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The Value of Proactive Mycotoxin Prevention in the Age of the Food Safety Modernization Act

INTRODUCTION

Full implementation of the Food Safety Modernization Act (FSMA) ushers in a new regulatory climate that raises profound implications for every food and agricultural industry stakeholder. This sweeping reform of food safety law not only calls for stricter FDA oversight of the way agricultural commodities are cultivated, transported, stored, processed, tested, and verified as fit for their intended use, but also authorizes the agency to enforce consistent industry-wide standards. The acquisition of these expanded powers marks a turning point in the FDA's 110-year history. By mandating proactive measures to prevent harmful substances from entering the supply stream, FSMA replaces the agency's longstanding policy of responding to outbreaks of contamination after the fact with a more assertive and far-seeing approach to food safety.

This white paper outlines the key changes in the FDA's stance on food safety since the passage of FSMA, the compliance challenges these changes raise, and the growing importance of upstream mycotoxin testing as a FSMA-informed strategy for staying one step ahead of a costly food safety problem.

BEFORE AND AFTER THE FSMA

The main impetus for the new food safety legislation was a spate of highly publicized food-borne illness outbreaks. Continuing concerns about not only the risk of a bioterror attack on the food supply, but also the challenges of maintaining safety and quality across an increasingly globalized supply chain also helped drive the push for stricter regulatory control.

Over the years, industry efforts to improve food safety have included increasingly widespread implementation of FDA-sanctioned approaches to contamination control such as Hazard Analysis Critical Control Points (HACCP) plans and Current Good Manufacturing Practices (CGMPs). Before the passage of FSMA, however, the adoption of many of the FDA's safety recommendations remained voluntary for most of the industry, as did the decision to recall contaminated products. Inspections of food facilities were typically sporadic, rarely included farms or grain elevators, and, in some cases, entailed no meaningful consequences for deviations from FDA guidelines.

With the shift from reactive to proactive regulatory policies, the FDA's emphasis on inspections and enforcement has increased significantly. As this change in the agency's focus reshapes the food safety landscape, the challenges of adapting to its defining features will require companies at every point in the supply chain to fortify their contamination control strategies with an extra measure of vigilance.

THE NEW REGULATORY SCENE: WHAT TO PREPARE FOR

Legally binding HARPC rules: FDA-registered food and feed facilities must now develop and carry out a food safety plan that identifies all reasonably foreseeable biological, chemical, and physical hazards. The plan must also stipulate appropriate control measures, such as CGMPs and ingredient and product testing, for each hazard. This new Hazard Analysis and Risk-Based Preventive Controls (HARPC) function incorporates many elements of the FDA's existing HACCP guidelines, but unlike those recommendations, it comprises legally binding rules for an extensive range of food and feed facilities,* including packing and shipping operations. These facilities must not only monitor the progress of their food safety plan but also keep written records detailing the results of their control efforts, including any food safety lapses that occur, subsequent remedial measures, and the effectiveness of those measures. Failure to provide this information at the request of an FDA inspector can result in corrective action. While the deadline for HARPC compliance has already passed for larger companies, small businesses (i.e., those with fewer than 500 employees) have till August 20, 2017, to satisfy this requirement. Companies that meet the FDA's "very small business" specifications have an additional year.

More frequent, far-ranging, and consequential inspections: In 2011, the FDA inspected more than 19,000 facilities,[1] nearly double the number conducted in 2001[2] and issued 52 percent more warning letters than it did in 2010.[3] The agency plans to schedule regular inspections of not only food and feed processing plants, but also farms, packing and shipping operations, and grain elevators and other storage facilities. The frequency of FDA visits will be based on the known safety risks of the food within a facility's purview and that facility's compliance history, as well as the rigor and effectiveness of the facility's food safety plan and preventive controls. Facilities deemed "high-risk" will be inspected at least every 3 years; visits to those that fall outside the high-risk category will occur at least every 7 years.

Expanded authority over the feed industry: FSMA requires feed and pet food manufacturers to comply with newly established CGMP rules and supply chain controls that emphasize preventing contamination in raw ingredients.

Mandatory recalls: FSMA authorizes the FDA to require responsible parties to recall products in cases of suspected as well as proven contamination. Companies that are required to recall products, as well as those that do so voluntarily, must develop a plan to prevent a reoccurrence of the problem and submit it to the FDA.

Stronger control of the global supply chain safety: Under FSMA, importers must verify that their foreign suppliers conform to the same safety standards, including preventive controls, as U.S. food producers.† Recommended methods of confirming suppliers' compliance include annual audits of suppliers' facilities, contaminant testing, or review of their food safety records. Foreign Supplier Verification Programs (FSVP) must be in place by April 31, 2017.

Enforceable safety standards for produce farms: In place of recommended guidelines, mandatory science-based safety requirements will apply to all fruits and vegetables that are consumed raw and not destined for processing. As defined by the FDA, the term "produce" also extends to raw mushrooms, sprouts, peanuts, tree nuts, and herbs. The deadline for compliance with these requirements is December 31, 2017, with the exception of small and very small businesses, which must comply by December 31, 2018, and December 31, 2019, respectively.

Tougher sanctions: Under FSMA, the FDA has gained the necessary clout to make sure its tougher safety standards stick. Breaches of these standards can lead to heavy financial and legal fallout, including steep re-inspection fees as well as complete shutdowns for facilities that fail inspections. In cases where food safety or purity is in doubt, regulators no longer need compelling evidence to take action. For instance, the FDA can suspend a company's registration, revoking its license to ship and import food commodities, if the agency has reason to suspect that one of the company's products poses a serious health hazard. A reasonable suspicion of contamination or adulteration also serves as sufficient grounds for temporarily detaining shipments. In addition, the agency aims to impose greater accountability on corporate officials, with updated policies recommending criminal prosecution of officials for food safety violations that happen on their watch, even if the official's failure to prevent the violation was unintentional. Individuals who commit serious violations can face up to 1 year of imprisonment and/or a maximum fine of $100,000 or $250,000, depending on whether or not the violation led to fatalities. For companies, the maximum fine for non-fatal offenses is $200,000; violations that result in death may entail fines of up to half a million dollars.

**Businesses that are exempt from this rule include grain elevators and facilities that meet the FDA's definition of a primary production or secondary activities farm. Farms that also engage in manufacturing and some types of processing may be subject to either the full requirements or a modified version of the rule. Seafood and juice processors that are already subject to a legally binding HACCP regulation are also exempt from HARPC requirements. (For more details see http://sustainableagriculture.net/blog/pc-rule-analysis-part-1/.)*

† Manufacturers that are already subject to HARPC rules are exempt from this requirement.

‡ The produce rule does not apply to farms that meet certain FDA-defined criteria. (See http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm334114.htm.)

Mycotoxin Contamination: Anatomy of a Chemical Hazard While the FSMA leaves it up to each facility to determine whether a particular contaminant warrants preventive controls, experts in some segments of the food industry see the inclusion of mycotoxin controls in their members' food safety plans as all but inevitable. According to a FSMA training module from the Iowa Grain Quality Initiative at Iowa State University, "at least one type of mycotoxin at every FSMA-regulated [grain] facility is likely to be deemed a *significant hazard* and need preventive controls."[4] Perhaps best known as a safety concern of corn and peanut dealers and buyers, the specter of mycotoxin contamination looms over upstream and downstream businesses in as variety of other markets as well. These potent naturally occurring toxins span commodities across the food chain from plant-based foods vulnerable to infection by mycotoxin-producing molds to products from animals that consume contaminated forages and processed feed (see Table 1).

FSMA guidance documents identify the first five mycotoxins listed in Table 1 as potential chemical hazards[5]; the two other mycotoxins listed are also considered a safety risk by many foreign and domestic buyers.

Table 1: Major Mycotoxins of Concern to the Food and Feed Industry

Mycotoxins of concern	Susceptible commodities
Aflatoxins	Grains, including corn, wheat, barley, rice and DDGs and other grain byproducts; grain-based foods (e.g., baked goods, dried pasta); peanuts; tree nuts; herbs and spices; dried fruit; animal products (e.g., dairy; eggs, dairy, meat, poultry)
Fumonisins	Corn and corn byproducts; animal products
Ochratoxin A (OTA)	Tree nuts; coffee; cocoa; grains and grain byproducts; herbs and spices; dried fruit; animal products
Deoxynivalenol (DON)	Grains and grain byproducts; wheat products; animal products
Patulin	Apples, pears
T-2 Toxin	Grains and grain byproducts; animal products
Zearalenone (ZEA)	Grains and grain byproducts; animal products

A profile of the main hazards associated with mycotoxin contamination (see Table 2) reveals the difficulty of controlling its spread across the production chain and the serious public health repercussions of failing to do so.

Table 2: Hazards Associated with Mycotoxin Contamination

Risk Criteria	Characteristics of Mycotoxin Contamination
Likelihood of contamination	Depends largely on unavoidable environmental factors; increases in conditions that favor mold growth (e.g., extreme weather, high temperatures and humidity, drought stress, increased insect activity)
Point in the production chain where contamination can occur	In the field, during harvesting and handling, in storage, and during shipping and manufacturing
Growth potential of mycotoxin-producing molds	Can spread rapidly, especially in warm, moist or hot, dry growing regions and under faulty storage or shipping conditions
Ability to control contamination introduced in the manufacturing process	Resistant to heat processing, irradiation; increased concentrations may result from some processes (e.g., creating grain byproducts and certain cheeses)
Toxicity	Exposure to ppm* and ppb† levels linked to negative health effects, especially in vulnerable human and animal populations; toxicity increases when two or more different mycotoxins occur together
Severity of illness	***Acute doses:*** potentially fatal mycotoxicosis, organ failure ***Chronic exposure to sub-acute doses:*** cancer, liver and kidney disease, neurological problems, gastrointestinal illness; immunosuppression, organ damage

** parts per million*
† parts per billion

The FDA has set recommended maximum limits for four mycotoxins (see Tables 3, 4, and 5). Companies that violate these recommendations can face serious repercussions. The action levels for aflatoxins, the strongest known human carcinogen, represent the point at which the FDA will pursue court action. Mycotoxin levels that exceed these or any of other of the FDA's recommended limits can also serve as evidence that a product is unfit for sale. The FDA plans to develop legally binding aflatoxin regulations,[6] which would relieve the FDA of its obligation to prove to the court that aflaxoxin contamination represents a significant health risk. In response to concerns about the carcinogenic potential of ochratoxin A, the agency is also currently collecting data on the occurrence of this mycotoxin to assess the need for maximum limits.[7]

Table 3: FDA Recommended Maximum Limits for Mycotoxins in Human Food6

Mycotoxin	Food	Maximum Limit
Aflatoxins*	Milk Other susceptible human foods (see Table 1)	0.5 ppb (aflatoxin M1) 20 ppb (total aflatoxins)
Fumonisins†	Dry milled corn products Corn intended for popcorn Whole or partially degermed dry milled corn products Dry milled corn bran Corn intended for masa	2 ppm 3 ppm 4 ppm 4 ppm 4 ppm
DON†	Finished wheat products	1 ppm
Patulin*	Apple juice	50 ppb

**Action level*
† Guidance level

Table 4: FDA Recommended Maximum Limits for Mycotoxins in Livestock Feed[6]

Animal	Mycotoxins	Commodity	FDA Level
Swine	Aflatoxin	Corn/peanut/other ingredients excluding cottonseed meal	200 ppb*
		Cottonseed meal	300 ppb†
	DON	Grain/byproducts	5 ppm
	Fumonisins	Corn/byproducts	20 ppm
Poultry	Aflaxoxin	Corn/peanut/other ingredients excluding cottonseed meal	100 ppb*
		Cottonseed meal	300 ppb†
	DON	Grain/byproducts	10 ppm
	Fumonisins	Corn/byproducts	100 ppm‡
Dairy cattle	Aflatoxin	Corn/peanut/other ingredients	20 ppb*
	DON	Grain/byproducts DDG/brewers grains/gluten	10 ppm 30 ppm
	Fumonisins	Corn/byproducts	60 ppm‡
Beef cattle	Aflatoxin	Corn/peanut/other ingredients excluding cottonseed meal	300 ppb*
		Cottonseed meal	300 ppb†
	DON	Grain/byproducts	10 ppm
		DDGs/brewers grains/gluten	30 ppm
	Fumonisins	Corn/bybroducts, not to exceed 50% of diet	60 ppm‡
Horses	Aflatoxin	Corn/peanut/other ingredients	20 ppb
	DON	Grain/byproducts	5 ppm
	Fumonisins	Corn/byproducts	5 ppm

**Action level for immature animals is 20 ppb; guidance level for breeding swine and cattle is 100 ppb.*

†All animals regardless of age or breed.

‡Advisory level for breeding animals is 30 ppm.

Table 5: FDA Recommended Maximum Limits for Mycotoxins in Pet Food[6]

Pets	Mycotoxin	Commodity	Level
Immature animals	Aflatoxins	Corn/peanut/other ingredients	20 ppb*
Adult pets	Aflatoxins	Corn/peanut/cottonseed meal/ other ingredients	20 ppb*
	DON	Grain/grain byproducts, not to exceed 40% of diet	5 ppm
	Fumonisins†	Corn/byproducts, not to exceed 50% of the diet	10 ppm

**Action level*

†A 5-ppm guidance level applies to rabbits and horses.

THE ROLE OF MYCOTOXIN TESTING IN FSMA COMPLIANCE

As the FDA's new approach to food safety continues to unfold, rigorous mycotoxin testing promises to become a cornerstone of a solid FSMA compliance strategy. To ensure this strategy doesn't impose an undue burden on businesses, FSMA rules allow food and feed facilities the flexibility to design testing programs that are appropriate for their needs. The test format, the frequency of testing, and the question of whether the program will employ in-house personnel or a third-party laboratory are left up to the facility's discretion.

These decisions should take into account a variety of company-specific factors:

- The FDA and business requirements that must be met
- The test data's intended use
- The likelihood of contamination
- The commodity to be tested
- The facility's budget and technical resources

At processing and manufacturing facilities, routine end-to-end monitoring promises to play an important part in documenting FSMA compliance and maintaining the quality and value of products. Testing at regular intervals before shipping, processing, and packing can reveal an upward trend in contamination levels before the problem leads to a failed inspection, substantial product losses, or rejected shipments. Equally important, a complete record of test results from critical control points enables midstream and downstream companies to not only verify the effectiveness of their hazard prevention plan and the reliability of their suppliers, but also trace contamination back to its source. By comparing test results across different growing regions, suppliers, in-house storage areas, and weather conditions, the processor or manufacturer can identify where and when potential food problems originate and how to prevent their recurrence. Based on these data, a company can make proactive changes like sourcing ingredients from another location, cleaning storage bins and rotating stock more often or increasing the frequency of testing during hot, dry spells and rainy springs. Timely interventions like these expand the role of traceability in food safety and brand protection, enabling it to serve as not only critical preparation for a recall, but also a cost-effective preventive strategy.

Even facilities that are exempt from the FSMA's preventive control and CGMP rules, such as grain elevators, will increasingly depend on accurate, reliable mycotoxin test data to sustain the confidence of their customers and confirm the merchantability of their products. Given that the receiver of a shipment will bear responsibility for any safety problems associated with that shipment, it's in the best interest of buyers to require their suppliers to thoroughly test every commodity load and verify its safety before delivery. In the event that an FDA audit of the buyer leads back to the supplier, that supplier will need comprehensive test data to demonstrate that the contaminant levels in its products met contractual requirements.

FSMA-READY MYCOTOXIN DETECTION AND CONTROL

While many upstream providers already test for mycotoxins, their test systems will have to address tougher regulatory demands and increasingly urgent bottom-line concerns in the wake of FSMA. The viability of frequent monitoring programs for these businesses ultimately hinges on the availability of practical, cost-effective screening tools, according to Patricia Jackson, a market development manager at the Massachusetts-based test developer VICAM. "While the best opportunity for mycotoxin prevention is just after raw commodities are harvested and before grain or feed processing, many growers, handlers, and grain elevators lack access to laboratory facilities. With advanced rapid quantitative methods like lateral-flow strip tests, onsite personnel can confidently and efficiently handle the challenges of accurately measuring mycotoxins."

Those challenges are both technical and practical. Mycotoxins tend to occur in pockets, or "hotspots" in widely scattered locations in large loads of commodities. The percentage of mycotoxins in a load is typically minute, yet the concentration in a few grains or kernels could exceed the FDA limit. To get a statistically valid measurement, multiple subsamples have to be collected from randomly selected locations throughout the load and then thoroughly ground and mixed together to create a test sample. "A fast, easy-to-use test method minimizes the additional time needed to get the test data in the hands of the person waiting to decide whether or not to accept the load," said Jackson.

A line of lateral flow strip tests made by VICAM adapts the company's advanced immunoaffinity technology to a simplified format that accurately measures mycotoxins at ppm or ppb levels in as little time as 5 minutes.

Unlike strip tests that require users to evaluate color changes, the VICAM line delivers results that require no interpretation. Numerical readings are displayed on the digital screen of a handheld optical reader. Jackson noted another important advantage. "The VICAM line include strip tests that require no organic solvents," she said. This helps reduce the financial burden and environmental impact of routine monitoring in the field and in storage and packing facilities, transport vehicles, and processing plants. Laboratories that need a fast, economical way to pre-screen samples also appreciate the combined benefits of this method."

To confirm test results obtained with screening methods, VICAM recommends using its line of AOAC and USDA-GIPSA approved immunoaffinity (IA) columns to prepare samples for instrumental analysis. By removing components of food that can interfere with accurate detection while efficiently extracting mycotoxins from samples, IA column cleanup minimizes the risk of false positives and false negatives. The simplicity of this method also greatly reduces the chances of procedural missteps.

Test methods that incorporate IA sample cleanup detect lower concentrations of mycotoxins and measure them more precisely than strip tests. Their cost varies according to their technical sophistication and performance level. The most economical option uses a fluorescence detection device that can be easily operated by onsite users in grain elevators and processing plants and at buying points, as well as by laboratory technicians. Accurate ppb results are available in less than 15 minutes. The VICAM Series-4EX® fluorometric reader offers processors and manufacturers the additional advantage of storing as many as 200 test results, streamlining the FSMA-mandated task of documenting their monitoring efforts. IA methods that require more specialized analytical skills provide the greatest degree of accuracy and precision for a tradeoff in price.

VICAM recommends combining IA column cleanup with high or ultra performance liquid chromatography (HPLC/UPLC®) or liquid chromatography – mass spectrometry (LC-MS) for exacting applications like documenting the geographical source of raw materials, verifying that foreign suppliers meet acceptable safety standards, and certifying products for export. The exceptional sensitivity of these sophisticated instrumental techniques enables laboratory analysts to precisely measure the very low levels of mycotoxins required to comply with mycotoxin limits in strictly regulated foreign markets. The IA column line includes a variety of multi-analyte methods that measure two or more mycotoxins in a single test run. Companies that deal with commodities such as grain and spices that are susceptible to multiple mycotoxins will find these columns particularly useful for determining which mycotoxins should be the focus of their preventive control efforts. Food and feed testing laboratories whose customers require exceptionally detailed and authoritative mycotoxin profiles should consider Myco6in1⁺ for LC-MS/MS, a powerful validated method that simultaneously determines aflatoxins, ochratoxin A, fumonisins, deoxynivalenol, zearalenone, the T-2 and HT-2 toxins, and nivalenol at or below EU guidance levels.

ESTABLISHING TRUST IN AN INCREASINGLY RISK-CONSCIOUS WORLD

With all its challenges, the advent of FSMA offers the food and feed industry an important opportunity to reaffirm its commitment to serving as responsible stewards of the world's food supply. In recent decades, consumers' awareness of the risks of food-borne contaminants has grown steadily, prompting a rising call for greater transparency and stronger assurances of quality and safety from the businesses that grow, process, and distribute their daily sustenance. The knowledge that these providers are striving to not just meet but consistently exceed the new FDA requirements promises to strengthen the public's loyalty to brands that achieve this goal and deepen their belief in an industry that embraces openness and accountability.

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