

Public Health Strategies for Preventing Aflatoxin Exposure

This is the second and final draft of a workgroup report for the International Mycotoxin Workshop: Public Health Strategies for Preventing Aflatoxin Exposure, which was sponsored by the World Health Organization and the U.S. Centers for Disease Control and Prevention and held in Geneva in July 2005.

I. Abstract

In response to consecutive outbreaks of acute aflatoxicosis in Kenya in 2004–2005 (responsible for over 150 deaths) a workshop of international experts and health officials was convened in Geneva, July 2005, by the United States Centers for Disease Control and Prevention and the World Health Organization. The goals of the workshop were to identify public health strategies for the reduction of morbidity and mortality associated with the consumption of aflatoxin-contaminated food in the developing world and to outline an integrated plan that more effectively combines public health and agricultural approaches to the control of aflatoxins. Following discussions concerning what is known about aflatoxins, participants were able to identify gaps in current knowledge about acute and chronic human health effects of aflatoxins, surveillance and food monitoring, analytic methods, and the efficacy of intervention strategies. Four themes emerged from the workshop and warrant immediate attention: 1) quantify the human health impacts and the burden of disease due to aflatoxin exposure; 2) compile an inventory, evaluate the efficacy, and disseminate results of on-going intervention strategies; 3) develop and augment the disease surveillance, food monitoring, laboratory, and public health response capacity of affected regions; and 4) develop a response protocol that can be used in the event of an outbreak of acute aflatoxicosis. This report summarizes the workshop findings.

II. Introduction

Aflatoxins, toxic metabolites of *Aspergillus flavus* and *Aspergillus parasiticus* fungi, are naturally occurring contaminants of food. Aflatoxins have been recognized as significant contaminants by the agricultural production community since the 1960s and control strategies have mostly eliminated harmful exposures in developed countries (Guo, Widstrom et al. 2000). The application of these strategies in developing countries is difficult, given differences in technology, agriculture, and trade practices, as well as other issues contributing to occurrence of aflatoxins and incidence of exposure. Consequently, over 5 billion people in developing countries worldwide are at risk of chronic exposure to aflatoxins through contaminated foods (Shephard 2003; Williams, Phillips et al. 2004). Aflatoxin associated health effects pervade the developing world despite the fact that these effects could be mitigated or prevented with the current state of agricultural knowledge and public health practice. The discussion of this problem and its remedies must be held in the context of the associated question of food insufficiency and more general economic challenges in developing countries.

Outbreaks of acute aflatoxin poisoning are a recurrent public health problem. In 2004, one of the largest, most severe aflatoxicosis outbreaks occurred in Kenya followed by another outbreak in 2005 (CDC 2004). Given that diseases in the developing world often go unreported, the Kenya outbreaks are likely to be an underestimation of the problem; furthermore, the burden of disease attributable to chronic aflatoxin exposure (e.g. hepatocellular carcinoma, impaired growth, immune suppression) remains undefined. These outbreaks emphasize the need to quantify and control aflatoxin exposure in developing countries and highlight the potential role of public health.

In July 2005, the United States Centers for Disease Control and Prevention (US CDC) and the World Health Organization (WHO) hosted a workshop to create an integrated plan intended to generate culturally appropriate, long-term, public health strategies to reduce aflatoxin exposure in developing countries. Participants included 40 internationally recognized scientists from diverse backgrounds (i.e. public health, agriculture, animal health, trade and social science) and key public health officials and stakeholders from countries heavily affected by aflatoxins. Through breakout sessions and roundtable discussions, participants identified gaps in current knowledge about the acute and chronic human health effects of aflatoxins, surveillance and food monitoring, analytic methods, and the efficacy of intervention strategies. Participants discussed public health strategies that could supplement agricultural efforts for the reduction or prevention of exposure to aflatoxins in the developing world. Lastly, participants discussed areas where efforts should be concentrated in order to reduce aflatoxin exposure and subsequently fill in the gaps in current knowledge.

III. Background

Well-known within the agricultural community, aflatoxins have been studied for over forty years due to their widespread occurrence and their significant impact on crops (Eaton and Groopman 1994; Wild and Turner 2002; Shephard 2003; Fung and Clark 2004; Williams, Phillips et al. 2004). Aflatoxins are toxic secondary metabolites produced by *Aspergillus* fungi. Aflatoxin B₁ (AFB₁) is the most potent and potentially lethal metabolite and is a known human carcinogen. Aflatoxins are most prevalent in areas located between latitudes 40°N and 40°S of the equator. Aflatoxins can affect a wide range of commodities including cereals, oilseeds, spices, and tree

nuts as well as milk, meat, and dried fruit. The major sources of exposure are maize and groundnuts as these are the foods that are most susceptible to contamination and consumed in the greatest amounts. The greatest risk for health impact lies within developing countries located in tropical regions, which rely on these commodities as their staple food source. Food insufficiency and lack of diversity substantially contribute to the susceptibility of individuals and communities to aflatoxins.

Many factors affect the growth of *Aspergillus* fungi and the level of aflatoxin contamination in food. Contamination can occur at any stage of food production from pre-harvest to storage (Wilson and Payne 1994). Factors that affect aflatoxin contamination include the climate of the region, the genotype of the crop planted, soil type, minimum and maximum daily temperatures, and daily net evaporation (Wilson and Payne 1994; Ono, Sugiura et al. 1999; Brown, Chen et al. 2001; Bankole and Mabekoje 2004; Fandohan, Gnonlonfin et al. 2005). Aflatoxin contamination is also promoted by stress or damage to the crop due to drought prior to harvest, insect activity, poor timing of harvest, heavy rains at harvest and post-harvest, and inadequate drying of the crop before storage (Hell, Cardwell et al. 2000; Ono, Sasaki et al. 2002; Hawkins, Windham et al. 2005; Turner, Sylla et al. 2005). Humidity, temperature, and aeration during drying and storage are also important factors.

The effects of aflatoxins on animal health have been observed in many species for over forty years (Patten 1981; Miller and Wilson 1994) beginning with the documentation of Turkey X disease in 1960 (Blount 1961). The primary target of aflatoxins is the hepatic system. Acute effects include hemorrhagic necrosis of the liver and bile duct proliferation while chronic effects

include hepatocellular carcinoma (HCC). In animals, suppression of immunity, growth retardation, and increased susceptibility to infectious disease due to aflatoxin exposure is well-documented (Patten 1981; Miller and Wilson 1994).

The effects of aflatoxins on humans, as with animals, are dependent upon dosage and duration of exposure. Acute exposure can result in aflatoxicosis, which manifests as severe, acute hepatotoxicity with a case fatality rate of approximately 25% (Cullen and Newberne 1994). Early symptoms of hepatotoxicity from aflatoxicosis can manifest as anorexia, malaise, and low-grade fever. Acute high level exposure can progress to potentially lethal hepatitis with vomiting, abdominal pain, jaundice, fulminant hepatic failure, and death. Outbreaks of acute aflatoxicosis are a recurring public health problem throughout the world (Krishnamachari, Bhat et al. 1975; Krishnamachari, Bhat et al. 1975; Ngindu, Johnson et al. 1982; Lye, Ghazali et al. 1995; CDC 2004).

Hepatocellular carcinoma (HCC) as a result of chronic exposure has been well documented, generally in association with hepatitis B virus or other risk factors (Qian, Ross et al. 1994; Wang, Hatch et al. 1996; Chen, Chen et al. 2001; Henry, Bosch et al. 2002; Omer, Kuijsten et al. 2004). The International Agency for Research on Cancer (IARC) first recognized aflatoxins as carcinogenic in 1976 and has subsequently reaffirmed naturally occurring mixtures of aflatoxins and aflatoxin B1 as Group 1 carcinogens (carcinogenic to humans) (IARC 2002). Additional effects of chronic exposure have not been widely studied but are thought to include immunologic suppression, impaired growth, and nutritional interference (Patten 1981; Cullen and Newberne 1994; Fung and Clark 2004; Williams, Phillips et al. 2004).

IV. Aflatoxins in Developing Countries

Baseline Levels of Exposure:

Although a few studies have provided estimates of daily exposure to aflatoxins during non-outbreak periods (Wild, Hudson et al. 1992; Wang, Huang et al. 2001; Park, Kim et al. 2004; Jiang, Jolly et al. 2005), more information is needed concerning baseline levels of chronic exposure for vulnerable populations. This would allow for a better quantification of the health risks associated with chronic exposure and for a better estimate of the level of aflatoxin exposure necessary to trigger an outbreak. Such knowledge will enable the public health community to understand health effects associated with chronic exposure and allow for the evaluation of future public health and agricultural interventions.

Health Impact and Burden of Disease:

HCC is the sixth most prevalent cancer worldwide with a higher incidence rate within developing countries (Parkin, Bray et al. 2005), however, the burden of HCC attributable to aflatoxins when accounting for other co-morbidities, such as hepatitis B (HBV), is not known. Several studies in China have indicated combined exposure to HBV and aflatoxins is associated with a much higher risk of HCC (Qian, Ross et al. 1994; Wang, Hatch et al. 1996). This interaction has not been studied in other high risk areas such as sub-Saharan Africa and the molecular mechanism of the interaction between HBV and aflatoxins is not known (Turner, Sylla et al. 2002; Wild and Turner 2002). Quantifying the proportion of HCC attributable to aflatoxin exposure, to HBV, and to the interaction of aflatoxin exposure and HBV will help identify the

best public health strategy to reduce HCC, including the benefits and limits of widespread HBV vaccination.

Additional health effects associated with chronic aflatoxin exposure have not been well studied. Without knowing the relationship between chronic exposure and health, the true human health impact and the resulting burden of disease in developing countries are not known. Preliminary evidence suggests that there may be an interaction between chronic aflatoxin exposure and malnutrition, immunosuppression, impaired growth, and diseases such as malaria and HIV/AIDS. Experimental animal evidence suggests that chronic exposure to aflatoxins may lead to impaired immunity, reduced uptake of nutrients from the diet, and growth retardation (Hall and Wild 1994; Miller and Wilson 1994). Several studies of children in Benin and Togo have shown an association between aflatoxin albumin adduct levels and impaired growth (Gong, Cardwell et al. 2002; Gong, Egal et al. 2003; Gong, Hounsa et al. 2004). In a recent study in Ghana, higher levels of aflatoxin B1-albumin adducts in plasma were associated with lower percentages of certain leukocyte immunophenotypes (Jiang, Jolly et al. 2005). A study in Gambian children found an association between serum aflatoxin-albumin levels and reduced salivatory secretory IgA levels (Turner, Moore et al. 2003). While the effects on immunity suggest the possible influence of aflatoxins on susceptibility to infectious disease, further investigation is needed.

Efficacy of Interventions:

Quantifying the baseline levels of exposure and the associated burden of disease in developing countries is essential for determining the efficacy of interventions intended to reduce exposure to

aflatoxins. Evidence exists for the effectiveness of various interventions to reduce aflatoxin contamination of foods in developed countries, but it is unclear whether these are applicable in developing countries (Phillips, Clement et al. 1994; Brown, Chen et al. 1999). Because of inherent differences between local (subsistence farmer) and commercial markets, regulations and practices, such as Hazard Analysis and Critical Control Point (HACCP) (Pineiro 2001), used in commercial markets may not directly apply to subsistence farmers. For example, while subsistence farmers consume their own grain, they also sell part of their harvest to local markets. They may later themselves purchase grain from these markets when their own supplies are depleted. Food commodities within these local markets are not tested for aflatoxins (Lewis, Onsongo et al. 2005). While general principles of HACCP and other commercial practices may be applicable at the individual farmer level, appropriate adaptation of these principles into effective and sustainable strategies is essential and currently missing.

An intervention to reduce exposure to aflatoxins can occur at various stages of food production and preparation (Table 1). Before crops are planted, efforts can be made to reduce the future burden of aflatoxins. Interventions can also occur before harvest, during harvest, and after harvest. The appropriate intervention or combination of interventions may differ depending on the crop and the country. Therefore further evaluation is needed with consideration towards the sustainability, cultural acceptability, economic feasibility, ethical implication, and overall effectiveness of potential interventions.

Table 1: Interventions for Preventing or Reducing Aflatoxin Exposure

Stage in Food Production	Interventions	References
Pre-Harvest	Timing of planting; Crop planted; Genotype of seed planted; Irrigation; Insecticides; Competitive exclusion; Timing of harvest;	(Cotty and Bhatnagar 1994; Wilson and Payne 1994; Dorner, Cole et al. 1999; Brown, Chen et al. 2001; Chen, Brown et al. 2001; Cleveland, Dowd et al. 2003; Munkvold 2003)
Post-Harvest: Drying & Storage	Hand sorting; Drying on mats; Sun drying; Storing bags on wooden pallets or elevated off ground; Insecticides; Rodent control;	(Hell, Cardwell et al. 2000; Ono, Sasaki et al. 2002; Munkvold 2003; Fandohan, Gnonlonfin et al. 2005; Hawkins, Windham et al. 2005; Turner, Sylla et al. 2005)
Post-Harvest: Food Preparation	Hand sorting; Winnowing; Washing; Crushing and dehulling; Nixtamalization; Acidification; Chemoprotectant; Enterosorption;	(Price and Jorgensen 1985; Voss, Bacon et al. 1996; Elias-Orozco, Castellanos-Nava et al. 2002; Munkvold 2003; Kensler, Egner et al. 2004; Mendez-Albores, Arambula-Villa et al. 2004; Castells, Marin et al. 2005; Fandohan, Zoumenou et al. 2005; Mendez-Albores, Arambula-Villa et al. 2005; Wang, Luo et al. 2005)

Pre-harvest interventions

The presence and growth of *Aspergillus* on pre-harvested crops is dependent on the environment.

Agricultural practices including proper irrigation and pest management can reduce aflatoxin contamination. Pre-harvest interventions include choosing crops with resistance to drought, disease, and pests and choosing strains of that crop which are genetically more resistant to the growth of the fungus and the production of aflatoxins (Cotty and Bhatnagar 1994; Chen, Brown et al. 2001; Cleveland, Dowd et al. 2003). Elimination of inoculum sources such as infected debris from the previous harvest may prevent infection of the crop (Olanya, Hoyos et al. 1997).

A biopesticide, consisting of a non-aflatoxigenic strain of *Aspergillus*, may competitively exclude toxic strains from infecting the crop (Dorner, Cole et al. 1999; Cleveland, Dowd et al.

2003) however, the allergenic and human health aspects of the atoxigenic strain need to be evaluated.

Post-Harvest Drying & Storage

Before storage, crops should be properly dried to prevent the development of aflatoxins. Sorting and disposing of visibly moldy or damaged kernels before storage has proven to be an effective method for reducing, but not eliminating, the development of aflatoxins (Fandohan, Zoumenou et al. 2005; Turner, Sylla et al. 2005). During storage, moisture, insect, and rodent control can prevent damage to the crop and reduce aflatoxin development. Aflatoxin contamination of maize is influenced by the structure used for storage, the length of time in storage, and the form of maize stored (i.e. with husk, without husk, or as loose grain) (Hell, Cardwell et al. 2000). A community-based intervention trial in Guinea, West Africa focused on thorough drying and proper storage of groundnuts in subsistence farm villages and achieved a 60% reduction in mean aflatoxin levels in intervention villages (Turner, Sylla et al. 2005). This study illustrates that simple and inexpensive post-harvest methods can have a significant impact.

Post-Harvest Food Preparation

Interventions during food preparation or consumption involve removing contaminated portions of food, diluting contaminated food with uncontaminated food, neutralizing aflatoxins present in food, or altering the bioavailability of the aflatoxins consumed. Aflatoxins are not largely affected by routine cooking temperatures, but simple food preparation methods such as sorting, washing, crushing, and dehulling may reduce aflatoxin levels (Lopez-Garcia and Park 1998; Park 2002; Fandohan, Zoumenou et al. 2005). Traditional methods of cooking food with alkaline

compounds (i.e. nixtamalization) have been used to reduce aflatoxin exposure; however, the chemical reaction may involve temporary inactivation of aflatoxins, a process that may reverse in the gastric acid of the stomach (Price and Jorgensen 1985; Elias-Orozco, Castellanos-Nava et al. 2002; Mendez-Albores, Arambula-Villa et al. 2004; Fandohan, Zoumenou et al. 2005). These methods do not always transfer well to other communities due to lack of acceptance. However, the principles could be used to create culturally appropriate methods.

Additional strategies for reducing aflatoxins, including enterosorption and chemoprotection, attempt to reduce the effects of aflatoxin exposure or the bioavailable portion of aflatoxins in food. These strategies are expensive and therefore difficult to implement in poor communities. Enterosorption is the use of clay, such as NovaSil, with a high affinity for aflatoxins (Phillips 1999; Phillips, Lemke et al. 2002; Wang, Luo et al. 2005). Clay has been used as an anti-caking additive in animal feed and has been shown to protect animals from ingested aflatoxins. Chemoprotection is the use of chemical (e.g. Oltipraz, Chlorophyllin) or dietary intervention (e.g., broccoli sprouts, green-tea) to alter the susceptibility of humans to carcinogens and has been considered as a strategy to reduce the risk of HCC in populations with high exposures to aflatoxins (Bolton, Munoz et al. 1993; Kensler, Davis et al. 1994; Wang, Shen et al. 1999; Kensler, Egner et al. 2004). The efficacy, safety, and acceptability of enterosorption and chemoprotection require further study.

Awareness Campaigns

Raising awareness of aflatoxins and disseminating relevant information to individuals is an important part of any intervention strategy. During the 2005 Kenya outbreak, individuals who

reported receiving information on maize drying and storage through an awareness campaign implemented by the Food and Agricultural Organization, the Ministry of Health, and the Ministry of Agriculture had lower serum aflatoxin levels than those who did not receive this information (CDC 2005). Awareness campaigns should utilize systems that are in place already for disseminating information to subsistence farmers (James 2005). Such campaigns should also include the dissemination of information to non-governmental organizations, public service associations, health care providers, and schools. Given diversity in culture and remote location of villages, multiple means for disseminating information as part of an awareness campaign may be necessary to reach a broad range of people. Populations not receiving messages from current campaigns and appropriate methods for reaching those populations need to be identified. Reasons for failure or unwillingness to adopt recommendations should also be identified.

Analysis of Food and Biological Specimens

The knowledge of the relationship between aflatoxin concentrations in food or biological specimens and potential health outcomes is central to quantifying and mitigating the aflatoxin burden in the developing world. From the standpoint of improving public health, the goals of laboratory testing in toxicology include establishing a baseline in humans and the environment (e.g., foods, communities, individuals), monitoring exposure, confirming exposure or diagnosis of poisoning, excluding other causes of disease, monitoring the effectiveness of prevention interventions, and guiding therapeutic interventions. Interpretation and application of aflatoxin results to achieve these goals are limited and vary based on the type of laboratory method and sample media.

Aflatoxin Food Concentrations

Testing food for aflatoxins is constrained by two limitations. First, obtaining a representative sample of food from subsistence farmers is difficult given (1) the need for large samples, (2) multiple vulnerable crops on one farm, (3) the distance between farmers, villages, and laboratories, and (4) the uneven distribution of aflatoxin contamination within a food supply. Second, there is a lack of information about threshold levels associated with adverse health effects. Agricultural data of the relationship between concentrations of aflatoxins in food and acute aflatoxicosis has resulted in a regulatory limit of 300 ppb for animal feed in the United States. Foods for human consumption in the industrialized world (including exports from developing countries) are enforced with regulatory limits varying from 4 to 20 ppb based on limited information from risk assessments of HCC (Henry, Bosch et al. 1999; van Egmond 2002). Little information is available concerning aflatoxin concentrations between 300 ppb and 20 ppb.

Aflatoxin B₁ Adducts & Urine Immunoassay

For epidemiologic studies, biomarkers in serum and urine provide a better estimate of aflatoxin exposure than food analysis. Aflatoxin metabolites in urine reflect recent exposure (i.e. 2-3 days) whereas the measurement of aflatoxin albumin adducts in blood reflects exposure over a longer period (i.e., 2-3 months) (Groopman, Wogan et al. 1994). These analyses, however, are labor-intensive and expensive (Wild, Jiang et al. 1990; Sheabar, Groopman et al. 1993; McCoy, Scholl et al. 2005). There is also limited information regarding the interpretation and application of aflatoxin B₁ adducts and urine immunoassays (Turner, Dingley et al. 1998; Wild and Turner 2001; Groopman and Kensler 2005). The detection of aflatoxin metabolites or adducts in urine

and serum indicate exposure but do not necessarily equate to adverse health effects. Some studies have correlated aflatoxin intakes to biomarker levels (Groopman, Hall et al. 1992; Wild, Hudson et al. 1992) and to disease (Qian, Ross et al. 1994; Wang, Hatch et al. 1996; Gong, Hounsa et al. 2004; Azziz-Baumgartner, Lindblade et al. 2005). More research is needed to determine aflatoxin levels in biological specimens that are associated with adverse health effects. Research must also clarify the relationship between aflatoxin levels in biological specimens and levels in food.

Appropriate Laboratory Methods for Developing Countries:

Current methods allow for the detection of aflatoxins and aflatoxin metabolites at very low concentrations in food and biological media; however, the application of these methods within developing countries is limited by practical considerations, such as resources and infrastructure. Methods for testing food and biological specimens need to be adapted to fit the surveillance and epidemiologic needs of developing countries. A simple screening method, adapted for developing countries, would benefit subsistence farmers as well as public health and agriculture institutions. Furthermore, these institutions would also benefit from sustainable yet reliable confirmatory methods for use in centralized laboratories.

Field Methods

Simple and inexpensive field screening methods are available to determine that food is sufficiently free of aflatoxins, but currently lack direct applicability to aflatoxin contamination issues in developing countries. Field methods can be performed with minimal training or equipment and can be performed on-site (i.e. at a farm or grain silo). Field methods for aflatoxin

analysis allow for rapid confirmation or exclusion of possible exposure at a reasonable cost, thus allowing officials to quickly determine whether further evaluation and intervention is necessary. Such methods would prove beneficial in developing countries given that the remote location of villages and long distances to a centralized laboratory make it impractical to take samples from villages, analyze them in the laboratory, and then travel back to the village to deliver the results.

Improving the cost, durability, ease of transport, and usability of field methods (e.g., simplicity of use, use in the absence of electricity) is necessary to optimize the public health approach to aflatoxin exposure in developing countries. One field method which could be useful involves dipsticks, which are developed to measure up to the cutoff value for aflatoxins in food that corresponds with trade agreements or regulations (Delmulle, De Saeger et al. 2005). However, cutoff values in developed countries are markedly lower than typical food levels in developing countries. Such field tests could prove effective if the cutoff value was adjusted based on chronic exposure, health effects, and action levels necessary for developing countries. Field methods for the analysis of biological samples have not been developed. However, the same concept of using dipsticks can be applied to field tests for biological specimens.

Laboratory Methods

Laboratory methods, which are more precise yet also more labor intensive and costly, can be used to confirm results of field tests. These methods require instrumentation or techniques not suited to working on-site. They require regular maintenance of instrumentation, training of personnel, and a ready supply of reagents and materials (Trucksess and Wood 1994). The best laboratory method for testing either food or biological specimen is one that balances the need for

quick, accurate results with limitations in resources and infrastructure. Current laboratory methods require further refinement to improve their usability in developing countries. Thin layer chromatography (TLC) is a well-suited laboratory method for testing food samples, given its reliability and simplicity (Stroka and Anklam 2000; Shephard and Sewram 2004), however, it is labor intensive and limited in the number of samples tested in a day. An alternative for food analysis is the VICAM AflaTest® immunoaffinity fluorometric method, which is less-intensive and faster, but also more expensive (VICAM 2001).

Early Warning System for Developing Countries:

In order to prevent future outbreaks, developing countries need an early warning system which is able to detect potential food contamination events with adverse health effects (Figure 1) (Park 1995). Public health surveillance is the ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health. Important characteristics of any surveillance system include simplicity, flexibility, data quality, acceptability, sensitivity, positive predictive value, representativeness, timeliness, and stability (CDC 2001). To create an effective and sustainable system, health surveillance and food and biological monitoring strategies must be adapted to meet the needs of developing countries. Early warning signs need to be validated and a response protocol needs to be developed.

Previous outbreaks in Kenya have been identified by physicians noticing an increase in cases of jaundice despite a lack of any organized or official reporting system (Azziz-Baumgartner, Lindblade et al. 2005). While a national reporting system for jaundice would prove beneficial for

developing countries, the baseline rate of jaundice and all its possible causes are not known. In addition, aflatoxicosis confirmation tests using biological markers are limited. An early warning system should also involve monitoring aflatoxin levels in food sources or individuals in order to prevent or reduce the health impact.

Monitoring aflatoxin levels in food or individuals to identify those at risk for disease is more difficult than monitoring rates of jaundice. However, food and biological monitoring may identify susceptibility sooner and allow for a more timely intervention. To maximize resources, monitoring or surveillance should target high-risk areas or populations and the most appropriate specimen – food, urine, or serum, – should be collected. A rapid, field test that analyzes aflatoxin adducts in biological samples would be ideal for an early warning system that incorporates biomonitoring.

Ultimately an early warning system should rely on multiple sources of information and triggers that would set in motion various responses for preventing or reducing an outbreak of aflatoxicosis. Triggers for action could also be based upon other factors which indicate or influence aflatoxin contamination, such as reporting of death among livestock or domestic animals which are often given lower quality grain. Modeling of aflatoxin contamination based on weather conditions from planting to post-harvest could also serve as a trigger (de la Campa, Hooker et al. 2005). Such modeling would require further validation and an infrastructure for weather monitoring and dissemination of information. But, it may be the easier and less expensive trigger to implement and would also allow for the earliest intervention in preventing further aflatoxin development.

An early warning system must also include a response protocol to prevent further aflatoxin exposure and associated health outcomes once a contaminated food source is identified. A protocol can only be effective if the infrastructure and funds to replace contaminated food exist and a method for identifying families in need has been determined. Inclusion of key members from various government agencies, the health care sector, and non-governmental organizations in an effective communication strategy and in all response efforts is necessary to ensure that an early warning system is successful.

Co-existence and Interactions of Multiple Mycotoxins:

Food commodities affected by aflatoxins are also susceptible to other types of mycotoxins and multiple mycotoxins can co-exist in the same commodity (Bankole and Mabekoje 2004; Fung and Clark 2004; Speijers and Speijers 2004). Various cereals affected by aflatoxins are also susceptible to contamination by fumonisins, trichothecenes (especially deoxynivalenol), zearalenone, ochratoxin A and ergot alkaloids. Maize can be contaminated with aflatoxins, fumonisin, trichothecenes, zearalenone and, rarely, ochratoxin-A, while wheat can be contaminated with aflatoxins, trichothecenes, ochratoxin-A, ergot alkaloids and zearalenone. Therefore individuals may be exposed to various combinations of mycotoxins (CAST 2003). The health effects associated with exposure to multiple mycotoxins are not well documented. Related mycotoxins are thought to have an additive effect while unrelated mycotoxins may have a synergistic effect (Speijers and Speijers 2004). A better understanding of exposure to multiple mycotoxins and the health effects associated with the interactions of multiple mycotoxins would clarify the true health impact of mycotoxins.

V. Conclusions

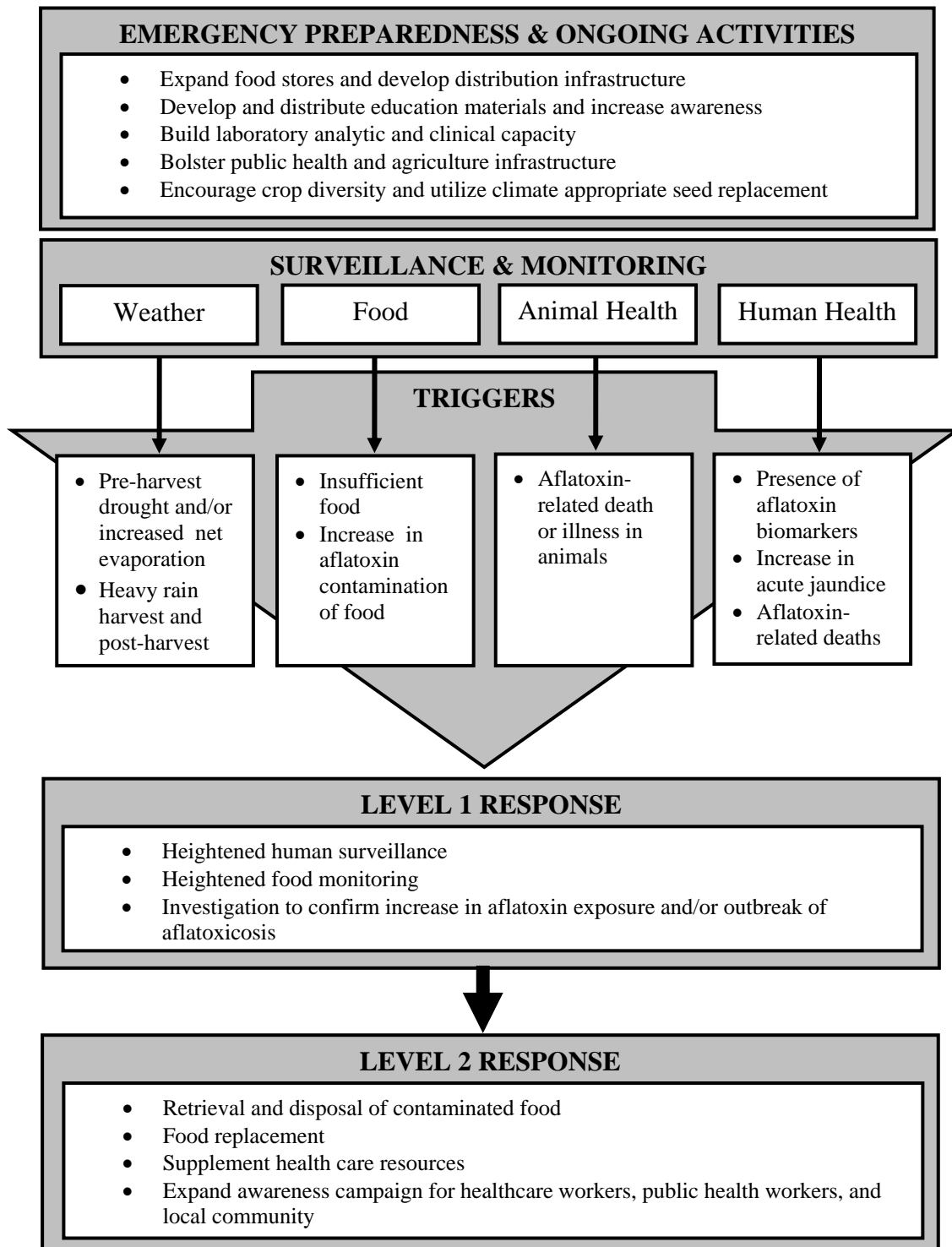
The aflatoxin workshop in Geneva brought together a diverse group of experts to develop an integrated plan intended to generate public health strategies, which complement agricultural strategies, to reduce and prevent aflatoxin exposure in developing countries. While a great deal is known about aflatoxins, much is not known about aflatoxin exposure and the resulting health effects in developing countries. Even without a complete understanding of the public health problem caused by aflatoxins, it is clear that acute aflatoxicosis is preventable and chronic exposure can be reduced.

The four recurrent themes that were evident throughout the workshop and warrant immediate attention are: 1) quantify the human health impacts and the burden of disease due to aflatoxin exposure; 2) compile an inventory, evaluate the efficacy, and disseminate results of on-going intervention strategies; 3) develop and augment the disease surveillance, food monitoring, laboratory, and public health response capacity of affected regions; and 4) develop a response protocol that can be used in the event of an outbreak of acute aflatoxicosis. These steps will provide much needed knowledge about the pattern and resulting health effects of aflatoxin exposure and will enable the development of effective, culturally appropriate interventions for reducing chronic levels of exposure.

Although aflatoxin exposure is not a new issue, it requires new strategies to address it effectively within developing countries, where aflatoxin exposure is intertwined with the issues of food

insecurity and insufficiency. Collaboration between the agricultural and public health communities, between the local, regional, national, and international governing bodies, and between different disciplines within public health and agricultural is necessary to reduce aflatoxin exposure. The consecutive outbreaks in Kenya emphasize the imperative for action.

Figure 1: Overview of Preparedness, Surveillance, & Response Activities for Preventing Acute Aflatoxicosis in Countries in Development



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