The Role of USDA-APHIS in the Regulation of Biotechnology in the United States

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Forum on Synthetic Biology
Inaugural Meeting
October 21, 2013

USDA United States Department of Agriculture
Animal and Plant Health Inspection Service

Coordinated Framework (1986)

Basic Principles:

- The safety risks of GE organisms are not fundamentally different from safety risks posed by non-GE organisms with similar traits.
- The *product* of the technology, rather than the *process*, should be regulated
- Regulation should be science-based and conducted on a case-by-case basis.
- The existing laws provide adequate authority

What Does APHIS Regulate?

Law: Title 7, Chapter 104 Plant Protection Act

Regulation: 7 CFR 340

Introduction of Organisms and Products Altered or Produced Through Genetic Engineering which are Plant Pests or which There is Reason to Believe are Plant Pests.

What Does APHIS Regulate?

"Regulated articles" (7 CFR part 340)

- If the organism has been altered or produced through genetic engineering ("the genetic modification of organisms by recombinant DNA techniques"), **and**
- The donor, recipient, or vector is a "plant pest" (as defined in the PPA), an unclassified organism, an organism whose classification is unknown, or an organism which the Administrator determines or has reason to believe is a plant pest

Is my GE organism a regulated article?

- www.aphis.usda.gov/biotechnology/am_i_reg.shtml

Introduction of Regulated Articles

APHIS regulates the following activities for regulated articles:

- Importation
- Interstate movement
- Environmental release/field test

Permit or notification procedures are used to authorize the activity

Confined Field Trials

Environmental releases are conducted under notification or permit such that the organism will be unlikely to:

- Persist in the environment
- Produce offspring that will persist
- Significantly impact non-target organisms

Petition Process for Nonregulated Status

Anyone can petition APHIS to determine "nonregulated" status

- If petition is accepted, the GE organism and all of its offspring are no longer subject to USDA-APHIS biotechnology regulations

Petition information should "substantiate that the regulated article is unlikely to pose a greater plant pest risk than the unmodified organism from which it was derived"

Petition Process for Nonregulated Status

APHIS conducts two evaluations

- Plant pest risk assessment to determine if the GE organism poses a plant pest risk (Plant Protection Act)
  - Relates directly to our decision making regulatory authority.
- Environmental assessment to evaluate whether the APHIS decision is likely to have significant environmental impacts (National Environmental Policy Act, NEPA)
  - Informs decision but does not provide decision-making authority

Public is given the opportunity to review and comment on the petition and APHIS assessments before a final decision

Petition Process: Key Considerations and Management Goals

No significant…

- Increase in pest or disease susceptibility or impact
- Increase in weediness
- Increase in weediness of sexually compatible plants
- Increase in harm to beneficial organisms
- Changes in agricultural practices that impact plant disease or pests or their management
- Impacts from transfer of genes to organisms with which the GE organism does not normally interbreed (horizontal gene transfer)

Petition Process: Key Considerations

Comparators

- Typically isogenic lines in self-pollinated species (often null segregants)
- For hybrid crops, some studies are conducted with the GE inbred and some with the GE hybrid; different comparators are used in each case.

Reference varieties

- When differences are detected between the regulated article and the comparator, the reference varieties often becomes the basis for concluding that the data for the regulated article is within normal ranges

Phenotypic assessment

Technological Advances

Areas of crop trait development with rapid growth

- Plant-derived biofuels
- Quality traits, e.g, improved oils and yields
- Traits to address environmental stress in plants
  - Drought, frost, and salt tolerant crops
- Plant-produced proteins
  - Biologics, vaccines, pharmaceuticals, anti-cancer drugs, enzymes, etc.

New and emerging genetic engineering technologies

- ZFN, TALEN, CRISPR/Cas
- Oligonucleotide-directed mutagenesis
- Plant artificial chromosomes
- Synthetic biology – all of the above?
- No plant pests as donors, recipients, or vectors

APHIS Regulations and Synthetic Biology

Has APHIS regulated any products arising from synthetic biology?

- Synthesized genes
- Metabolic engineering (e.g. high oleic acid soybean)

"Synthetic biology does not necessarily raise radically new concerns or risks … in many ways, synthetic biology is an extension of genetic engineering"

- Presidential Commission for the Study of Bioethical Issues. Dec, 2010

APHIS Regulations and Synthetic Biology

Does the nature of synthetic biology in any way challenge the regulatory framework APHIS follows in assessing risk and benefits?

- To answer, must first define “synthetic biology” and identify how, if at all, it differs from “traditional” genetic engineering
- Challenge to comparative risk assessment

> “One of the biggest challenges in the oversight of synthetic biology … is its capacity to create novel entities that are increasingly dissimilar to known agents or organisms, making potential risks harder to assess. As the field begins to develop more complex, novel, and artificial agents and products, assessing the risks posed will be challenging, particularly for those products with the potential to be released into the environment. - PCSBI, Dec, 2010.

APHIS Regulations and Synthetic Biology

What issues associated with synthetic biology is APHIS most concerned about?

- Risk identification and regulatory triggers
  - When does a synthetic biology product pose a potential plant pest risk (or noxious weed risk) and should be regulated?
- Risk assessment
  - Will we have sufficient knowledge, familiarity and comparators for effective risk assessment?
  - If so, at what point? Does answer differ for microbes and plants?
  - Will synthetic biology be evolutionary, allowing us to build off previous experience?
- Containment methodologies for microbes and plants with sexually compatible relatives

APHIS Regulations and Synthetic Biology

What might the Forum focus on?

- Is synthetic biology a distinct scientific and product development approach or discipline that merits a distinct discussion of regulatory issues?
  - If so, what are those distinctions?

- Do “synthetic biology” approaches or any of the projected products of “synthetic biology” raise unique issues regarding risk or uncertainty?
  - If so, what are those issues?
  - If so, are new risk assessment paradigms required?
  - When?

APHIS-BRS Website

- Main Page URL:

  http://www.aphis.usda.gov/biotechnology/brs_main.shtml

- Petition Guidance

  http://www.aphis.usda.gov/biotechnology/petitions.shtml

- Notification Guidance

  http://www.aphis.usda.gov/biotechnology/notifications.shtml

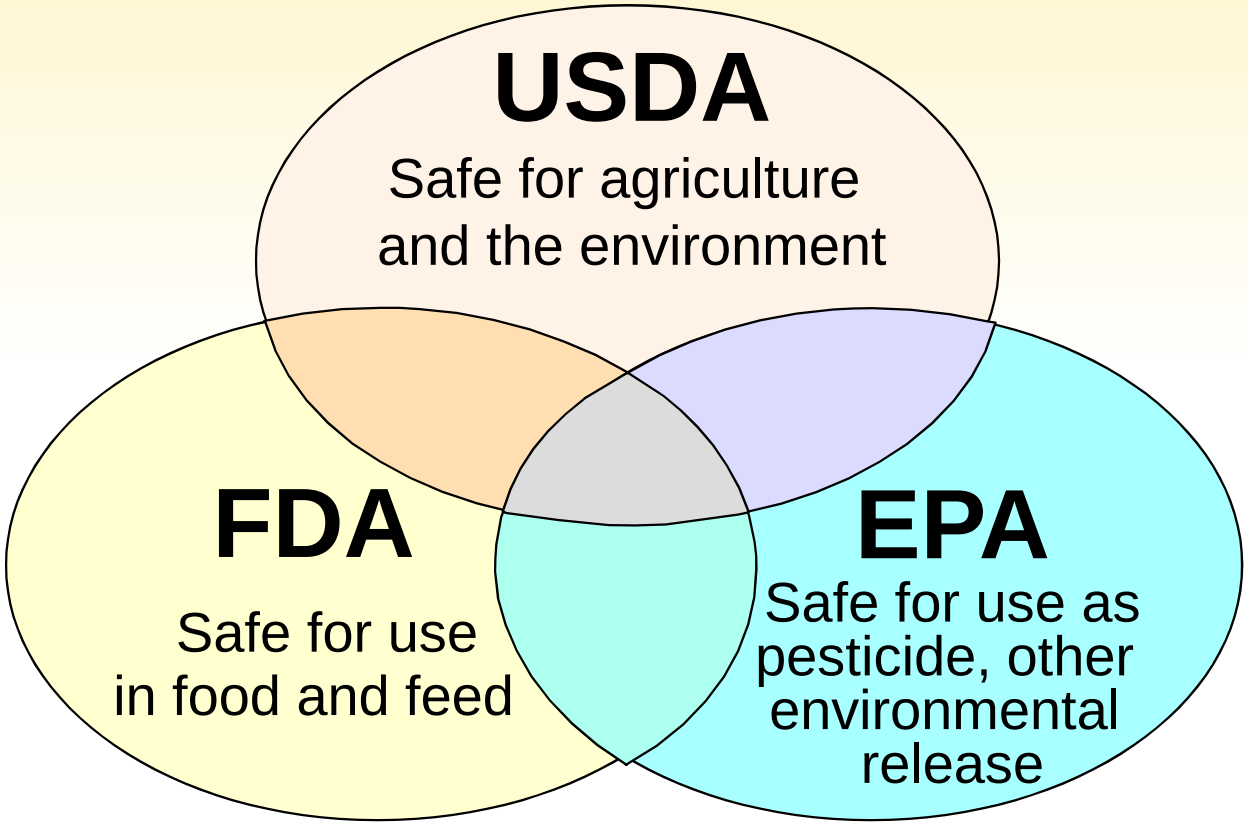
- Permit Guidance

  http://www.aphis.usda.gov/biotechnology/permits.shtml


THANK YOU……

Extra Slides

Coordinated Framework



Products can be regulated by more than one agency

What Does APHIS Regulate?

The Plant Protection Act defines "plant pest" as:

Any living stage of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product:

- **a protozoan**
- **a nonhuman animal**
- **a parasitic plant**
- **a bacterium**
- **a fungus**
- **a virus or viroid**
- **an infectious agent or other pathogen**
- **any article similar to or allied with any of the articles specified in the preceding subparagraphs**

Compliance, Inspection, and Enforcement

- APHIS conducts inspections and tracks compliance with the conditions of the permit
  - Applicants are legally obligated to comply with conditions permits and to report any non-compliance
  - Permits are subject to inspections and reporting requirements
  - Violations may be subject to fines

Petition Process for Nonregulated Status

§ Petition Evaluation

- Comprehensive scientific review
- Crop biology and taxonomy
- Genotypic differences
- Phenotypic differences
- Field test reports for all releases conducted in the U.S.
- Relevant experimental data, publications and other data upon which to base a determination

GE Plants with Nonregulated Status

- APHIS has made determinations of nonregulated status in response to over 100 petitions, representing 16 plant species
- The determination of nonregulated status extends to the GE plant and its offspring
- Once APHIS determines nonregulated status, the GE organism can be freely moved and planted without APHIS regulatory oversight
- Actual commercialization of GE plants with nonregulated status is determined by market demand, not the APHIS decision

APHIS Regulations and Synthetic Biology

Holdren Memo, March 2011

- Protection of safety, health, and the environment while avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating trade barriers
- § Regulatory Principles
  - Decisions based on best obtainable scientific, technical, economic, and other information
  - Regulations developed with firm commitment to fair notice and public participation
  - Benefits of regulation should justify costs
  - Regulations should promote innovations while also advancing regulatory objectives
  - When no significant oversight issue can be identified, consider the option not to regulate
  - Regulatory approaches should be performance-based and provide predictability and flexibility