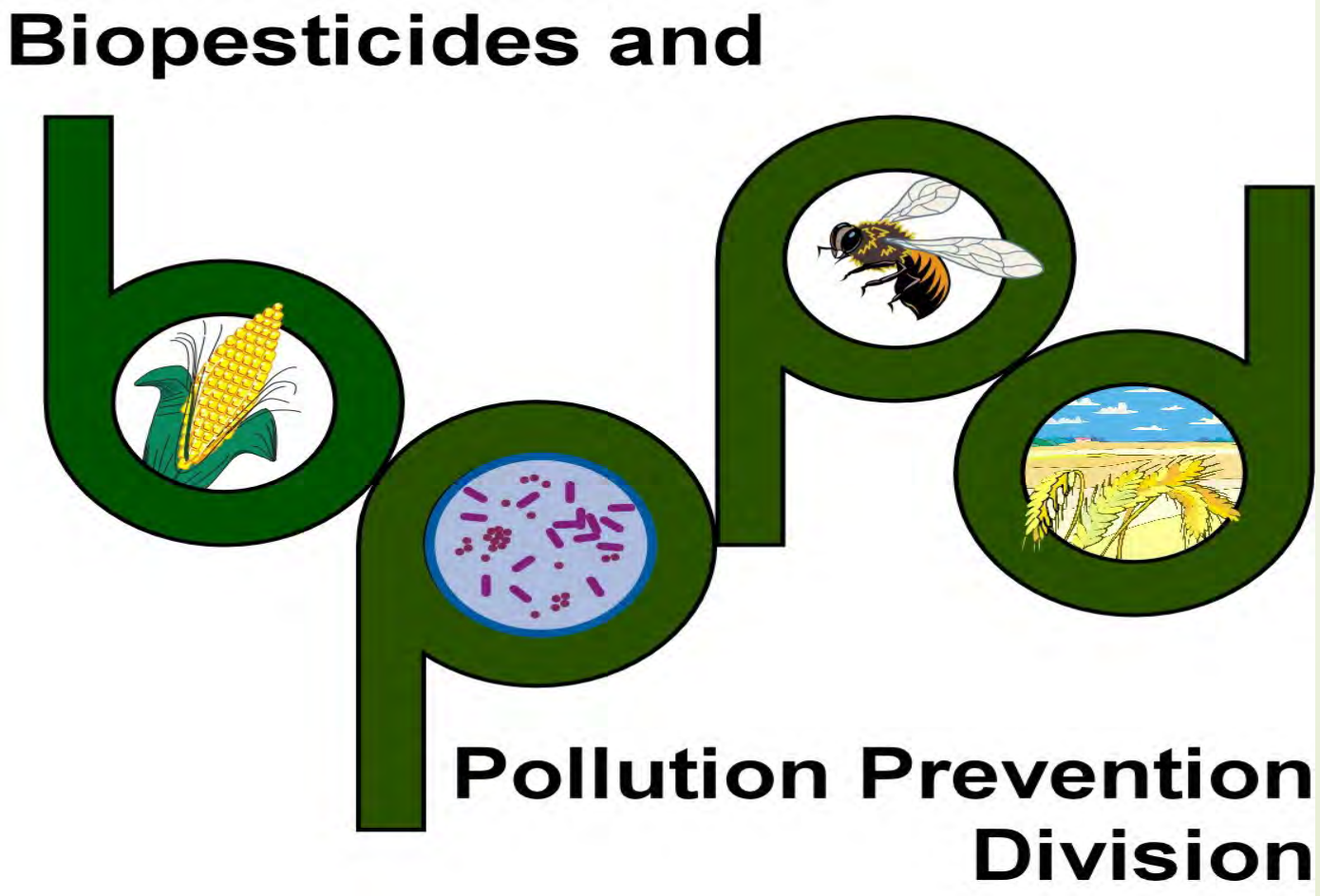
OPP's Role in Agricultural Biotechnology Today and Tomorrow

Opening Remarks

- Robert McNally, Director



OPP's Role in Agricultural Biotechnology Today and Tomorrow

- White House memo from July 2015: 3 key Points:

https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

- Today -- Coordinated Framework Update – USDA, EPA (FIFRA and TSCA) and FDA
  - Coordinated Framework has existed for 30 years
  - Clarify current roles and responsibilities in the regulatory process
- Tomorrow – Long term Strategy
  - New products are in development
  - Ensure Federal gov't is equipped to efficiently address any risks with future products of biotech
- Tomorrow – National Academy of Sciences (NAS)
  - Commission an expert panel to scan the horizon to determine the future landscape of biotech products

Implementation of White House memo

- 2015/2016 Process – 3 public meetings, about 900 public comments
- Results:
  - Sept. 16, 2016 Revised CF out for 40 day public comment
  - Sept 16 Long term strategy posted on web for public review
  - NAS Initial Meeting: Summer 2016 - report expected first half of 2017

Today's Focus

- Provide broad overview of all three activities CF Update, Long term Strategy, and National Academy of Sciences effort
- Use two case studies that are pesticide specific to illustrate the "Today" work of the CF and the "Tomorrow" work of the Long Term Strategy
  - Case Study #1: Bt Corn PIPs – how the CF works today to regulate/oversee these;
  - Case Study #2: GE Mosquitoes – How the three agencies are involved in this technology of tomorrow

BPPD's Role

- Why is BPPD Involved in this Coordination and Strategy?
- BPPD's Mission: "Protect human health and the environment by reducing risks of pesticides through regulating biopesticides and through encouraging pollution prevention practices."
- Biopesticides: In general:
  - Considered to be "reduced risk" pesticides
  - Affect only the target pests and closely related organisms
  - Less toxic than conventional pesticides
  - Decompose quickly

What are Biopesticides?

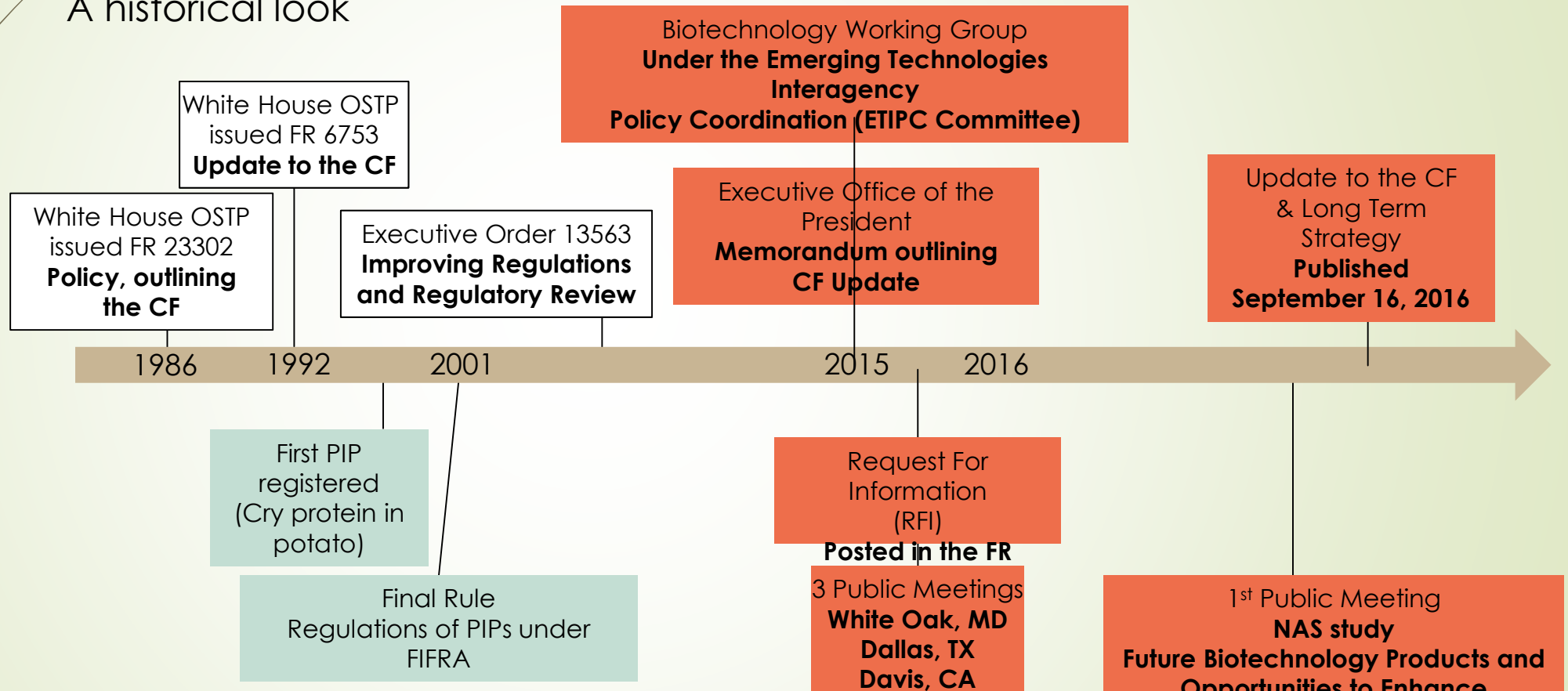
- Biopesticides fall into three areas:
  - Biochemicals – naturally occurring chemical substances that control pests with non-toxic mode of action
  - Microbials – microorganisms that control pests
  - Plant-Incorporated Protectants – pesticidal substances produced by plants and the genetic material necessary to produce them (PIPs)

Plant-Incorporated Protectants

- Plant-Incorporated Protectants (PIPs) – Plants containing PIPS may be regulated by FDA and USDA.
- The Coordinated Framework for Biotechnology was established 30 years ago to coordinate efforts across all three agencies on things like PIPs.
- September 2016 Coordinated Framework Update
  - Bt Corn Case Study will illustrate how the 3 agencies coordinate today on these products, and in doing so describe the key elements of the Framework as it relates to pesticides and OPP's role

The Coordinated Framework for Regulation of Biotechnology (CF)

A historical look



The Coordinated Framework for Regulation of Biotechnology (CF)

July 2, 2015 Executive Office of the President's Office of Science and Technology Memorandum - Modernizing the Regulatory System for Biotechnology Products

Goals and guidance

- Federal agencies that regulate biotechnology products should continually strive to:
  - Improve predictability
  - Increase efficiency
  - Reduce uncertainty in their regulatory processes and requirements
- It is critical that these improvements:
  - Maintain high standards that are based on the best available science and that deliver appropriate health and environmental protection
  - Establish transparent, coordinated, predictable, and efficient regulatory practices across agencies with overlapping jurisdiction
  - Promote public confidence in the oversight of the products of biotechnology through clear and transparent public engagement

The Coordinated Framework for Regulation of Biotechnology (CF)

Modernizing the Regulatory System for Biotechnology Products

1) Update the Coordinated Framework for the Regulation of Biotechnology,
2) Develop a long-term strategy to ensure that the Federal biotechnology regulatory system is prepared for the future products of biotechnology, and
3) Commission an expert analysis of the future landscape of biotechnology products to support this effort.

Clarifying Current Roles and Responsibilities

The September 16, 2016 proposed Update to the Coordinated Framework offers a complete picture of a robust and flexible regulatory structure that provides appropriate oversight for all products of modern biotechnology.

The proposed Update to the Coordinated Framework; presents information about agency roles, and responsibilities in several forms, including:

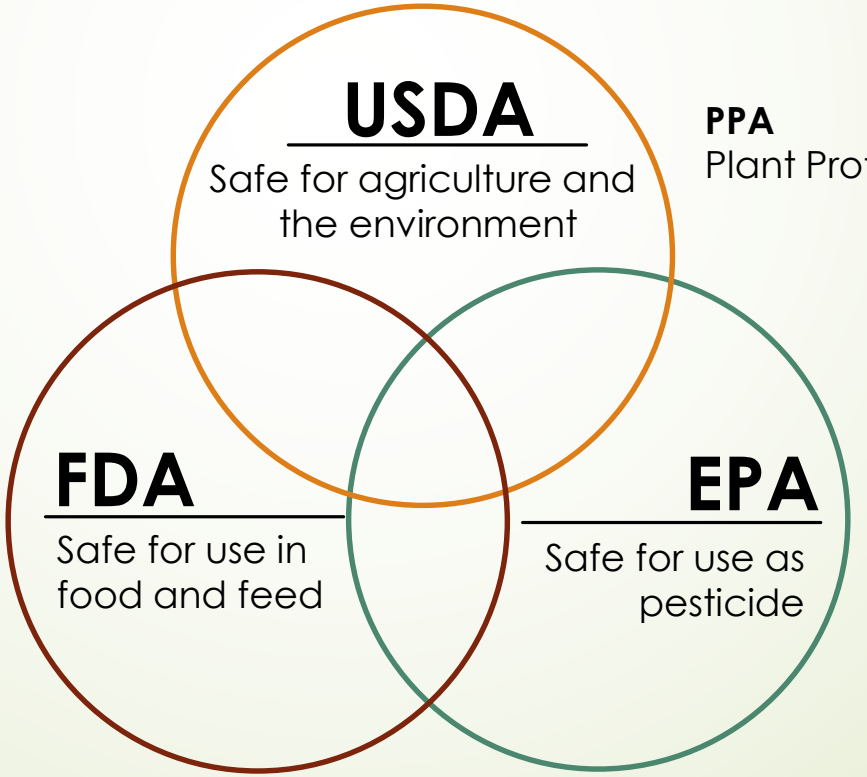
- graphics
- case studies
- a comprehensive table

Product Area	Source Organism or Culture			
	Genetically Engineered Plant	Genetically Engineered Animal	Genetically Engineered Microbe or Cultured Cell	Cell-free Synthesis
Pesticide	EPA/OPP If plant-incorporated protectant is produced by plant, EPA/OPP regulates the pesticide trait and related genetic material for human and environmental safety, including the safety of dietary exposures to pesticide residues in human and animal food USDA/APHIS/BRS If plant poses a plant pest risk FDA/CFSAN If human food, FDA/CFSAN oversees non-EPA-regulated aspects of the food for safety for human consumption FDA/CVM If animal food, FDA/CVM oversees non-EPA-regulated aspects of the food for safety for animal consumption	EPA/OPP If an animal is used as a pesticide, EPA/OPP ensures safety of human and animal food by regulating as chemical pesticide residues any animals or animal parts in the human or animal food, e.g., predatory insects, predatory insect parts, or nematodes in grain. USDA/APHIS/BRS If animal poses a plant pest risk FDA/CVM	EPA/OPP If pesticide is a genetically engineered microbe, EPA/OPP regulates the microbial pesticide for human and environmental safety, including the safety of dietary exposure to pesticide residues in human and animal food. This also includes genetically engineered bacterial symbionts that are part of a nematode-bacterial entomopathogen complex. USDA/APHIS/BRS If microbe poses a plant pest risk EPA/OPPT Evaluates and potentially regulates a living genetically engineered microbe used as a pesticide intermediate, i.e., where the "pesticide" product is the dead microbe FDA/CFSAN If human food, FDA/CFSAN oversees non-EPA-regulated aspects of the food for safety for human consumption FDA/CVM If animal food, FDA/CVM oversees non-EPA-regulated aspects of the food for safety for animal consumption	EPA/OPP If nucleic acids produced via cell-free synthesis are used for pesticidal purposes, these products are regulated by EPA/OPP for human and environmental safety, including the safety of exposures to pesticide residues in human and animal food

The Coordinated Framework for Regulation of Biotechnology (CF)

Regulatory oversight over genetically engineered plants

- Each Federal Agency has their specific triggers for regulatory oversight associated with own protection goals



PPA
Plant Protection Act

FFDCA
Federal Food Drug and Cosmetic Act

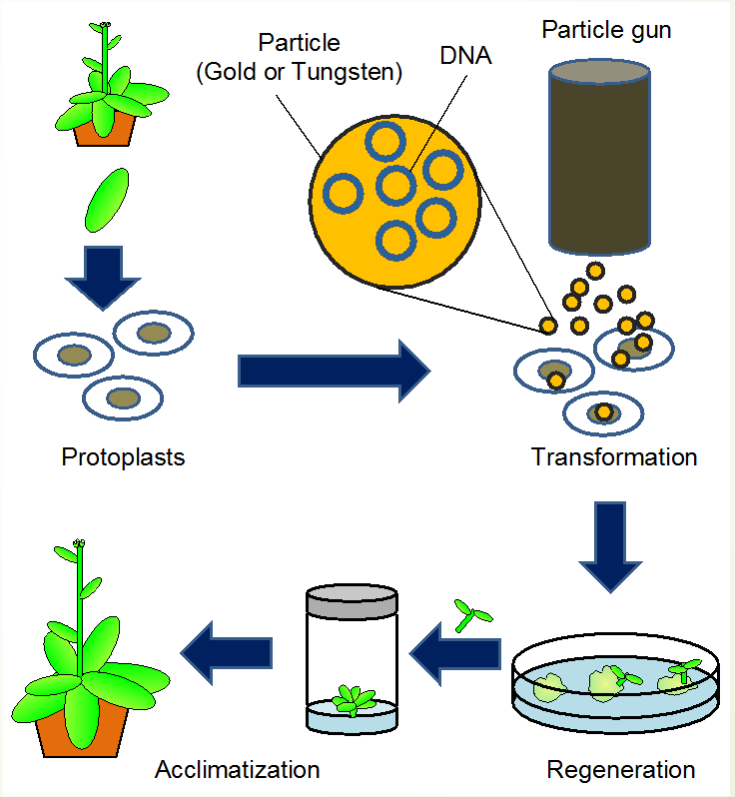
FIFRA
Federal Insecticide Fungicide and Rodenticide Act

FFDCA
Federal Food Drug and Cosmetic Act

Bt Crops and the PPDC

- In 1999, OPP asked PPDC whether Bt-PIPs are a "public good" to be conserved
  - Bt used for many years by organic growers
  - PIPs expressed constitutively by crop on millions of acres season after season
    - Potential for resistance
- PPDC agreed Bt should be conserved as a "public good"
- With PPDC guidance, OPP instituted "insect resistance management" or "IRM" for Bt-PIPs
- Program now a model for other resistance management programs

Moving Genetic Information into the Plant – Making Bt Corn



Case Study #1 - Bt Corn Submitted Data

- Acute oral toxicity, heat stability, amino acid sequence analyses compared to known toxins and allergens, *in vitro* digestibility
- Molecular characterization, protein expression levels
- Non-target organism toxicity, environmental fate, and gene flow
- Insect resistance management
- EPA will provide the appropriate scientific review to ensure we are protecting human health and the environment.
- PRIA deadlines for registration actions shorter and costs lower compared to conventional pesticide

Bt Corn – Safety Findings

- EPA evaluates pesticidal substance and the genetic material necessary for its production, e.g. Bt Cry protein and *cry* gene in corn.
- No toxic effects to humans or non-targets. No allergenicity.
- Non-target invertebrates are generally more abundant in *Bt* cotton and *Bt* corn fields than in non-transgenic fields managed with chemical insecticides.
- Do not bioaccumulate. Bt proteins readily susceptible to metabolic, microbial, and abiotic degradation
- No short term effects. No long term effects – no bioaccumulation. No effects on bees, workers, groundwater, etc
- Prescribe IRM requirements to ensure continued prevention of evolution of resistance in target pests.

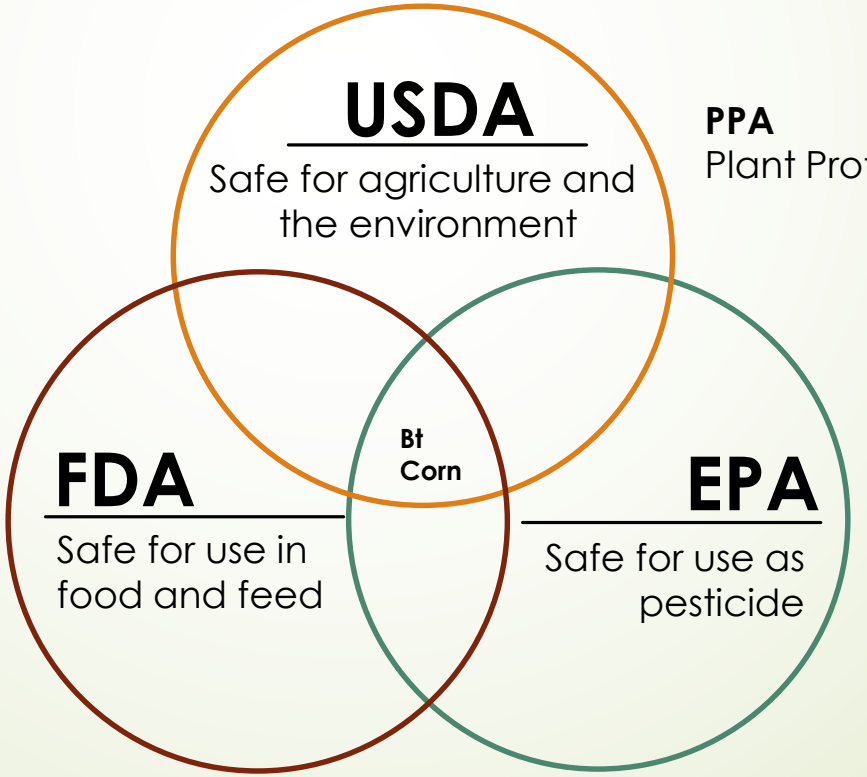
Bt Corn – Other Benefits

- Reduced use of conventional pesticides.
- Reduction in use of broader spectrum, harsher conventional chemical pesticides, e.g., Bt-PIPs reduced conventional chemical pesticide use by 12.5 million pounds of active ingredient over 7.5 million corn acres in the first 3 years for corn rootworm control

The Coordinated Framework for Regulation of Biotechnology (CF)
-Bt Corn-

Regulatory oversight over genetically engineered plants

- Each Federal Agency has their specific triggers for regulatory oversight associated with its own protection goals



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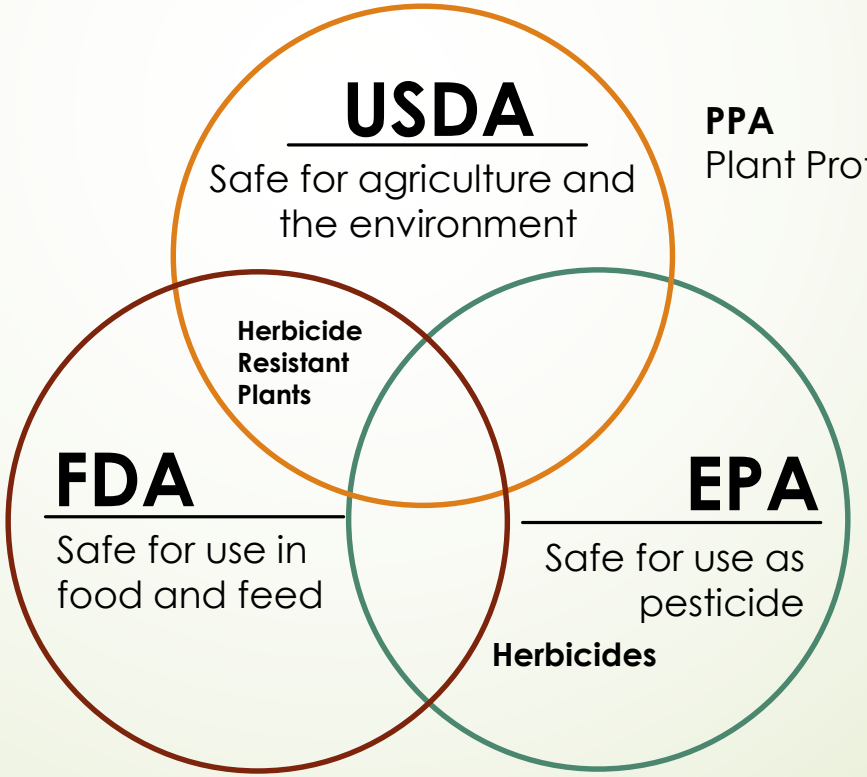
Herbicide Resistant Plants

EPA regulates the chemical herbicides used on herbicide resistant plants, not the plants.

The Coordinated Framework for Regulation of Biotechnology (CF)
-Herbicide Resistant Food Plants-

Regulatory oversight over genetically engineered plants

- Each Federal Agency has their specific triggers for regulatory oversight
  - Associated with own protection goals



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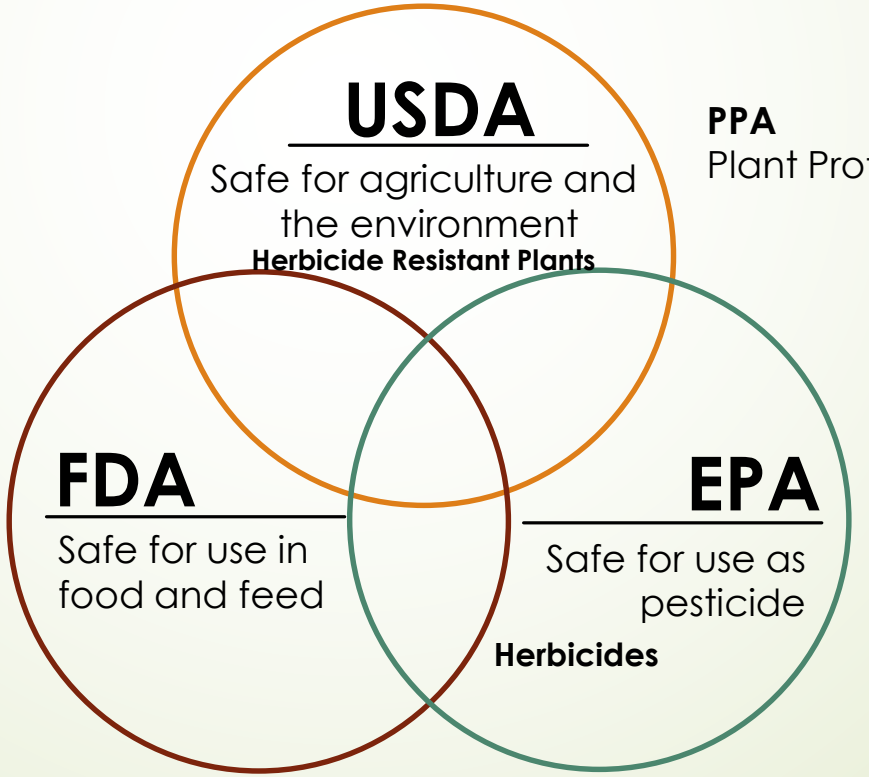
The Coordinated Framework for Regulation of Biotechnology (CF)
-Herbicide Resistant Non-Food Plants-

Regulatory oversight over genetically engineered plants

- Each Federal Agency has their specific triggers for regulatory oversight
  - Associated with own protection goals



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Biotech Strategy – Preparing for the Future

- The September 16, 2016 *National Strategy for Modernizing the Regulatory System for Biotechnology Products* sets forth a vision for:
  - ensuring Federal regulatory system equipped to assess efficiently risks, if any, associated with future products of biotechnology
  - supporting innovation,
  - protecting health and the environment,
  - maintaining public confidence in the regulatory process, increasing transparency and predictability, and
  - reducing unnecessary costs and burdens.

- In the *Strategy*, the Federal agencies demonstrate their sustained commitment to ensure the safety of future products of biotechnology, increase public confidence in the regulatory system, and prevent unnecessary barriers to future innovation and competitiveness.

- The *Strategy* highlights many existing and new activities at EPA, FDA, and USDA. RNAi, etc. would be future areas to coordinate among federal partners

Biotech Strategy - Coordination

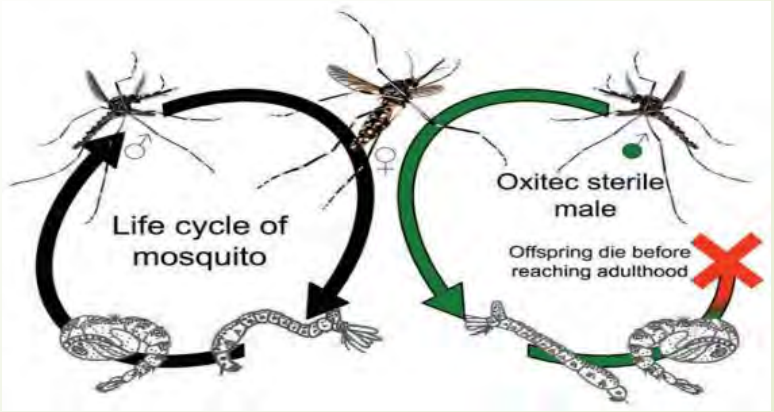
- EPA, FDA, and USDA commit to interagency communication that helps with:
  - timely decisions on regulatory jurisdiction
  - clarifying for developers which regulatory agency(ies) have oversight responsibility for a novel biotechnology product
- EPA, FDA, and USDA will enhance collaborations to optimize use of scientific data for scientific and regulatory assessments.

Future Regulatory Challenges: Genetic Modification of Insects as Pest Control

- Even today, vector borne diseases such as malaria, kill hundreds of thousands of people or result in devastating consequences, e.g., zika
- New technologies and information are resulting in the development of new means of reducing the population of disease vectors, e.g., mosquitoes
- And BPPD may play some role in evaluating and ensuring the safety of genetically modified insects used to reduce pest populations
- At this time, BPPD has under review non-GE mosquitoes that can be used to reduce mosquito populations
  - These mosquitoes contain variants of a microorganism, *Wolbachia pipientis*
  - *Wolbachia pipientis* is a microorganism that is naturally found in many types of insects
  - Some *Wolbachia* can adversely impact mosquito fertility
    - Large numbers of male mosquito containing such *Wolbachia* would be reared in laboratories and then released into the environment to mate with wild females that do not carry the *Wolbachia*. Eggs from females that mate with these males do not hatch

Case Study # 2 - GE Mosquito Control Product

- Another type of mosquito control product currently in the testing pipeline
- Also intended to reduce mosquito populations, but using genetic engineering of mosquito
- Like *Wolbachia pipientis* approach, interferes with mosquito's ability to reproduce
  - Gene modified through genetic engineering stops mosquito cells from functioning normally
    - Protein produced from the gene ties up cellular machinery – other important proteins not produced
- Involves releases of large numbers of male mosquitoes to mate with wild female mosquitoes, produce defective offspring unable to grow into adults
- Male mosquitoes do not bite



Biotech Strategy - Insects

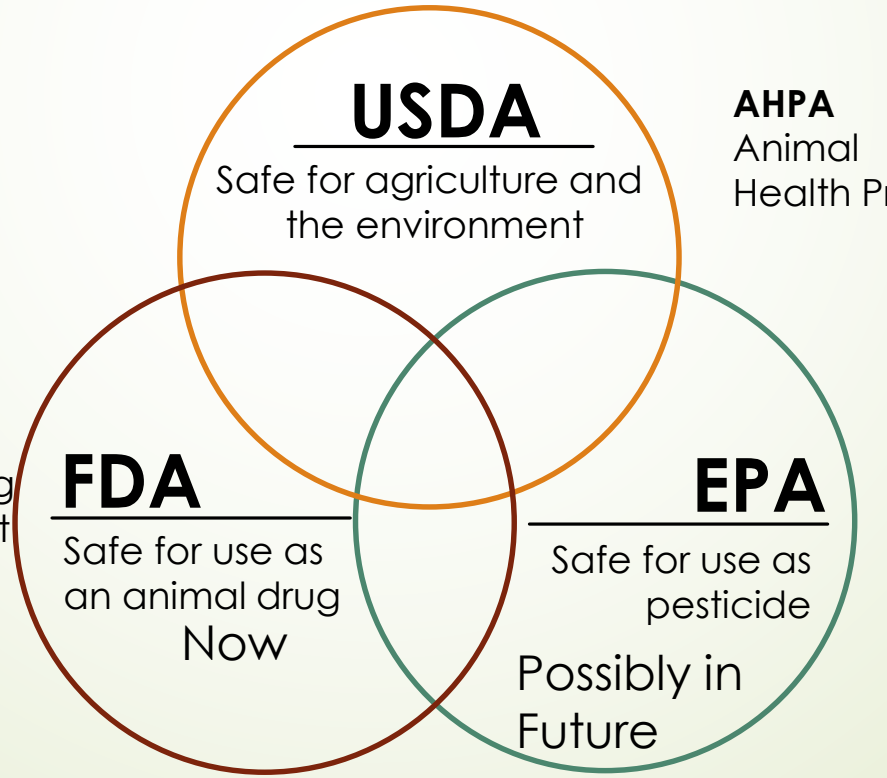
- **EPA, FDA and USDA will** continue to examine their regulatory structures with the goal of **clarifying how the U.S. Federal Government will regulate genetically engineered insects** in an integrated and coordinated fashion to cover the full range of potential products. The agencies are working **to better align their responsibilities over genetically engineered insects with their traditional oversight roles, for example, considering mechanisms that would enable EPA to regulate genetically engineered mosquitos under FIFRA when the developer claims they are intended to control population levels,** and FDA to regulate them under FD&C Act when the developer makes a disease claim. USDA will continue to exercise its authorities for control of certain plant or animal pest insects.

Biotech Strategy - Insects

With respect to GE insects, EPA has already noted the specific wording in the Strategy document. ***FDA and EPA are currently determining how best to delineate responsibilities and provide additional direction and clarity****, including assessing how to exercise their authorities for regulation of GE mosquitoes based on the developer's intended use of the product. For example,* ***the agencies are looking at ways that would enable EPA to regulate GE mosquitoes under its FIFRA pesticide authority when the developer claims they are intended to control population levels of wild mosquitoes.*** *FDA would continue to regulate under the FD&C Act GE mosquitoes that are intended to prevent or mitigate disease transmission. FDA plans to issue a draft guidance or regulation that would clarify regulatory oversight for GE mosquitoes. We are working closely with EPA and APHIS to ensure that any such guidance or regulation takes into account and accurately reflects their regulatory authorities.* ***In the interim, FDA will continue to review GE mosquitoes under its new animal drug authorities.***

The Coordinated Framework for Regulation of Biotechnology (CF)
-GE *Aedes aegypti Mosquito for Population Control*-

- Each Federal Agency has their specific triggers for regulatory oversight associated with own protection goals



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The Coordinated Framework for Regulation of Biotechnology (CF)

Modernizing the Regulatory System for Biotechnology Products

- Commission an expert analysis of the future landscape of biotechnology products to support this effort, https://www8.nationalacademies.org/cp/CommitteeView.aspx?key=49773

- NAS initial meeting held Summer 2016

NAS Study Tasks

- Major advances and potential types of new products in next 10 years
- Describe risk analysis system and how it pertains to agencies' authorities
- Project whether potential future products could present novel types of risks
- What scientific capabilities, expertise, tools could be useful to the regulatory agencies

Summary of Key Points

- CF Update comment period closed November 1st. The CF Update is posted on the web at https://www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_coordinated_framework.pdf
- Long term strategy is posted on the web at https://www.whitehouse.gov/sites/default/files/microsites/ostp/biotech_national_strategy_final.pdf
- National Academy of Science (NAS) effort is ongoing and a report should be issued by early 2017.
- OPP's review is science based and thorough.
- Fewer data requirements and lower PRIA fees than conventional pesticides
- Focus is on the product – is it a pesticide or not – not the process used to develop it.

Summary of Key Points

- Over 100 Bt PIP pesticides registered over the last two decades have not had any traditional risk issues to manage
  - No bee issues
  - No worker mitigation
  - No effects on non- targets
  - No FQPA concerns
- New Technology is coming down the road – GE Mosquitoes, RNAi.
  - These efforts will be handled in coordination with FDA and USDA as needed.
  - EPA will provide the appropriate scientific review to ensure we are protecting human health and the environment.