

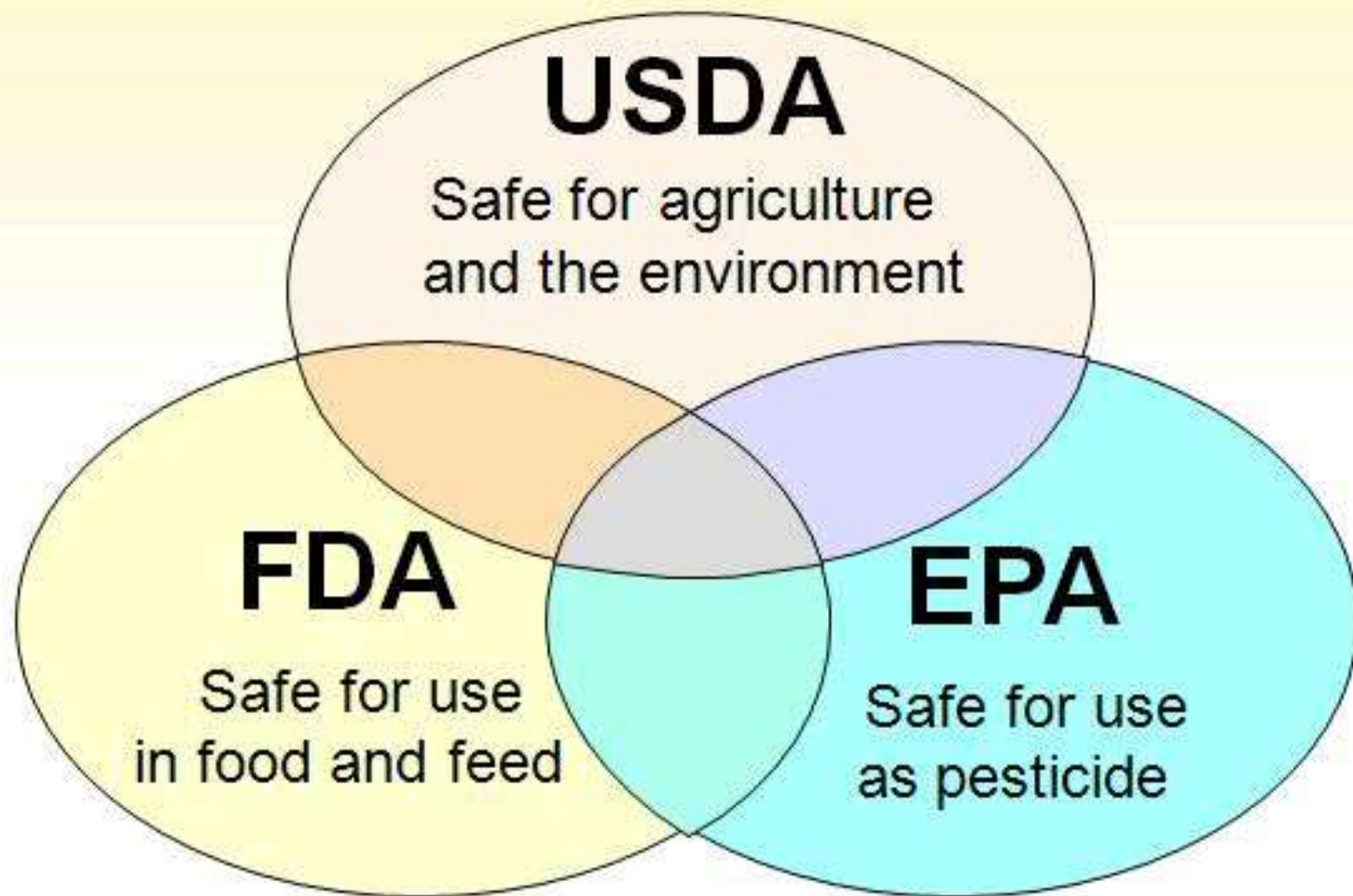


Overview of US EPA Regulation of Plant-Incorporated Protectants



Presentation for NRC's Genetically Engineered Crops Comm.

*EPA Office of Pesticide Programs
December 10, 2014*





EPA's Statutory Authority

- **Federal Insecticide, Fungicide and Rodenticide Act – (FIFRA) - pesticides**
 - **No unreasonable adverse effects upon man and the environment**
- **Federal Food Drug and Cosmetic Act – (FFDCA) - food and feed safety**
 - **Reasonable certainty of no harm from aggregate exposure**



Background

In order to protect human health and the environment, the EPA Office of Pesticides regulates the sale, distribution, and use of all pesticides in the US, as well as the pesticide residues in food and animal feed.

Pesticides include:

- **Conventional chemicals (herbicides, insecticides, etc.)**
- **Plant-Incorporated protectants (PIPs)**
- **Microbial and biochemical Pest Control Agents**



What is a Plant-Incorporated Protectant (PIP)?

“ . . . a pesticidal substance that is intended to be produced and used in a living plant, or in the produce thereof, and the genetic material necessary for production of such a pesticidal substance. “

It also includes any inert ingredient contained in the plant, or produce thereof.” (40 CFR Sec. 174.3)

- e.g., antibiotic or herbicide tolerance marker used in the selection of a PIP product
- **NOTE: EPA does not regulate the plant, only the pesticidal substance and associated gene(s)**



Plant-Incorporated Protectants

- Cotton, Maize, Potato and Soybean expressing insecticidal toxins from *Bacillus thuringiensis* (e.g., Bt-maize)
- Virus resistant potato, European plum, yellow squash and papaya



FIFRA Registration

- **FIFRA is a licensing statute – pesticides require initial premarket review and periodic reevaluation, as well as annual maintenance fee for sale and distribution in the US**
- **Registration typically follows an Experimental Use Permit [Section 5 FIFRA]**
- **Adverse events require reporting to EPA for the life of the product [6(a)2 FIFRA]**



Experimental Use Permits (EUPs)

- ✓ **EUP required for field testing above cumulative acreage of ≥ 10 Acres (4 Hectares) per year per pest**
- ✓ **Food / feed tolerance exemption (or crop destruction) required (at any size)**
- ✓ **EUPs are all time limited and require reporting of results as well as any adverse events – [6(a)2 of FIFRA]**
- ✓ **Pesticides under EUPs are not eligible for sale, advertising, or promotion**
- ✓ **EUPs are for research purposes; collection of data needed to support registration**



Herbicide Tolerant Crops

- OPP licenses the herbicide for use on genetically modified or conventionally bred crops
 - EPA establishes terms and conditions of the herbicide registration with the registrant
 - Approves product label for users (growers, applicators, and consultants)
- *Goal is to have effective resistance management and maintain flexibility for growers*
- *Enlist Duo® recently approved for use on corn and soybeans*



Food / Feed Tolerance

- **Federal Food Drug and Cosmetic Act**
- **Residue of pesticide on food or feed requires a tolerance or exemption**
- **Toxicity profiles are used to determine safety of pesticide residues**
- **FDA enforces tolerance violations**



FFDCA - Tolerances

- **Tolerance actions include inert ingredients (markers)**
- **Tolerances can be for all crops / commodities or more restricted**
- **Trade with unapproved PIPs in commerce can be problematic**



Regulation of Agricultural Biotechnology

- Transparent and accessible
- Flexible and case-by-case evaluation
- Evolves with time and discovery
- Scientifically based and responsive to novel technologies and developments



RISK



Ecological
(acute & chronic)

Human Health
(acute & chronic)



Aquatic

Terrestrial

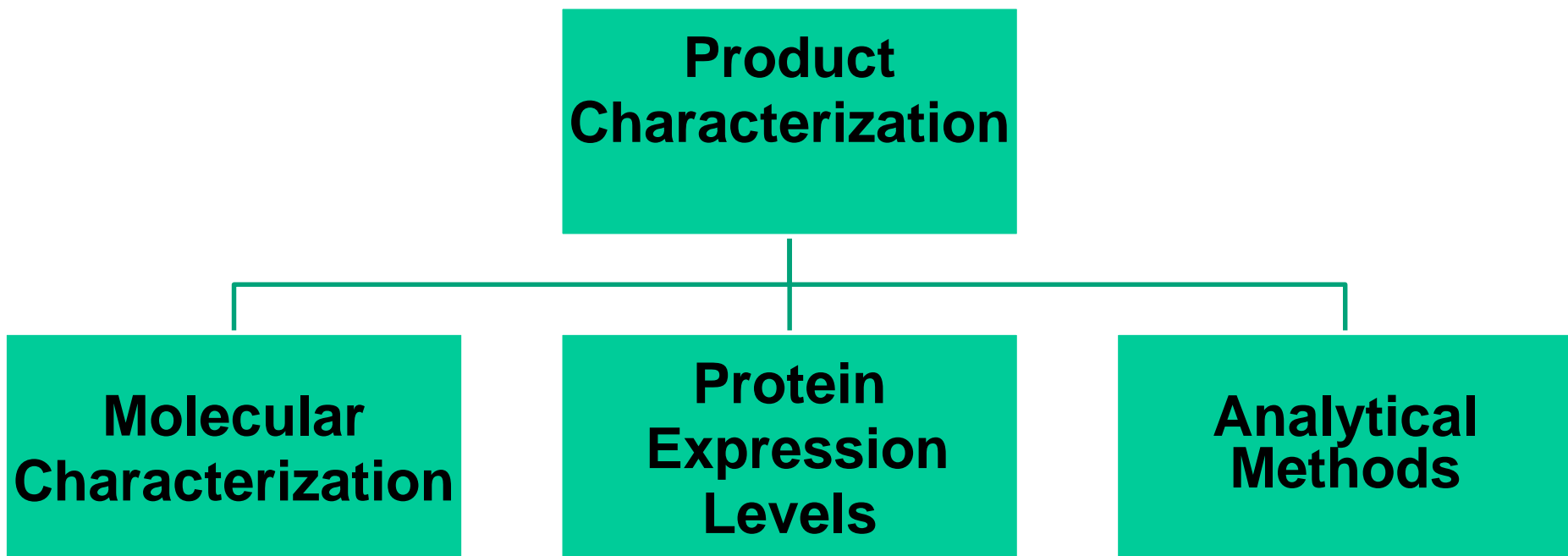


Populations & Subpopulations

Special protection for children

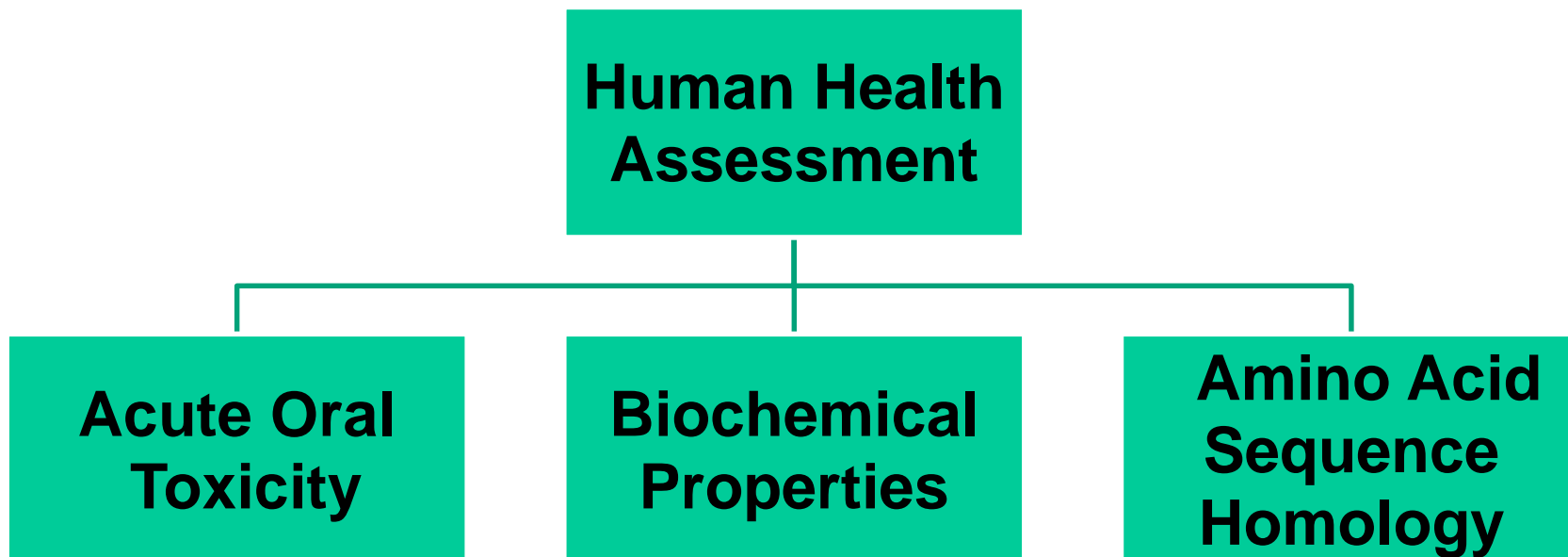


How EPA Characterizes PIPs



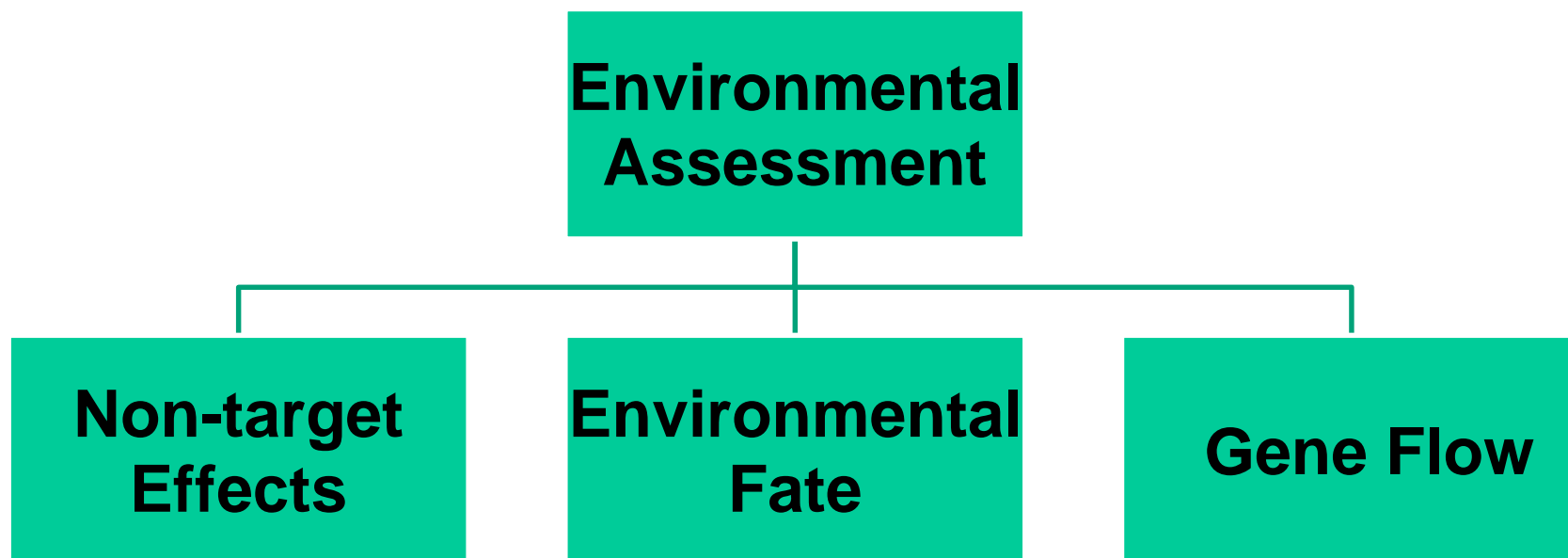


How EPA Assesses Human Health Effects for PIPs





How EPA Assesses Environmental Effects for PIPs





Insect Resistance Management

- **Bt-based biopesticides are considered as ‘in the public good’- therefore,**
 - **IRM plan is required** for each *Bt* product as a condition of registration
- **IRM was instituted to maintain *Bt* efficacy and reap the benefits of reduced environmentally persistent, chemical insecticide application**
- **Both microbial and PIP expressed Cry proteins remain effective against target pest complexes, however, CRW resistance noted**



Insect Resistance Management for Bt Crops

- **Public Good**
 - **Benefits due to pesticide reduction in corn and cotton (USEPA 2001)**
 - **Human health, non-target species, and environment**
- **Preserve the lifetime of microbial Bt sprays**
- **Higher selection pressure for resistance with PIPs than conventional insecticides**
 - **Season-long expression of Bt toxins**
 - **Many target Pests have multiple generations per year (up to 6 for bollworm)**
 - **Some pests feed almost exclusively on corn or cotton (ex. European corn borer, corn rootworm, pink bollworm)**
- **Resistance to PIPs is deemed an adverse effect**



New Breeding Technologies

- **Site directed DNA modification**
 - CRISPR / Cas9 / TALENs / ZFN
- **Oligonucleotide directed modification**
- **Epigenetics / methylation**
- **Reverse breeding**
- **Synthetic genomics**



NBTs – How will they be regulated (or not?)

- EPA regulates pesticides based upon intent and phenotype
- Which NBT may be used to create the product is not as relevant as the product
- Practical considerations need to be included in discussions of regulation
- Risk-based analysis



Useful websites

- <http://www.epa.gov/pesticides/biopesticides/regtools/biotech-reg-prod.htm> [**Biotech Pesticide Regulation**]
- http://www.epa.gov/scipoly/sap/meetings/2000/october/brad3_enviroassessment.pdf [**PIPs Risk:Benefit**]
- http://www.epa.gov/pesticides/biopesticides/reg_of_biotech/eparegofbiotech.htm [**Biotech Pest Management**]
- <http://www.epa.gov/scipoly/sap/meetings/2009/022509meeting.htm> [**PIP Data Requirements**]
- <http://www.epa.gov/scipoly/sap/meetings/2014/january/012814minutes.pdf> [**RNA interference report**]