Aflatoxin and the Food Quality Protection Act of 1996

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Introduction

After years of debate and Congressional hearings, the nation's laws regulating food uses of pesticides were amended in 1996. The Food Quality Protection Act of 1996 (FQPA) requires the EPA to consider additional risk factors while reducing the consideration of benefits of a pesticide's use when establishing food tolerances for carcinogenic compounds. One benefit that Congress explicitly directed USEPA to consider under the new Law concerns the presence of naturally-occurring mycotoxins in foods. If a carcinogenic pesticide reduces the presence of a carcinogenic naturally-occurring compound in foods, the EPA is to determine which compound poses the greater risk. Congress used a hypothetical example to illustrate the application of this benefit provision. Since EPA has begun implementing the FQPA, it is appropriate to determine the extent to which pesticides are used currently to reduce the presence of cancer-causing, naturally-occurring compounds in foods.

The Food Quality Protection Act

In August 1996, President Clinton signed into law The Food Quality Protection Act (FQPA), which had passed both houses of Congress unanimously. The FQPA amends the two laws that regulate pesticide use in the United States -- The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Federal Food and Drug and Cosmetic Act (FFDCA). FIFRA directs EPA to register and label all pesticide products used in the United States. FFDCA requires EPA to assign pesticide residue tolerances (maximum residue limit) to each pesticide that has been labeled to be used on food consumed by humans. A separate tolerance is assigned to each crop included on the pesticide label. The tolerances are designed to help protect the public against exposure to potentially harmful chemical residues that may be found at low levels on food products.

Most major environmental statutes are risk-driven and prohibit consideration of economic costs in setting health-based standards. FIFRA is one of the few statutes

administered by EPA that explicitly requires the Administrator to consider the risks and benefits of a chemical. If in some or all circumstances, a chemical's risks outweigh its benefits, regulatory action is taken to restrict or ban its continued use. Conversely, if EPA determines that a pesticide's benefits outweigh its risks, its registration is continued. However, since policymakers were concerned that health risks were not being adequately addressed by FIFRA, Congress included provisions in the FQPA to broaden the consideration of human health risk factors before a tolerance may be granted.[28]

In particular, the new law emphasizes the health risks pesticides pose to children and infants. Evidence suggests that they are more likely than adults to experience health problems associated with exposure to pesticide residues. Two of the provisions of the FQPA are particularly noteworthy. First, the FQPA mandated EPA to develop a comprehensive screening program to determine if each pesticide is capable of disrupting the endocrine system. Second, the FQPA requires EPA to assess the potential risks associated with aggregate pesticide exposure. Previously, EPA only considered exposure to pesticide residues in food. Now, all exposure pathways, including water and residential uses, are considered. Further, the residues of compounds that have the same mode of action, such as the organophosphate insecticides, must be jointly considered if two or more are used on the same food commodity. Prior to FQPA, pesticide risks were considered individually.[28]

The FQPA also significantly reduced EPA's mandate to consider the benefits of pesticides when the Agency assigns tolerances. Under the old Law, EPA was required to consider the benefits of retaining the tolerances previously granted for carcinogenic pesticides that posed non-negligible risks. Among other things, the benefit considerations included the economic impacts, such as higher producer and consumer costs, that would result if certain pesticides were removed from the market. Under the new Law, the benefits derived from using carcinogenic pesticides are only considered

if at least one of two conditions exists. First, the pesticide protects consumers against adverse health effects that are greater than the health risks posed by the pesticide itself. Second, the pesticide is needed to avoid a significant disruption of the domestic production of an adequate, abundant and economical food supply. If either of these conditions is met, the EPA Administrator may leave a tolerance in effect, even if it poses a non-negligible cancer risk.

The legislative history of the Food Quality Protection Act makes clear congressional intent to protect consumers from adverse health effects that pose a greater risk than the dietary risk from the pesticide chemical residue. In this instance, eating food treated with the pesticide chemical is safer for consumers than eating the same food that is not treated with the pesticide.[27] To illustrate this condition, the legislative history uses the example of aflatoxin, a naturally-occurring, cancer-causing fungus. Congress recognized that there currently are no pesticides that directly kill the aflatoxin fungus. However, Congress used the hypothetical example that if such a pesticide were to be developed, it would be a candidate for a tolerance, even if it posed a non-negligible cancer risk if its dietary risks were lower than the dietary risks of aflatoxin.[27]

Although Congress was correct in concluding that no pesticide currently in use controls aflatoxin directly, several currently used pesticides control insects that spread aflatoxin. By controlling the insects, these insecticides are important in limiting aflatoxin to low levels in food. Several of the insecticides that help to limit aflatoxin contamination are in the organophosphate class of chemistry, which is the first group of chemicals that EPA has designated for consideration under FQPA's aggregate risk and common mechanism of toxicity requirements. Thus, in considering whether to maintain current tolerances of organophosphate insecticides, that may pose a greater than non-negligible cancer risk, the EPA must consider whether eliminating their use would lead to a greater risk of aflatoxin ingestion, that, in turn, may lead to a greater risk of cancer. The benefits conferred by organophosphate pesticides in reducing cancer risks must be

included as part of the review. If their cancer reducing benefits are greater than their cancer risks, some of the organophosphate pesticides may be granted tolerances.

Background of Aflatoxin

Aflatoxins are powerful tasteless, odorless and colorless mycotoxins, which are chemical metabolites, produced by certain strains of *Aspergillus* fungi. Aflatoxins are mutagenic, carcinogenic, teratogenic and acutely toxic to most animals and humans.[22] They can cause animals, including humans, to lose their appetite, decrease their feeding efficiency, and / or cause death.[14] Evidence suggests that aflatoxins are one hundred times more likely to induce cancer than polychlorinated biphenyls (PCBs).[16] When aflatoxin is present in the grain fed to dairy cows, it metabolizes and forms other carcinogenic compounds that eventually find their way into milk. Aflatoxins also inhibit the body's immune system and reduces the effectiveness of vaccines. For example, an outbreak of hepatitis in India was linked to moldy corn that contained aflatoxin.[14] It also was found in the tissue of Asian children who suffered from Reye's syndrome. Concern exists for possible adverse effects from long-term exposure to low levels of aflatoxins in food.[21] A major concern is the possible role of aflatoxin exposure in the development of liver cell cancer.[21] Ten to twenty parts per billion of aflatoxin consumed regularly by sensitive young animals can result in fatal liver cancers.[14]

In the United States, the aflatoxins are the only mycotoxins that are specifically regulated.[21] Aflatoxins are regulated under the Food, Drug, and Cosmetic Act (FFDCA). In 1965 the FDA established specific guidelines for acceptable levels of aflatoxins in human food and animal feed (*i.e.*, action levels) that allow for the removal of violative lots from interstate commerce.[21] The action levels for human food are 20 parts per billion (ppb) total aflatoxins, with the exception of milk, that has an action level of 0.5 ppb for aflatoxin M_1 (a metabolite of aflatoxin B_1).[21] For feeds the action level for aflatoxins is also 20 ppb with the exception of a 300 ppb action level for

aflatoxins in cottonseed meal used in feeds, a 300 ppb action level for corn used for finishing (feedlot) beef cattle, 200 ppb for corn destined for finishing swine (*i.e.*, >100 lbs.), and 100 ppb aflatoxins in feeds used for breeding cattle, breeding swine, and mature poultry.[21]

There have been several serious outbreaks of aflatoxin which have caused significant agricultural losses. In 1977, aflatoxin contaminated more than sixty percent of the corn grown in the southeastern portion of the U.S.[14] In 1988, a severe drought in the Midwest caused aflatoxin to contaminate between 5 and 25 percent of the region's corn crop.[16] After the aflatoxin was discovered, a significant amount of milk, which had been produced in more than five states, had to be destroyed because the dairy cows had been fed aflatoxin tainted corn.

Although many fungi are controlled with chemicals, the *Aspergillus* fungi have proven largely immune to tested pesticides.[4] In order to minimize aflatoxin contamination in crops, a variety of approaches are used, including the use of insecticides to control insects that spread the fungal infestations. Aflatoxin causing fungi live on dead plant debris, producing spores that are distributed by wind and insects.

Aflatoxin and Peanuts

The fungi which produce aflatoxin are commonly found in the light soils used to grow peanuts.[3] Peanuts are frequently contaminated by aflatoxin if their pods develop during drought conditions and / or if the pods are partially eaten by an insect -- the lesser cornstalk borer. Prior to 1960, the contamination of peanuts by aflatoxin was not considered to be a significant problem. By 1960, the peanut industry was much more concerned after it was discovered that animals had been poisoned by aflatoxin.[1] For example, farmers in Georgia reported that their swine had been poisoned after consuming moldy peanuts. Also, more than one hundred thousand turkeys in England died after they consumed moldy peanut meal.[1] Hot and dry conditions that favor

development of aflatoxin also favor population outbreaks of the lesser cornstalk borer. The caterpillars inhabit the upper soil and feed on plant stalks at or just below the soil surface.

When the cornstalk borer larvae feed on peanut pods, they often weaken or pierce the shell. This provides a point of entry for the aflatoxin producing fungi.[24] The amount of aflatoxin found in seed penetrated by insects is thirty to sixty times greater than the aflatoxin levels found in undamaged pods.[5] Tests conducted in Alabama during 1990 found a 94 percent correlation between damage caused by the lesser cornstalk borer and the number of aflatoxin producing fungi.[3] Peanut field studies found that over 50 percent of the lesser cornstalk borer larvae sampled were contaminated by aflatoxin fungus spores. Researchers also have found propagules of aflatoxin fungus in the gut of the lesser cornstalk borer larvae.[5]

Research has shown that the judicious use of pesticides significantly reduces the damage to peanut pods caused by the lesser cornstalk borer. Thus, insecticides indirectly reduce aflatoxin levels found in peanuts. When peanuts are treated with a single application of the organophosphate insecticide chlorpyrifos thirty days after planting, and again either forty-five or seventy-one days after planting, the damage caused by the lesser cornstalk borer larvae and the levels of aflatoxin are consistently lower than when no insecticides are applied.[3] Chlorpyrifos reduces the insect's population by approximately 80 percent, while the most efficacious non-organophosphate insecticide reduces the population by approximately 40 percent.[17] Insecticide treatments for lesser cornstalk borer control in peanuts have been rising in recent years because of a succession of drought years and recent research that shows the relationship between lesser cornstalk borers and aflatoxin in peanuts.[25]

Aflatoxin and Cotton

Cottonseed produced in California and Arizona is used to feed dairy cows in a number of states. Unfortunately, the cottonseed can be a significant source of aflatoxin. Cotton plants become infested with aflatoxin when the cotton bolls are open and/or when chewing insects, such as the pink bollworm and *Heliothis*, chew holes in the bolls.[6] In Arizona and the Imperial Valley of California, 100 percent of the cotton acreage is infested with pink bollworms.[19] The holes enable fungus spores to reach the moist lint which then germinate and grow on the lint fibers. Eventually, the fungus enters the cottonseed and produces aflatoxin which is a by-product of its normal metabolic activity. Research has shown that all of the highly contaminated cotton lots (>10,000 ppb of aflatoxin) are from bolls that have been damaged by the pink bollworm.[9] Over 90 percent of the total aflatoxin detected in one experiment was in seed produced from pink bollworm damaged bolls.[7]

The fungus is only able to infest cotton plants if the temperature and humidity are high and the moist lint is exposed. When night temperatures consistently fall between 70°F and 75°F, which is the case in most cotton growing areas, infection levels are generally low. However, in the deserts of Arizona, California and the Rio Grande Valley of

Texas, aflatoxin production is usually high between early August and mid-September due to the prevailing high temperatures and humidity.[6]

Prevention of aflatoxin contamination is based on a strategy of preventing pink bollworm damage to bolls in the early and the middle of the season.[8] Research has demonstrated that chemical control of the pink bollworm reduced amounts of bright greenish-yellow fluorescence associated with aflatoxin producing fungi. Levels of aflatoxin were maintained below 20 ppb when populations of pink bollworm were held at or below the economic threshold, but this was only achieved by numerous insecticide applications.[15] Pink bollworm infested acres are treated approximately three times with insecticides, including the organophosphate insecticides azinphos methyl and methyl parathion.[19]

Aflatoxin and Corn

Aflatoxin contaminates corn grown in the cornbelt and in the southern states.[13] Insects act as a vector for aflatoxin contamination of corn. Research has shown that aflatoxin levels are higher on corn damaged by insects than on undamaged corn ears.[14]

Corn earworms are responsible for much of the spread of aflatoxin since they cause breaks in the pericarp that have been linked to increased aflatoxin production.[12] When insecticides were used during experimental trials to control corn earworms, the incidence of corn plants infected with aflatoxin was much lower.[11] However, at present, insecticides are not used to reduce the corn earworm population in field corn. As a result , during years in which aflatoxin production is favored and field corn becomes contaminated, it has sometimes been necessary to allow aflatoxin contaminated grain to be diluted with other grains to reduce the aflatoxin level below 20 ppb. For the 1988 corn crop, the FDA allowed a blending of corn containing aflatoxins with non-contaminated corn to produce a total level of contamination below

the action levels for animal feeds only.[26] The use of insecticides to control insects in the field has been proposed as a means of eliminating most of the toxic contamination of field corn.[10]

Insecticides are used to control corn earworms on sweet corn since marketing standards regarding insect damage are much more stringent. In Florida, the largest domestic producer of sweet corn for the fresh market, experiments have shown that without pesticide applications, essentially 100 percent of the sweet corn would be infested with corn earworms.[20] Insecticides, which include the pyrethroids, thiodicarb and methomyl, are usually applied between seven and fifteen times to prevent corn earworms from damaging Florida sweet corn.[18]

Aflatoxin and Almonds

The two major insect pests of California almond orchards are the navel orangeworm and the peachtwig borer. Navel orangeworm larvae enter damaged nuts and go directly into the kernel to feed. Aflatoxins are associated with almond kernels damaged by navel orangeworm larvae.[22] The larvae attack the almond fruit while they are still drying on the tree. During drying, high temperatures in the orchard and moisture in the hulls provide an environment especially suited for the production of aflatoxin. Research has shown that the most direct means of controlling aflatoxin contamination of almonds is to reduce insect damage.[22] Early season feeding damage from the peachtwig borer creates openings for the navel orangeworm to enter. The frass excreted by peachtwig borer larvae attract navel orangeworm females to damaged nuts. Navel orangeworm do not attack undamaged nuts.

Since in-season applications of insecticides provide only 50 to 60 percent control of navel orangeworm, non-chemical controls and dormant season controls are recommended. The current recommendation for insect control in almond orchards is to spray almond trees every year in the winter with a dormant spray of oil and

organophosphate insecticides.[23] The major organophosphate insecticides used in almond orchards include azinphos methyl, chlorpyrifos, diazinon, methidathion and phosmet.

Summary and Conclusions

Pesticides are one of the primary methods used to keep aflatoxin contamination of food within the safety standards set by FDA. Although pesticides do not directly reduce the level of aflatoxin, certain pesticides may meet the benefit standards required by the Food Quality Protection Act of 1996 by controlling insects that spread aflatoxin. Thus, any review of the pesticides for continued food tolerances and registration must consider the risk-risk tradeoff with aflatoxin. Congress clearly intends that EPA grant tolerances to pesticides that are known carcinogens if they reduce another risk more than the risk posed by the pesticide. Although chemical pesticides, such as organophosphate insecticides, pose certain dietary risks, it will be necessary for the EPA to determine the potential of increased dietary risk from aflatoxin ingestion that might be expected if those uses were canceled.

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