

Bt corn's reduction of mycotoxins: The fact, the fiction, and regulation

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Presentation outline

- ◆ Mycotoxins in corn
 - Background
 - Economic and health risks
- ◆ Bt corn's reduction of mycotoxins: the facts and the fiction
 - Evidence from field trials
 - Purported health effects
 - Economic impacts
- ◆ Why Bt corn's benefits are absent in regulatory decision-making on GMOs
 - But how they may play a role in the future

What are mycotoxins, & why should we care about them?

- ◆ Toxic & carcinogenic chemicals produced by fungi
- ◆ Long history of mycotoxins affecting society
 - 11th century: *Claviceps purpurea* producing ergot alkaloids in rye → St. Anthony's Fire
 - Mysterious human & animal deaths in more recent years (Great Depression horses)
 - Recent discovery of mycotoxins
- ◆ To protect human and animal health, regulatory standards on mycotoxins exist worldwide
 - But standards vary enormously!



Push for harmonized mycotoxin regulations

- ◆ 2003 Council for Agricultural Science & Technology (CAST) Mycotoxin Report:
 - One 21st-century goal is development of uniform regulations worldwide for foodborne mycotoxin contamination
- ◆ Why harmonized standards are important
 - Disagreements between importing and exporting countries on food import standards
 - Crucial trade issue for U.S. & some less developed countries
 - Effects of strict mycotoxin standards can be severe
- ◆ But whose standards will the world adopt?
 - Tradeoff: health vs. economic costs

Assessing risks, benefits, and economics of mycotoxin standards

- ◆ Which nations are most at risk of *economic losses* from stringent mycotoxin standards?
- ◆ Which populations worldwide would experience greatest potential *health benefits* from stringent fumonisin & aflatoxin standards?
- ◆ Do the health benefits justify the export market losses?
- ◆ Case study: corn
 - Fumonisin
 - Aflatoxin



Fumonisin: Health effects & standards

- ◆ 1988 discovery: human cancer, horse deaths
- ◆ Produced by *Fusarium verticillioides*, *F. proliferatum*
- ◆ **Postulated** human health effects
 - Esophageal cancer
 - Neural tube defects
- ◆ Animal effects
 - Equine leukoencephalomalacia
 - Porcine pulmonary edema
 - Liver, kidney cancer in rodents
- ◆ Few nations have fumonisin standards
 - U.S.: 2 mg/kg in corn for human consumption
 - EU proposed standard: 0.5 mg/kg



Photo: Gary Munkvold

Aflatoxin: Health effects & standards

- ◆ Earliest mycotoxin discovered: produced mainly by *Aspergillus flavus*
- ◆ Most potent chemical liver carcinogen known
- ◆ Human health effects
 - Liver cancer
 - Synergistic with the carcinogenic hepatitis viruses (10X ordinary potency)
 - Stunting in children; immune disorders
- ◆ Animal effects
 - Liver, kidney damage; immune disorders
 - Decreased egg production in hens, brittle eggshells
- ◆ Many nations have standards
 - U.S.: 20 µg/kg; EU: 4 µg/kg



Empirical model: economic impact of standards

$$\text{Export Loss}_{i,j,k} = P_i * V_{ij} * r_{i,j,k} \quad (1)$$

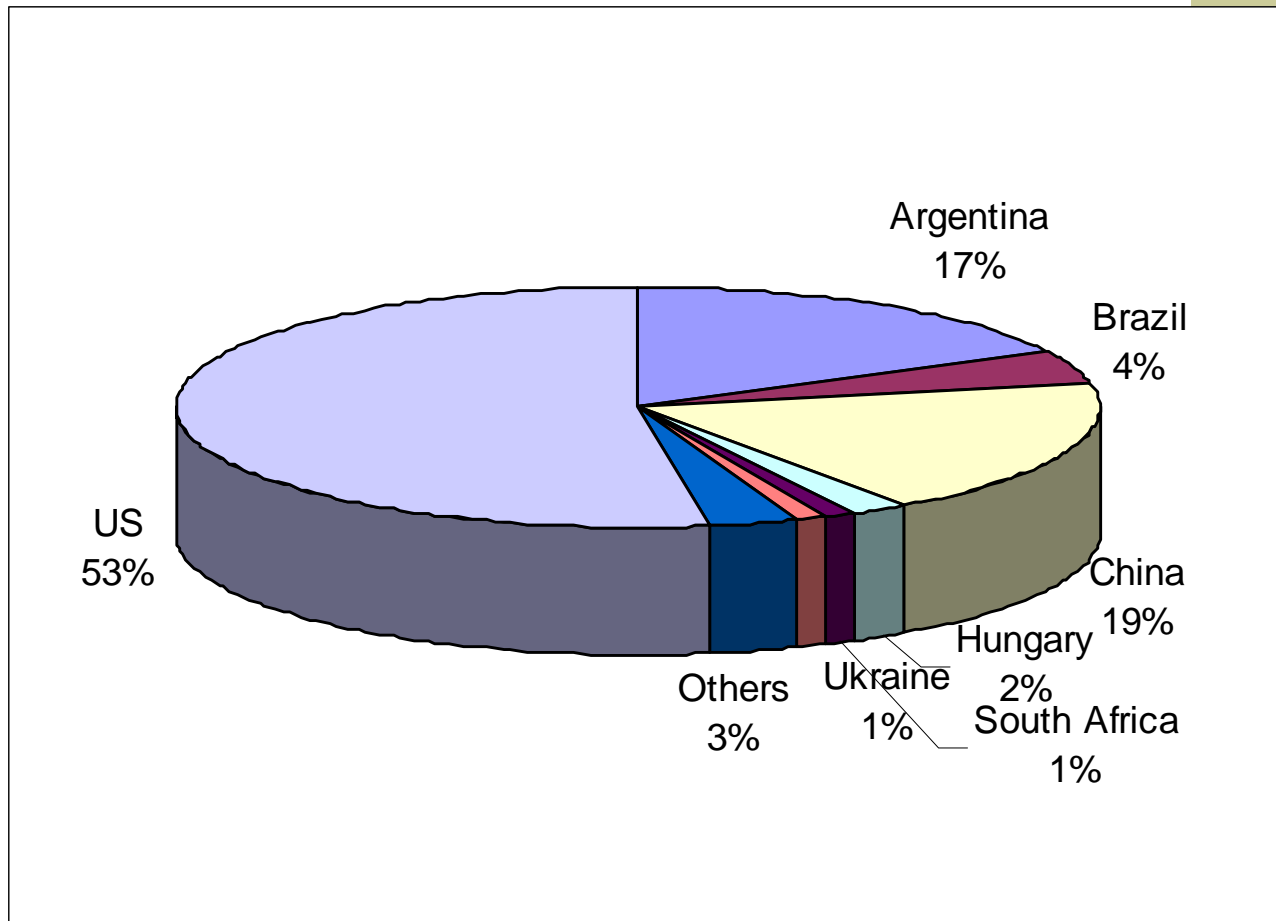
where

- i = crop (e.g., corn),
- j = nation,
- k = international mycotoxin standard,
- P_i = world price for food crop i per unit volume,
- V_{ij} = export volume of crop i from nation j , and
- $r_{i,j,k}$ = % export volume of crop i from nation j rejected at international mycotoxin standard k .

$$r_{i,j,k} = 1 - \int PDF_{i,j,k} dk, \quad (2)$$

where $PDF_{i,j,k}$ is the probability density function of % crop i from nation j having mycotoxin levels at or lower than standard k , and its integral over k represents the cumulative distribution function.

Relative corn export market volumes of prominent corn-exporting nations (2004)



If the world adopted US vs. EU standard for fumonisin...

- ◆ US: 2 mg/kg in food
 - ◆ Annual losses to:
 - US: \$40M
 - China: \$30M
 - Argentina: \$30M
 - ◆ Total losses to 3 major corn exporters: **\$100M**
- ◆ EU: 0.5 mg/kg in food
 - ◆ Annual losses to:
 - US: \$170M
 - China: \$60M
 - Argentina: \$70M
 - ◆ Total losses to 3 major corn exporters: **\$300M**

If the world adopted US vs. EU standard for aflatoxin...

- ◆ US: 20 $\mu\text{g}/\text{kg}$ in food
- ◆ Annual losses to:
 - US: \$9M
 - China: \$30M
 - Argentina: \$1M
- ◆ Total losses to 3 major corn exporters: **\$40M**
- ◆ EU: 4 $\mu\text{g}/\text{kg}$ in food
- ◆ Annual losses to:
 - US: \$44M
 - China: \$72M
 - Argentina: \$8M
- ◆ Total losses to 3 major corn exporters: **\$124M**

F. Wu [2004], "Mycotoxin Risk Assessment for the Purpose of Setting International Regulatory Standards," *Environmental Science & Technology* **38**(15), 4049-4055

Conversely: who experiences health benefits of stringent mycotoxin standards?

- ◆ Fumonisin: *We don't know.*
 - IARC 2B carcinogen, Proposition 65 listed
 - Effects unquantifiable: No reliable biomarker
- ◆ Aflatoxin: *No one!*
 - JECFA estimated effects of tightening regulatory standard from 20 to 10 $\mu\text{g}/\text{kg}$
 - Where 25% pop. has hepatitis B/C, tighter standard reduces liver cancer by 300 cases per year per billion persons
 - Where 1% pop. has hepatitis B/C, tighter standard reduces liver cancer by **2 cases per year per billion persons**
 - Undetectable by epidemiological methods



Countervailing risks & policy implications

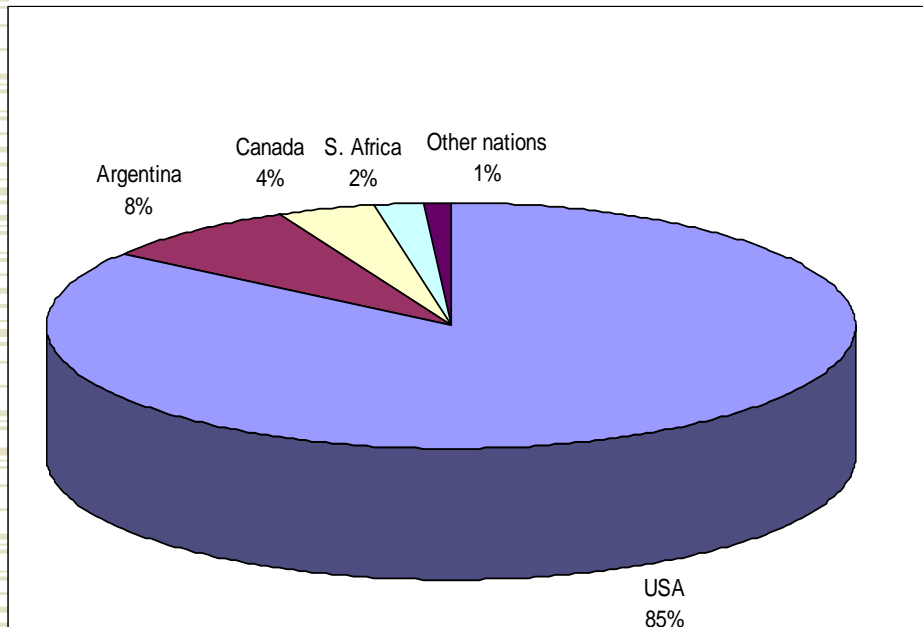
- ◆ Where are populations with hepatitis B/C?
 - High hepatitis populations: China (major corn exporter), Africa
 - Low hepatitis populations: industrial world (corn importers!)
- ◆ Health policy dilemma:
 - To preserve market, China with HIGH hepatitis prevalence likely to export best corn and keep worst domestically, increasing health risks
 - Importers experience insignificant health benefit
 - But: public unlikely to accept weaker standard to protect food safety where stronger existed
- ◆ So best solution for corn-exporting nations is to find technologies or methods to reduce mycotoxin contamination
 - *Bt corn may be one solution...*

Background on Bt corn



- ◆ What is Bt corn?
 - *Bacillus thuringiensis*: pest-protective properties
 - Effective against Lepidopteran corn pests
 - Harmless to mammals, other non-target species
 - More effective than other pesticides
 - Sprays cannot reach inner corn parts where pest feeds
 - Sprays easily degraded, blown or washed off
 - Bt corn produces toxin in all parts of corn

Bt corn planting around the world



- ◆ 10M ha (25M acres) Bt corn planted globally
- ◆ 8 nations: U.S., Canada, Spain, Germany, Argentina, Honduras, South Africa, Philippines
- ◆ Field trials in China

Bt corn and mycotoxin reduction: The facts

- ◆ Insects one primary cause of fungal disease on corn
 - Both pre-harvest & post-harvest
 - Kernel damage; insects as vectors
 - ECB, SWCB directly linked to mycotoxins (Dowd 1998)
- ◆ Bt corn can reduce mycotoxins
 - Less insect pest damage
 - Potentially improved animal & human health
 - Improved market acceptance of corn



Fumonisin and aflatoxin reduction

- ◆ Fumonisin lower in Bt corn worldwide
 - Because fumonisin so closely associated with insect damage
 - Bt corn success in U.S. (Munkvold & Hellmich 1997, 1998, 1999; Dowd 2001; Hammond et al. 2003)
 - Bt corn success in Argentina, South Africa, France, Italy, Turkey (Hammond et al. 2003)
- ◆ Aflatoxin: mixed success
 - Aflatoxin often caused by insects other than ECB, SWCB; and more affected by *A. flavus* infection method
 - Bt corn mixed record of success in U.S.
 - Where ECB & SWCB are main pests, lower aflatoxin in Bt corn
 - No field trials elsewhere in world

Bt corn's impacts on human health: The fiction

- ◆ Bt corn has never been shown to reduce neural tube defects!
 - Bt corn has lower fumonisin levels than non-Bt isolines
 - But fumonisins not the only cause of NTDs
 - High NTD rates: Central America, Texas/MX border
 - Pregnant women's diets highly unvaried
 - Low in folate and choline
 - Most fumonisin in Hispanic diet hydrolyzed through nixtamalization
 - Many barriers to getting Bt corn planted in these regions
- ◆ In fact, Bt corn has not been clinically proven to have ANY health benefits to either humans or animals
 - But someday may be proven: likely for animals

Benefits of Bt's mycotoxin reduction in U.S.

(Wu 2006, *Transgenic Research* 15:277-289)

	Fumonisin	Deoxynivalenol	Aflatoxin
	<i>\$US millions, average (95% Confidence Interval)</i>		
Market loss	39 (14 to 86)	52 (17 to 120)	163 (73 to 332)
Animal health loss	0.27 (0.05 to 2)	0	N/A
Total US losses	40 (14 to 88)	52 (17 to 120)	163 (73 to 332)
<i>Benefit from Bt corn</i>	8.8 (2.3 to 31)	8.1 (2.6 to 16)	14 (6.2 to 28)

Total annual benefit of Bt corn's mycotoxin reduction in U.S.:
~\$30 million (\$1.50/Bt acre): mostly *market benefits*

Why aren't Bt corn's benefits part of regulatory decision-making?

- ◆ Lack of benefits analysis in GMO regulations
- ◆ New state of science on Bt/mycotoxin link
- ◆ Public opinion



Benefits analysis in GM crop regulations: United States (1)

- ◆ 1986 Coordinated Framework for Regulation of Biotechnology
 - 10 years before Bt corn was even grown commercially
 - Existing statutes adequate to regulate GMOs
 - 3 agencies share oversight of Bt corn: US Dept of Agriculture, Environmental Protection Agency, Food & Drug Administration

Product class	Lead agency	Federal statutes
Plants	USDA	NEPA, PPA
Pesticides	EPA	FIFRA, FFDCA
Food & additives	FDA	FFDCA

Benefits analysis in GM crop regulations: United States (2)

- ◆ FIFRA & FFDCA: explicit benefit-risk mandates
 - Relevant to EPA & FDA
- ◆ EPA: 2001 Biopesticides Registration Action Document (BRAD) for Bt corn does include benefits analysis
 - Yield increase, reduction in pesticide usage, mycotoxin reduction!
 - Unclear how benefits would be weighed against risks if EPA determined that Bt corn had risks, which they didn't
- ◆ FDA: GM foods “substantially equivalent” to non-GM foods (1992)
 - Granted GM foods GRAS status: *Generally Recognized As Safe*
 - No mandatory analysis; no labeling requirement

Benefits analysis in GM crop regulations: worldwide

- ◆ Among other nations with GMO policies, only China & Argentina's include benefits analysis specifically
 - China: Implementation Regulation on Agricultural Biological Genetic Engineering (Ministry of Agriculture)
 - Environmental assessment considers benefits as well as risks of GMOs
 - Economic benefits of each application taken into account
 - Argentina: National Directorate of Agrifood Markets (DNMA) assesses benefits and costs of each GM crop on Argentina's exports
- ◆ EU: Directive 2001/18/EC has specific mandate to consider “ethical implications” of GMOs
 - To extent that Bt corn's mycotoxin reduction has ethical dimensions, benefit would also be considered here
 - But so far, GMO ethical issue has been framed the *opposite* way

Science linking Bt corn & mycotoxin reduction fairly new

- ◆ Fumonisin one of most newly-discovered mycotoxins (1988)
 - Human health effects still not fully known
 - News-breaking potential effects re: neural tube disorders only confirmed in 2004
- ◆ Aflatoxin known since 1960, but link with Bt corn weaker
 - Mixed record in U.S.
 - No conclusive field trials elsewhere in world
- ◆ The scientific evidence must be fairly well-established before it enters into GMO regulatory policies.

Policymakers and industry not eager to alert public to foodborne mycotoxins

- ◆ Policymakers and industry want to maintain public confidence in their abilities to ensure food safety & quality
- ◆ Even at generally harmless levels (as in U.S.): if people knew extent of food contamination by molds, a significant public perception problem could arise
- ◆ This could outweigh any benefit to be gained by advertising Bt corn's effect on reducing mycotoxins

Discussion

- ◆ Mycotoxins cause significant economic / health problems worldwide
 - Significant impacts to U.S., China, Argentina
- ◆ Bt corn has lower levels of mycotoxins
 - Fumonisin reduction proven worldwide; aflatoxin mixed success
- ◆ This benefit is unlikely to directly affect regulatory decision-making in near future
 - Benefits analysis not part of many GMO regulatory frameworks
 - Science on Bt corn / mycotoxin link still new and unfinished
 - Policymakers not eager to publicize mycotoxin problem
- ◆ But indirect effects could be important
 - Especially to countries with severe mycotoxin problems
 - Word-of-mouth among farmers
 - As mycotoxin standards grow harder to meet, control technologies gain popularity