Regulation of Agricultural Biotechnology in the United States: Overview

Webinar for:

National Agricultural Law Center

July 15, 2015

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Animal and Plant Health Inspection Service

History of Plant Breeding

Pre-1900's

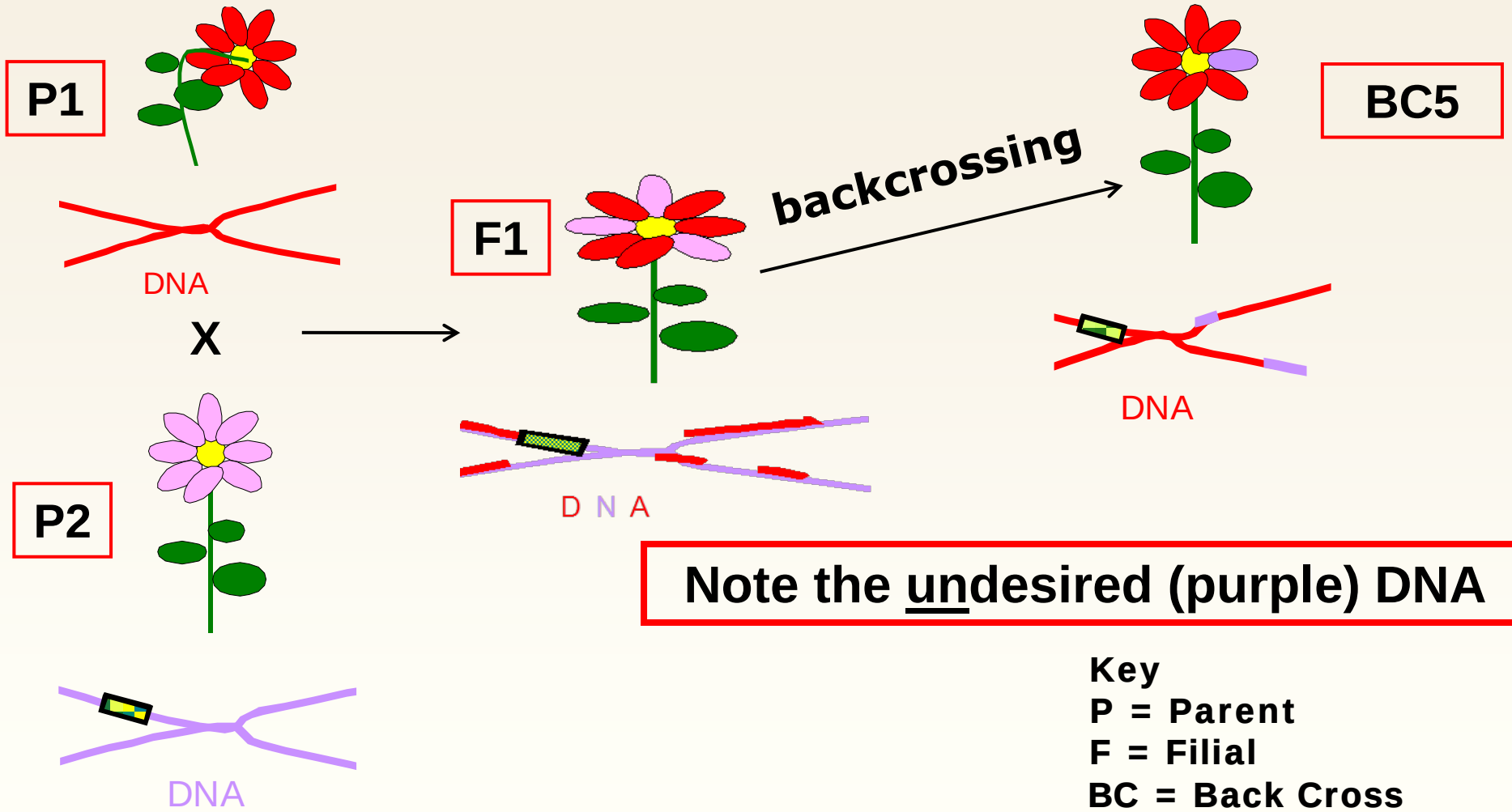
- Cross Two Plants
- Select Among Progeny

1900's

- Cell Fusion
- Chemical Mutants
- X-Ray Mutants

1980's Insert Specific DNA Fragments

Classical (Conventional) Breeding



Note the undesired (purple) DNA

Key
P = Parent
F = Filial
BC = Back Cross

Cell Fusion

- Fusing two cells to form a single cell
- Somatic cell hybridization / protoplast fusion
  - One type of cell fusion
  - Cells from two different plants placed together in container
  - Cell walls removed with chemicals or electricity
  - Resulting cell has genetic material from both plants
- Hundreds of commercial plant varieties have been developed using this technique

Chemical and X-Ray Mutagenesis
("Traditional" Breeding Techniques)

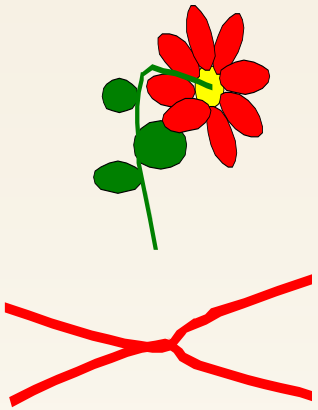
Select for different traits for breeding or marketing

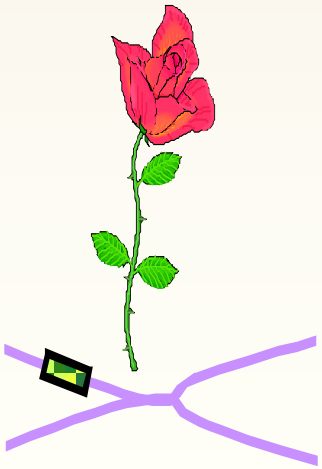
- **2,500+ plant varieties have been developed using radiation mutagenesis**
- **Star Ruby and Rio Red grapefruit varieties**

What is Genetic Engineering?

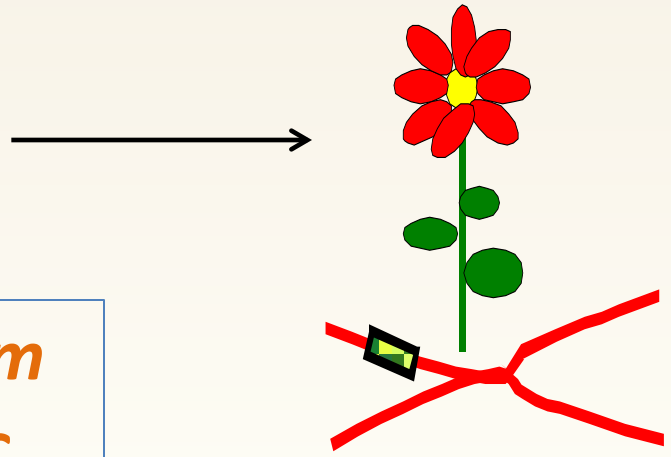
- "The genetic modification of an organism by recombinant DNA techniques." (7CFR340.1)
  - Changes the genetic makeup of the organism
  - DNA may be from the same or different organism
- Many terms are often used interchangeably:
  - Biotechnology
  - GM or GMOs (genetic modification)
  - GE or GEOs (genetic engineering)
    - US regulatory agencies use the term GE
  - Transgenic, Recombinant, Transformed

Genetic Engineering





Use *Agrobacterium*
"Nature's genetic engineer"



Note the lack of undesired DNA

Product Types Regulated by the Federal Government

Not Regulated	Regulated
Classical Breeding	Genetic Engineering
Cell Fusion Chemical Mutants X-Ray Mutants	

Brief History of U.S. Biotechnology Regulations

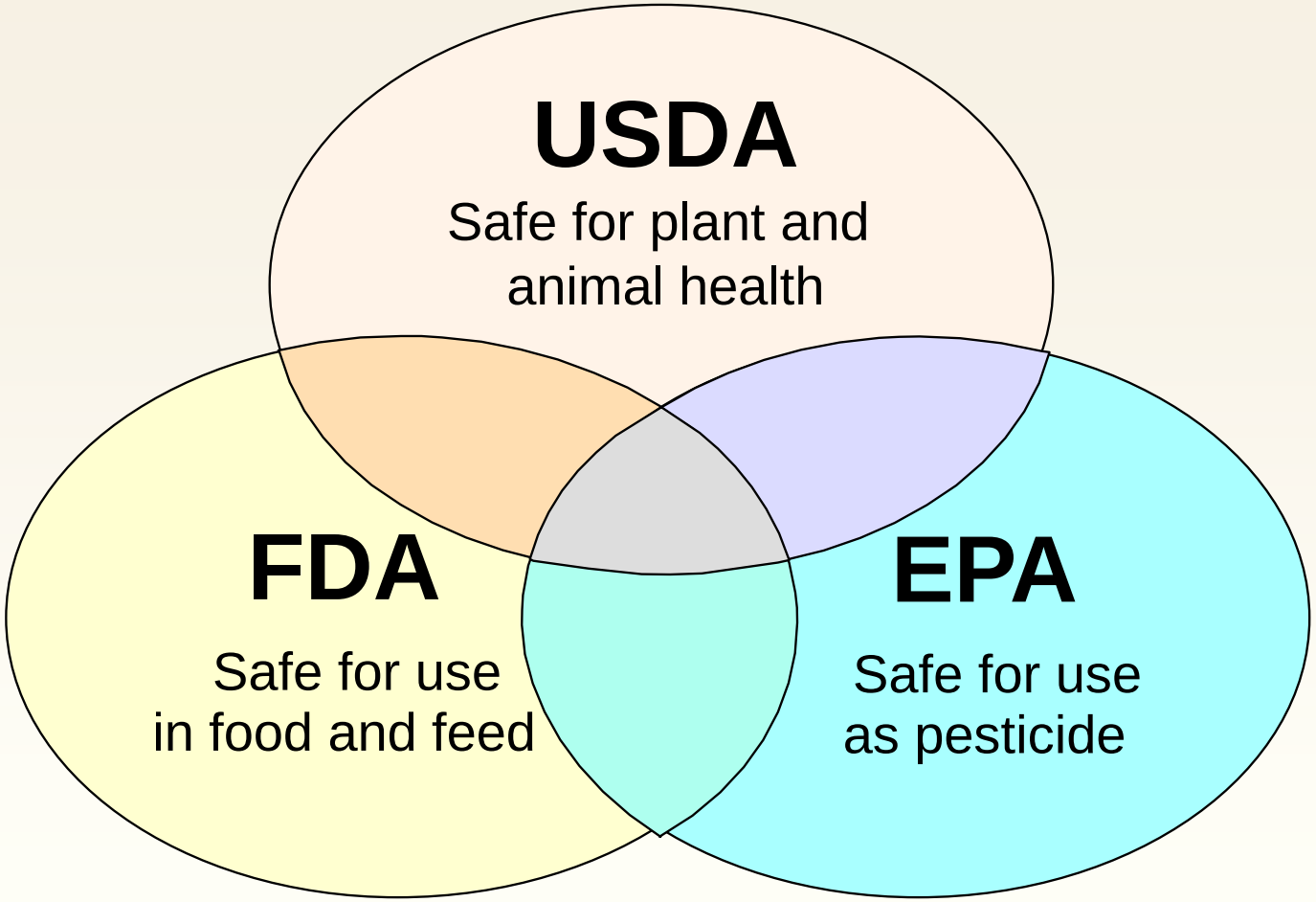
- 1970's – NIH Guidelines
- 1986 - "Coordinated Framework for Regulation of Biotechnology"
- 1987 – GE organisms that are plant pests (7 CFR part 340)
- 1993 – Notification authorizations (7 CFR part 340.3)
- 1997 – Notification authorizations expanded

Coordinated Framework (1986)

Federal role in the safe use of biotechnology:

- The safety risks of GE organisms are not fundamentally different from safety risks posed by non-GE organisms with similar traits
- The existing laws provide adequate authority
- Regulation should be science-based and conducted on a case-by-case basis

Regulation Under the Coordinated Framework



Regulatory Framework

- US Environmental Protection Agency (EPA)
  - Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
  - Federal Food, Drug and Cosmetics Act (FFDCA)
  - Toxic Substances Control Act (TSCA)
- US Food and Drug Administration (FDA)
  - Federal Food, Drug and Cosmetics Act (FFDCA)
- US Department of Agriculture (USDA)
  - Plant Protection Act (PPA) of 2000
    - Federal Plant Pest Act (FPPA) in 1987

Regulation Under the Coordinated Framework

New Trait/Crop	Agency	Review
Insect resistance in food crop (Bt corn)	USDA EPA FDA	Protection of plant health Environmental, food/feed safety of pesticide Food/feed safety
Herbicide resistance in food crop (glyphosate resistant soybeans)	USDA EPA FDA	Protection of plant health New herbicide use Food/feed safety
Herbicide resistance in ornamental crop (glufosinate resistant tulips)	USDA EPA	Protection of plant health New herbicide use
Modified oil in food crop (high oleic acid soybeans)	USDA FDA	Protection of plant health Food/feed safety
Modified flower color (blue poinsettias)	USDA	Protection of plant health

What Does APHIS-BRS Regulate?

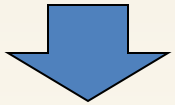
- "Regulated articles" (7 CFR part 340)
  - If the organism has been altered or produced through genetic engineering, **and**
  - If there is a possibility that the GE organism could be a plant pest, i.e.,
    - Donor, recipient, or vector organism is a plant pest
    - "Plant pest" is defined by statute

"Introduction" of Regulated Articles

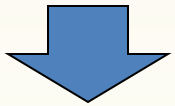
- APHIS-BRS regulates activities with regulated articles:
  - Importation
  - Interstate movement
  - Release (confined) into the environment (*e.g.,* field test)
- Permit or notification procedures are used to authorize

GE Plant Variety Development

LABORATORY / GREENHOUSE
(not regulated by APHIS)



FIELD TESTING
(regulated by APHIS)



COMMERCIALIZATION
(not regulated after attaining non-regulated status)

Release Notifications and Release Permits

	Notification	Permit (Non PMPI *)
Organisms	Plants	Plants, Microorganisms & Animals
Genes	Known function	Any non-PMPI gene (intent-based)
Confinement	Performance Standards	▪Applicant provides confinement details ▪APHIS issues supplemental permit conditions
Inspections	Percentage based on risk	At least one site per state per permit
Reports	▪Activity Report (Planting) ▪Unintended Effects ▪Unintended Release ▪Field Test Report	▪Activity Report (Planting) ▪Unintended Effects ▪Unintended Release ▪Volunteer Monitoring Report ▪Final Field Test Report

*** PMPI = Plant-made Pharmaceutical or Industrial**

- All PMPI are under permit, but with separate requirements

PMPI Permits

- Most rigorous permit type
- Case-by-case permit conditions
  - pre-notification of planting, flowering, harvest, etc
- Five inspections before/during planting
- Two additional inspections post-harvest
- Dedicated equipment (equipment cleaning is required in most other cases)

Containment vs. Confinement

- Containment Procedures
  - Procedures to prevent exposure of GE plants to the environment
  - Refers to use in greenhouses and during transport
  - *Probability of release should be near zero*
- Confinement Procedures
  - Procedures used during Confined Field Trials to ensure that the GE plant does not persist in the environment
  - These include reproductive isolation and post-harvest monitoring
  - *Probability of persistence should be near zero*

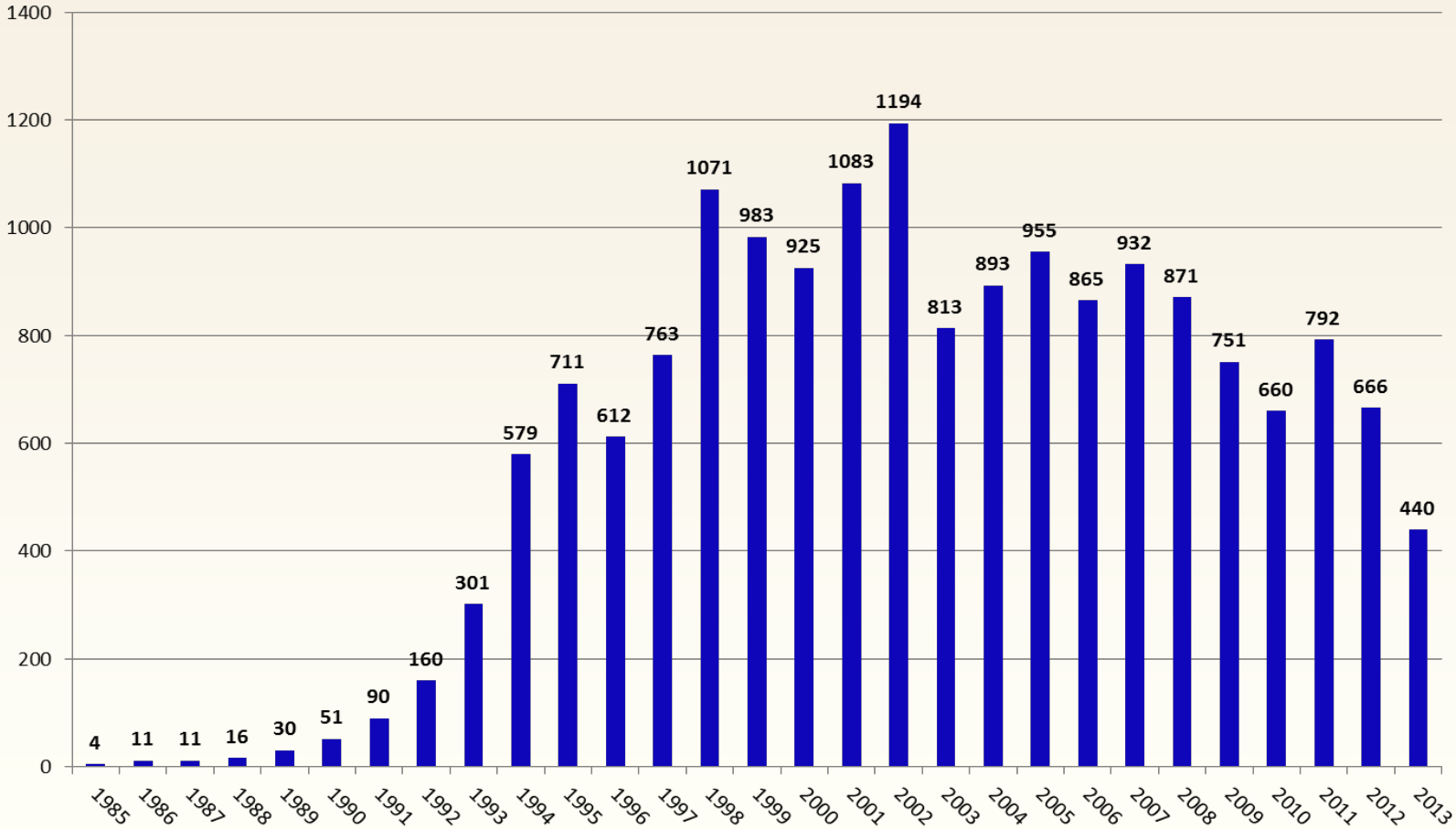
Authorized Activities with Regulated Articles, 2014 (1 of 2)

		Import Only	Interstate Only	Release (Field Trial)	TOTAL
Notification	Received	322	396	436	1154
	Authorized	317	368	391	1076
Permit	Received	49	116	195	360
	Authorized	33	91	181	305

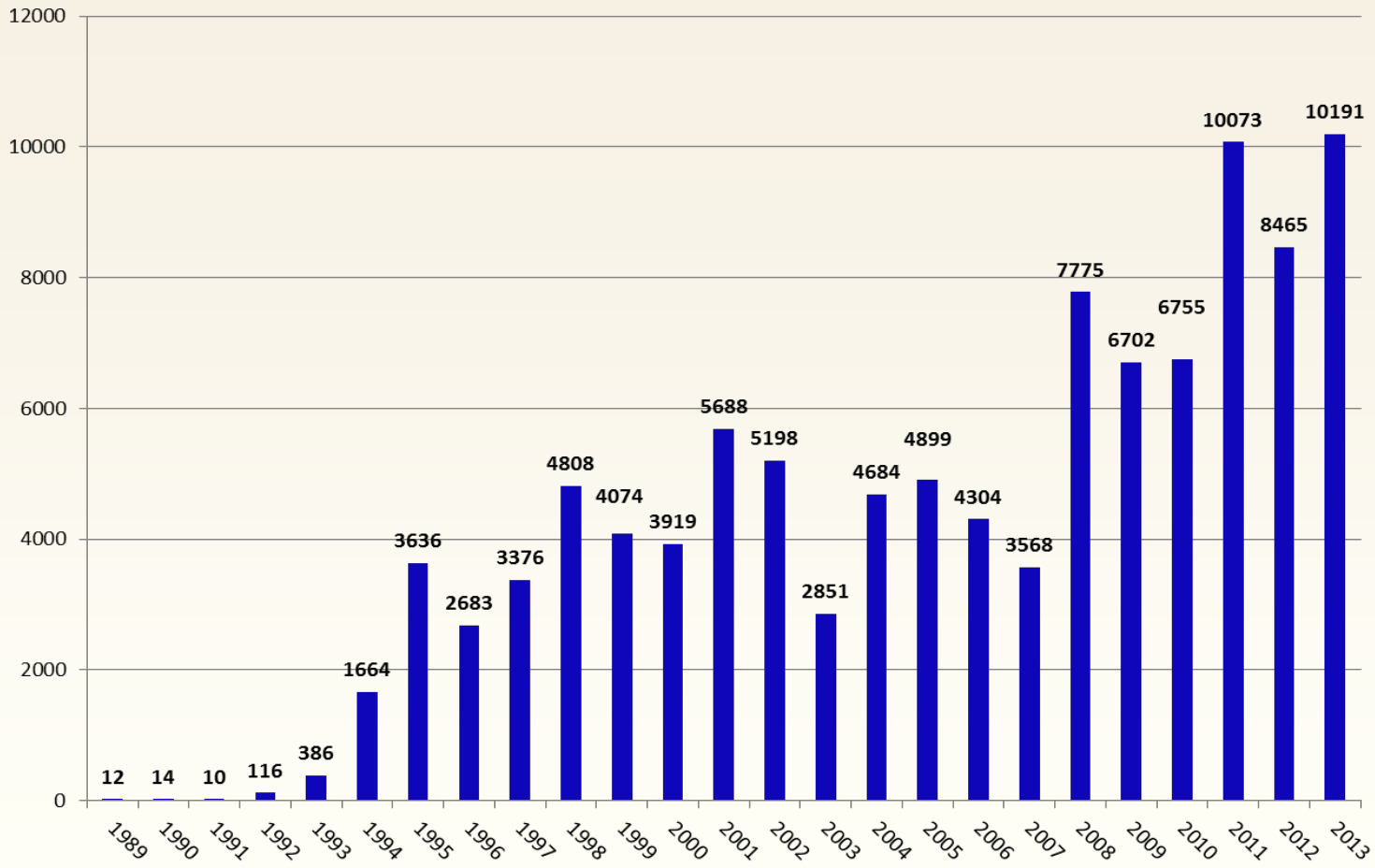
Authorized Activities with Regulated Articles, 2014 (2 of 2)

Number of Release Authorizations	Number or Release Sites	Number of Phenotypic Designations (crop-trait combination)
572	11,938	49,552

Release Authorizations



Authorized Field Release Sites



Three Components of Compliance

- Compliance Assurance
  - Manage planting reports and schedule inspections
  - Train inspectors and conduct inspections
- Compliance Enforcement
  - Manage and evaluate compliance incidents
  - Coordinate investigations
  - Issue incident responses
- Compliance Assistance
  - Provide assistance to facilitate compliance

Compliance Assurance

- Management of planting report information
- Management of inspections
- Training of inspectors
- Participate in field investigations
- Proactively promote compliance
  - Participate in education and outreach activities
  - Serve as a resource
  - Provide guidance

Inspections of Field Trial Sites

- Inspections verify compliance to the regulations
- All field trial sites are eligible for inspection
- Timely submission of planting reports is necessary
- Permittees must allow access
- Compliance is based upon observations, records, interviews, mapping, and measurements
- Potential incidents are referred to the Compliance Evaluation and Enforcement Branch

Compliance Enforcement

- An "incident" is a distinct event of reported, apparent, non-compliance to APHIS regulations (7 CFR part 340)
  - Associated with an acknowledged notification
  - Associated with an issued permit
  - Without a valid BRS authorization
- Examples:
  - Inadvertent planting in non-permitted area
  - Failure to submit required planting reports
  - Release without a valid BRS authorization

Compliance Evaluation

- Did the incident violate APHIS regulations
  - If so, what sections were violated
  - Have effective corrective actions, preventative actions, and or mitigating actions been taken
  - Should the compliance response be elevated
    - Seriousness
    - Culpability
    - Prior compliance history
    - Cooperation

Volunteer Corn in Soybean Follow-Crop

Petition Procedure for Nonregulated Status under 7 CFR part 340

- Anyone can petition APHIS-BRS to determine "nonregulated" status (the GE organism would no longer be subject to this regulation)
  - Petition information must support the conclusion that the GE organism is not likely to pose plant pest risk
  - Public reviews petition and APHIS evaluation before final APHIS determination

Petition Procedure for Nonregulated Status under 7 CFR part 340

- APHIS-BRS does two evaluations:
  1. Plant Pest Risk Assessment (PPRA)
     - determine whether GE organism poses plant pest risk
     - Authority for decision, Plant Protection Act
  2. Environmental Assessment (EA) or Environmental Impact Statement (EIS)
     - Pursuant to National Environmental Policy Act (NEPA)
     - Evaluate significance of any environmental impacts that may arise from the APHIS-BRS decision
     - **NEPA provides no additional authority for decisions**

GE Plants with Nonregulated Status under 7 CFR part 340

- APHIS-BRS has made determinations of nonregulated status in response to 115 petitions, representing 17 plant species
- The determination of nonregulated status extends to the GE plant and its offspring
- Actual commercialization of GE plants with nonregulated status is determined by market demand, not the APHIS decision

GE Plants with Nonregulated Status

- Alfalfa – HT
- Canola – HT, AP, PQ
- Corn – HT, IR, AP, PQ
- Cotton – HT, IR
- Papaya – VR
- Soybean – HT, IR, AP, PQ
- Sugar Beet – HT
- Rose – PQ
- Squash – VR
- Tobacco – PQ
- Potato – IR, VR, PQ
- Apple – PQ
- Chicory – AP
- Flax – HT
- Plum – VR
- Rice – HT
- Tomato – PQ

- Major Commercial Production
- Minor Commercial Production
- No Commercial Production

HT – Herbicide Tolerant
IR – Insect Resistant
VR – Virus Resistant
AP – Agronomic Properties
PQ – Product Quality

Current Petitions

1. Creeping Bentgrass: Glyphosate Resistant
2. Eucalyptus: Freeze Tolerant
3. Cotton: 2,4-D/Glufosinate Resistant
4. Corn: Rootworm/Glyphosate Resistant
5. Potato: Late Blight Resistant, Low-Acrylamide Potential, Reduced Black Spot Bruising
6. Corn: Increased Ear Biomass

* Additional details on web page (see next slide)

Transparency: Petitions under 7 CFR part 340

- See BRS web page
  - http://www.aphis.usda.gov/biotechnology/petitions_table_pending.shtml
- Provided for approved and current petitions:
  - Incoming Petition for Non-regulated Status
  - Environmental Assessment or Environmental Impact Statement
  - Plant Pest Risk Assessment
  - Determination of Non-regulated Status

Transparency: Field Trials

- VA Tech Website
- See link below for more information on accessing and using the VT Website search functions to obtain field trial data:

http://www.aphis.usda.gov/biotechnology/downloads/vt_isb_search.pdf

Other APHIS Biotech Activities

- Recently closed Proposed Rule from 2008
- Webinars asking for input on next steps
  - Held May 6, 12 and 20, 2015
- OSTP-led effort to update Coordinated Framework
  - https://www.whitehouse.gov/blog/2015/07/02/improving-transparency-and-ensuring-continued-safety-biotechnology

Other APHIS Biotech Activities: International Efforts

- OECD (Organization of Economic Cooperation and Development)
  - ~ 40 countries
- GLI (Global Low Level Presence Initiative)
- Cartagena Protocol
- Country to Country meetings/briefings, focus on
  - Information exchange
  - Optimize harmonization
  - Scientific aspects of national regulatory systems

History of Plant Breeding

Pre-1900's

- Cross Two Plants
- Select Among Progeny

1900's

- Cell Fusion
- Chemical Mutants
- X-Ray Mutants

1980's Insert Specific DNA Fragments

2000's NPBT (New Plant Breeding Technologies) (*e.g.*, modify existing DNA)

"Am I Regulated" (AIR) Process

- Recall definition of "Regulated Article" from previous slide
  - Altered or produced through genetic engineering, and
  - Possibility the GE organism could be a plant pest
    - Donor, recipient, or vector organism is a plant pest
- Developers ask whether their product is a regulated article
  - Submit "Letter of Inquiry" to APHIS
- Not all approaches to genetic engineering have a plant pest nexus… may not be regulated
- Our web page shows all of the incoming letters and responses since 2011 (n=29) when we formalized process

For More Information

- USDA-APHIS-BRS on the web:

http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/biotechnology

- Become a BRS Stakeholder:
  - See the link below for instructions to register as a BRS Stakeholder to receive important news and information:

http://www.aphis.usda.gov/biotechnology/downloads/brs_sh_how_to_register.pdf

Questions?