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General Interest

Framework for Managing Mycotoxin Risks in the Food Industry

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ABSTRACT

We propose a methodological framework for managing mycotoxin risks in the food processing industry. Mycotoxin contamination is a well-known threat to public health that has economic significance for the food processing industry; it is imperative to address mycotoxin risks holistically, at all points in the procurement, processing, and distribution pipeline, by tracking the relevant data, adopting best practices, and providing suitable adaptive controls. The proposed framework includes (i) an information and data repository, (ii) a collaborative infrastructure with analysis and simulation tools, (iii) standardized testing and acceptance sampling procedures, and (iv) processes that link the risk assessments and testing results to the sourcing, production, and product release steps. The implementation of suitable acceptance sampling protocols for mycotoxin testing is considered in some detail.

The food processing industry is noteworthy for its emphasis on risk mitigation and hazard prevention to ensure that finished food products are safe for consumption when used as intended. This emphasis is evinced by the widespread adoption of the well-known hazard analysis and critical control point (HACCP) methodology, which provides a systematic, science-based approach for preventing food safety risks throughout the production process. This food industry approach is in contrast with the ''inspection and sorting of finished products'' approach that is often used for quality management in some other manufacturing industries. Adoption of the HACCP approach in the food industry is tied to the serious public health consequences associated with food safety incidents and the indisputable need for effective risk mitigation. In addition, the HACCP approach ensures an efficient, sustainable food production process that minimizes waste and offers a viable business operating model, which is vital in light of the stringent safety and testing requirements imposed on the finished product. The exhaustive testing of finished food products is not only prohibitively time-consuming and expensive, but it may also be entirely impractical because the testing process itself invariably renders the final product unsuitable for further distribution and consumption. Therefore, HACCP principles, along with good manufacturing practices, which incorporate the best practices for sanitary procedures in food processing plants, have been widely accepted and incorporated worldwide into government regulations and food industry standards, such as ISO 22000 *(15)*.

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In recent years, there has been great interest in applying these well-established product safety and quality management processes to a wider range of food products: to unprocessed foods, which, to date, have rarely been managed using HACCP, and to processed foods, to introduce control points and control processes outside the manufacturing facility and throughout the entire food production and consumption pipeline (the ''farm to fork'' approach). There is considerable evidence that failure to extend the use of these processes may place consumers and businesses at a higher risk for certain kinds of food safety incidents. For instance, at the ''farm end'' of this pipeline, in the United States in 1999 to 2003, among food safety incidents that could be traced back to raw material, production, distribution, or consumer mishandling prior to consumption, 60% were linked to raw material, far outnumbering the other categories *(16)*. Similarly, food safety monitoring and feedback at the ''fork end'' of this pipeline have resulted in the identification of sources of cross-contamination during finished-product transportation and storage, as well as the isolation, recall, testing, and cessation of contamination-related product batches and production processes *(3)*.

Mycotoxin contamination predominantly affects raw materials, such as cereals, fruits, and nuts, which are widely used both as primary food stocks and as ingredients in various processed foods *(2)*. Although HAACP programs have been described for specific mycotoxins and raw materials, such as aflatoxin in cereals *(1)* and ochratoxin A in coffee *(10)*, in general, mycotoxin risk management presents a significant challenge to the food industry. This is due to the geographic scope and extent of the problem, the

volume and diversity of the raw material to be tested, the variety of toxins that need to identified, and, above all, the lack of effective remediation controls for mycotoxins within the manufacturing plant itself. This lack of effective remediation controls for mycotoxins is in contrast with the routine use of controls such as sterilization and pasteurization, which are highly effective for reducing or eliminating microbiological contaminants. Therefore, whereas food processing facilities invariably locate a control point for mycotoxin testing at the inlet supply dock for raw material, the difficulties associated with mycotoxin remediation make it imperative to direct a significant focus toward managing the risks across the entire raw material pipeline. The resulting risk profiles and quality metrics for the raw material sources must be incorporated into the mycotoxin testing protocols at the inlet supply dock and must be integrated into an effective program for production and product release verification *(5)*.

A FRAMEWORK FOR MYCOTOXIN RISK MANAGMENT

In principle as well as in practice, mycotoxin risk management requires a holistic approach that includes all the processes for raw material acquisition, production planning, and finished product release. These considerations may be similar to those encountered in traditional HACCP programs, in that the overall risk management process is only as strong as its weakest link; however, in the case of mycotoxins, the weakest link is likely to be located outside the factory environment, related to events that occur prior to the arrival of the raw material at the factory gate. Therefore, the entire process must be rigorously reviewed to ensure that these risks are effectively identified and appropriately managed through each stage in the procurement, production, and product release pipeline, from the raw material to the finished product. Even when testing resources may be limited and mitigation actions may be confined to the manufacturing facility, a ''one size fits all'' risk management process is inappropriate because the mycotoxin risk profile changes with each new crop year and with each new procurement source of raw material. These changes in the mycotoxin risk profile may be local, due to regional weather conditions during crop planting, growth, harvesting, and storage, and may be further influenced by factors such as seed selection, crop disease, pest infestations, harvesting stress, and the extent to which farmers and suppliers adhere to good agricultural practices.

For mycotoxin contamination, the risk management process focuses on agronomic data and crop surveys, supplier quality assurance, factory gate and finished product verification, and sampling and testing protocols.

Agronomic data and crop surveys. One of the most important steps in the mycotoxin risk management process is the collection of crop-specific agronomic data and regional crop surveillance information for each new crop year. This data provides scientific information on potential mycotoxin prevalence that can be used for quantitative risk assessments, directing food stock purchasing strategies, evaluating supplier quality-assurance requirements, and fine-tuning the sampling and testing protocols (e.g., based on the type of mycotoxin that is encountered, the associated levels of contamination relative to the regulatory requirements, and the provenance and risk profile of raw material sourced from regional areas and crop locations that have been affected by heat, drought, and other types of environmental stress, etc.).

Supplier quality assurance. Raw material suppliers must understand the potential mycotoxin risks associated with the crops that they grow or acquire, store, and later sell for use as primary food stocks or as ingredients for the processed-food industry. Their responsibilities include an understanding of the local regulatory requirements and the equivalences across multiple regulatory jurisdictions. They must also adhere to the relevant food safety standards and ensure that effective processes are in place for measurement, monitoring, and control of the raw material attributes associated with elevated mycotoxin risks (e.g., moisture, water content, protein content, fat content, sugar content, excessive dockage and breakage, etc.). For food manufacturers, the supplier quality assurance process requires working with the raw material supplier base to audit the effectiveness of their mycotoxin control programs to ensure that the potential upstream raw material risks are appropriately managed prior to being shipped (and possibly rejected upon arrival at the food processing facilities). The use of statistical process control methods for supplier assurance, certification, and ranking has been widely advocated in the total quality management literature *(8)* and is standard practice in many other industries, and these templates and case studies may be adapted to the mycotoxin supplier quality assurance process as well.

Factory gate and finished product verification. Mycotoxin risk management at the food processing facility starts with inspection and testing at the inlet supply dock, where the industry-standard processes for sampling and testing are performed on the inbound loads, according to the raw material quality and food safety requirements. This particular testing requirement is an example of an operational prerequisite program in the food industry, which is a program identified by the hazard analysis as essential in order to control the likelihood of introducing food safety hazards and/or the contamination of or proliferation of food safety hazards in the product or the processing environment. The testing protocols that are part of this operational prerequisite program may be risk based, inasmuch as the information and data coming from the agronomic and crop data surveys, as well as from the supplier assurance ratings, can be used to determine the scope and extent of inbound sampling and testing (e.g., to determine whether all inbound loads from a supplier are to be tested, or only a specified fraction of loads, based on an evaluation of the potential mycotoxin risk for a particular supplier or particular origination of the raw material). Note that when sampling is performed on a subset of the inbound loads, these must be randomly selected to avoid selection bias. The outcome

from the testing is an accept-reject decision on an inbound load, along with other follow-up actions that may include a supplier audit and suspension. The effectiveness of the inbound testing can be considerably enhanced by information on the provenance of the raw material and any other associated crop and supplier risks.

Finished product verification is also risk based, whereby the finished products on positive release that are produced from higher-risk raw material may undergo tighter scrutiny and audit at levels that may even be above the customary regulatory requirements or food industry norms. Conversely, finished products produced from lower-risk material may be audited less frequently. The use of risk-based modifications to the finished product verification is important for calibrating the food safety assurance, as well as for ensuring the cost-effective and judicious management of the plant and production operations, with the limited testing resources focused on the most critical operations and with the limited audit resources directed to the most vulnerable scenarios. We note that the audit processes during finished product verification are not intended to supplant the up-front testing and controls but to ensure that their effectiveness is not somehow compromised. An independent audit process is a basic strategy in quality management in many manufacturing industries; for example, it is an essential component of the well-known Plan-Do-Check-Act cycle, which is sometimes termed the Shewhart-Deming Cycle, which in turn is often the prerequisite for implementing continuous improvement (e.g., Kaizen).

Sampling and testing protocols. The importance of implementing a standardized and scientifically validated approach for sampling, sample preparation, and analytical testing cannot be understated. The sampling strategy for the inbound raw material needs to be customized with a particular emphasis on the presence of possible ''mycotoxin pockets,'' which leads to a common and challenging situation when the testing results may display considerable variability even for samples from the same inbound load *(4)*. The sample preparation steps must be validated to ensure that they are compatible and appropriate for the mycotoxin quantification method that is being employed, which is typically high-performance liquid chromatography (HPLC) or enzyme-linked immunosorbent assay (ELISA). A survey of analytical methods for the detection and quantification of mycotoxin levels is provided in Rahmani et al. *(14)*. The sample preparation and analytical methods used in the testing protocols must be validated to ensure that the methodology is consistent and the results are reproducible. This can be achieved by checking the quantification accuracy by routine calibration versus a recognized proficiency authority (e.g., FAPAS in the United Kingdom). This calibration also enables the benchmarking of results that may be obtained across many different raw material, testing laboratories, measurement techniques, mycotoxin varieties, and mycotoxin contamination levels.

The possible presence of ''mycotoxin pockets,'' as mentioned above, is manifested by a clumped rather than a uniform or random distribution of the contaminant within each raw material lot. This leads to a situation in which the probability of detecting any elevated mycotoxin measurement in a single sample from this raw material lot is rather low; therefore, these ''pockets'' may go undetected unless an inordinate amount of sampling and testing is performed. The use of composite sampling techniques, which involve aggregating multiple raw material samples taken from different locations in each lot, is of considerable help in reducing the time and cost of the analytical measurements, as well as in enhancing the ability of the testing process to detect these ''mycotoxin pockets.'' A key aspect of the composite sampling methodology is that the acceptance sampling decisions, which ideally should be based on the distribution of the mycotoxin levels in the original noncomposited samples, can also be suitably obtained from the composite sample measurements *(13)*. Note that the use of composite sampling for testing of bulk raw material is also indicated by the nature of the subsequent food processing pipeline, which is often comprised of batch production processes that originate with the individual lots of raw material and that involve considerable mixing, homogenization, and mass averaging.

To develop testing procedures, it is important to retain and analyze individual mycotoxin test data for each combination of raw material and supplier across a rolling set of inbound lots, to understand the causes of variation and to identify changes in behavior and trends that might require attention in the inbound testing process. These raw material and supplier combinations are identified and tracked in this way based on rational subgrouping concepts *(17);* the subgroups are chosen so that any assignable causes of process variation due to differences among the subgroups can be isolated from the random causes of process variation that would be prevalent for the samples within each subgroup. The sequential tracking of measurements from multiple inbound loads in this way also enables the testing and acceptance sampling protocols to be appropriately modified to correct for the correlations in the sample measurements that are often seen within successive inbound loads.

The use of process capability indices is common in statistical process control, and an extensive description and treatment can be found in Kotz and Johnson *(9)*. In particular, the process capability index, $C_U = (U - \hat{\mu})/3\hat{\sigma}$, which measures the average process deviation below a certain upper specification limit U, with $\hat{\mu}$ and $\hat{\sigma}$ being the estimates for the process mean and standard deviation, respectively, can be used for comparisons among suppliers for the same raw material (in this case, because the comparisons involve the mycotoxin measurement levels, U is based on the applicable regulations and norms). The value of C_U for a given raw material and supplier combination should typically be greater than 1.0 to ensure that, given the natural variability that can be expected in the measurements for the specific rational subgroup, the process mean is at least 3 standard deviations on the safe side from the upper specification limit. If C_U is less than 1.0, then there is a higher than acceptable risk that a raw material inbound load that contains elevated mycotoxin levels may bypass the front-end sampling and testing program; therefore, further actions would be required to determine

how to reduce the potential risks of the given supplier. The use of the one-sided upper process capability index C_U is appropriate here, because, from the food-safety point of view, only the detection of elevated mycotoxin levels above the upper specification limit is of concern. However, the process capability index, $C_p = (U - L)/6\hat{\sigma}$, where L can be taken as the so-called minimum detectable concentration limit, should also be measured and is of general interest in characterizing the variability of the measurements in the testing process. The C_p index can be used to ensure the data integrity of the process measurements, to implement supplier quality assurance and preferential supplier partnerships, or to negotiate quality-based pricing agreements with suppliers.

Example: corn at high risk for aflatoxin. The informal ideas presented in the focus areas outlined above are clarified in the following example. Crop survey and agronomic data had shown that the 2012 U.S. corn crop would contain elevated levels of aflatoxin, with the highest risk areas being in the Midwest and Southeast regions. Based on this, the supplier quality assurance team assessed the ability of suppliers to consistently deliver inbound loads of shelled corn to meet food safety specifications. The supplier assessment indicated that some corn suppliers in the North and Northwest regions of the United States would be able to meet the required specifications. However, this supply source would not be sufficient to meet the production demand. Based on this, a mycotoxin management process was put in place across the entire U.S. production network to ensure that the potential high risks were being adequately managed. The measures included a heightened testing program at both the supplier and factory front gate, with every inbound lot tested for aflatoxin level. In addition, for manufacturing facilities receiving corn supplies from the Midwest and Southeast regions, every lot of finished product was placed on positive release (as per the documented requirements in the food safety standards) pending the test and audit results that the raw material and products met the required food safety specifications. Compared to 2011, this represented a 100% increase in overall testing and a 25% increase in held product pending positive release. The net outcome of the efforts in 2012 to 2013 was very successful. Thanks to the upfront work based on the crop survey and agronomic data, the magnitude of the risk was understood and an appropriate tactical response was put in place to quickly and effectively manage the potential mycotoxin risk in the supply and production pipeline, to ultimately meet the goal of delivering safe products to consumers.

STATISTICAL ACCEPTANCE SAMPLING AND TESTING ASPECTS

Mycotoxin acceptance sampling review. An informal assessment of the current practice for mycotoxin testing of inbound loads suggests that, even though the sampling and testing protocols may be implemented as per standard plant practice and industry norms, the accept-reject decisions are often made without guidance and insight from the relevant statistical theory. We first motivate and justify this assessment and then suggest how the relevant statistical acceptance sampling theory can be adopted for mycotoxin testing.

As a specific example, consider the sampling and testing process for aflatoxin in an inbound load of shelled corn at a food manufacturing facility (see Fig. 1). At the inlet supply dock to this facility, a set of corn samples is obtained from the inbound load, either manually using a trier or using a robotic sampler. A portion of these samples is set aside for grading and various other quality measurements, while another portion of the samples is aggregated, mixed, and ground to a fine particle size. Finally, subsamples are taken from the resulting ground material for the quantification of the mycotoxin levels, using ELISA. Typically, three different measurements are obtained, and, if any one of these aflatoxin measurements exceeds 20 ppb, then the entire inbound load is rejected. This reject decision may lead to other actions, such as further testing or an audit inspection at the supplier. The threshold value for the measurements (i.e., 20 ppb for aflatoxin) is a regulatory requirement and, as such, incorporates safety factors and represents the scientific consensus on the smallest possible level of the aflatoxin contamination that is deemed acceptable for food stocks. This threshold cannot be set to an arbitrarily small value, however desirable that might seem, since there may be no supplier capable of delivering this quality. Similarly, it is not possible to guarantee that every potential sample measurement from the inbound lot will be below this threshold value because this would require exhaustive sampling of the lot, which is clearly impractical.

In this context, we observe that, although there is a considerable literature on the application of statistical acceptance sampling methods in food safety applications, the emphasis is almost entirely focused toward methods that are primarily appropriate for testing for microbiological contaminants (e.g., *(7, 11)*). This testing methodology for microbiological contaminants typically involves taking n samples from each inbound lot. (Note that a lot is assumed to comprise a batch of raw materials, product intermediaries, or finished products, as appropriate, whose units have more or less the same provenance.) The entire lot is rejected if even one of the samples in it tests positive for the presence of the contaminant (e.g., when testing for a virulent pathogen such as *Salmonella*) or, in some alternatives, if the sample measurement exceeds a certain threshold value. (For example, certain coliforms regarded as indicators for sanitation issues are tested in raw material and during processing; although coliforms may not be directly harmful, their presence suggests the possibility of more serious issues with undetected co-occurring pathogens.) In statistical acceptance sampling theory, these plans are known as zero-tolerance, attribute sampling (ZT-AS) plans, and the only parameter in them is the number of samples (n), which can be specified to achieve the desired acceptance sampling objectives. For instance, if θ is the unknown probability for the presence of *Salmonella* in an inbound load, then, in the ZT-AS plan, this lot will be accepted only 5% of the time (i.e., consumer's risk) for $n = 5$ for θ greater than 0.450,

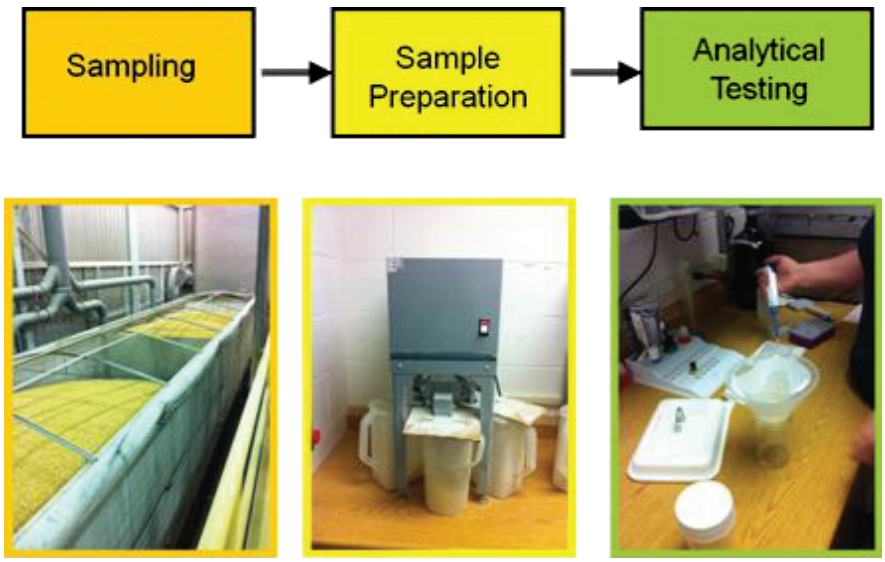

FIGURE 1. *Sampling and mycotoxin testing of corn at a factory inlet supply dock.*

and for $n = 30$ with θ greater than 0.095. Also note that, for ZT-AS plans, the n individual samples may be merged and homogenized into a single aggregate before the analytical test is performed, as long as the ensuing contaminant dilution does not affect the test sensitivity for either the contaminant presence or for the exceedance of its threshold value. The value of n that is chosen in the ZT-AS plan will depend on many factors that require asserting θ to be some suitably small value; these factors include regulatory requirements, the level of safety protection required based on the virulence of the microorganism, the cost of additional sampling, and the nature of the remaining processing and storage steps, including remediation. Finally, note that the ZT-AS plan is different from a ''zero-defective'' plan, which is only achievable through exhaustive testing of the entire lot and is, therefore, not feasible for microbiological contamination given the destructive nature of the testing process.

Given this context, it seems evident that the current acceptance sampling practice for aflatoxin in shelled corn, as described earlier, is quite similar to the ZT-AS plan above in many respects (albeit the condition for lot rejection is based on the sample ELISA measurement being greater than the 20 ppb threshold). For many reasons, this approach seems to be inefficient and unsatisfactory for mycotoxin testing. First, given the serious toxic nature of the contaminant, and the impracticality of any remediation, the threshold violation for mycotoxin contamination has more serious implications than a similar threshold violation for a sanitation indicator organism such as coliforms (which are not direct health hazards, as discussed above in the context of the ZT-AS plan). Second, given these concerns, it is unclear what is to be done if the ELISA measurement is close to but less than the threshold, and how much additional confirmatory testing must be carried out. Finally, the other ELISA measurements that were taken as part of the testing on the same lot are ignored, although their inclusion might provide a more comprehensive view of the acceptance sampling risk in the borderline situations.

For these reasons, we advocate the use of variables sampling (VS) plans for more relevant, as well as more cost-effective, mycotoxin acceptance sampling. As may be surmised, the VS plans are not widely used in food safety applications and are rarely considered for microbiological contaminants. For instance, see Midura and Bryant *(11)* for a discussion of VS plans, wherein they state (page 19), ''Disadvantages include the calculations involved in evaluating a lot. … For these reasons, variables sampling plans are not widely used in the food industry for microbiological measurements.'' However, in our view, the use of VS plans is appropriate and well justified for mycotoxin testing.

Background statistical theory. We believe that the VS plans would be widely adopted for mycotoxin testing if the background assumptions and underlying mathematics were better clarified for practitioners. The primary mathematical difficulty is due to the use of small-sample distribution theory, but this is an important aspect to retain for mycotoxin sampling and testing, in which, invariably, for practical reasons, only a small number of sample measurements are taken. For this reason, we have identified a set of topics that covers the basic principles and relevant statistical theory for VS plans, including

1. Normality-inducing transformations.
2. Sampling theory for the normal distribution.
3. Variables (VS) acceptance sampling plans.
4. Operating characteristic (OC) curve.
5. Variance partitioning for sampling and measurement variance.
6. Composite sampling.

Normality-inducing transformations include, for example, Box-Cox transformations of the raw observation values, which then enable the well-developed theory for the normal distribution to be used for acceptance sampling. A basic concept in acceptance sampling is the OC curve, which if appropriately formulated, fully characterizes the risks of a given acceptance sampling plan, both for the producer as well as for the consumer. Specifically, assuming that the true, albeit unknown, value of the lot quality metric is such that

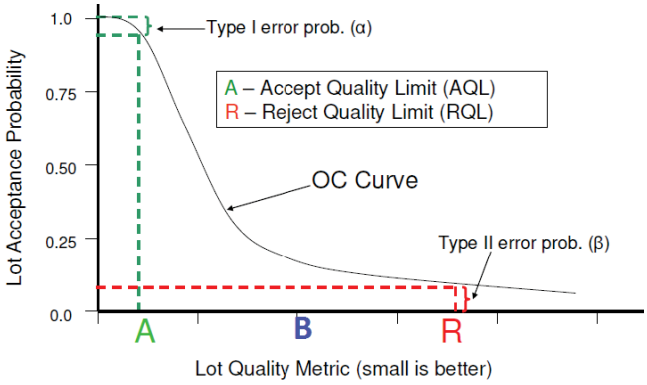

FIGURE 2. *Example of operating characteristic (OC) curve for acceptance sampling.*

small values of this quality metric correspond to better quality, then the OC curve for a given acceptance sampling plan can be depicted as shown in Figure 2; here, from the consumer's perspective, β is the probability that a lot with the quality metric at the reject quality limit (RQL) will be accepted, and similarly, from the producer's perspective, α is the probability that a lot with the quality metric at the accept quality limit (AQL) will be rejected (typical values for α and β can be 0.05 to ensure that the requirements of both the consumer and producer are satisfied in the chosen acceptance sampling plan). The technical details of the determination of the OC curves for VS plans cannot be adequately covered here, but we intend to provide a review elsewhere; in addition to covering the six topics listed above, this review will also include additional topics of relevance, such as tolerance regions, process capability indices, autocorrelation and batch correlation effects, and experimental design.

A key aspect in understanding the application of these topic areas to mycotoxin testing is the use of realistic mycotoxin measurement data for illustrative purposes. However, in the real world, mycotoxin measurement data are often proprietary and, therefore, difficult to obtain and impossible to share, and the distributions of these measurements are only imperfectly known. We therefore also advocate using simulated data, for which dither distributions can be specified, and random number generators can be used to obtain representative sample measurements from these distributions for the understanding and application of the statistical methodologies.

We reiterate that the use of VS plans for mycotoxin acceptance sampling is relatively new; and, although these have been widely studied in the total quality management or statistical process control literature, our goal is to motivate its relevance for food safety and, specifically, for mycotoxin risk management. Finally, we note that a recent report *(12)* contains additional background information and considers some other advanced topics that are relevant to the further development of mycotoxin testing applications.

Steps for establishing a mycotoxin acceptance sampling plan. The following steps are suggested as guidelines for a mycotoxin testing and acceptance sampling plan at the inlet dock for raw material for a manufacturing facility:

1. Specify and record all the details of the sampling and testing methodology, which include the method for identifying random locations from where the samples will be taken in each lot; the size of each individual sample; the number of samples in each composite sample; the method for selecting the individual samples that are assigned to each composite sample; the grinding time and grinding equipment used for homogenizing each composite sample; the number and size of analytical samples taken from each composite sample for quantification; and, finally, all the details and method steps for the quantification of the mycotoxin measurement in each analytical sample. Note that many of these sampling details may already be specified and available as per industry norms or standard plant practice. Note also that many of the details of the quantification will also be available as per instructions from the manufacturers of the analytical testing equipment and kits.
2. Collect and record any other observations about the samples, including supplier and truck identifiers, moisture, protein content, discoloration, fraction of dockage, etc., because these may be used to modify the acceptance sampling procedures for certain inbound loads based on the ensuing risk perception.
3. Specify the upper threshold limit for the mycotoxin measurement U, the allowable threshold exceedance probability θ, and the consumer's risk β. Given these specifications and given the number of composite samples n, find the appropriate value of the acceptance sampling parameter k (which can be obtained from a suitable computer program for the VS plan).
4. If $\bar{Y}$ and S denote the sample mean and standard deviation of the measurements in each lot, then accept the lot if $\bar{Y} + kS < U$ and otherwise reject.
5. Record $\bar{Y}$ and S (or any other equivalent and acceptable measure of the within-lot sample spread such as the interquartile range) on statistical process control charts.

Note that, because of the time and cost for the sampling and testing, in many cases, for each inbound load, it may only be possible to obtain a single composite sample; and, further, it may only be possible to obtain a single analytical measurement from this composite sample. (This, in fact, may be the sensible thing to do, if, for example, there is essentially no variation in the measurements within each lot, between different composite samples, or between multiple analytical measurements for each composite sample.) However, with only a single measurement, it is no longer possible to estimate S, and, therefore, it may be necessary to redefine the lot to now comprise a sequence of inbound loads from the same supplier or storage facility (e.g., based on the rational subgroup concept). The VS plan is then applied to the measurements obtained from the entire sequence of inbound loads that comprise this redefined lot. This situation would then require accepting or rejecting the entire sequence of inbound loads, and this may not be possible if some of the earlier inbound loads have already been moved into the processing stage.

In practice, most testing situations will involve the intermediate case, when the acceptance sampling protocol must be applied to multiple inbound loads, but with multiple measurements on each of these inbound loads. This issue, among others, is discussed further in the case study below.

Case study and insights. An important aspect of the implementation of statistical process control or acceptance sampling is the identification of the rational subgroups in the measurement data, so that the variations in the sample measurements that are attributable to assignable causes can be identified and, simultaneously, the magnitude of the remaining process variation can also be estimated within each identified rational subgroup. Many of these aspects have not been explicitly studied for mycotoxin measurement data; and, therefore, we briefly describe a data collection exercise that we carried out at a pet-food processing plant in Asia during a 1-week period in December 2011 to explicate these issues.

Sample measurements of aflatoxin measurements were taken from a set of 62 inbound truckloads of shelled corn originating from five different suppliers. Variables in this multifactorial study included supplier of origin, the compositing scheme (e.g., number of samples included in each composite [10, 20, or 40]), the sample preparation technique (e.g., the extent and uniformity of sample grinding, as measured by the number of grinding passes [1 or 2]), and the quantification technique (HPLC or ELISA). An experimental design was devised so that all the relevant contrasts could be estimated from the measurement data; this involved taking multiple measurements from each inbound truck.

We have omitted the details of the preliminary data analysis and statistical evaluation. However, we highlight a few interesting conclusions obtained from the data, with the caveat that more work is required to generalize the conclusions across the possible broad range of foreseeable mycotoxin measurement data.

First, we showed that supplier quality assurance was possible using this data. In terms of the mean level of mycotoxin measurements, of the five suppliers, one was rated as poor, three were rated as medium, and one was rated excellent (the three suppliers rated medium were virtually indistinguishable from each other and, hence, could be combined into the same rational subgroup for all practical purposes). As for mycotoxin measurement variance, the supplier rated as excellent also had a smaller variance and was, therefore, low risk in all aspects.

Second, some of the observed variation in the measurements could be ascribed to use of two grinding passes, as compared to one; for instance, the former increased the mycotoxin measurement level by about 7% (on the log concentration scale) for the poor-rated supplier, although this increase was relatively smaller for larger measurements. This is perhaps not surprising because the extraction efficiency for the mycotoxin quantification technique is improved by a more uniform grinding and by a reduction to a smaller average particle size from the aggregated raw material, although this relative effect may be less important at larger mycotoxin concentrations.

Finally, we were able to estimate the variance partition coefficient (VPC), which for both the poor- and medium-rated suppliers was about 0.186 (the VPC is defined as the ratio of the between-truck variance to the sum of the between-truck and the within-truck variances). This is a somewhat intermediate magnitude for the VPC; but, because it is closer to 0 than to 1, this indicates that the measurements on a single inbound truck are fairly representative of the measurements across all trucks and that, therefore, it may be possible to carry out a supplier qualification based on just the multiple measurements from a single truck without greatly compromising the statistical accuracy of this assessment.

Overarching risk management framework. Finally, we emphasize that we envision a mycotoxin risk management framework comprising the following parts:

(i) An information repository with all relevant crop, supplier, and factory test data;

(ii) A collaborative infrastructure to host this repository, providing remote and shared access to data analysis tools and site-specific dashboards for risk evaluation and compliance;

(iii) Effective, standardized procedures for mycotoxin testing and acceptance sampling with statistical controls that are adaptive and responsive to the changing profile of food safety risks; and

(iv) Linkage of food-safety testing results to production processes, to sourcing and supplier management, and to the positive release verification of the finished product.

DISCUSSION

The evolution of the farming and food production process now involves global supply chain networks with many agricultural sources, intermediaries, and manufacturing facilities involved in the transformation of raw material to finished products. The upcoming challenges faced by the food industry now include providing food security and adequate nutrition to the increasing world population, reducing waste and managing the environmental impact of the production of agricultural raw material, expanding international trade and supply chain diversification, and promoting good industrial and food handling practices throughout all geographies including the developing regions. Whereas this evolution of the food industry has, on the one hand, led to the increasing application of scientific methods and standardization efforts to food safety issues, on the other it has also led to a welter of supply chain networks and regulatory practices that must be monitored and harmonized from a risk perspective.

In this respect, the food supply networks resemble other critical infrastructure networks such as transportation, communication, finance, and utilities, all of which are expected to function with an uncompromising degree of trust, reliability, and service; but these networks, by their very complex nature, are also subject to failures and malicious attacks and attract high-profile attention in these situations. The approach that is increasingly being adopted

in some of these critical infrastructure networks is to introduce diversification, redundancy, transparency, communication, distributed control, and self-correcting processes into the network design. Some of these ideas may also provide some valuable lessons and templates for safety and hazard prevention in the food supply chain as well.

Increasingly, food safety practitioners will interact with data repositories that contain a variety of relevant material, including regulatory requirements, background agronomic information, educational and research content, provenance and testing data, and retail and consumer reviews and feedback. These interactions will be mediated by modern technology platforms that are based on collaborative services for information organization, search and retrieval, analytics and simulation, and training and expertise sharing. For instance, the postmarket surveillance of consumer data may continue to involve survey design, focus groups, and controlled experiments; but, increasingly, these traditional data collection methods are being replaced with data and content gleaned through informal sources such as product forums, service channels, news media articles, and social networking sites. In many cases it may be necessary to track this data in real time, using tools that are quite different from those developed in classical experimental design and statistics. For example, Doyle *(5)* describes the real-time analysis of news data carried out using text mining and sentiment analysis to identify and predict emerging food security issues.

Given the complexity and expertise requirements of industrial food safety management, we foresee a critical need for technologies that can assist with risk identification and severity diagnosis and that can provide appropriate guidelines for actions leading to risk mitigation. In this respect, the use of question and answer technologies would enable the food safety practitioner in a focused context to access the entirety of the deep expertise in unstructured information from scientific research, news and social media, controlled experimental studies in laboratory reports, and regulatory requirements from multiple jurisdictions in multiple languages and to integrate this information with process and production data. Such question and answer systems are already being pursued in other domains; Ferrucci et al. *(6)* describe a system for clinical diagnosis in health care that is based on the open-domain Watson system used in the celebrated Jeopardy! game show challenge, but with some significant adaptations to make it applicable for the decision support requirements in domain-specific applications such as clinical diagnosis or financial counseling. The architecture of question and answer systems makes extensive use of natural language processing technologies for query, analysis, and result generation, in conjunction with machine learning technologies for hypothesis generation, evidence collection, and results ranking; and these technologies are combined with goal-oriented dialog systems for question refinement and resolution. The augmentation of such question and answer systems to provide operational guidance that is coupled to and influenced by the tactical forecasting of potential adverse risk events, or even the observational data from actual hazards in progress, may be highly relevant to food safety applications.

We believe that the methodological framework outlined here is a significant step toward addressing the challenges of mycotoxin contamination. Furthermore, although mycotoxin contamination may be the most cogent food safety problem for these developments, these ideas, with appropriate modifications, may also be relevant for mitigating the food safety risks associated with many other sources of contamination, including chemical and microbiological hazards, harmful commercial additives, and adulterants.

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