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Evaluating the technical feasibility of aflatoxin risk reduction strategies in Africa

Felicia Wu^{a,*} and Pornsri Khlangwiset^a

^aDepartment of Environmental and Occupational Health, University of Pittsburgh, 100 Technology Dr, Pittsburgh PA 15219, USA

Abstract

Public health interventions must be readily accepted by their target populations to have any meaningful impact, and must have financial and infrastructural support to be feasible in the parts of the world where they are most needed. At the same time, these interventions must be assessed for potential unintended consequences, either to the environment or to human health. In this paper, we evaluate the technical feasibility of interventions to control aflatoxin risk, to be potentially deployed in parts of Africa where aflatoxin exposure poses a significant public health concern. We have applied a conceptual framework for feasibility to four interventions, one associated with each of four different stages of aflatoxin risk: biocontrol (pre-harvest), a post-harvest intervention package (post-harvest), NovaSil clay (dietary), and hepatitis B vaccination (clinical). For each intervention, we have assessed the following four components of technical feasibility: 1) characteristics of the basic intervention, 2) characteristics of delivery, 3) requirements on government capacity, and 4) usage characteristics. We propose ways in which feasibility of each intervention is currently high or low from the perspective of adoption in Africa, how public education is crucial for each of these interventions to succeed, and how to align economic incentives to make the interventions more suitable for less developed countries.

Keywords

aflatoxin; risk; technical feasibility; control strategies; Africa; public health interventions; economic incentives

Introduction

Aflatoxin, produced by the fungi *Aspergillus flavus* and *A. parasiticus* on crops such as maize, peanuts, and tree nuts, is recognized to be an important food safety risk worldwide. Aside from causing acute poisoning at high doses (acute aflatoxicosis), aflatoxin can also cause liver cancer (hepatocellular carcinoma, or HCC), immunomodulation (Bondy and Pestka 2000; Williams et al. 2004; Jiang et al. 2005, 2008; Meisssonier et al. 2008), and stunted growth in children at chronic lower-level doses (Gong et al. 2002, 2008; Turner et al. 2003). More recent evidence shows that aflatoxin may also play a role in global cirrhosis morbidity (Kuniholm et al. 2008). Most of these health problems associated with aflatoxin exposure occur in less developed countries (LDCs) in tropical and subtropical areas of the world, where the *Aspergilli* thrive and where food safety measures are less stringent.

* Corresponding author. few8@pitt.edu, Tel: 1-412-624-1306.

An interesting aspect of the aflatoxin public health issue is that the risk can be mitigated at so many different levels, in multiple different ways. This stands in contrast to other foodborne risks such as harmful bacteria (e.g., *Escherichia coli*): no enterosorbents could reduce their levels in the gastrointestinal system, and no vaccines could mitigate their impacts. Aflatoxin accumulation could be reduced in crop fields, in food storage, or in food processing. Additionally, even if aflatoxin is present in consumers' food, certain dietary additives or clinical practices can mitigate adverse effects of the toxin in the body. Hence, many different interventions have been developed either to reduce aflatoxin directly in the field and in food (preharvest and postharvest interventions), or to reduce aflatoxin's harmful effects in the body once it is ingested (dietary and clinical interventions). These categories of interventions are described in greater detail in Khlangwiset and Wu (2009) and Wu and Khlangwiset (2009).

Regulations on maximum allowable levels of aflatoxin in food could also reduce aflatoxin exposure. These regulations are generally effective in controlling aflatoxin in industrial nations; commodities that contain aflatoxin levels exceeding regulatory guidelines for human food or animal feed are discarded, or sold at a lower price for a different use (Wu 2004, Wu et al. 2008). However, aflatoxin regulations in many LDCs do little to protect public health, as there is limited enforcement of food safety regulations, especially among rural communities where food quality is rarely formally inspected (Shephard 2008). Subsistence farmers and local traders sometimes have the luxury of discarding obviously moldy maize and groundnuts. But in drought seasons, people often have no choice but to eat moldy food or starve. Thus, regulations do little to help reduce aflatoxin and its related health effects in LDCs (Shephard 2008, Williams 2008). Rather, the focus should be on promoting adoption of strategies that can control aflatoxin and its associated risks, in the field, in postharvest conditions or in the diet (Wu and Khlangwiset 2009).

This dichotomy between the feasibility of aflatoxin regulations against the feasibility of other kinds of public health interventions highlights the need for mycotoxin researchers to consider whether the control strategies they develop could actually be implemented widely to improve public health. It is crucial that an intervention be technically feasible in the places where it is most needed. The purpose of this paper is to highlight key components of technical feasibility, which are then applied to analyzing four specific interventions that control aflatoxin risk.

Framework to consider feasibility of aflatoxin control strategies

The cost-effectiveness of selected public health interventions to control aflatoxin-induced liver cancer has been assessed (Wu and Khlangwiset 2009). Yet cost-effectiveness of a strategy is not enough to ensure its successful adoption. More questions must be posited, such as: Are there countervailing health or ecological risks to the strategy? What would the delivery mechanism be, and would locally-available infrastructures support the mechanism? Do governmental regulations inhibit or promote the intervention? Is the intervention culturally appropriate and easy to adopt by the target population (Wu and Khlangwiset 2009)? If an intervention to reduce aflatoxin fails in any or all of these points, then it is not likely to be adopted on a global scale, no matter how cost-effective it may be.

A conceptual framework to evaluate the technical complexity – and hence the feasibility – of public health interventions for less developed countries has been developed (Gericke et al. 2005). There are four relevant dimensions (see Figure 1):

1. Characteristics of the basic intervention
2. Characteristics of delivery
3. Requirements on government capacity

4. Usage characteristics

Aflatoxin control strategies

Multiple public health interventions exist by which to control aflatoxin or its burden in the body, to prevent HCC. Several of these are listed in Table 1, adapted from Wu and Khlangwiset (2009). We are beginning to understand more about the cost-effectiveness of these interventions; what remains to be found is how technically feasible they would be in many parts of the world.

Interventions to reduce aflatoxin risk can be roughly grouped into three categories: 1) agricultural (preharvest and postharvest), 2) dietary, and 3) clinical. *Agricultural* interventions are methods or technologies applied either in the field (preharvest) or in drying, storage and transportation (postharvest) to reduce aflatoxin levels in food. Agricultural interventions can thus be considered “primary” interventions, because they can reduce actual aflatoxin levels in food. *Dietary* and *clinical* interventions can be considered “secondary” interventions. They cannot reduce aflatoxin levels in food, but can ameliorate aflatoxin-related illness; by reducing bioavailability either of aflatoxin (e.g., through enterosorption) or of its reactive oxygen species that binds to DNA to initiate cancer (e.g., through induction of Phase 2 enzymes that detoxify the aflatoxin-8,9-epoxide).

We assess the technical feasibility of one intervention from each of these categories, specifically for human use:

1. Biocontrol (preharvest)
2. A postharvest intervention package (postharvest)
3. Calcium aluminosilicate clay (NovaSil) as an enterosorbent (dietary)

Hepatitis B vaccine is included in our analyses, even though it is not literally considered as an aflatoxin control intervention. The vaccine itself has no impact on actual aflatoxin levels in diets, but it prevents the synergistic impact of HBV and aflatoxin in inducing liver cancer.

For each of these, we evaluate characteristics of each intervention according to the aforementioned dimensions of the intervention's basic characteristics, delivery characteristics, government capacity requirements, and usage characteristics. In addition, we describe economic issues associated with wide-scale adoption of each intervention. We describe the areas in which the characteristics of each intervention lend themselves to being more or less feasible in LDCs, with a focus on sub-Saharan Africa, where these interventions have shown success in field and clinical trials.

Application of technical feasibility framework to aflatoxin risk-reduction interventions

Biocontrol: Technical feasibility

Agricultural biocontrol involves the use of biological agents to control pests or toxin production. Specifically, biocontrol of aflatoxin refers to using organisms to reduce the incidence of toxigenic *Aspergilli* in susceptible crops, and thereby to reduce aflatoxin contamination. The most widely used biocontrol method for aflatoxin employs nontoxigenic strains of *Aspergilli* that can competitively exclude toxigenic strains from colonizing crops. Grain seeds (of wheat, barley, sorghum, or other small grains) are either briefly colonized by or coated with conidia of a nontoxigenic strain, and these seeds are applied to agricultural fields during a period favorable for competitive exclusion of toxigenic strains.

These biocontrol methods have been used in maize, groundnuts, and cottonseed in several regions of the world (Cotty and Bhatnagar 1994, Dorner et al. 1999, Bandyopadhyay et al. 2005, Pitt and Hocking 2006, Cotty et al. 2007, Atehnkeng et al. 2008). Importantly, nontoxigenic *A. flavus* strains have been found in sub-Saharan Africa, which show promise for controlling aflatoxin in African maize (Bandyopadhyay et al. 2005, Atehnkeng et al. 2008). Biocontrol methods, though applied in the field, can result in reduced aflatoxin in crops for months postharvest (Dorner 2006).

Table 2 summarizes the characteristics of biocontrol as an aflatoxin reduction intervention in African countries that determine its overall feasibility.

Biocontrol: Basic characteristics—Three main elements are important to consider here: the basic product design (stability, standardization, safety profile, and ease of storage and transport), supply requirements, and equipment needed. Biocontrol agents have a shelf life in the United States of up to six months (Cole and Dorner 2001), which may be lower in the tropics depending on quality of storage conditions, including susceptibility to insect damage. Standardizing biocontrol is highly important, to ensure that each application unit contains sufficient amounts of nontoxigenic fungi to competitively exclude toxigenic strains in the field.

Safety is an important consideration regarding biocontrol use in Africa. Because of the potential risk of invasive aspergillosis from *A. flavus* exposure among immunocompromised individuals (as highlighted in Krishnan et al. 2009 and Hedayati et al. 2007), it is important to ensure that the biocontrol material is manufactured and applied in such a way as to minimize direct inhalation of spores. The biocontrol methods used commercially and in field trials in various parts of the world, in which the nontoxigenic *Aspergilli* are applied in an oil or molasses mixture to seeds (Cotty et al. 2007, Pitt and Hocking 2006) that are then applied to fields, minimize potential inhalation risks. At the present time, no aspergillosis cases have been reported as a result of biocontrol manufacturing or application. In the United States, it is recommended that applicators wear protective gear – a long-sleeved shirt, long pants, shoes, sock and gloves—when working with biocontrol (EPA 2004), because of concerns regarding potential moderate eye or skin irritation, though no cases have thus far been reported (ACRPC 2007). These precautions should be followed in other parts of the world where biocontrol is used.

Several conditions are necessary for optimal storage and transport. Grains colonized by nontoxigenic *Aspergilli*, once dried, should be kept in moisture-protected, insect-proof bags, which should not be exposed to high relative humidity or extreme temperatures, such as over 80% RH, over 50° C, or below freezing (ACRPC 2007). In most parts of Africa, these temperature constraints would pose no problem; however, relative humidity could be higher than optimal for storage of biocontrol agents.

High-technology equipment, basic supplies, and trained professional staff are necessary to produce and maintain biocontrol agents: to maintain the cultures used, to manufacture the large numbers of nontoxigenic fungal spores needed for application to the substrate (the grains used to convey the spores in the field), to sterilize the substrate on a large scale, and to mix the spores and substrate with a binder (such as oil or molasses) to allow the spores to adhere (Pitt and Hocking 2006, Wu and Khlangwiset 2009). The ability of African countries to meet these high-technology requirements varies from nation to nation. Nigeria would benefit from the support of the Ibadan-based International Institute of Tropical Agriculture (IITA), with an active research and outreach group for biocontrol adoption. Biotechnology has also flourished in certain African countries such as Kenya, Zimbabwe, Egypt and South Africa (Serageldin and Juma 2004). These countries may thus be more capable of producing biocontrol agents than others, although training needs for biocontrol specifically may be minimal

There are potential supply constraints as well. The substrate itself, such as wheat, rice, or sorghum grains (Yin et al. 2008), must be available; this may be problematic to obtain in situations of food insecurity, when the grains would be better used as a food source rather than as a substrate to convey biocontrol agents. Maize cobs have been proposed as a potential substrate on which nontoxigenic fungi can be applied and then dispersed in fields (Bandyopadhyay et al 2005), which would alleviate grain supply concerns.

Biocontrol: Delivery characteristics—Specifics of biocontrol delivery in Africa may vary by nation. There may be centralized laboratories and facilities to provide the biocontrol materials; or the facilities may be more widely distributed within the target population, particularly if individual farmers will apply the biocontrol to their fields. If farmers are already using agricultural chemicals such as pesticides and fertilizers, the biocontrol agents could be obtained through the same venues.

There are benefits and costs associated with both centralization and dispersion of facilities to produce and maintain biocontrol, and individuals who apply biocontrol to fields. For example, transportation costs to get biocontrol materials to the places they are needed are lower if the facilities are more dispersed within a community; but having a greater number of facilities necessitates having trained professionals at each location, which may cause a strain on human resources. Likewise, hiring trained professionals to apply biocontrol to crop fields would ensure better quality control of application. However, it leads to questions of who would pay for and train these professionals, and whether there would be a sufficient number of them to ensure that the biocontrol was applied at exactly the right time to allow competitive exclusion of aflatoxin-producing fungi in the field. Ultimately, it should be the individual farmers who apply biocontrol, with guidance either from a local agricultural extension worker or from the biocontrol packaging materials.

Biocontrol: Government capacity requirements—Two items should be considered: governmental regulations on use and commercialization of the intervention, and regulatory support and enforcement to ensure optimal benefits and minimal risk. Biocontrol for aflatoxin reduction was first registered in the United States, by the Environmental Protection Agency (EPA 2003). A lengthy review ensured no evidence or likelihood of risks to human health or to the environment. The review included tests with laboratory mammals to assess oral or lung infectivity, toxicity, and allergenicity; soil and air monitoring studies for environmental quality; survival tests of the fungi after crop processing, and ecological risk assessments of endangered species encountering the fungi. In all cases, risks were shown to be minimal or nonexistent (Cotty et al. 2007).

With this precedent to guide further health and environmental risk assessments in different parts of the world, governmental regulatory barriers may be minimal. The International Institute of Tropical Agriculture (IITA) has held workshops aiming to create harmonized biopesticide regulation for African countries. The biopesticide regulation system within the member countries of the Permanent Interstates Committee for Drought Control in the Sahel (CILSS) has been proposed as a protocol of harmonized regulation for biopesticide registration. Pesticides registered by CILSS can be used in any CILSS member nations (IITA 2008). If this approach is developed and accepted by African countries, biocontrol application in Africa could be implemented on a wide scale. Moreover, stakeholder involvement in select nations has been mobilized. Recently, a stakeholder consultative meeting on biological control was held in April 2009 at Ibadan-based IITA, Nigeria; to discuss biocontrol application in maize to lower aflatoxin levels, as well as its potential usefulness in other staple crops (AATF 2009).

Monitoring should also be conducted regularly, to ensure that the nontoxigenic strains do indeed continue to produce no aflatoxin in field conditions. Recently, an inexpensive aflatoxin test kit was developed by IITA and ICRISAT: a mere \$1–\$2 per analytical sample. This kit is purported to be effective even for analyses in the most remote rural areas of Africa (CGIAR 2007).

Biocontrol: Usage characteristics—The three aforementioned considerations regarding the end user - the ease of usage, pre-existing demand, and black-market risks – are legitimate concerns regarding widespread biocontrol adoption. Eventually, individual farmers must be the ones to apply biocontrol in African crop fields to control aflatoxin. The education and outreach process could be complicated – both in convincing the farmers of the need for this product, and in providing guidance on how much and when to optimally apply the biocontrol (Cotty et al. 2007). There is little if any pre-existing demand for this product specifically, as it is a new technology; although there is pre-existing demand more generally for aflatoxin control. Finally, it is possible that black markets may arise that provide materials that are not truly nontoxigenic. This is why monitoring processes and quality control for marketed products are extremely important.

Biocontrol: Economic issues—The low cost of biocontrol (\$10–\$20 per hectare) and its effectiveness at aflatoxin reduction (50–90%) make biocontrol a very cost-effective intervention in reducing aflatoxin-induced disease (Wu and Khlangwiset 2009). However, individual farmers may not have incentive to pay even this relatively small amount if they do not understand the risks of aflatoxin, and moreover, have very little discretionary monies.

Therefore, initially, governments (in partnership with internal and external funding agencies) would most likely need to provide the resources for widespread biocontrol application. Alternatively, governments and/or commodity industries could establish a marketing system that provides a premium to growers for low aflatoxin levels (or penalizes high aflatoxin levels, which may be less successful). This system would provide economic incentives for the growers to pay for biocontrol, and is, most likely, the rational long-term approach. Meanwhile, public education on the health effects caused by aflatoxins and the method to manage aflatoxins at the field level must be provided regularly in order to encourage people to adopt this new technology, and change their behavior to protect themselves from aflatoxins exposure.

Postharvest intervention package: Technical feasibility

In industrial nations, food storage and processing practices usually prevent postharvest development of mycotoxins, but postharvest mycotoxin accumulation remains a threat in many LDCs. Hence, attention to key critical control points during harvesting, drying, and storage of food is essential, to reduce postharvest aflatoxin in LDCs (Magan and Aldred 2007, Wagacha and Muthomi 2008). Reducing postharvest aflatoxin accumulation can begin with simple physical methods. Mechanical sorting can separate aflatoxin-contaminated kernels from relatively cleaner ones, and proper drying can further reduce risks. To prevent the growth of *Aspergilli* in food storage, it is necessary to control moisture, temperature, and pests (Kabak et al. 2006).

Combinations of these methods to reduce postharvest aflatoxin have been tested for efficacy in actual storage conditions. Turner et al. (2005) describe a postharvest intervention package to reduce aflatoxin in groundnuts, tested in Guinea. The package consisted of six components: education for groundnut farmers on hand-sorting nuts, natural-fiber mats for drying the nuts, education on proper sun drying, natural-fiber bags for storage, wooden pallets on which to store bags, and insecticides applied on the floor of the storage facility under the wooden pallets.

After five months in the Guinea groundnut intervention study, individuals who had received and practiced the postharvest intervention package had on average 57.2% lower aflatoxin-albumin concentrations in the blood (8 pg/mg), compared with individuals in the control group (18.7 pg/mg; Turner et al. 2005). Indeed, the adduct levels in the intervention group after five months was similar to the adduct levels in both groups immediately postharvest, while the average adduct level in the control group increased by over 100%. Because this biomarker can be directly correlated with aflatoxin exposure in the diet (Wild et al. 1990), the results of the Guinea study imply that the postharvest intervention package could essentially prevent aflatoxin from accumulating beyond its immediate postharvest level, even after five months of storage. We evaluate the technical feasibility of the entire package in this study. Table 3 summarizes the characteristics of the postharvest intervention package as an aflatoxin reduction intervention in African countries that determine its overall feasibility.

Postharvest intervention package: Basic characteristics—A beneficial feature of the postharvest intervention package is that most aspects of it are simple modifications of already-existing, culturally appropriate practices. Groundnut growers throughout Africa are already employing various methods to dry and store – and even apply insecticides to – groundnuts. The intervention builds upon what is already being done, with a specific goal of reducing aflatoxin accumulation.

Hence, the package's basic characteristics are simple and not substantially different from those of current practices for postharvest groundnut treatment in Africa. The recommended drying and storage materials (natural fiber mats and bags, wooden pallets) could last 3 to 4 years if kept properly (Dr. Christopher Wild, personal communication). The mats and bags are, however, susceptible to mold and toxin contamination if not dried and stored properly; and people may use the wooden pallets for firewood or other uses if wood is scarce. The materials themselves are generally safe; the only potential health risk is through exposure to the insecticide. There is not likely to be additional risk, as insecticide recommendations for this package are based on what is already being used by growers. Most raw materials are locally available (Turner et al. 2005).

Postharvest intervention package: Delivery characteristics—In order to deliver the postharvest intervention package to groundnut growers, provisions must be made for both facilities and human resources. As described above, wooden pallets should be custom-made and sold or distributed at local markets. Natural-fiber mats and bags can likely be purchased locally or made at home, with materials from cloth retailers.

A critical issue in the success of the postharvest package is public education. Hence, the human resource requirement is possibly the most important aspect of this intervention, as well as potentially the most difficult. Farmers must be shown how to identify groundnuts that are visibly moldy or damaged, and to discard them before storage. They must be shown how to judge the completeness of sun drying (on fiber mats) by shaking the kernels to listen for the free movement of the dried nuts. They must also be educated on the proper way to store the dried nuts: in natural fiber bags, on wooden pallets, with insecticide spread underneath (Turner et al. 2005). A substantial network of agricultural extension workers is needed to provide this education in rural groundnut-growing villages of Africa, to ensure the broader adoption that can lead to population health benefits. With proper training from extension staff, individuals in communities may be able to educate and train other farmers in their communities to apply the postharvest intervention package properly. It is crucial to develop community interest and support for such an intervention to succeed.

Postharvest intervention package: Government capacity requirements—

Presuming that the insecticides used are already registered in the target countries, no special regulation is required for wide-scale adoption of the intervention package anywhere in Africa. Collaborative efforts between health and agricultural sectors would likely be beneficial in the efforts to educate groundnut growers throughout the nation, and to provide the necessary materials where growers would not be able to afford them. Funding from external agencies may be desirable to aid in the public education efforts, as well as to offset the initial costs of the packages.

Postharvest intervention package: Usage characteristics—As described above, this intervention would rely heavily on user knowledge of and adherence to practices that reduce aflatoxin in postharvest conditions. Fortunately, growers are already practicing many of these post-harvest activities (sorting, drying, storage) in some form; it is a matter of optimizing the activities to reduce aflatoxin accumulation. The activities included in this intervention are culturally appropriate for many rural groundnut growers in Africa. There may be, however, difficulties in changing current practices. A previous study on a different postharvest intervention showed that only 6.3% of farmers in the Southern Guinea Savannah adopted an improved “crib” storage structure for crops, recommended by the Food and Agriculture Organization (Hell et al. 2000), though it was promoted in those communities. Behavioral change, even if beneficial, may be slow among communities.

Postharvest intervention package: Economic issues—As with biocontrol, the main challenge to widescale adoption of the postharvest intervention package is providing the right economic incentives. Individual groundnut growers need the motivation to undergo the education and all the actions and costs needed to implement this package, which can be difficult if aflatoxin is not recognized as a significant public health or market problem. In this case, unlike biocontrol, the package cannot be applied by agricultural staff going from household to household; the growers themselves must implement the intervention. Moreover, the total package was estimated in 2005 to cost \$50 per household (Turner et al. 2005). The wooden pallet, the largest cost in the total intervention package, is the most difficult part for groundnut growers to be able to make on their own. These must be purchased or otherwise distributed from retail outlets.

Economic issues of a different nature concern the incentives of poor growers who do not understand or seriously regard the extent of aflatoxin-induced illness. First, one must consider the fate of groundnuts sorted out because of high aflatoxin levels. Even if growers are trained to do this with a high degree of accuracy (as part of the postharvest intervention package), it is not known what would happen to those contaminated nuts. If they are kept out of the marketplace, then indeed, consumers who can afford to buy nuts from markets will be better-protected. But if they are consumed by poor households who cannot afford to discard the nuts, then the poorest people in Africa would still suffer the greatest burden of aflatoxin-induced risk. Second, if wood is a scarce resource in poor households, the wooden pallets may be destroyed for alternative uses (such as firewood) rather than used for their intended purpose: to elevate the stored groundnut bags for postharvest protection against aflatoxin accumulation.

Hence, as part of this intervention package, public education on health risks of aflatoxin is absolutely crucial, to ensure the right economic and health incentives for groundnut growers to adopt the intervention and to remove highly contaminated nuts from the human food chain.

NovaSil: Technical feasibility

A variety of dietary interventions can reduce aflatoxin-related health risks. One simple dietary intervention, where feasible, is to consume relatively less maize and groundnuts, in favor of other food crops that usually have lower aflatoxin levels such as sorghum and pearl millet (Bandyopadhyay et al. 2007). Where it is not easy to make such a conversion, however (e.g., where maize and groundnuts have traditionally been staples in the diet), other dietary interventions may prove helpful. Dietary additives to reduce aflatoxin-induced risk include enterosorbents that “trap” aflatoxin in the gastrointestinal (GI) tract, facilitating elimination (Phillips et al. 2008, Egner et al. 2001); agents that induce Phase 2 enzymes to conjugate aflatoxin's reactive oxygen species in the liver (Talalay and Fahey 2001, Kensler et al. 2005, Groopman et al. 2008); or anti-inflammatory agents (Fujiki et al. 2002, Tang et al. 2008).

We focus on NovaSil clay, an enterosorbent of aflatoxin. Enterosorbents can be blended into food or feed, or taken separately (e.g., in capsule form) during mealtimes to bind aflatoxin in the GI tract, resulting in reduced aflatoxin bioavailability in the body. Several materials have varying degrees of this ability to bind aflatoxin, including bentonites, zeolites, diatomaceous earth, activated charcoal, yeast cell walls, and fibers from plant sources. One material that has proven effective in animal feed and is showing promise in human trials is calcium montmorillonite, marketed as NovaSil clay (NS). NS has been shown to prevent aflatoxicosis in many animal species when included in their diet, by binding aflatoxin with high affinity and high capacity in the GI tract (Phillips et al. 2008). Importantly, in humans, aflatoxin-albumin adducts in both low-dose and high-dose NS intervention arms were significantly lower than those in the control arm after three months, with a roughly 25% reduction: 0.89-0.90 pmol/mg adducts in albumin compared to 1.20 pmol/mg in the control arm. However, only the high-dose group shows the significant lower levels of AFM1 after three months (Wang et al. 2008).

One advantage of including NS (or other effective enterosorbents) in a comprehensive plan to reduce aflatoxin risk is that it can mitigate adverse health effects even if preharvest and postharvest conditions were conducive to high aflatoxin levels in food. NS could conceivably be used in “emergency” situations when aflatoxin levels are determined to be high in foodstuffs – by then, it is too late to change preharvest or postharvest practices to improve the food available to people at that moment, and few other options to reduce aflatoxin risk are possible. While NS does not directly reduce aflatoxin levels in food, it can reduce aflatoxin bioavailability. The feasibility of including NS as an aflatoxin risk-reduction intervention is summarized in Table 4.

NovaSil: Basic characteristics—NS is one of only several types of clays that can properly adsorb aflatoxin in the GI tract; hence, it is important to distinguish NS in any public education effort, to prevent the belief that any clay would have the same property. NS is stable under normal conditions of temperature and moisture; it loses aflatoxin-binding capacity if heated to over 200 °C for over 30 minutes (Gilbert 2008). Standardization is important, whether NS is administered in capsules or blended into maize or groundnut meals, to ensure effective and safe doses for humans. Although mild GI symptoms were reported in an initial human trial, Phase I (Wang et al. 2005) and Phase II (Afriyie-Gyawu et al. 2008) clinical trials confirm the safety of NS for use in human food, and provide assurance that it does not bind and result in elimination of nutrients such as vitamins A and E. Indeed, NS has a notable preference and capacity for aflatoxin (Phillips et al. 2008).

A regular supply of NS would be needed in aflatoxin-vulnerable regions, because of daily consumption requirements; i.e., NS should be consumed whenever aflatoxin is present at potentially risky doses in food. Because not every African geographic region has types of clays

necessary to bind aflatoxin (Phillips et al. 2008), NS (or other adsorbent clays) must be imported. Hence, it is not necessary to set up the extensive high-technology equipment and infrastructure needed to produce and maintain NS throughout Africa. However, because NS must be supplied from elsewhere on a regular basis, transportation and delivery costs may be high.

NovaSil: Delivery characteristics—Depending on the delivery method to consumers (capsules, blended into meal, or other options), NS can be purchased or distributed in food markets or local health centers. If any part of the production chain is carried out locally (including blending the clay into the meal), trained personnel are required.

If NS must be imported, as described above, transportation and delivery issues to at-risk populations are among the top priorities that need to be planned in advance. To whom, and how, will the clay be delivered, and what is the anticipated cost? Is this a universal coverage intervention? If not, which populations are the target groups? Will this intervention be used every day for an extended period of time, or only occasionally, when high levels of aflatoxin are detected in food crops? All these issues must be resolved to understand and budget for demands on delivery mechanisms.

NovaSil: Government capacity requirements—NS may be subject to regulations governing food additives in target nations. National and local governments, in collaboration with outside partners, need to make a financial investment for the initial subsidy of NS, as many of the most aflatoxin-vulnerable populations do not have sufficient funds to purchase quantities necessary to reduce risk through NS consumption on a regular basis. There is also a need for government-funded inspection and monitoring to prevent potential counterfeiting of NS products; i.e., producing and marketing clays that do not bind aflatoxin and may indeed cause adverse health effects. Depending on the delivery mechanism of NS, coordination is needed among agricultural, health, pharmaceutical, and food-related government sectors.

NovaSil: Usage characteristics—When considering who would use NS, and under what conditions, it is important to consider likelihood of adherence to a demanding regimen. For optimal effectiveness, consumers should take NS at every meal in which aflatoxin-contaminated foodstuffs (such as maize or groundnuts) were present. However, it is impossible under most circumstances for consumers to know whether their foods have high aflatoxin levels, so taking NS with *every* meal, regardless of aflatoxin exposure, is a possible recommended regimen.

If NS were administered in capsule form, many people would likely object to the idea of taking a capsule with every meal for extended periods of time, especially if they do not understand or appreciate aflatoxin-related health risks. Blending NS into maize and/or groundnut meal eliminates the problem on adherence issue and has the advantage of including the product only with foodstuffs (maize and groundnuts) that could have high aflatoxin levels.

As to whether the product itself would be accepted culturally: Geophagy, the practice of consuming clay(s), is widely accepted in many parts of Africa, as well as in several other parts of the world, such as China (Phillips et al. 2008). Certain African populations consume clay for several purposes, such as detoxifying dietary toxins, treating GI symptoms, and neuropsychological comfort (Abrahams 2003). Even though promotion of NS clay as a dietary prevention is unlikely to be difficult from a cultural standpoint, promoting the right clay is important. Public educational efforts are necessary to explain the benefits of NS-enriched meal (or NS capsules; for example, in the case of emergencies), and to direct consumers toward using the right product.

NovaSil: Economic issues—The cost of the product itself is less than one dollar per year per person for 3-gram estimated daily dose (Dr. Timothy Phillips, personal communication). Even such a low cost, however, may be unaffordable on a daily basis in certain parts of the world, where poverty is rampant and aflatoxin is a significant problem. In all likelihood, governments in collaboration with external funding agencies would need to provide the resources to deliver NS to populations in need. Indeed, this low product cost may be insignificant compared with the higher cost of transporting the material from another part of the world. NS proves most cost-effective when other methods – preharvest and postharvest – fail to prevent dangerously high levels of aflatoxin from entering the food supply. More economic research is needed on whether it is more cost-effective to only supply NS during “emergency” situations, or whether NS should become a semi-regular part of diets in certain regions of the world.

Hepatitis B vaccination: Technical feasibility

Hepatitis B is an infectious disease that affects the liver. The hepatitis B virus (HBV) can cause acute illness, characterized by GI symptoms, tiredness, jaundice, and muscle and joint pain. In about 10% of cases, HBV can also cause chronic infection, which can result in liver cancer, cirrhosis, and death. HBV is spread through contact with body fluids of an infected person. In LDCs, individuals are most commonly infected with HBV through maternal-to-child transmission. HBV is also transmitted through contact with body fluids through breaks in the skin, contact with objects that have body fluids on them, unprotected sex with infected individuals, and needle sharing (CDC 2007).

A regular practice now in the US and other developed nations, HBV vaccination in children is still rare in many parts of the world. Vaccinating children against HBV has been shown, over the last three decades, to significantly decrease HBV infection in several regions including Europe (Williams et al. 1996, Bonanni et al. 2003), Taiwan (Chen et al. 1996), and Thailand (Jutavijittum et al. 2005). This vaccine has already had, and will continue to have, significant impacts on liver cancer incidence, particularly in Africa and East Asia.

Though the HBV vaccine itself does not affect actual aflatoxin levels in diets, it reduces aflatoxin-induced HCC by lowering HBV risk, thereby preventing the synergistic impact of HBV and aflatoxin in inducing liver cancer. For individuals who are chronically infected with HBV (common in China and Africa), aflatoxin consumption raises by up to thirty-fold the risk of liver cancer compared with either exposure alone (Groopman & Kensler 2005). Hence, lowering the risk of chronic HBV infection through HBV vaccination could reduce by 30 times the risk of aflatoxin-induced liver cancer, and may also play some role in reducing aflatoxin-induced cirrhosis (Kuniholm et al. 2008). However, the vaccine may not prevent other adverse effects caused by aflatoxin (e.g., immunomodulatory effects). The feasibility of including the HBV vaccine as an aflatoxin risk-reduction intervention is summarized in Table 5.

HBV vaccine: Basic characteristics—The HBV vaccine is made from a part of the virus, and cannot cause infection. It is usually given as a series of 3 or 4 shots, each one conferring ever-greater protection against chronic HBV infection risk. It is recommended that all children receive their first dose of HBV vaccine at birth, because of the maternal-to-child transmission risk (Kew 2002, Francois et al. 2008) and complete the vaccine series by 6-18 months of age. Additionally, any child, adolescent, or adult who has not been previously vaccinated should receive the vaccine (CDC 2007).

To maintain product stability, the vaccine should be stored between 36-46 °F (refrigerated, but not frozen; Drugs.com 2009). Generally, vaccines have been standardized during their manufacturing processes. This is necessary to ensure that all vaccine doses are the same, and

at safe and effective doses, for the target population. The HBV vaccine has been used for decades safely, with low risk of significant side effects; the most common side effect is pain and swelling at the site of injection (NFID 2009). However, it is crucial that needles be kept sterilized and not shared, and that the vaccine remains refrigerated at all times before use.

One main technological challenge for many parts of rural Africa lies in providing and maintaining cold storage for the vaccines (Francois et al. 2008). Cold storage is difficult where electricity is not available. Indeed, the rate of accessibility to electricity in sub-Saharan African populations was approximately 15% in 2005 (Estache 2005). It is also not optimal for individuals to have to travel too far in order to receive the vaccine (e.g., to the clinic of the nearest village that does have electricity), as incentive to receive the vaccine may decrease. Other types of equipment/supplies needed include needle syringes and antigen-antibody titer checks. A regular supply of the vaccine is needed throughout populations in Africa, to vaccinate children when they are born, and to others who have not previously received the vaccine.

HBV vaccine: Delivery characteristics—Vaccines could be delivered in at least two different general methods in Africa, to reach as much of the population as possible. One is to deliver the vaccine at existing hospitals, clinics, and other health care centers. This would be the main means by which to reach urban populations and more technologically sophisticated villages.

Another option is to deliver the vaccine through a mobile vaccination service, traveling door-to-door as necessary with cold storage in the medical vehicle: focusing at first on reaching everyone who had never been previously vaccinated, then focusing primarily on reaching newborn babies (if possible). Even if it were impossible to perfectly target the households with newborn babies, simply vaccinating the mothers in a broad vaccination outreach could dramatically reduce the risk of HBV transmission to babies. To this end, the vaccine must be kept cold but not frozen during transport. It is recommended to use frozen packs for hot-weather conditions or refrigerated packs for cold-weather conditions during transportation. Proper insulation such as crumpled paper or bubble wrap should be used to keep the vaccine from direct contact with frozen pack or shifting during transport. Moreover, insulated containers should be kept in a cool place in the vehicle if possible (Immunization Action Coalition 2006). Even with this mobile vaccination option, reaching a broad population in Africa may be difficult; as averaged transport access rate by road in sub-Saharan Africa in 2005 ranged from 60% – 70% (Estache 2005).

Vaccines must be provided by a reliable source to ensure efficacy, cleanliness, and proper dosage. Nurses, medical assistants, or other trained personnel can administer the vaccines. Aside from administration of the vaccine, outreach services should also be provided to educate the public on the importance of vaccination and completing the recommended regimen.

HBV vaccine: Government capacity requirements—Initiating, preparing, and maintaining a vaccination program is an extremely complex task; and requires governmental coordination at the administrative, technical, medical, logistic, educational, financial, and political levels (Francois et al. 2008). Clinics and other health care centers must be connected with vaccine supply outlets, and staff should be trained on how to properly administer the vaccines, especially to avoid cross-contamination through needles.

External funding is almost certainly necessary in most sub-Saharan African countries, because in order to achieve widespread immunity to the disease among a population, continuity of the program is a vital part. Fortunately, the Global Advisory Group of the Global Alliance for Vaccines and Immunization (GAVI), supported by UNICEF, WHO, and the Bill and Melinda

Gates Foundation, has specifically recommended that HBV vaccination be integrated into national immunization programs in all countries of the world (Manzila et al. 2002). GAVI provides funds and other resources to implement HBV vaccination in nations whose gross national income is below 1000 USD per capita per annum. Hence, most sub-Saharan African nations qualify for GAVI assistance, and efforts have been made to spread HBV vaccination there since the early 1990s. Yet as of 2008, 20% of all unvaccinated children globally were in sub-Saharan Africa (Francois et al. 2008). (The only place in the world that has a greater number of HBV-unvaccinated children is India.) African nations that accepted GAVI aid now have between 50-96% coverage of infant HBV vaccination, while Nigeria, which qualifies but did not accept GAVI aid, has HBV vaccination coverage of only 27% (Francois et al. 2008).

HBV vaccine: Usage characteristics—The goal of any vaccination program is to immunize as many individuals as possible, so as to prevent spread of the disease. It is important to promote and educate about the HBV vaccination program to encourage individuals to complete their vaccination regimen (3 boosters on average to provide near-lifetime immunity). For example, for individual boosters, coverage rate of HBV immunization in a large cohort of infants in Venda, South Africa dropped rapidly from 99% to 53% and 39% for the first dose, second dose, and third dose, respectively (Schoub 1991).

HBV vaccine: Economic issues—Economic considerations for the HBV vaccine are not substantially different from those of other common vaccines in less developed countries. The vaccine itself is extremely inexpensive, considering its lifetime benefit: less than \$1 per dose (Evans and Kaslow 1997), with three doses are recommended per individual to provide up to 95% efficacy in HBV protection (Viviani et al. 1997).

Even so, in order to impact as many people as possible, HBV vaccination programs in relatively poor African nations may require external funding to be initiated and/or sustained. Currently, as described above, HBV vaccination in several African countries is financially supported by GAVI. As a result of GAVI funding and other resource support, HBV vaccination among infants has increased enormously in the last decade (Francois et al. 2008). Still, there are many African nations that do qualify for GAVI funding but have not yet applied for it.

Economic issues surrounding HBV vaccination in Africa are largely out of the hands of individuals. Governments need to decide that HBV vaccination is a priority, and to contribute funds or apply for funds in order to reduce the burden of HBV-related disease. As populations in many of these nations are also vulnerable to high aflatoxin levels in their food, reducing HBV risk becomes an even more important problem, regarding liver diseases such as cancer and cirrhosis. This information on the synergistic risks of aflatoxin and HBV should be conveyed to governments to emphasize the importance of reducing either, or both, risk factors.

Discussion

No one intervention to reduce aflatoxin risk in Africa emerges as being “most feasible” in all categories. Each has its unique benefits and drawbacks for wide-scale adoption in Africa. For example, biocontrol is highly cost-effective and reduces aflatoxin at its earliest stages. However, professional staff and training requirements may be high. The postharvest intervention package has the benefits of cultural appropriateness and adaptability to multiple different local settings, as well as low technology and equipment requirements. However, there is a high public education component for proper sorting and drying practices, and compliance requirement for health benefits. NovaSil may prove a life-saver in emergency situations when preharvest and postharvest means have failed in keeping high aflatoxin levels out of food, but long-term public adherence may be problematic. The HBV vaccine has high global-level

support and needs only be administered three times in a lifetime to ensure high protection against liver-related diseases, but clinical and facility requirements are high.

As different as these interventions are from each other, certain general trends emerge from a technical feasibility study. The first is that public and governmental education on aflatoxin risk is absolutely crucial to provide economic incentives to adopt interventions. Even if an intervention to reduce aflatoxin risk is cost-effective, in terms of lives saved and quality of life improved (Wu and Khlangwiset 2009), there may still be no incentive to implement it unless health and market effects of aflatoxin are fully understood. It is worth noting that aflatoxin exposure in Ghana has been shown to be significantly correlated with farmers' knowledge of aflatoxin risk (Jolly et al. 2006), while farmers' knowledge of aflatoxin risk in Benin has been correlated with the motivation to implement aflatoxin-reduction interventions (Jolly et al. 2009).

Education must take place in at least three different levels. Government policymakers must first receive information about the burden of aflatoxin-induced disease in their nations – both in terms of health and market effects – as well as information about possible interventions, their cost-effectiveness in reducing aflatoxin, and their technical feasibility requirements. Obtaining the appropriate information will motivate them to provide the finances and other resources necessary to initiate the interventions. Also, depending on the intervention characteristics, either the farmers, or the consumers, or both these groups must receive education on why aflatoxin is a concern and how to implement the intervention in question. Finally, international health and agricultural organizations must be informed about the extent to which aflatoxin can affect both food markets and public health. This will provide incentive to aid nations in which aflatoxin is still a significant problem in food.

The second trend is that interventions would ideally be combined in a suite to solve aflatoxin problems in LDCs. The ones analyzed in this study represent preharvest, postharvest, dietary, and clinical solutions to the problem. Each one, taken alone, could reduce a significant burden of aflatoxin risk; but potential failures in the overall system could result in gaps through which high contamination events could occur. Biocontrol would help reduce preharvest aflatoxin accumulation from the start, to ameliorate any potential problems further along the food chain. The postharvest intervention package significantly reduces aflatoxin in storage so that even food stored for longer periods of time would have greater safety. NovaSil can serve as an enterosorbent to reduce aflatoxin risk in cases where food is already highly contaminated. The HBV vaccine lowers the overall risk of specific liver diseases for which aflatoxin is a risk factor.

The third trend is that, after appropriate funds are obtained, *delivery* of the intervention to people and places in need may be the most significant challenge to implementing aflatoxin risk-reduction interventions. In three of the four case studies described in this study, the delivery would cost more than the intervention itself – in some cases, significantly more. The one exception is the postharvest intervention package, whose materials can be obtained locally. In the other cases, either the intervention must be imported, or significant effort is needed to establish the equipment and personnel necessary in various parts of the country to reach the target population.

Understanding constraints to feasibility of interventions aids scientists and policymakers to think beyond efficacy, and even beyond material costs. For interventions to succeed in less developed countries, governments, scientists, international organizations, farmers, and consumers must work collaboratively to overcome challenges in implementing the intervention – challenges in terms of human resource needs, equipment and technology and transportation

requirements, financial aid, and user adoption constraints. Feasibility analyses can indicate research and development priorities in order to improve likelihood of adopting interventions that can improve public health and market outcomes.

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Figure 1.
Framework to assess technical feasibility of public health interventions.

Table 1

Sampling of interventions to reduce aflatoxin risk in field, dietary, and clinical settings.

Setting		Intervention
Agricultural	Preharvest	<ul style="list-style-type: none"> • Suitable hybrid choice • Transgenic or conventional breeding for plant host resistance • Biocontrol • Chemical control (insecticides, fungicides) • Good agricultural practices • Antioxidants (e.g., caffeic acid, gallic acid)
	Postharvest	<ul style="list-style-type: none"> • Cleaning • Mechanical sorting and segregation • Improved storage / drying / transportation conditions • Ammoniation • Ozonation • Chemical control (insecticides, fungicides)
Dietary		<ul style="list-style-type: none"> • Enterosorbents (e.g., calcium aluminosilicates, glucomannan, chlorophyllin) • Chemopreventive agents (e.g., Oltipraz, isothiocyanates, triterpenoids) • COX-2 inhibitors • Green tea polyphenols
Clinical		<ul style="list-style-type: none"> • HBV vaccination

Table 2

Technical feasibility characteristics of biocontrol for aflatoxin control in Africa.

Category	Criteria	Intervention
Intervention Characteristics		
Basic product design	Stability	Shelf life ~ 6 months; dependent on temperature and moisture control
	Standardization	Needed to ensure that each application unit of biocontrol contains sufficient amounts of living nontoxigenic fungi to competitively exclude toxigenic fungi
	Safety profile	Low risk of inhalation aspergillosis and skin and eye irritation; minimal risk of toxicity and infectivity
	Ease of storage and transportation	Must be stored and transported at low relative humidity and avoiding either temperature extreme
Supplies	Need for regular supplies	Nontoxigenic spores must be maintained in cultures, and grains must be provided regularly as a substrate
Equipment	High-technology equipment and infrastructure needed	Equipment to manufacture and maintain fungal spores, sterilize substrate, and mix spores and substrate with a binder
Delivery characteristics		
Facilities	Retail sector	Needed if biocontrol application is done by farmers
	Outreach services	Monitoring proportion of nontoxigenic spores in the field to ensure continued effectiveness Educating growers on why aflatoxin is an important problem, and how to optimally apply biocontrol
	Laboratories	See "Equipment" above
Human resources	Trained scientific professionals	Professional staff to produce and maintain nontoxigenic spores, operate equipment to produce all parts of biocontrol, and to apply it (in situations where farmers cannot themselves)
	Outreach staff	Community volunteers, agricultural and health care providers to highlight the importance to control aflatoxin in food and feed stuffs. Laboratory workers to routinely monitor aflatoxin levels in agricultural goods. Agricultural extension service to provide advice, suggestion or recommendation on biocontrol.
Communication and transport	Dependence of delivery on communication and transport infrastructure	Crucial for biocontrol to reach diverse parts of African countries where maize and other aflatoxin-vulnerable crops are planted
Government capacity requirements		
Regulation/legislation	Need for regulation	Need for biopesticide registration in African countries
	Need for monitoring and enforcement	Need for aflatoxin monitoring in agricultural goods

Category	Criteria	Intervention
		Need for monitoring potential health effects produced by biocontrol agents (e.g., skin irritation, aspergillosis)
		Need for monitoring potential changes in toxigenicity of nontoxigenic fungi
Collaborative action	Collaborative efforts within government sectors and between government and other groups	<p>Collaborations among ministries of agriculture and health could provide a stronger basis for biocontrol as a means of improving public health through farming technologies.</p> <p>International organizations (e.g., IITA, WHO, Foundations) have made, and should continue to make, important contributions toward aflatoxin reduction in Africa (funding, staff, etc.).</p>
Usage characteristics		
Ease of usage	Need for information, education, supervision	If biocontrol application in hands of farmers: instructions can be printed on packages, agricultural outreach staff can assist and supervise in some areas. More broadly, education is needed to inform farmers why aflatoxin is an important problem and how biocontrol can reduce risk.
Pre-existing demand	Need for promotion	Little if any pre-existing demand for biocontrol in most African nations; promotion essential among farmers
Black-market risk	Need to prevent counterfeiting	Counterfeiting is possible but unlikely: toxigenic fungi could be packaged and sold as biocontrol to farmers

Table 3

Technical feasibility characteristics of postharvest intervention package for aflatoxin control in Africa.

Category	Criteria	Intervention
Intervention Characteristics		
Basic product design	Stability	Drying/storage materials could last for 3-4 years if kept properly
	Safety profile	Extremely safe. Only potential health risk concerns insecticide use; not expected to be a problem if already locally available and a familiar product to farmers.
	Ease of storage and transport	Most raw materials are locally available; fiber mats and bags and pallets may need to be stored away from moisture and pests to extend lifetime
Supplies	Need for regular supplies	Drying/storage materials could last for 3-4 years if kept properly
Equipment	High-technology equipment needed	None; entire intervention relies on community-based technology and materials
	Maintenance needed	Fiber bag, mat and wooden pallet can become contaminated with fungi; sun drying and proper storage after use may reduce risk
Delivery characteristics		
Facilities	Retail sector and outreach services	If drying and storage materials are not made by each household, large scale production of these materials could be an option (e.g., for pallets). Local retail stores could provide the finished mats, bags, and pallets.
Human resources	Skill level required for service provision	Community volunteers/ agricultural extension staff or local agricultural authorities, to educate growers on the risks of aflatoxin and the methods of using the complete intervention to reduce aflatoxin
Government capacity requirements		
Regulation / legislation	Need for regulation	No special regulation required
Collaborative action	Collaborative efforts within government sectors and between government and other groups	Collaboration between health and agricultural sectors, as well as between national and local level governments, is important. Outreach staff are an important part in this community based intervention.
		Funding from external agencies may be desirable to offset the initial costs of the packages.
Usage characteristics		
Ease of usage	Need for information/education	While the need for information and education is high (e.g., hand-sorting, drying, specific storage requirements), usage itself should be simple because of the cultural familiarity of the overall practices

Category	Criteria	Intervention
Pre-existing demand	Need for promotion	Though the practices of drying and storage are familiar, the specifics (e.g., wooden pallets, fiber mats and bags) may not be, and growers may not understand the need for them. Hence, the need for promotion is crucial.
Black-market risk	Counterfeit prevention	Low risk of counterfeiting

Table 4

Technical feasibility characteristics of NovaSil clay for aflatoxin risk reduction in Africa.

Category	Criteria	Intervention
Intervention Characteristics		
Basic product design	Stability	Stable under normal conditions; loss of binding capacity (primary mechanism to reduce aflatoxin bioavailability) if heated ≥ 200° C over 30 minutes (Gilbert 2008)
	Standardization	Needed for human consumption purposes, to ensure reliable dose whether in capsule form or blended in meal
	Safety profile	No significant changes in hematology, liver, kidney function, vitamin A and E levels, and mineral levels. Mild gastrointestinal symptoms have been observed. Sterilization and standardization necessary.
	Ease of storage / transport	No special requirements for storage. Transportation is needed from other parts of world where clays have shown aflatoxin-binding properties and can be sterilized and standardized.
Supplies	Need for regular supplies	A regular supply is needed in aflatoxin-vulnerable regions, because of daily consumption requirements
Equipment	High-technology equipment and infrastructure needed	If imported, no local high-technology equipment is needed. If produced locally, sophisticated manufacturing and packaging equipment is needed.
Delivery characteristics		
Facilities	Retail sector and outreach services	Depending on delivery method (capsules, blended into meal, etc.), can be purchased or distributed in food markets or local health centers
Human resources	Skill level required for service provision	Staff are needed to distribute NS in the appropriate manner to the general public (e.g., blending the product into meal, selling or providing caplets). If production is done locally, trained scientists are required for manufacture and maintenance of the product.
Government capacity requirements		
Regulation/legislation	Need for regulation	May be subject to food additive regulations in target nations
	Need for monitoring and enforcement	Monitoring needed to prevent potential counterfeiting / inappropriate health claims of untested clay
Management systems	Need for sophisticated management systems	Need for government financing and management to subsidize NS if it is incorporated in major food products, or if distributed for free in capsule form. It is also necessary to manage potential risks of counterfeiting and compliance (Gilbert 2008).
Collaborative action	Collaborative efforts within government sectors and between government and other groups	Depending on NS's delivery mechanism, coordination is needed between agricultural, health, pharmaceutical, and food-related governmental sectors.
		Community volunteers can help government to monitor inappropriate use or the presence of counterfeiting.
		Because this intervention requires continuous action (monetary support), funding from international organizations may be crucial.
Usage characteristics		

Category	Criteria	Intervention
Ease of usage	Need for information/education	In aflatoxin-vulnerable areas, education is needed on when, why, and how often to consume NS. May be difficult for individuals to remember or to desire to take NS capsules with each meal, so alternative delivery mechanisms should be considered (e.g., blending NS into maize or groundnut meal).
Pre-existing demand	Need for promotion	Geophagy is common in certain parts of world; however, there is a need to promote NS specifically as distinguished from common clays, and why aflatoxin is an important risk to control.
Black-market risk	Need to prevent resale/counterfeiting	Potential risk of counterfeiting with common clays that do not adsorb aflatoxin in the GI tract

Table 5

Technical feasibility characteristics of Hepatitis B vaccination for aflatoxin risk reduction in Africa.

Category	Criteria	Intervention
Intervention Characteristics		
Basic product design	Stability	Vaccine should be stored between 2°C to 8°C (refrigerated, not frozen) (Drugs.com 2009)
	Standardization	Necessary to ensure that all vaccine doses are the same for a given target group, and safe for that group
	Safety profile	This vaccine is very safe. The most common side effect is pain at the site of injection. There is no clear association to other serious side effects (NFID 2009). However, it is crucial that needles be kept sterilized and that vaccines be kept refrigerated.
	Ease of storage and transport	Vaccines require cold storage (See above; applies to transportation conditions as well)
Supplies	Need for regular supplies	To reduce HBV prevalence, multi-generation vaccination is needed. Therefore regular supply of vaccine is required
Equipment	High-technology equipment and infrastructure needed	Cold storage is necessary to preserve the vaccines, which can be a challenge in areas without electricity. Existing infrastructures in hospitals and other health centers can facilitate vaccination.
	Number of different types of equipments	Temperature controlled chambers/containers Needle syringe Antigen-antibody titer check
Delivery characteristics		
Facilities	Retail sector	Vaccines must be provided by a reliable source to ensure efficacy, cleanliness, and proper dosage
	Outreach services	Mobile vaccination services (door-to-door) may be possible and desirable in certain communities
	First level care	Community education on HBV's health effects and how to prevent infection is desirable
	Hospital care	Clinics can provide vaccination to infants and previously unvaccinated, uninfected people
Human resources	Skill level required for service provision	Nurses, medical assistants or other trained personnel to administer vaccines
	Skill level required for staff supervision	Medical staff required
	Intensity of professional services (frequency/duration)	Regular service is required to supply vaccines to health care facilities
	Management and planning requirements	Because this vaccine is not locally manufactured in most of the high-HBV-prevalent countries, planning and management of vaccine inventories and funding are two requirements. Planning should also cover how the vaccine reaches the target population, evaluation, and up-scaling of the program.

Category	Criteria	Intervention
Communication and transport	Delivery dependence on communication and transport infrastructure	Cold storage needed. To reach large proportions of the target population, it is important to distribute this vaccine to every part of the country: all local clinics and health centers, if possible.
Government capacity requirements		
Regulation/ legislation	Need for regulation	No special regulation is required, but government must see HBV vaccination as priority to mobilize resources
Management systems	Need for sophisticated management systems	Clinics and other health care centers must be connected with vaccine supply outlets, and staff should be trained to administer vaccines.
Collaborative action	Collaborative efforts within government sectors and between government and other groups	Health departments within each nation should coordinate with each other and international health organizations to provide vaccines regularly where needed. External funding is necessary, because in order to achieve widespread vaccination, continuity of the program is a vital part. Without external funding or support from external agencies, it can be difficult for poorer nations to maintain this program.
Usage characteristics		
Ease of usage	Need for information / education	Individuals must understand need for vaccine as well as where and how often to obtain it, for themselves and their children.
Pre-existing demand	Need for promotion	Vaccination has already been promoted in many African nations, but especially in rural areas, greater effort is needed to educate the public on benefits of vaccines.
Black-market risk	Need to prevent resale/ counterfeiting	Low risk of resale or counterfeiting