Review

Food Safety in the Context of Bioterrorism: The Challenge of Mycotoxins

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Posted Date: 11 June 2026

doi: 10.20944/preprints202606.0976.v1

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 doi:10.20944/preprints202606.0976.v1

Review

Food Safety in the Context of Bioterrorism: The Challenge of Mycotoxins

Running title: Food Defense and Mycotoxin Risk

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Abstract

This manuscript examines food safety through the lens of bioterrorism, emphasizing how deliberate contamination of food and water systems can cause not only illness and death but also fear, economic disruption, and erosion of public trust. It reviews the public health and regulatory foundations of food defense, including preventive controls, vulnerability assessments, surveillance, and traceback systems, and situates mycotoxins within this broader security framework. Historical incidents of intentional contamination with microbial pathogens demonstrate that foodborne agents can be weaponized, while mycotoxins represent a distinct but credible concern because of their persistence, difficulty of detection, and capacity to contaminate widely distributed staple commodities. The manuscript synthesizes major mycotoxin classes, their exposure pathways, toxicologic mechanisms, analytical detection methods, and mitigation strategies, with attention to cross-cutting risk drivers such as climate, storage conditions, masked toxins, and co-contamination. Collectively, the evidence supports integrating microbial and mycotoxin hazards into food-defense planning and strengthening coordination among surveillance, laboratory, regulatory, and emergency response systems to improve preparedness and resilience.

Keywords: bioterrorism; food defense; food safety; intentional adulteration; mycotoxins; aflatoxins; surveillance; traceback

1. Introduction

When viewed through the lens of bioterrorism, food safety issues center on the deliberate contamination of food or water supplies to harm human health and disrupt society. Unlike ordinary foodborne outbreaks, which are usually caused by accidental contamination, poor sanitation, or failures in food-handling practices, bioterrorism introduces an element of intent. The need for food safety has become especially pressing as modern food systems rely on large-scale production, global supply chains, rapid distribution, and complex processing networks, all of which can allow contamination to spread quickly across communities, regions, or even countries.

Unsafe food remains a major public health concern worldwide; the World Health Organization estimates that foodborne diseases cause about 600 million illnesses and 420,000 deaths globally each year (1). In the United States, foodborne illness continues to affect millions of people annually, with

 doi:10.20944/preprints202606.0976.v1

federal estimates commonly citing about 48 million illnesses, 128,000 hospitalizations, and 3,000 deaths each year (2,2a,2b). These risks explain why food safety has shifted from a reactive model to a preventive one, as reflected in the U.S. Food Safety Modernization Act (3), which emphasizes preventing contamination rather than merely responding after illnesses occur. In the context of bioterrorism, this need is even greater because the purpose of deliberate contamination is not only to cause illness but also to create fear, undermine public confidence, damage the economy, and strain emergency response and public health systems (4a).

Because food and water systems are complex, widely distributed, and dependent on many points of production, processing, transportation, storage, and retail, they can be difficult to protect. Effective prevention requires a food defense approach, meaning facilities must identify where intentional contamination could occur, limit unauthorized access, train employees to recognize suspicious activity, and maintain written plans that are not only developed but also implemented, tested, reviewed, and updated. The FDA's Intentional Adulteration Rule under the Food Safety Modernization Act requires covered facilities to prepare a written food defense plan that includes vulnerability assessments, mitigation strategies, monitoring procedures, corrective actions, and verification activities (3a,4). For meat, poultry, and processed egg establishments, USDA guidance similarly emphasizes functional food defense plans that are documented, implemented, tested, and reviewed regularly to reduce the risk of intentional harm and economic loss (5b-c).

Preparedness also depends on strong surveillance and rapid outbreak detection. In the United States, CDC's PulseNet system uses laboratory data, including whole-genome sequencing, to connect cases of similar illness across locations and help identify potential outbreaks more quickly (5,6). Once an outbreak is detected, investigators use three major types of evidence: epidemiologic data showing who became sick and what they ate, traceback data showing where the food moved through the supply chain, and food or environmental testing showing whether the same pathogen or contaminant is present in food, facilities, or production environments (5a). FDA traceback investigations can follow suspected food from consumers back through distributors, processors, farms, or production facilities, allowing agencies and companies to remove contaminated products from the market and warn the public when necessary.

Water safety requires similar planning because drinking water systems are critical infrastructure. Under America's Water Infrastructure Act, community water systems serving more than 3,300 people must complete risk and resilience assessments and emergency response plans that address malevolent acts, physical security, cybersecurity, monitoring practices, chemical handling, treatment, storage, and distribution systems. EPA also provides resources to help water and wastewater utilities prepare for contamination incidents, supply chain disruptions, and cybersecurity threats, and to support emergency response, recovery, and coordination with other critical sectors, including healthcare, energy, emergency services, and chemical infrastructure (6a,6b). In the context of bioterrorism, these measures are essential because even a limited contamination event can have consequences beyond illness, including public fear, product recalls, business losses, loss of trust, and pressure on public health, law enforcement, and emergency management systems.

Multiple agencies work together to prevent nuclear or radiological terrorism and involve the National Nuclear Security Administration (NNSA), EPA and NRC; the FDA has oversight over treatment for accidental or deliberate exposure to radioactivity. There are strict regulations to guide facilities, material phase-outs, and emergency preparedness. Large amounts of sealed radioactive material went missing from government oversight in developing countries and the former Soviet Union (6c). In the United States, a water cooler in Building 37 at the National Institutes of Health was deliberately contaminated with radioactive phosphorus. In that incident, twenty-six people including a pregnant female working in the laboratory were found to be contaminated with radioactive phosphorus. She was exposed to between 8-12.7 rem, well above the Nuclear Regulatory Commission's annual limit of 5 rem. Her seventeen week old fetus was exposed to between 5.1-8.1 rem. Luckily, none of the other water coolers in the more than sixty buildings at the

 doi:10.20944/preprints202606.0976.v1

NIH were contaminated with radioactive material. The perpetrator was never found in that incident (6d).

Food-related bioterrorism has clear microbial examples. One of the most cited cases is the 1984 Rajneeshee salmonellosis outbreak in The Dalles, Oregon, in which restaurant salad bars were deliberately contaminated with Salmonella typhimurium (7) Investigators reported 751 cases of salmonellosis, most linked to restaurants with salad bars; a later criminal investigation found that members of a religious commune had intentionally contaminated the salad bars (8), and a strain from the commune's laboratory was indistinguishable from the outbreak strain (7). Another example occurred in Texas in 1996, when muffins and doughnuts in a medical-center laboratory break room were intentionally contaminated with *Shigella dysenteriae* type 2. In that incident, 12 of 45 laboratory workers developed severe diarrhea, four were hospitalized, and isolates from patients, an uneaten muffin, and a missing laboratory stock strain were indistinguishable (9).

Microbial toxins are also relevant to food bioterrorism; for example, the CDC identifies botulinum toxin as a potential bioterrorism threat because it could be released into the food supply and is not easily seen, smelled, or tasted (10). These examples show that microbial pathogens have been used in confirmed food attacks, while fungal toxins pose a serious food-defense concern because they can contaminate widely distributed staple foods and cause both health and economic consequences.

Historically, naturally occurring fungal-toxin outbreaks include ergotism in medieval Europe caused by *Claviceps purpurea* on rye (11); alimentary toxic aleukia during World War II in Russia from overwintered grain infected with trichothecene-producing Fusarium (12); and the 1960 "Turkey X disease" outbreak in the United Kingdom (13), where aflatoxin-contaminated peanut meal killed more than 100,000 turkeys, helping launch modern mycotoxin research. Although confirmed food bioterrorism attacks using fungal toxins are rare, the threat is historically credible because aflatoxins, produced by certain fungi and naturally associated with crops such as corn, peanuts, and tree nuts, were reportedly part of Iraq's biological weapons program (14). UNSCOM determined in 1995 that Iraq had produced, filled, and deployed munitions containing botulinum toxin, anthrax spores, and aflatoxin. These examples show that microbial pathogens have been used in confirmed food attacks, while fungal toxins pose a serious food-defense concern because they can contaminate widely distributed staple foods and cause both health and economic consequences.

These incidents show why public health agencies treat foodborne pathogens such as *Salmonella*, *Shigella*, and *E. coli* O157:H7 as food safety threats in the bioterrorism context, alongside microbial toxins such as botulinum toxin, epsilon toxin of *Clostridium perfringens*, and staphylococcal enterotoxin B. CDC specifically notes that botulinum toxin, produced by *Clostridium botulinum* and related fungal toxins, is a bioterrorism concern because it could be released into the food supply, although no reported U.S. botulism cases have been linked to bioterrorism. Although confirmed food-delivered bioterrorism using fungal toxins is rare, aflatoxin has appeared in biological-weapons history: after the Gulf War, Iraq admitted to UNSCOM that it had produced 2,200 liters of aflatoxin and had prepared biological-warfare munitions that included aflatoxin, although Iraq did not use them (15).

Table 1. Several pathogens are high-risk because they spread easily or cause severe illness.

Agent	Possible Effects
Salmonella	Food poisoning, diarrhea, fever
Escherichia coli O157:H7	Severe gastrointestinal disease, kidney damage
Clostridium botulinum toxin	Paralysis, respiratory failure
Listeria monocytogenes	Severe infection in pregnant women and immunocompromised people16
Bacillus anthracis	Respiratory failure; septic shock15
Norovirus	Rapid outbreaks of vomiting and diarrhea17

1. Mycotoxins

 doi:10.20944/preprints202606.0976.v1

Fungal toxins (mycotoxins) are widely found in foods such as cereals, nuts, spices, dried fruits, apples, coffee beans, corn, rice, peanuts, and tree nuts (18-19). Historical mycotoxin events include ergotism in Europe from contaminated rye, alimentary toxic aleukia in the Soviet Union during the 1940s from *Fusarium*-contaminated grain, and the 1960 "Turkey X disease" outbreak in England, in which aflatoxin-contaminated groundnut meal was associated with the deaths of large numbers of turkeys (13,20). Mycotoxins are low-molecular-weight secondary metabolites produced by filamentous fungi and can cause illness or death in vertebrates. Their relevance spans human foods, animal feeds, companion-animal foods, and especially baby foods, where routine testing is warranted. Liquid chromatography coupled with mass spectrometry is the standard confirmatory method for measuring mycotoxin levels. Exposure severity varies with age, genetics, diet, immune status, medical condition, sex, exposure duration, dose, and co-exposure to other toxicants (21-22). Poor nutrition and calorie deficiency may further increase susceptibility and compound the risk of microbial disease in impoverished populations (21).

Mycotoxin production is highly probable when fungi gain access to grain in the field or during storage. Crop damage, insects or bird injury, high relative humidity, warm temperatures, poor storage conditions, and substrate humidity in the 10-20% range can promote fungal growth and toxin production. Climate change is an important independent driver because warming may expand the geographic range of toxigenic fungi and increase aflatoxin and fumonisin contamination in historically cooler regions (23). These conditions create a continuum from field damage to storage contamination, and if contaminated commodities are consumed in sufficient quantities, they can lead to human or animal illness.

Risk assessment is complicated by masked mycotoxins and co-contamination. Masked forms can evade detection because their polarity or binding state is altered, yet the gastrointestinal tract and microbiome may convert less toxic, conjugated, or bound forms back into more toxic parent compounds (24-25). Because contamination data and toxicological profiles are often incomplete for modified forms, and because foods may contain multiple mycotoxins or other toxicants such as pesticides, single-analyte assessments may underestimate hazard (26). Aflatoxins, deoxynivalenol, fumonisins, patulin, and ochratoxin A are the U.S. FDA focal mycotoxins in human food.

2. Cross-Cutting Risk Drivers

Across toxin classes, risk is shaped by interactions among fungal ecology, host-plant injury, weather, harvest timing, storage control, food processing, and host susceptibility. Field injury allows fungi to colonize plant tissues before harvest, whereas inadequate drying, poor aeration, high temperatures, and elevated moisture can permit further post-harvest accumulation. These drivers are especially important because mycotoxins are chemically stable enough that routine cooking or processing may not reliably eliminate them, and because vulnerable populations may experience greater harm at similar exposure levels (23,27). Table 2 consolidates the recurring risk drivers and practical implications across toxin classes.

Table 2. Main risk drivers and implications.

Driver	How it increases risk	Practical implication
Fungal access to grain	Fungi can colonize crops in the field or during storage when kernels or plant tissues are damaged.	Monitor crop damage, insect injury, bird damage, harvest timing, and storage integrity.
Warm temperatures and humidity	Tropical and subtropical conditions, high relative humidity, and 10-20% substrate humidity favor toxin production.	Temperature and moisture control are central to prevention.

 doi:10.20944/preprints202606.0976.v1

Driver	How it increases risk	Practical implication
Drought followed by warm, wet weather	This pattern is highlighted for fumonisins and aflatoxins, especially in maize/corn.	Target pre-harvest monitoring during drought stress and late-season weather changes.
Climate change	Warmer regions may expand fungal ranges and shift toxin occurrence into historically cooler areas.	Surveillance plans should be updated geographically rather than based only on historical risk zones.
Poor storage conditions	Post-harvest contamination can occur when humidity and temperature favor mold growth.	Use drying, aeration, temperature control, and removal of damaged or over-mature crops.
Masked mycotoxins	Chemical binding or polarity changes can reduce detectability while later gastrointestinal conversion may restore toxicity.	Risk assessment should consider modified forms, not only parent compounds.
Co-contamination	Multiple mycotoxins or other toxicants can occur together, creating uncertain additive or synergistic effects.	Testing panels and risk assessments should consider mixtures rather than single analytes only.
Vulnerable hosts	Age, immune status, nutrition, genetics, and disease can alter susceptibility.	High-risk foods and populations need stricter surveillance, especially infants and malnourished populations.

3. Major Mycotoxin Classes at a Glance

The major toxin classes differ in fungal source, favored commodities, primary target organs, stability, and preferred analytical methods. A comparative overview is useful because management decisions often require parallel surveillance for multiple toxins rather than a single-target approach, particularly when environmental stress and commodity damage increase the likelihood of co-contamination (26). Table 3 summarizes the major toxin classes.

Table 3. Comparative overview of major mycotoxin classes.

Class	Primary producers/forms	Common commodities or exposure routes	Key health concerns	Processing/detection notes
Fumonisins	Primarily *Fusarium verticillioides* and *F. proliferatum*; also *F. nygamai, Alternaria alternata f.* sp. lycopersici; low levels from *Aspergillus niger*. FB1 is emphasized as the most toxic and most important for contamination.	Maize/corn and corn-based foods; also grapes, wine, dried vine fruits, coffee at lower levels; reports in cow milk and breast milk.	Animal diseases include equine leukoencephalomalacia, porcine pulmonary edema, liver damage, and rodent liver cancer. Human associations include esophageal cancer and infant neural tube defects in high-maize-consumption regions.	Hydrophilic; extracted using aqueous methanol or acetonitrile and analyzed by liquid chromatography with fluorescence detection. Milling has limited effect; nixtamalization and high-temperature processing can reduce levels.

 doi:10.20944/preprints202606.0976.v1

Class	Primary producers/forms	Common commodities or exposure routes	Key health concerns	Processing/detection notes
Trichothecenes	More than 60 sesquiterpenoid metabolites from *Fusarium*, *Myrothecium*, *Phomopsis*, and *Stachybotrys*. Important examples include DON, DAS, NIV, T-2, and HT-2.	Corn, wheat, barley, rice, oats, soybeans, moldy grain, and moldy hay.	DON causes nausea, vomiting, diarrhea, reduced appetite, and weight loss in pigs. T-2 is highly toxic, can be absorbed through skin, and is linked with alimentary toxic aleukia symptoms in historical moldy-grain outbreaks.	Measured by gas chromatography and high-performance liquid chromatography combined with mass spectrometry. Toxins and metabolites are generally removed in urine or stool within one day according to the source text.
Ochratoxins	Produced by *Penicillium verrucosum* and *Aspergillus ochraceus*, *A. carbonarius*, and *A. niger*. OTA is the most prevalent and toxic member.	Primarily damaged grains; barley, oats, wheat, coffee beans, dried fruit, beer, red wine, pork and poultry meat, milk, cheese, and possible workplace inhalation exposure.	Kidney is the main target. OTA is linked in experimental models to mutagenicity, teratogenicity, and carcinogenicity; human epidemiologic evidence remains inconclusive in the source text.	Relatively heat stable. Baking/roasting reduce content about 20%; boiling has no effect. Adsorbents, radiation, UV-B, activated carbon, and natural materials have been proposed for removal/detoxification.
Zearalenone (ZEN)	Produced by Fusarium species, especially *F. graminearum*, *F. culmorum*, *F. verticillioides*, and *F. sporotrichioides*.	Corn, wheat, barley, sorghum, rye, cow-based infant formula metabolites, poultry organ parts, and fish feed.	Estrogenic endocrine effects; hyperestrogenism in swine at low ppm levels; reproductive problems in swine, cattle, and sheep at higher levels; possible hepatotoxicity and cancer associations require better controlled studies.	Detected most often by HPLC-MS, often after immunoaffinity-column cleanup. Heat stable and does not degrade readily during processing.

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Class	Primary producers/forms	Common commodities or exposure routes	Key health concerns	Processing/detection notes
Aflatoxins	Produced by *Aspergillus flavus* and *A. parasiticus*. Major forms include AFB1, AFB2, AFG1, AFG2, and AFM1. AFB1 is the most potent genotoxic and carcinogenic form.	Groundnuts/peanuts, tree nuts, maize, rice, figs, dried foods, spices, crude vegetable oils, cocoa beans, animal feed, milk, and meat products through carryover.	Acute nausea, vomiting, abdominal pain, convulsions; chronic hepatotoxicity, immunotoxicity, teratogenicity, and hepatocellular carcinoma. AFB1 is a major liver-cancer risk in developing countries.	Fluorescence spectrophotometry can quantify aflatoxins rapidly in the ppb range. Other methods include GC, HPLC, and thin-layer chromatography. Competitive exclusion with atoxigenic strains and NovaSil clay are discussed as controls.

4. Detailed Consolidated Profiles

4.1. Fumonisins

Fumonisins are ubiquitous toxic secondary metabolites primarily produced in maize by *Fusarium verticillioides* and *F. proliferatum*, with additional production reported from *F. nygamai* and *Alternaria alternata* f. sp. lycopersici (28-30). *Aspergillus niger* can also produce lower concentrations in grapes, wines, dried vine fruits, and coffee (31). Several Fusarium mycotoxins, including moniliformin, enniatins, and fusaproliferin, have been detected in food crops across diverse geographic regions, underscoring the need to consider fumonisins as part of broader patterns of Fusarium contamination (32-34).

Fumonisin risk increases when kernels are damaged by birds or insects, when crops experience drought stress followed by warm, wet weather late in the growing season, and when harvested grain is stored under harsh conditions (35-37). Although fumonisin contamination is primarily associated with maize and corn-based foods, reports of contamination in cow's milk and breast milk indicate that exposure assessment may need to include carryover into animal- or human-derived matrices (38). High-exposure settings are especially important in regions where maize is a dietary staple, including parts of Africa, South and Central America, and China, where intake may exceed acceptable levels (39).

Processing effects are uneven. Milling has little impact on fumonisin levels in flour or related fractions, whereas nixtamalization reduces fumonisins effectively by soaking and cooking corn in an alkaline solution, followed by washing and hulling (40). Fumonisins are generally stable and are not eliminated by normal food processing, cooking, baking, or pasteurization, although heating above approximately 160°C, high-temperature extrusion, or industrial processing can reduce levels (27,37,40). Apparent reductions may also reflect binding to food components and formation of conjugated or masked forms rather than complete detoxification (41). Because fumonisins are hydrophilic, extraction is commonly performed using aqueous methanol or acetonitrile, followed by liquid chromatography with fluorescence detection (42).

Toxicologically, fumonisin B1 is the most abundant and toxic fumonisin and is associated with porcine pulmonary edema, equine leukoencephalomalacia, and liver injury across multiple animal species (43-45). Species-specific target-organ effects include lung injury in pigs, brain injury in horses, kidney injury in rats, rabbits, and sheep, and hepatocarcinogenicity in rodents (46-50). Epidemiologic data have linked consumption of corn contaminated with *F. verticillioides* to esophageal cancer and infant neural tube defects, with low-income populations described as having greater risk in several settings (51-55).

 doi:10.20944/preprints202606.0976.v1

Mechanistically, fumonisins resemble sphingosine and competitively inhibit sphinganine and sphingosine N-acyltransferase, thereby disrupting ceramide synthase activity and sphingolipid metabolism. Because complex sphingolipids contribute to membrane integrity, caveolar microdomains, extracellular matrix interactions, microbial and viral binding sites, and second-messenger systems, fumonisin-induced perturbation can influence inflammation, apoptosis, cell trafficking, proliferation, organ injury, and carcinogenesis (56-60). Removal of tricarballylic side chains can form AP1, which is converted to palmitoyl-AP1 and may inhibit ceramide synthase more potently than the parent compound, reinforcing the need to evaluate downstream sphingolipid disruption when interpreting fumonisin pathophysiology (52).

4.2. Trichothecenes

Trichothecenes comprise more than sixty sesquiterpenoid secondary metabolites produced by filamentous fungi in genera such as Fusarium, Myrothecium, Phomopsis, and Stachybotrys (61). Important cereal contaminants include deoxynivalenol (DON) and its derivatives, diacetoxyscirpenol, nivalenol, T-2 toxin, and HT-2 toxin (62). The group is defined by a 12,13-epoxytrichothecene skeleton and is divided into types A through D; type A toxins, such as T-2 and HT-2, lack a carbonyl group at C-8, type B includes DON and nivalenol, type C contains two epoxy rings, and type D includes macrocyclic toxins such as satratoxin and roridin (63).

Table 4. Trichothecene classification.

Type	Distinguishing feature	Representative toxins
Type A	Lack a carbonyl group at C-8.	T-2 and HT-2 toxins.
Type B	Include deoxynivalenol and nivalenol.	DON and NIV.
Type C	Contain two epoxy rings, one between C-7/C-8 or C-9/C-10.	Croton and baccharin as stated in source text.
Type D	Macrocyclic structure between C-4 and C-15.	Satratoxin and roridin.

Trichothecenes occur in corn, wheat, barley, rice, oats, soybeans, and moldy hay, with fungal growth favored by temperatures from 30° to 40°C and relative humidity above 70%. Tropical and subtropical environments are therefore more prone to fungal damage than many temperate regions (63). DON, also produced by *F. graminearum*, can cause nausea, vomiting, and diarrhea, and lower doses can reduce appetite and body weight in pigs (64). T-2 toxin is highlighted as uniquely capable of dermal absorption among this group and as highly toxic, with fowl described as particularly sensitive based on oral lesions, skin inflammation, intestinal irritation, and poor appetite (63,65).

Historical outbreaks also illustrate the severity of trichothecene exposure. During World War II, villagers in the former U.S.S.R. reportedly consumed moldy grain infected by *F. sporotrichioides* and *F. poae*, and T-2 toxin and diacetoxyscirpenol may have contributed to alimentary toxic aleukia, a syndrome involving skin inflammation, vomiting, hematopoietic injury, oral cavity necrosis, bleeding, and central nervous system disorders (66,67). Consumption of moldy hay containing Stachybotrys was likewise associated with high horse mortality in the Russian literature, and investigations of trichothecenes as potential bioweapons were reported during World War II (63,68). Analytical measurements are performed using gas chromatography and high-performance liquid chromatography coupled with mass spectrometry, and most ingested toxins and metabolites are excreted in urine or stool within 1 day (63,69).

The toxicological mechanism centers on potent inhibition of eukaryotic protein synthesis. Trichothecenes can interfere with initiation, elongation, and termination and appear to bind the 60S ribosomal subunit, inducing oxidative stress and apoptosis in immune cells (70-72). Rapidly dividing cells, including immune cells, red blood cells, and gastrointestinal epithelial cells, are especially vulnerable, which is consistent with bloody diarrhea, hemorrhage, intestinal epithelial necrosis, and

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skin and oral lesions (73-76). T-2 and DON also induce mitochondrial dysfunction, oxidative stress, and neuronal apoptosis through MAPK, ras, p53, and nrf-2/HO-1-related pathways, while interactions among T-2, zearalenone, and ochratoxin A suggest that mitochondrial apoptosis and reactive oxygen species can differ by toxin (77-78).

4.3. Ochratoxins

Ochratoxins are secondary metabolites produced by *Penicillium verrucosum* and *Aspergillus ochraceus*, *A. carbonarius*, and *A. niger*, and they primarily contaminate damaged grains. The family includes ochratoxin A (OTA), ochratoxin C, 4-hydroxyochratoxin A, ochratoxin B, and ochratoxin alpha, with ochratoxin A identified as the most prevalent and toxic form and non-amide forms described as less toxic (79). OTA primarily contaminates barley but also occurs in oats, wheat, coffee beans, dried fruit, beer, red wine, and other commodities (80). Carryover into animal-origin foods such as pork, poultry, milk, and cheese may contribute to human exposure, and inhalation exposure is possible in abattoirs and packing facilities (81,82).

OTA is relatively heat-stable. Baking and roasting reduce content by approximately 20%, whereas boiling has no effect, and accumulation can occur during storage when humidity and temperature favor mold growth (83.84). Prevention therefore depends on screening for insect damage, promptly removing over-mature crops during harvest, and controlling temperature and humidity during storage (85.86). These storage-management steps are especially important because heat alone is not a reliable detoxification strategy for OTA-contaminated commodities.

The kidney is the primary target organ for OTA in humans and animals, although effects on the liver, central nervous system, and immune system have also been described. Experimental models report mutagenic, teratogenic, and carcinogenic effects, and Balkan endemic nephropathy, urinary tract tumors, and chronic interstitial nephropathy have been proposed as possible outcomes associated with OTA (87,88). However, confirmatory epidemiological evidence linking OTA exposure to adverse human effects remains limited or absent, apart from a preliminary study of highly exposed individuals that did not adequately control for confounders such as infection, diabetes, lupus, or hypertension (89,90).

Proposed mechanisms of OTA toxicity include oxidative stress, mitochondrial dysfunction, inhibition of protein synthesis, lipid peroxidation, and prolonged albumin binding (79,91,92). Reactive oxygen species such as hydroxyl radicals and peroxynitrite can promote peroxidation of membrane polyunsaturated fatty acids, potentially contributing to nephrotoxicity, while serum albumin binding extends their persistence in the body, and a reported half-life of approximately 35 days may support deposition in tissues and fluids (92,93). Proposed OTA reduction methods include physical adsorption, gamma radiation, ultraviolet B light, natural adsorbents, activated carbon, and related approaches, although their usefulness depends on the food matrix and implementation context (94-100).

Regulatory and health-based assessments reflect uncertainty and concern. IARC classified OTA as a Group 2B possible human carcinogen based on sufficient animal evidence and inadequate human evidence (101). Health Canada recommended a tolerable weekly intake of 21 ng/kg body weight, lower than the EFSA CONTAM Panel value of 120 ng/kg body weight. The Commission Regulation (EC) No. 2022/1370 established maximum OTA levels for multiple foods (102-103). The United States FDA has not established formal OTA limits for foodstuffs, although levels at or below 20 ppb are considered of no further concern.

4.4. Zearalenone (ZEN)

Zearalenone is produced by several Fusarium species, especially *F. graminearum*, *F. culmorum*, *F. verticillioides*, and *F. sporotrichioides*, and can contaminate corn, wheat, barley, sorghum, and rye (104,105). ZEN can accumulate before harvest, but poor storage conditions may also promote post-harvest production, especially under warm and wet conditions (106,107). High-performance liquid chromatography coupled with mass spectrometry is the most common detection approach, often

 doi:10.20944/preprints202606.0976.v1

with immunoaffinity column cleanup. The toxin is heat-stable and does not readily degrade during processing (108,109).

ZEN and its metabolites have been reported in multiple food and feed matrices, including cereals, cow-based infant formula, poultry organ tissues, and fish feed, indicating that exposure assessment may need to extend beyond raw grains (110-112). At the same time, a single-source study found no detectable ZEN in cow milk after administering 544.5 mg ZEN per day for three weeks to a single cow, suggesting that milk carryover may not always represent a major human health risk under the tested conditions (113). These observations supported commodity-specific surveillance rather than broad assumptions about uniform carryover (114).

The defining biological concern for ZEN is its estrogenic activity. ZEN is structurally similar to endogenous estrogens, binds alpha and beta estrogen receptors in humans, and can activate estrogen-response-element-mediated gene transcription (106,115-118). The cis isomer has a greater affinity for estrogen receptors than the trans isomer and reduced or related metabolites such as alpha-zearalenol and alpha-zearalanol can have greater estrogenic activity than the parent compound (118,119). Dietary exposure near one ppm may induce hyperestrogenic effects in swine, whereas higher exposures are associated with conception difficulties and abortion in swine, cattle, and sheep (120-123). Enterohepatic cycling of glucuronide metabolites can prolong elimination, and alpha-zearalanol has been used as a growth promoter in beef cattle in North America but was banned in the European Union in 1985 (118,124,125).

Beyond endocrine disruption, concerns have been raised about hepatotoxicity and genotoxicity. ZEN has been associated with altered liver function tests and liver cancer in some reports, although more controlled studies are needed to clarify the relationship with cancer (126-129). Experimental findings include DNA adduct formation, DNA fragmentation, chromosomal abnormalities, and apoptosis (130). EFSA has set a tolerable daily intake of 0.25 ug/kg body weight per day for ZEN and modified forms, while the FDA and WHO have set a maximum allowable level of 0.5 ug/kg body weight for human food and animal feed (107,118,131-133)

4.5. Aflatoxins

Aflatoxins are toxic secondary metabolites produced mainly by *Aspergillus flavus* and *Aspergillus parasiticus* from polyketide pathways (134,135). Major forms include AFB1, AFB2, AFG1, AFG2, and AFM1, with AFB1 identified as the most common and most potent genotoxic and carcinogenic aflatoxin. Aflatoxins occur in groundnuts, tree nuts, maize, rice, figs, other dried foods, spices, crude vegetable oils, cocoa beans, animal feed, and downstream foods such as milk and meat when animals consume contaminated feed (136-140).

Formation is favored by warm temperatures and drought, including conditions described for the southern and midwestern corn belt of the United States. Asexual spores are spread by wind or insects, and loss of the seed coat or plant tissue integrity allows fungal growth on developing grain (141). Because a single contaminated raw commodity, such as peanuts, can be processed into peanut oil, bottled peanuts, peanut butter, animal feed, milk, and meat products, contamination can propagate through several branches of the food chain if not detected and controlled.

The aflatoxin gene cluster in Aspergillus comprises approximately 30 genes regulated by aflR and aflS, and the cluster shows high homology between *A. flavus* and *A. parasiticus* (142-145). A key species-level distinction is toxin profile: *A. flavus* mostly produces B aflatoxins, whereas *A. parasiticus* produces both B and G aflatoxins (146,147). This distinction is useful for interpreting contamination patterns and potential risk across commodities.

Aflatoxins target the liver and can cause acute symptoms such as fever, malaise, vomiting, anorexia, abdominal pain, hepatitis, nausea, convulsions, and abdominal pain, while chronic exposure is associated with hepatotoxicity, immunotoxicity, teratogenicity, and hepatocellular carcinoma (148,149). Immunosuppressive effects have been described in animals and humans, and hepatocellular carcinoma is a major concern in developing countries where exposure may be high (150-152). AFB1 is activated by cytochrome P450 enzymes to an 8,9-epoxide, especially the exo

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isoform, which binds DNA to form mutagenic adducts, inhibits RNA synthesis, impairs mitochondrial function, promotes oxidative injury, and binds proteins such as albumin after conversion via dihydroxydiol and dialdehyde intermediates (84,136,140,153-155). In people with chronic hepatitis B and aflatoxin exposure, a p53 codon 249 mutation has been reported and may contribute to hepatocellular carcinoma pathogenesis (156).

Aflatoxins can be measured rapidly by fluorescence spectrophotometry in the 5-5000 ppb range, and other methods include gas chromatography, high-performance liquid chromatography (HPLC), and thin-layer chromatography, with HPLC and thin-layer chromatography commonly used for determination (157,158). Control strategies include competitive exclusion using atoxigenic Aspergillus strains and dietary binding with NovaSil clay, which binds aflatoxins in the gastrointestinal tract and can reduce bioavailability without impairing the use of vitamins and micronutrients (159-161). AFB1 is classified by IARC as a Class 1 human carcinogen, and the U.S. FDA maximum levels is 20 ug/kg in human and animal food except milk, where the limit is 0.5 ppb, with animal limits varying by species, sex, and production use (102).

5. Mechanisms of Toxicity

Although each toxin class has a distinct primary target, several mechanistic patterns recur, including disruption of sphingolipid metabolism, inhibition of protein synthesis, oxidative stress, mitochondrial dysfunction, activation of endocrine receptors, and genotoxic adduct formation (Table 5). These mechanisms provide a useful framework for interpreting the target-organ patterns described above and for prioritizing analytical surveillance when multiple toxin classes may co-occur (26).

Table 5. Consolidated mechanisms and target outcomes.

Toxin class	Primary mechanism summarized	Likely target systems or outcomes
Fumonisins	Structural similarity to sphingosine; competitive inhibition of sphinganine/sphingosine N-acyltransferase and ceramide synthase; altered sphingolipid metabolism; AP1/palmitoyl-AP1 may be more toxic than parent FB1.	Liver, lung in pigs, brain in horses, kidney in rats/rabbits/sheep; organ damage and likely cancer-related pathways.
Trichothecenes	Inhibition of eukaryotic protein synthesis through effects on initiation, elongation, and termination; binding to 60S ribosomal subunit; oxidative stress and apoptosis.	Rapidly dividing cells including immune cells, red blood cells, gastrointestinal epithelium; oral/skin lesions, bloody diarrhea, hemorrhage, intestinal necrosis, CNS effects.
Ochratoxins	Oxidative stress, mitochondrial dysfunction, protein synthesis inhibition, lipid peroxidation, albumin binding, and prolonged persistence.	Kidney as primary target; possible liver, CNS, immune effects; experimental mutagenicity, teratogenicity, and carcinogenicity.
Zearalenone	Estrogen receptor binding and estrogen-response element activation; more estrogenic metabolites; enterohepatic cycling of glucuronide forms.	Endocrine disruption, reproductive effects, hyperestrogenism, possible hepatic and genotoxic effects.
Aflatoxins	P450-mediated activation of AFB1 to 8,9-epoxide; DNA/RNA/protein adduct formation; oxidative damage and lipid peroxidation; possible p53 codon 249 involvement with hepatitis B co-exposure.	Liver toxicity, immunosuppression, teratogenicity, hepatocellular carcinoma.

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6. Detection and Analytical Methods

Analytical confirmation generally relies on chromatographic separation and mass spectrometric detection, but the toxin's chemistry influences the preferred extraction and detection workflow (Table 6). Hydrophilic fumonisins require aqueous organic extraction; trichothecenes are commonly measured by gas chromatography (GC) or HPLC with mass spectrometry (MS); ZEN is often measured by HPLC-MS after immunoaffinity cleanup; and aflatoxins can be screened or quantified using fluorescence-based methods in addition to chromatographic approaches (22,42,69,108,157,158).

Table 6. Detection methods consolidated.

Method or approach	Used for	Notes from source text
LC-MS	General mycotoxin confirmation; ZEN frequently detected by HPLC-MS/LC-MS workflows.	Presented as the standard confirmatory approach for mycotoxin levels; ZEN analysis often includes immunoaffinity-column cleanup.
Aqueous methanol or acetonitrile extraction plus LC with fluorescence detection	Fumonisins	Fumonisins are hydrophilic, making extraction and analysis challenging.
Gas chromatography and HPLC combined with mass spectrometry	Trichothecenes	Used to measure trichothecenes, including DON, T-2, and HT-2-related toxins.
Fluorescence spectrophotometry	Aflatoxins	Can quantify aflatoxins in the 5-5000 ppb range in less than five minutes according to the source text.
GC, HPLC, and thin-layer chromatography	Aflatoxins	HPLC and thin-layer chromatography are described as commonly chosen methods for determining aflatoxin levels.

LC, liquid chromatography; MS, mass spectrometry; HPLC, high pressure liquid chromatography.

7. Processing, Storage, and Mitigation Options

Prevention and mitigation are most effective when applied across the production chain. Field-level strategies reduce fungal access to crops; storage controls, such as low humidity, cool temperatures and intact grain,limit post-harvest growth; processing methods such as nixtamalization or high-temperature extrusion can reduce specific toxins; and binding or biological competition strategies may reduce bioavailability or field contamination. However, stability varies by toxin, and normal cooking, baking, boiling, pasteurization, or milling may be insufficient for several toxin classes, so mitigation should not substitute for surveillance and prevention [Table 7] (27,40,83,159,160).

Table 7. Processing, storage, and mitigation strategies.

Intervention	Most relevant toxins	Purpose and source-text notes	Limitations or cautions
Routine testing and surveillance	All major mycotoxins	Companion-animal foods, food-animal feeds, human foods, and especially baby foods should be routinely analyzed.	Sampling plans must account for heterogeneous contamination and masked/co-contaminated toxins.

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Intervention	Most relevant toxins	Purpose and source-text notes	Limitations or cautions
Drying, temperature control, and humidity control during storage	All storage-related toxins; especially OTA, fumonisins, ZEN	Higher humidity and temperature after harvest increase fungal growth; storage controls reduce post-harvest accumulation.	Cannot reverse contamination that already occurred before harvest.
Removal of damaged or over-mature crops	OTA and general grain toxins	The source text highlights screening for insect damage and prompt removal of over-mature crops.	Requires field-level and storage-level quality control.
Nixtamalization	Fumonisins	Soaking/cooking corn in alkaline solution, washing, and hulling reduces fumonisin levels effectively.	May not apply to all grain products or industrial formats.
High-temperature extrusion/processing	Fumonisins	Heating above about 160 degrees C, or 150-200 degrees C in processing, can reduce fumonisin levels.	Normal cooking, baking, pasteurization, and routine processing may not eliminate toxins.
Baking or roasting	Ochratoxin A	Reduces OTA content by about 20% according to the source text.	Boiling has no effect; heat is generally limited as an OTA detoxification strategy.
Physical adsorption and adsorbents	OTA and aflatoxins	OTA: physical adsorption, natural material adsorbents, activated carbon, gamma radiation, and UV-B are discussed. Aflatoxin: NovaSil clay binds toxins in the GI tract and reduces bioavailability.	Effectiveness varies by matrix and toxin; must avoid reducing nutrient bioavailability or introducing new risks.
Competitive exclusion with atoxigenic strains	Aflatoxins	Atoxigenic Aspergillus strains are used to reduce toxigenic aflatoxin-producing strains in the field.	Requires appropriate strains, agricultural implementation, and ongoing monitoring.

8. Regulatory Classifications and Guidance Values

The regulatory landscape differs by toxin and jurisdiction. Fumonisin B1 and ochratoxin A are described as IARC Group 2B possible human carcinogens, whereas AFB1 is classified as an IARC Class 1 human carcinogen; EFSA, JECFA, Health Canada, FDA, WHO, and EU documents provide health-based guidance or commodity limits for selected toxins (101-103,118,162,163). Guidance values are reported in Table 8 and should be treated as a verification checklist rather than a final compliance table.

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Table 8. Regulatory classifications and guidance values**.

Toxin or group	Classification/guidance body	Value or limit reported in source text	Notes
Fumonisin B1/fumonisins	IARC; JECFA; U.S. FDA	IARC Group 2B, possibly carcinogenic to humans. JECFA provisional maximum tolerable daily intake: 2 ug/kg body weight/day. U.S. FDA maximum level for corn products for human consumption: 2-4 ppm. Corn and by-products under 5 ppm considered safe for all animal feed; species/stage-specific maximum recommendations range from 5-100 ppm.	The duplicated fumonisin regulatory paragraph in the source text was consolidated here.
Trichothecenes/T-2/HT-2	Food safety experts; EU; U.S. FDA as reported in source text	T-2 and HT-2 in infected unprocessed cereals including corn: 0.1-0.25 ppm. Lowest observed adverse effect level for dairy cows, beef cattle, and goats: 10 ug/kg body weight/day. EU maximum levels for combined T-2 and HT-2 in foods: 10-1250 ug/kg. FDA values reported: 1 ppm humans, 2 ppm dairy cows, 10 ppm cattle.	The source text describes fowl as extremely sensitive to T-2 toxin.
Ochratoxin A	IARC; Health Canada; EFSA; EU; U.S. FDA as reported in source text	IARC Group 2B possible human carcinogen. Health Canada TWI: 21 ng/kg body weight/week. EFSA CONTAM Panel TWI: 120 ng/kg body weight/week. EU maximums: infant food 0.5 ug/kg, wine 2.0 ug/kg, roasted coffee 5.0 ug/kg, unprocessed cereals 5.0 ug/kg, date syrup 15 ug/kg. U.S. FDA has not set regulatory limits; source text states FDA considers levels at or below 20 ppb to be of no further concern.	OTA is noted for kidney toxicity and long body persistence.
Zearalenone	EFSA; FDA/WHO as reported in source text	EFSA tolerable daily intake: 0.25 ug/kg body weight/day for ZEN and modified forms. FDA and WHO maximum allowable level reported as 0.5 ug/kg body weight for human food and animal feed.	ZEN is estrogenic; metabolites may be more potent than parent compound.
Aflatoxins/AFB1/AFM1	IARC; U.S. FDA; EU as reported in source text	AFB1: IARC Class 1 human carcinogen. U.S. FDA maximum level: 20 ug/kg (ppb) in human and animal food, except milk at 0.5 ppb. Animals: 20-300 ppb depending on species/sex. EU levels reported as 2-15 ppm for typical foods, 0.5 ppm for baby and medical foods, and AFM1 in milk at 50 ng/kg.	AFB1 is the most potent genotoxic and carcinogenic aflatoxin; AFM1 is a milk metabolite of AFB1.

**Regulatory limits can change, and some secondary-source unit reporting may be inconsistent; values should be verified against current official regulatory documents before publication or compliance use.

9. Discussion

Food safety in the context of bioterrorism should be conceptualized as extending beyond the prevention of accidental contamination. Deliberate adulteration of food or water supplies can cause not only illness and mortality but also fear, economic destabilization, and erosion of public trust in essential systems. As this analysis demonstrates, food defense is inseparable from contemporary public health preparedness, particularly because modern food and water distribution networks are

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highly integrated, involving many businesses and different parts of the country that can amplify the consequences of a single contamination event across geographically dispersed populations (1-3)

A central implication of this framework is the necessity of shifting from reactive response toward anticipatory prevention. The global burden of unsafe food remains substantial, with WHO estimating approximately 600 million cases of foodborne disease and 420,000 deaths annually worldwide, while recent CDC estimates continue to indicate millions of illnesses, tens of thousands of hospitalizations, and hundreds of deaths each year in the United States (1,2). Deliberate contamination magnifies that burden by introducing intent, strategic targeting, and the potential for disproportionate societal disruption. Regulatory frameworks such as the Food Safety Modernization Act and the Intentional Adulteration Rule reflect this preventive orientation by requiring covered facilities to conduct vulnerability assessments, implement mitigation strategies, and maintain written food defense plans that are monitored, verified, reviewed, and periodically updated rather than treated as static compliance documents (3,4,5a-c). Accordingly, food defense should be understood not merely as a regulatory obligation, but as a core component of risk reduction for both public health protection and economic resilience.

Surveillance and traceback capacity are equally fundamental to preparedness. Systems such as PulseNet strengthen outbreak detection by linking clinically and genetically similar cases across jurisdictions, while epidemiologic investigation, traceback analysis, and laboratory confirmation collectively provide the evidentiary basis for source attribution and product removal from commerce (5,6). This layered approach is especially important in intentional contamination events, for which early recognition may limit both direct exposure and the broader social consequences of public alarm. A parallel rationale applies to drinking water systems, where risk and resilience planning are essential because contamination can rapidly compromise critical infrastructure and undermine community confidence in basic public services (3,4).

The historical record further demonstrates that intentional food contamination is not merely a theoretical concern. The Rajneeshee *Salmonella* outbreak in The Dalles, Oregon, resulted in 751 illnesses and illustrated the vulnerability of restaurant salad bars as vehicles for deliberate contamination (7,8). Similarly, the Texas *Shigella dysenteriae* outbreak among laboratory workers showed that intentional contamination of food with a highly pathogenic strain could lead to severe illness and hospitalization (9). Taken together, these incidents support the conclusion that routine foodborne pathogens should also be considered potential bioterrorism agents when exposure patterns are unusual, tightly clustered, or accompanied by evidence suggestive of deliberate intent. Their public health significance extends beyond case counts alone, as even relatively limited outbreaks may precipitate recalls, substantial business losses, and enduring damage to consumer confidence.

Mycotoxins occupy a somewhat distinct position within this landscape because they are often naturally occurring contaminants rather than agents primarily transmitted from person to person. Nevertheless, their relevance to food defense remains substantial. Historical episodes including ergotism, alimentary toxic aleukia, and aflatoxin-associated outbreaks demonstrate that fungal toxins have repeatedly caused severe disease through contamination of staple commodities (11-13,164). Their chemical stability, persistence in globally traded foodstuffs, and relative resistance to routine cooking or processing make them especially important from both food safety and food defense perspectives. This concern extends beyond human food to animal feed, where contamination may propagate through the food chain and generate broader economic and agricultural consequences (165).

The bioterrorism relevance of aflatoxin is particularly noteworthy because it links naturally occurring mycotoxicology with the historical development of biological weapons programs. Iraq acknowledged to UNSCOM that it had produced 2,200 liters of aflatoxin and prepared biological warfare munitions containing anthrax, botulinum toxin, and aflatoxin, although aflatoxin was not ultimately used operationally (14,15,166). This history strengthens the rationale for explicitly incorporating mycotoxins into food defense planning, especially because contamination may be

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difficult to detect visually or organoleptically and may evade simple field-based screening methods. From a regulatory and analytical perspective, this also supports the use of confirmatory methods such as liquid chromatography-mass spectrometry and the need to account for masked forms and co-contamination, both of which may contribute to underestimation of true exposure.

Several limitations should be acknowledged in interpreting these findings. First, confirmed cases of food-delivered bioterrorism involving fungal toxins remain rare; consequently, much of the concern derives from historical precedent, toxicologic plausibility, and evidence of prior weaponization rather than from frequent documented occurrence. Second, risk is not uniform across settings; it varies by commodity type, climatic conditions, storage practices, and population susceptibility, so generalized conclusions may not apply equally across all contexts. Third, detection and surveillance capacities differ substantially across regions, increasing the likelihood that both accidental and intentional contamination events are underrecognized or incompletely characterized (1-2a-b,3,3a,4).

Notwithstanding these limitations, the central conclusion is unambiguous: food safety, food defense, and critical infrastructure protection are closely interdependent domains. Effective preparedness requires integrating preventive controls, workforce training, functional surveillance systems, analytical capacity, and rapid coordination among public health, regulatory, and emergency management institutions. Within this framework, both microbial pathogens and mycotoxins should be recognized as relevant hazards—not because they present identical threat profiles, but because each may be deliberately exploited or inadvertently introduced in ways that threaten health, commerce, and social stability. Ultimately, the resilience of a society may be measured by how effectively it protects its food and water systems, for in safeguarding them it protects not only health, but also public trust, economic stability, and national security (1-4).

Author: Contributions. Writing (AWH); Original draft preparation (AWH, AMM, PP); review and editing (AWH, AMM, PP).

Funding: None.

Acknowledgments.: No artificial intelligence was used to prepare this manuscript.

Conflicts of Interest: None.

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