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Recollections on the Evolution of the US Regulation of GE Crops

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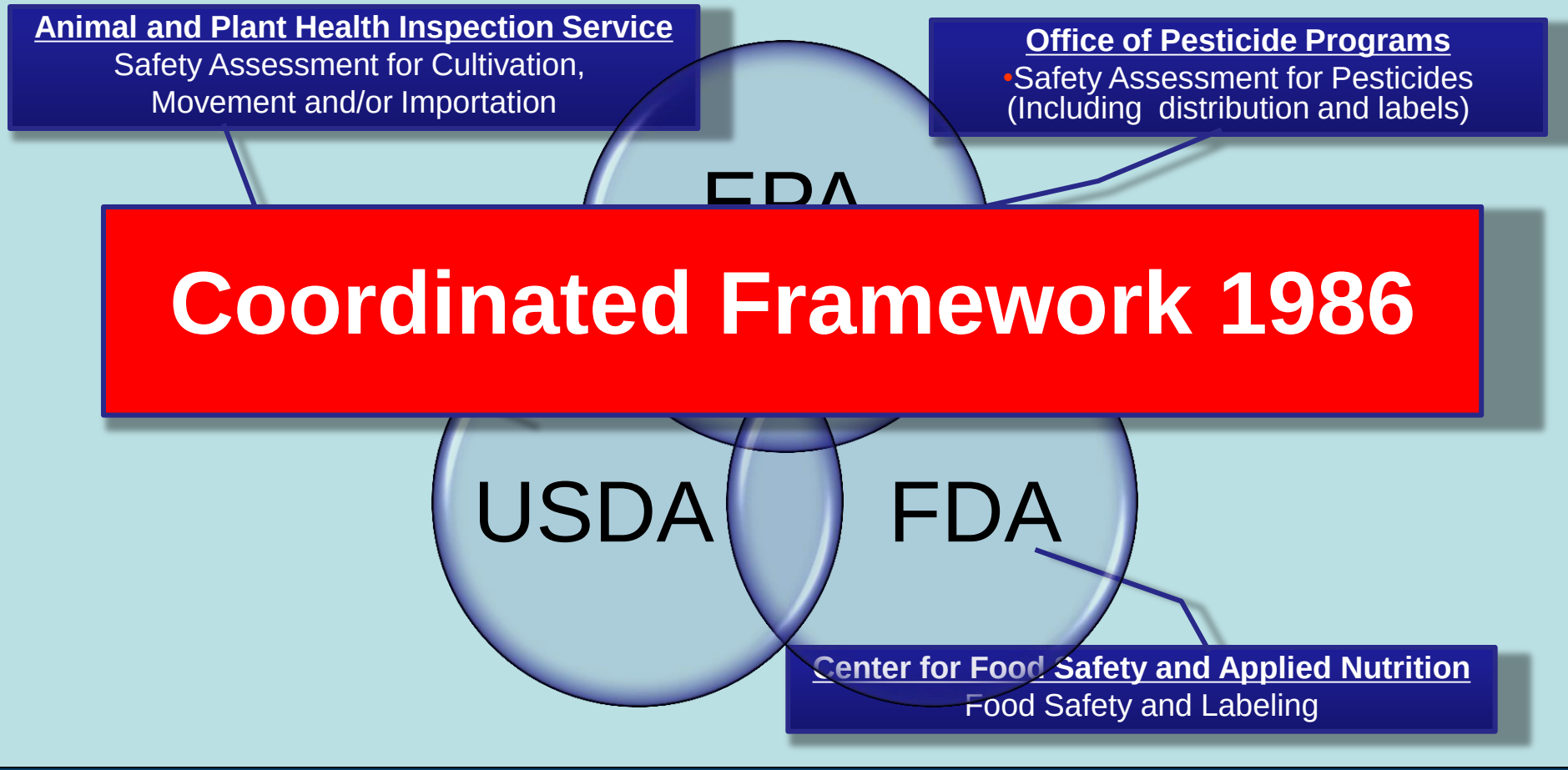
US Regulation of Biotechnology Products: A Coordinated Framework



Statutes Used By EPA for Biotechnology Regulation

- Toxic Substances Control Act (TSCA)
- Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)*
- Federal Food Drug and Cosmetic Act (FFDCA)
- Food Quality Protection Act (FQPA) 1996
- Endangered Species Act
- Migratory Bird Treaty Act

*Risk Benefit Statute

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FIFRA is a Risk/Benefit Statute

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RISKS

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BENEFITS

4

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EPA sponsored or cosponsored with other Federal agencies, six conferences relevant to development of its approach to plant-incorporated protectants

- October 19–21, 1987--“Regulatory Considerations: Genetically Engineered Plants”
- September 8–9, 1988--“Transgenic Plant Conference”
- November 6–7, 1990--“Pesticidal Transgenic Plants: Product Development, Risk Assessment, and Data Needs”

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EPA sponsored or cosponsored with other Federal agencies, six conferences relevant to development of its approach to plant-incorporated protectants

- April 18–19, 1994-- “Conference on Scientific Issues Related to Potential Allergenicity in Transgenic Food Crops”
- July 17–18, 1997-- “Plant Pesticide Workshop”
- December 10–12, 2001--“Assessment of the Allergenic Potential of Genetically Modified Foods”

Plant Incorporated Protectants Rule

- First Proposed in 1994 – Published 2001

- Defines PIP active ingredient:
  - Plant incorporated protectants are pesticidal substances produced by plants and the genetic material necessary for the plant to produce the substance.

*Volume 40 of the Code of Federal Regulations

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Science based implementation

Science Based Regulation

Science key to strong regulatory program for this cutting edge technology:

- Defines the risks and the benefits
  - Provides the data necessary to do credible risk assessment
  - Determines what mitigation would be appropriate and effective
  - Provides predictive models (e.g., for product longevity, environmental monitoring strategies)

Developing a Science Based Risk Assessment Approach

- US EPA relies on internal and external science experts to develop risk assessment approach
  - literature reviews
  - recommendations from science experts
- Consultation with other Agencies
- Public* input

The “Public” is broadly defined to include the general Citizenry as individuals or organizations, e.g., industry groups or NGO’s.

Examples of Scientific Advisory Panel Meetings

- 2006: Evaluation of the Resistance Risks from Using 100% Bollgard and Bollgard II Cotton as Part of a Pink Bollworm Eradication Program in the State of Arizona
- 2006: Analysis of a Natural Refuge of Non-Cotton Hosts for Monsanto's Bollgard II Cotton
- 2009: Evaluation of the Resistance Risks from Using a Seed Mix Refuge with Pioneer's Optimum AcreMax1 Corn Rootworm-Protected Corn
- 2009: Scientific Issues Associated with Data Required to Register Plant-Incorporated Protectants
- 2010: Insect Resistance Management for SmartStax™ Refuge-in-the-Bag, a Plant- Incorporated Protectant (PIP) Corn Seed Blend

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Risk Considerations

- Toxicity
- Allergenicity
- Implications of pollen spread (e.g., weediness)
- Insect resistance development
- Antibiotic resistance
- Affects on non-target organisms

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PIPs Data Collection and Analysis

- Product characterization
  - Source of the genes
  - What protein(s) are made
  - Expression- In what parts of the plant are the proteins found and at what level
  - Includes review of any marker genes
- Environmental fate
  - Protein expression
  - Protein persistence and degradation
  - Gene transfer

PIPs Data Collection and Analysis

Human health effects

Direct:

- Toxicity testing (e.g., feeding the protein to mice)

Indirect:

- Allergenicity and toxicity potential estimation via comparison of structure of the protein including amino acid sequence
- Stability/breakdown of protein in digestive fluids

PIPs Data Collection and Analysis

Ecological effects

- Effects on non-target organisms
  - Birds, fish and other aquatic species, and invertebrates
- Endangered Species
- Post release follow-up (Monitoring)

Transparency in the PIPs Regulatory Process

- All applications announced in Federal Register (FR)
- All non-confidential business information (CBI) is made publicly available during the review process
- Numerous public meetings and open Science Advisory Panels
- Extensive Use of Website

Science Evaluation: The use of Expert Panel Meetings

- EPA prepares a paper on potential risks
- Paper given to the panel of experts and made available to the public at least 30 days before a public meeting
  - EPA presentation with questions for Panel
  - Public comments are taken
  - Panel raises questions/discusses issues
  - Written report given to EPA and to public

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Built-in Review

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BT Corn/Cotton Reassessment

- Improved yield/profitability
- Improved crop management effectiveness
- Reduction in farming risk
- Reduced pesticide application
- Reduced production costs

Total Annual Benefit: Corn ……. $219M
Cotton ….. $6 to120M

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Dynamic nature of EPA's regulatory process (2 examples)

Science Issue 1: Monarch Butterfly Impacts

- 1995 risk assessment concluded no significant exposure to Lepidoptera
- Letter to Nature (1999)—Bt corn pollen toxic to Monarch butterflies
- Industry immediately launched research effort
- Public science meeting re. data requirements
- Additional Congressional funds for follow-up research
- Published papers conclude no significant exposure (PNAS 2001)

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Impact on Regulation

- Testing of relative(s) of the target pest now required before commercial approval
- Continuing effort to evaluate and improve non-target organism testing for PIPs
- Tested EPA's responsiveness to new information—changes can and will be made, but they must be based on science

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Science Issue 2: Insect Resistance Development

- Lots known about how to kill a pest, but much less known on basic biology
  - Where mates, how many eggs laid, etc.?
- Frequency of resistant alleles?
- Modeling used to predict years-to-resistance
- Methods to monitor for resistance development?

Impact on Regulation

- Registration requirements
  - Research and monitoring
  - IRM plan for each Bt product
  - Reports on compliance and adoption
- Bt crops IRM program is unique—aimed at protecting Bt microbial pesticide
- Wide support for IRM—original pressure from NGO's is now backed by growers, industry, and other stakeholders
- First time many entomology researchers directly involved in regulation

EPA Registrations since 2008

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>30 Current & Previously Registered Section 3 PIP Registrations

Plant-Incorporated Protectant	Registrant	Date	
		Registered	Expires
Vip3Aa20 (MIR162) in corn	ta 67979-14	11/26/ 2008	12/31/2011
Bt Cry 1Ab (Bt11) + Vip 3Aa 20 (	ta 67979-12	2/13/2009	12/31/2011
Bt Cry 1Ab (Bt11) + Vip 3Aa 20 (MIR 162) + modified Cry3A (MIR 604) in corn	Syngenta 67979-13	2/13/2009	12/31/2011
(SmartStax) Bt Corn Events MON 89034 x TC1 x MON 88017 x DAS-59122-7 (PDF)	524- Dow 3467-7	7/20/2009	11/30/ 2011
Optimum AcreMax 1 (OAM 1) Seed Blend of Herculex Xtra + Herculex I (PDF)	Pioneer/Dupont	4/30/2010	9/30/2012
Optimum AcreMax RW (OAM RW) Seed Blend of Herculex RW + Non-Bt corn		4/30/2010	9/30/2012
C5 HoneySweet Plum (C5) Coat Protein Gene of Plum Pox Virus	USDA/ARS 11312-8	5/7/2010	5/7/ 2011
1507 (PO Cry1F) x MON 810 (PO Cry1Ab)	Pioneer/Dupont 29964-7	2/24/2010	10/31/2010
1507 (PO Cry1F) x 59122 (PO Cry34Ab1 + Cry35Ab1) x MON 810 (PO	Pioneer/Dupont 29964-8	2/24/2010	10/31/2010
59122 (PO Cry34Ab1 + Cry Cry1Ab)	ioneer/Dupont 29964-9	2/24/2010	10/31/2010
Bt Cry1Ac Soybean MON-877Ø1-2	Monsanto 524-594	9/9/2010	9/30/2011

Vegetative Insecticidal protein

Seed blend

Viral coat protein

Bt soybean

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Useful websites

- http://www.epa.gov/pesticides/biopesticides/regtools/biotech-reg-prod.htm
- http://www.epa.gov/scipoly/sap/meetings/2000/october/brad3_enviroassessment.pdf
- http://www.epa.gov/pesticides/biopesticides/reg_of_biotech/eparegofbiotech.htm
- http://www.epa.gov/scipoly/sap/meetings/2009/022509meeting.htm

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Planning ahead is not a bad thing!
Thank You