foodborne bacteria are responsible for 400,000 to 410,000 cases and 5,500 to 6,300 hospitalisations.

Extrapolated to the EU level, this would mean that **we have to consider at least 3.2 million cases and 50,000 hospitalisations per year due to mycotoxins.** According to WHO (2016), it costs between EUR 130 and 230 per day to be in a hospital in major EU member states such as Germany, France, Spain and the UK. Therefore, the extrapolated EU hospitalisations (assuming at least two days) caused by mycotoxins would have cost EUR 13 to 23 million per year. This is minor compared to what mycotoxins cost in terms of missing societal income. According to Eurostat (2015), the average Gross Domestic Product (GDP) per capita per (working) day at market prices is around EUR 110. During illness, labour productivity is (almost) zero. Hence, 3.2 million cases of mycotoxin-borne short term (two working days) illnesses, cost more than EUR 700 million per year.

This still does not include high cost for treating cancer and other severe diseases. To take an example: Treating just one (mycotoxin-related) case of liver cancer in high-income countries such as EU member states costs not less than EUR 20,000 per year; when including the economic burden of lost or disability life years it actually costs (much) more than EUR 50,000 per year (see also Hanly et al., 2014; Luengo-Fernandez et al., 2013). Indeed, following Catana et al. (2014) one might assume that direct treatment costs alone amount to EUR 150,000 to 300,000 per case. In the EU, approximately 250,000 new cases of liver cancer are diagnosed per year, and the mortality is still high - close to 95 percent (Ferlay et al., 2013). If only 2 percent of all these cases would be attributed to mycotoxins (a conservative estimate) this implies annual costs of at least EUR 100 million (directly with health care) to 250 million (including economic losses due to lost productive working time).

The aggregated human health costs from mycotoxin intoxications including short-term hospitalisations, lost working days due to diarrhoea-like illnesses and cases of liver cancer is illustrated in Figure 19. These alone **accumulate to EUR 1 billion still neglecting other diseases and associated costs caused by mycotoxins in the EU.**

Figure 19 ~ Illustration of the Potential Human Health Costs of Mycotoxins in the EU per Year (in EUR million)



Source: Own figure based on own calculations.

The above-mentioned accords with what Schmale and Minkvold (2014) have reported. **Diseases modulated by mycotoxins accounted for 40 percent of lost disability-adjusted life years around the globe.** However, the number "40 percent" needs clarification: The concept mentioned by Schmale and Minkvold (2014) measures life years lost due to illness and death. Globally, many infants and very young children still die because of diarrhoea (due to mycotoxins and other causes) and the loss of life years (measured in terms of potential life years) is extremely high. Indeed, globally many lives are lost from mycotoxins. In Kenya, to take an example, 125 people died in 2004 from just one outbreak of AF from contaminated maize, which is a staple food there (Schmale and Munkvold, 2014). Whilst in the "more sophisticated" supply chains of the EU, such an outbreak is far less likely, mycotoxins still accelerate or cause deaths. Our own calculations described above should be seen in this perspective.

3.3.2 Preventing Food Waste

To end chapter 3, another societal challenge caused by mycotoxins is briefly highlighted. The FAO estimates that **a quarter of all the world's grain crops are affected by mycotoxins each year** (Schmale and Munkvold, 2014). This was over 20 years ago. Some of this 25 percent is not discarded but used for alternative purposes such as for livestock feed. However, if this FAO estimate is correct, the indirect costs of mycotoxins through food waste might be one of the largest. Park et al. (1995) estimated that **the production of food commodities globally, which is at 'high risk' of mycotoxin infestation to be about 100 million tonnes**.

Demographers predict we will have a global population of 10 billion people in 2050 (we currently have 7.3 billion). Food demands per person will also be higher, meaning that food production should increase by 70 percent from today's levels (FAO, 2012). To achieve these levels, we will globally have to waste less in general and reduce wastage from mycotoxin contamination in particular. Otherwise it will be difficult to achieve an important Sustainable Development Goal, namely Goal 2: End hunger, achieve food security and improved nutrition and promote sustainable agriculture. Accordingly, it shall be stated: **Good agricultural management including the sensible use of fungicides to combat mycotoxins is key to feeding the world population in decades to come.**

4 MYCOTOXINS IN LIGHT OF HAZARDS AND RISKS

4.1 HAZARDS AND RISKS: A GENERAL COMPARISON

So far, we have shown that mycotoxins are a hazard and as such they can be found everywhere; thus they increasingly may create risks throughout the agricultural value chain and beyond. But is the relevance of mycotoxins for today's agricultural and food production appropriately reflected in public discussions?

Every day we expose ourselves to risks (such as the risk of falling down the stairs, being run over in the street, or being poisoned by foodborne diseases during a meal). Thus, every day we have to manage such risks (for example, by holding onto banisters when on the stairs, looking before crossing a road or ensuring food is clean by smelling it or checking the dates). It becomes apparent: Risks are ubiquitous and risk management is a common practice in human lives. In this respect, risks have to be clearly distinguished from hazards as defined by Barlow et al. (2015):

- A hazard is an inherent property of an agent having the potential to cause adverse effects when an organism or population is exposed to it.
- A risk is the probability of an adverse effect to an organism or population caused by exposure to an agent.

To make it more visual: There are hazards that some individuals are not exposed to, e.g. a tree falling which is not going to land on somebody, meaning it is not a risk for a person seeing it falling but standing far away. Thus, risk is the hazard multiplied by the likelihood of it (the exposure) affecting you. This can be visualised in a formula as follows:

Risk	=	Hazard	X	Exposure

Consequently, we can define two different ways on how to deal with risk: Firstly, risk can be reduced by removing the hazard, or secondly by reducing the exposure to it. Talking again in imaginary terms: Keeping away from a falling tree reduces the chance of being hit by it even though it is still going to fall. This reduces the exposure and consequently the risk. Not planting a tree in the first place would remove the hazard and, therefore, also the risk. Consequently, we observe that risk assessment is more than simply hazard assessment, because we need to consider the exposure as well. This is highly relevant when exploring the risks of mycotoxins versus fungicides.

4.2 HAZARDS AND RISKS RELATED TO MYCOTOXINS VS. FUNGICIDES

The difference between hazard and risk is central when deciding as a society which conditions we want to ensure low human and animal exposure to mycotoxins and what means society uses to achieve this goal. So, how does our society evaluate mycotoxins and fungicides in terms of regulatory means?

Regarding food safety, EU legislation applies both hazard and risk-based approaches. Mycotoxins in particular are legislated on a risk-based approach, meaning the regulation will only tighten if considered necessary for human health due to increasing exposure. On what basis is such an approach taken?

- It is well known on the one hand that food contaminants such as mycotoxins are hazardous in nature, e.g. toxic, but cannot totally be removed from food and feedstuffs.
- According to Marin et al. (2013), on the other hand, there is not yet much data on the exposure of specific populations to mycotoxins. Thus, there is no full regional or even global picture of the real exposure of human beings to mycotoxins.

Despite the lack of information on exposure to mycotoxins, policy-makers have decided to regulate them according to the risk-based approach. This is because being naturally ubiquitous, mycotoxins cannot be kept out of the food system without losing substantial amount of food. Today, some people including those who try to represent the civil society (lobbyists) and also selected EU policy-makers consider hazards to be the same as risks and that regulators should remove them all. This is even if there is plenty of evidence that considerable benefits to society of hazardous but not necessarily risky agents exist which would be lost. This clearly refers to favouring a hazard-based regulation approach neglecting exposure. A typical example for such a perspective is fungicides or more particularly azoles and triazoles currently controversially discussed as having an endocrine disruptor effect. Because of this potential health hazard, it is argued that they should be removed, despite the obvious benefits fungicides provide such as removing mycotoxins or adding food on our tables and therefore, on balance, making the world a safer and more abundant place. This is also despite the minimal risk to human health they pose when properly used.

Consequently, there is broad debate in the EU about how plant protection products such as fungicides should be regulated: Should regulation be based on a meaningful risk-based assessment including an analysis of both hazard and exposure or solely a "narrower" hazard-only evaluation? A number of commentators, ourselves included, argue that fungicides need to be regulated on a risk-based system

– just as mycotoxins are. Critically, the exposure of plant protection products to humans is very well studied and consequently there is no need to exclude this knowledge by conducting only a hazard-based analysis. This is summed neatly by Nordlander et al. (2010) who state that regulating chemicals should aim to strike the right balance between minimising risks to humans and the environment while maintaining the benefits to society.

This statement also reflects on another disadvantage of purely hazard-based regulation of fungicides and their role as counteracting agents: the exclusion of a benefit comparison (Barlow et al., 2015). The following easily understandable example explains what it would mean to count solely on hazard-based regulation. Pure hazard-based policy would mean that all modes of transport, including bicycles and cars, would be banned as they each provide hazards. Luckily, their benefits to society are understood and recognised as greater than the risks they cause (e.g. likely deaths and injuries in case of accidents). So they are regulated according to the risk-based approach where the hazard is kept but people's exposure to it is minimised with driving regulations, air bags, speed controls, and so on, all of them trying to limit the likelihood of occurrence of the specific circumstances mentioned above.

This shows that the broader public accepts transportation – and mycotoxins – should rightly be regulated according to risk-based policy. However, such acceptance is not so widespread with plant protection products. This is as their hazards are stressed in public and policy debate rather than their benefits. Clearly though, plant protection products, similar to transportation, present numerous benefits as well as some hazards to society.

Indeed, different studies show that the consumers' perception of risk between fungicides and mycotoxins is very much biased towards synthetic compounds as being the greater hazard (see, e.g., Muri et al., 2009). In the Eurobarometers of 2005 and 2010 (EC, 2005; 2010) people were asked the following question: What are all the things that come to your mind when thinking about possible problems or risks associated with food? In 2005, "Chemicals, pesticides and toxic substances" were the second most answered issue (14 percent of all respondents) after "food poisoning". This number increased in 2010 to 19 percent, thereby becoming the most common concern of consumers in terms of food safety.

This stands in stark contrast to an evaluation of the situation on food safety by experienced scientists. A study of Muri et al. (2009) shows in a risk assessment evaluating the health impact of fungicides and mycotoxins that neither of the compounds under investigation provided alarming results. Much more the authors concluded that neither fungicides nor mycotoxins gave concern to cause a health risk in humans for at least 99 percent of the population. In addition, the authors stressed that fungicides are thoroughly studied concerning their toxic potential, while mycotoxins have so far been much less under scientific observation, even concerning their toxic potential. In any case, this shows that a risk comparison between fungicides and mycotoxins is very differently evaluated by the different actors depending on their knowledge, interest as well as belief system.

Such a great difference in risk evaluation between different actors is also mirrored by the following example. Salomon (2016) – based on information mainly provided by the Austrian Agency for Health and Food Security (see AGES, 2015a; b) – listed a ranking of food-related risks evaluated by consumers, journalists and trained experts. The findings are displayed in Figure 20. It becomes apparent that **neither consumers nor journalists think about mycotoxins as a food-related risk, but highlight risks of pesticides on top.** Contrary to that, **experts consider mycotoxins as an important risk whereas plant protection products are not even listed in the Top-Five.** In this respect, the survey of AGES (2015a) shows that the risk perception especially of consumers greatly differs from the one of experts when evaluating food-related risks and that this can be related to a considerable knowledge gap.

Figure 20 ~ Food-Related Risks Evaluated by Consumers, Journalists and Experts (Priority Ranking)

Rank	Consumers	Journalists	Experts
1	**Pesticides**	Residues of medicaments and hormones	Pathogen microorganisms
2	Genetically modified organisms	**Pesticides**	Obesity and wrong nutritional behaviour
3	Residues of medicaments and hormones	Toxic elements (heavy metals)	**Mycotoxins**
4	Food additives	Genetically modified organisms	Allergens
5	Toxic elements (heavy metals)	Migrating substances (plastic particules, etc.)	Toxic elements (heavy metals)

Source: Own figure based on Salomon (2016).

It is beyond the scope of this research to close this knowledge gap and to assess and discuss all relevant variables. However, the following example may illustrate that **mycotoxins are much more hazardous than fungicides once a person becomes fully exposed to them.** Figure 21 depicts the lethal dosage level that causes 50 percent of a group (of animals) to die once a specific mycotoxin vs. fungicide has been orally obtained via feed. It becomes apparent that **the toxicity of mycotoxins is considerably higher than that of fungicides – and here we speak about magnitudes of hundreds and thousands, not only a few percent.**

Figure 21 ~ Lethal Dosage to 50 Percent of Rats/Mice (in mg per kg body weight)

Mycotoxins		Fungicides	
Aflatoxins	5 – 9	Benzimidozoles	~ 6,640
Deoxynivalenol	46 – 70	Dicarboximides	~ 10,000
Ochratoxin	20 – 30	Dithiocarbamates	3,000 – 8,000
Patulin	25 – 35	Strobilurines	> 5,000
T2-/HT2-Toxin	4 – 9	(Tri-)azoles, among them: - Epoxiconazole - Prothiconazole	> 2,000 3,000 – 5,000 > 6,200
Average	**25**	**Average**	**5,620**

Source: Own figure based on Brimer (2011), Coda-Cerva (2016) and EPA (2007a; b)

Figure 21, shows how much of each chemical is required to kill half the population. It demonstrates **the mycotoxins are on average more than 200 times more toxic than the fungicides that are controlled, managed, have short half-lives and kill the mycotoxins.**

What do such differing perceptions on hazards and risks related to mycotoxins and fungicides as their counteracting agents imply for future risk communication and risk governance? It has been shown above that a clear controversy exists in assessing risks. The main challenge for future risk communication is to find common ground for all stakeholders involved. This means to recognize that there are different risk perceptions between stakeholders. Consequently, what is needed is a willingness by all stakeholders to consider the other perspective (Barlow et al., 2015). Research on risk perception shows that actors are willing to adjust their behaviour when confronted with reliable information on exposure and consequences of given hazards as well as options for protective measures (Wachinger et al., 2013).

These findings should be used in pragmatic ways. It implies the importance of transparency of data collection and evaluation. The information provided above may be used in this respect. Indeed: Outcomes as well as uncertainties of risk assessments must be fully explained to ensure public trust in the results of analyses. Essentially, the hazards of banning certain fungicides as "counter agents" of mycotoxins have to be compared to the hazards of potentially replacing them (Barlow et al., 2015). These are important steps towards a balanced and dialogue-based risk communication on mycotoxins and pragmatic ways to manage them.

4.3 PRAGMATIC WAYS TO MANAGE RISKS ASSOCIATED WITH MYCOTOXINS

It becomes apparent: **Managing mycotoxins is necessary and managing the associated risks requires a multi-disciplinary approach.** It involves good agricultural practice and integrated crop management at farm level, thorough testing including due diligence by the store, merchant and primary manufacturer and it means keeping food clean, dry and cool. The FAO provides advice on managing mycotoxins and recommends a series of **strategies starting at (1) primary prevention, (2) fungal growth inhibition and (3) decontamination of mycotoxins** (see Semple et al., *1989*). We will also use these three headlines to discuss management options **to combat mycotoxins** in primary agricultural produce as well as feed and food.

4.3.1 Primary Prevention

Preventing mycotoxins at farm level is considerably cheaper and far more effective than removing them at a later stage of the agricultural value chain (see also the discussion above in sub-chapter 3.2.1). The top list of actions consists of:

- Development of fungal resistant varieties of growing plants;
- Control field infection by fungi of planted crops;
- Sensible cultivations and rotations;
- Lowering moisture content of plant seeds, after harvesting and during storage;
- Store commodities at low temperature whenever possible;
- Using fungicides and preservatives against fungal growth;
- Control insect infestation in the field and stored bulk grains with approved insecticides.

Secondary and tertiary prevention measures then cover re-drying and re-cooling the grains, removing contaminated goods and isolating them from non-contaminated goods.

4.3.2 Fungal Growth Inhibition

Fungal growth can be inhibited by using chemical measures (i.e. fungicides, but also insecticides), biological treatments (e.g. varietal choice and bio-pesticides) as well as agronomic measures (e.g. crop rotation and soil preparation) and physical measures. The physical measures involve the harvested crop and include drying grain in store, removing damaged grains as this can provide an access for fungal spores to take hold, ensuring the crop is stored at the correct temperature and ensuring the commodity is in a suitable and pest-proof storage. The chemical measures also cover both the growing plant and also the stored crop. Fungicides to prevent infestation in the first place are most effective and least costly.

4.3.3 Decontamination of Mycotoxins

Decontamination of mycotoxins in feed and food by absorbing agents (additives) is a difficult and very expensive process. The application of additives may cost up to EUR 60 per tonne of feed (Noleppa, 2015). Semple et al. (1989) in this respect discuss percentages of mycotoxins removed from grain as only being in the range of 10 to 70 percent; not enough for most cases. The authors therefore also discuss hand picking the "clean" cobs from stores, irradiating crops, and cooking in oil under pressure as potential management options to decontaminate. Clearly, this is very costly and most people would still be suspicious of consuming food following such processes, considering the resilience mycotoxins demonstrate to heat and other physical and chemical decontaminants.

Other experts, e.g. Whitney (2016), suggest at this point screening the grain to remove chaff and fines, feeding the grains to livestock (in small numbers) to test for reactions, and to beef cattle and sheep before pigs (as they are generally less susceptible) while not feeding young stock as they are also more susceptible. Other advice refers to good agricultural and storage practices already discussed.

4.4 LEARNING FOR THE FUTURE

The amount of mycotoxin poisoning in the EU is lower than in most African states and other developing and emerging countries. This could provide us with lessons for how to minimise the chances of mycotoxin infections in the future on a global scale. Since mycotoxins are most often created in the field, the key solutions for their elimination or at least reduction are also field-based. Rotations, cultivations, varietal choice and particularly effective fungicide applications are necessary in commercial scale agriculture but also in small-scale farming to minimise the risks of mycotoxins, protect the value of the crop growing and ripening in the field, and keep the consumers safe from toxic poisoning.

5 CONCUDING REMARKS AND RECOMMENDATION

5.1 CONCLUSIONS

This paper has taken a "deep-dive" into the economic and health issues of mycotoxins in the human food and animal feed supply chains with an EU perspective. The issues explored are not solely those of the region or supply chains discussed here, but of all developed agricultural and food supply chains that have to tackle the natural killer.

Mycotoxins have always been a lethal natural poison. They have caused disruption, inefficiencies, sickness, and death to animals and also humans long before they were identified. They eluded the scientific, political and medical elite for many years, being difficult to comprehend and often a lesser killer than some bacterial killers such as E. coli. Yet, their toxicity, coupled with their persistence make them just as lethal or even more dangerous in many situations. Mycotoxicology, a relatively new science of only about 50 years, developed following some distinct cases of mycotoxin poisoning, ironically more from animal deaths than human. Whilst the level of ignorance on mycotoxins is still high, science is now working on methods to better manage them and to save lives, both animal and human. However, the obvious challenge is still not appropriately mirrored in public discussions and policy-making.

It is plain to see from several examples in the study, that supressing the fungi that cause mycotoxins is by far the safest, most reliable and low-cost way to control mycotoxins. This paper demonstrates that the agricultural, feed and food supply chains are impacted by mycotoxins at several levels. The most effective way to manage them is to keep them outside the supply chains in the first place, i.e. to combat them in field. If they do enter the food or feed supply chains it is too late and they can wreak havoc at every stage on both economic and health levels.

Whilst the risk of being affected by mycotoxins from the supply chains is still small in the EU, the impact once affected will most likely be very high. In this respect, it has to be noted that we all take risks every day; they are impossible to avoid, especially if we lead a relatively normal life. However, we all have a different attitude to risk so when an individual or "competent-authority" is charged with creating policy to manage it, no outcome will ever satisfy everybody.

Yet, most people would be pleased to see a situation where the majority of people's interests are protected. There are not many consumers (and public decision-makers) who consider mycotoxins hazardous but many who consider fungicides to be harmful. Yet, nobody should deny that the risk of being exposed to the hazard of mycotoxins is many hundreds of times greater. This identifies the social benefits of agrochemical products, in particular fungicides which are meaningfully applied. Of course, if something is causing more harm to society or the environment than the benefits they offer, they should not be made available, but when considerable benefits are provided at such minimal risks to society and the environment, their removal from markets through regulation appears to be led by weak policy-making. This might be the case when asking for a removal of useful fungicides combating mycotoxins.

Plant protection product regulators (including the roles of regulators and lobby groups) are, by definition, focussed on the subject of regulation. They are not good at looking at the broader trade-offs as it's not part of their remit. We don’t know how fast mycotoxins will develop in the future, but we can be certain they are here to stay and need careful management and regulating to prevent unnecessary cost, injury and death. This should be kept in mind when making decisions for the future which will surely affect our well-being, i.e. our economic and health performance. A real risk assessment analysing hazards and exposures in combination with a thorough cost-benefit-analysis should lead policy decision-making.

5.2 RECOMMENDATIONS TO FARMING, POLICY MAKERS, SCIENCE, THE PUBLIC

The following recommendations are based on the findings of this study and come in a series of comments targeted at different sectors of society. In particular, our recommendations target the (1) arable farmer, (2) the livestock farmer, (3) supply chain managers, (4) policy makers, and (5) the broader public.

Arable Farmers

1. Select crop varieties resistant to fungal infections if possible.
2. Consider rotations and cultivations carefully.
3. Keep crops clean from disease from sowing to harvest by using relevant fungicides legally and at the recommended rates and tank mixes.
4. Keep good records and complete paperwork accurately coupled with necessary tests at farm level.
5. Ensure grain storage facilities meet top specifications in terms of cleanliness and grain management.
6. Monitor the grain condition regularly in store, keeping it dry and cool.

Livestock Farmers

1. Observe and be suspicious of unexplained small changes in livestock performance.
2. Examine all animal feed carefully on delivery for freshness, testing it if unsure.
3. Use trusted and reliable animal feed companies.
4. Take care when feeding home grown grains.
5. Use feeding additives if mycotoxins are detected in feed (only if feed is compliant with levels below allowed maximum limits).
6. Store feed appropriately, keep feed stores clean and dry.

Supply Chain Managers

1. Focus on measures that will facilitate the prediction of mycotoxins. This particularly includes increased sophistication with the mapping process to identify fields and individual farmers as well as hot spot regions.
2. Keep grain storage facilities dry, cool and clean
3. Use the passport, grain tests and due diligence to predict mycotoxin contamination but continue to remain vigilant of all batches of grain.
4. Arrange shared due diligence with other firms to multiply the value of information.

Policy Makers

1. Ensure crop protection compounds in general and fungicides in particular are governed in the same way as mycotoxins, i.e. on a risk-based approach.
2. Demonstrate strong policy-making based on properly weighting costs and benefits, pros and cons, advantages and disadvantages of a policy measure.
3. Particularly compare the benefits to society of meaningfully using fungicides against any adverse impacts to the environment and health they might cause.
4. Keep mycotoxin management legislation simple and effective so they are easily understood and manageable by everybody.

Broader Public

There is much noise made by a very small minority of people about the safety of tools used to manage mycotoxins. Almost no noise is made about the mycotoxins which are many times more lethal.

1. It is therefore important to be able to focus on the more important issues regarding food safety for the family and what threats can be more harmful to them.
2. The necessary information needs to be made available to everyone. Public information and monitoring systems need to be communicated better and to improve their outreach. This includes science.
3. Source food from reliable supply chains that has used mycotoxin mitigation measures. This doesn’t mean interrogating everybody that has been involved in the supply chains of your food, but to consider the robustness of alternative food supply chains.

5.3 FINAL WORD

Mycotoxins are likely to become a greater issue for the feed and food supply chains in the future. Better science to understand and predict their presence will help manage them and minimise mycotoxin-related foodborne and feedborne illnesses. **Mycotoxins should be considered an emerging concern of which we still know precious little and so all the tools to keep them under control and at low risk to the consumer, should be used to combat them.** An array of tools to control their precursor fungi will save lives and keep more people healthy while saving costs in the short and long term. Any private and public decision-making should be aware of this and help to manage what is considered by us – the authors of this study – an emerging challenge for mankind that can be met by setting the right incentives and meaningfully weighting hazards and risks associated to mycotoxins and means to combat them.

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ANNEX A: MAJOR MYCOTOXINS OF THE FOOD AND FEED CHAIN: SOME BASIC FACTS ON SOURCES OF EXPOSURE, TOXICTY AND DISEASES

Mycotoxins (Group of ...)	Description
Aflatoxins (AF)	Major sources of this group of mycotoxins are Aspergillus genera of fungi. Crops affected are mainly maize and peanuts, but also cotton seeds, peppers, rice, pistachios, tree nuts and oilseeds as well as dried fruits and spices. It may develop pre-harvest but also post-harvest (by poor storage conditions) and has also been found in milk and dairy products, proving that AF can pass the digestive tract of, e.g., cattle. AF emerge in wet conditions and at temperatures well above 25°C. Stress to plants is key for a contamination, especially under drought stress and if temperatures are above 30°C. If heavily affected, animals or humans suffer from a loss of enzymes, necrosis, immune suppression and liver problems, including cancer. Animals' growth rate decreases and feeding efficiency falls. Anaemia may occur. Altogether, AF are immune suppressive, mutagenic, teratogenic, and carcinogenic and have been linked to increased mortality in farm animals. The AF B1 is the most toxic in this group of mycotoxins and is considered as one of the most potent naturally occurring carcinogens. Young animals and children are more susceptible to AF than are adults.
Deoxynivalenol (DON) and other Trichothecenes (TCT)	Several species of Fusaria particularly infect corn, wheat, barley and other small grains, but also figs, vegetables and other crops with TCT. DON is the most frequent Fusarium mycotoxin, and most hazardous next to DON is also the so-called T-2 toxin. The latter is cytotoxic and causes haemorrhage as well as necrosis of skin tissue. DON has a special importance for the livestock sector. It develops best in warm humid conditions (24-30°C), other TCTs need between 15-30°C and causes feed refusal and emesis (or vomiting – the name "vomitoxin" is also used for this particular mycotoxin) as well as grave lack of appetite. More generally, TCT result in necrosis, bleeding, nausea, and other acute effects on the digestive tract, decreased bone marrow and weaker immune functions. Also, the alimentary toxic aleukia can be related to TCT.
Ergot alkaloids	Small grains such as rye, barley, wheat and oats carry ergot alkaloids, the mycotoxins causing ergotism. What is today classified as ergotism has been known since biblical times and is recognised as an important cause of human death. Since the Middle Ages and until the 20th century there have been mass poisonings due to the consumption of food and feed containing ergots. The first time the illness came to public attention was in relation to the so-called St Anthony's Fire which affected many parts of Europe in the year 943. Infected people suffered from hallucinations and swollen limbs with burning sensation. Subsequent necrosis led to a loss of appendages. Ergot alkaloids can be isolated from Claviceps and cultivate best under warm and humid conditions. Clinical signs are oedema of the legs with severe pain, necrosis, increased body temperature, pulse and respiration rate, hyper-excitability and tremors, heat intolerance, nausea, vomiting and giddiness as well as blindness and paralysis.
Fumonisins (FUM)	These are a group of toxic metabolites primarily produced by Fusaria. They are most frequently found in corn and other grains such as sorghum and rice. They cause abdominal pain and diarrhoea and are hepatotoxic and carcinogenic. The oesophagus and kidneys can be damaged as well as neural tubes in human babies.

Mycotoxins (Group of …)	Description
Ochratoxins (OT)	These mycotoxins are generated by Aspergillus and Penicillium genera of fungi. Optimal conditions for toxin production are at 24-30°C. OT is produced primarily in barley, oats, corn, and wheat, but have also been found in very many other foods such as coffee, beer and wine meaning, it can be carried through the whole food chain. It can be found in kidneys and blood serum and disrupts protein synthesis as well as carbohydrate metabolism of affected animals and humans. Vomiting, diarrhoea, dehydration and depression may follow as well as fatigue, weight loss, immune suppression, carcinogenesis and haemorrhage. Most toxic members of OT are considered potent nephrotoxic and nephrocarcinogenic causing kidney damage as well as liver necrosis and enteritis.
Patulin	Patulin is a mycotoxin that is produced by species of the genera Aspergillus und Pecicillium. Apples as well as apple juice and cider made from affected fruits are the major potential dietary sources of patulin, since it is a common spoilage microorganism in apples. However, patulin can occur as well in other molding fruits, for example in pears and grains, like barley, wheat and corn. Thus, it can also be found in products like jam, and it has also been detected in shellfish. It is reported that patulin does not pose a safety concern for most foods because of the manufacturing and consumption processes. However, mainly apply juice seems to be an exception in that regard for which the avoidance of molding or rotten fruits for juice production is strongly recommended. While not considered a particularly potent toxin, patulin is assessed to occasionally be genotoxic, i.e. it may be a carcinogen. Patulin has also shown some antimicrobial properties against various microorganisms.
Zearaleone (ZEA)	This mycotoxin is a metabolite from Fusaria and develops with corn, wheat and other small grains. High moisture and alternating high and low temperatures (7-21°C) provide favourable conditions. The toxin functions as a weak oestrogen and, thus, has an impact on reproductive functions especially of monogastrics such as pigs and humans. Clinical signs are infertility, ovarian dysfunction, abnormal spermatozoa, vulval oedema, vaginal prolapse, and mammary hypertrophy. It is also linked to the early onset of puberty in children and human breast tumorigenesis. ZEA is often associated to DON too.

Source: Own figure based on Aidoo (2009), Ashiq (2015), BfR (2004), Bhat and Miller (1991), Bhat et al. (2010), CAST (2003), FAO (2001), FDA (2001), Hollmichel (2015), Marin et al. (2013), Noleppa (2015), Peraica et al. (1999), Schwarzer (2009), Walker (2015), WHO (2011), Wild et al. (2015), and Zain (2011).

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