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

Key
P = Parent
F = Filial
BC = Back Cross

Note the undesired (purple) DNA
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)

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

Select for different traits for breeding or marketing
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

<table>
<thead>
<tr>
<th>Not Regulated</th>
<th>Regulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical Breeding</td>
<td>Genetic Engineering</td>
</tr>
<tr>
<td>Cell Fusion</td>
<td></td>
</tr>
<tr>
<td>Chemical Mutants</td>
<td></td>
</tr>
<tr>
<td>X-Ray Mutants</td>
<td></td>
</tr>
</tbody>
</table>
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
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

- **USDA**: Safe for plant and animal health
- **FDA**: Safe for use in food and feed
- **EPA**: Safe for use as pesticide
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

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

<table>
<thead>
<tr>
<th>Notification</th>
<th>Permit (Non PMPI *)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisms</td>
<td>Plants</td>
</tr>
<tr>
<td>Genes</td>
<td>Known function</td>
</tr>
</tbody>
</table>
| 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)

<table>
<thead>
<tr>
<th></th>
<th>Import Only</th>
<th>Interstate Only</th>
<th>Release (Field Trial)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Notification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received</td>
<td>322</td>
<td>396</td>
<td>436</td>
<td>1154</td>
</tr>
<tr>
<td>Authorized</td>
<td>317</td>
<td>368</td>
<td>391</td>
<td>1076</td>
</tr>
<tr>
<td><strong>Permit</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received</td>
<td>49</td>
<td>116</td>
<td>195</td>
<td>360</td>
</tr>
<tr>
<td>Authorized</td>
<td>33</td>
<td>91</td>
<td>181</td>
<td>305</td>
</tr>
</tbody>
</table>
### Authorized Activities with Regulated Articles, 2014  (2 of 2)

<table>
<thead>
<tr>
<th>Number of Release Authorizations</th>
<th>Number or Release Sites</th>
<th>Number of Phenotypic Designations (crop-trait combination)</th>
</tr>
</thead>
<tbody>
<tr>
<td>572</td>
<td>11,938</td>
<td>49,552</td>
</tr>
</tbody>
</table>
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
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
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**
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

- 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:

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
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:

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