BT PIP Insect Resistance Management: An Overview

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EPA Resistance Management Activities

- Voluntary Resistance Management Mode of Action Rotation Labeling Guidelines
  - PR Notice 2001-5
- Section 18s
- 6(a)2 reporting of substantiated instances of resistance
- EPA began resistance management effort in 1992 for all pesticides
  - 1995 1st Bt registered

EPA Resistance Management Activities

- USDA/APHIS and EPA/OPP joint efforts to address herbicides and herbicide tolerant crops

- Insect Resistance Management (IRM) Requirements for Bt Crops (PIPs*)

*Plant Incorporated Protectar

Background

- What is IRM?
  - Strategies/Plan to manage/mitigate/delay insect resistance
  - Centers on reducing the selection for insects carrying one copy of an allele for resistance at a given locus (i.e., RS) in favor of those carrying no such alleles (i.e., SS)
- How is it regulated?
  - IRM evaluated under FIFRA, but no specific data requirements or regulations

Background

- Compared to other conventional pesticides, IRM plans for Bt PIPs are unprecedented
- More detailed, prescriptive, proactive
- Why is it regulated for Bt PIPs?
  - Bt susceptibility is in the “Public Good”
  - Preserve environmental benefits

Background

- IRM plans required for all Bt PIPs
  - Potato
  - Sweet corn (Attribute – Cry1Ab)
  - Field corn (not all are listed)
    - YieldGard - Cry1Ab
    - Herculex -Cry1F
    - YieldGard RW -Cry3Bb
    - YieldGard Plus - Cry1Ab + Cry3Bb
  - Cotton

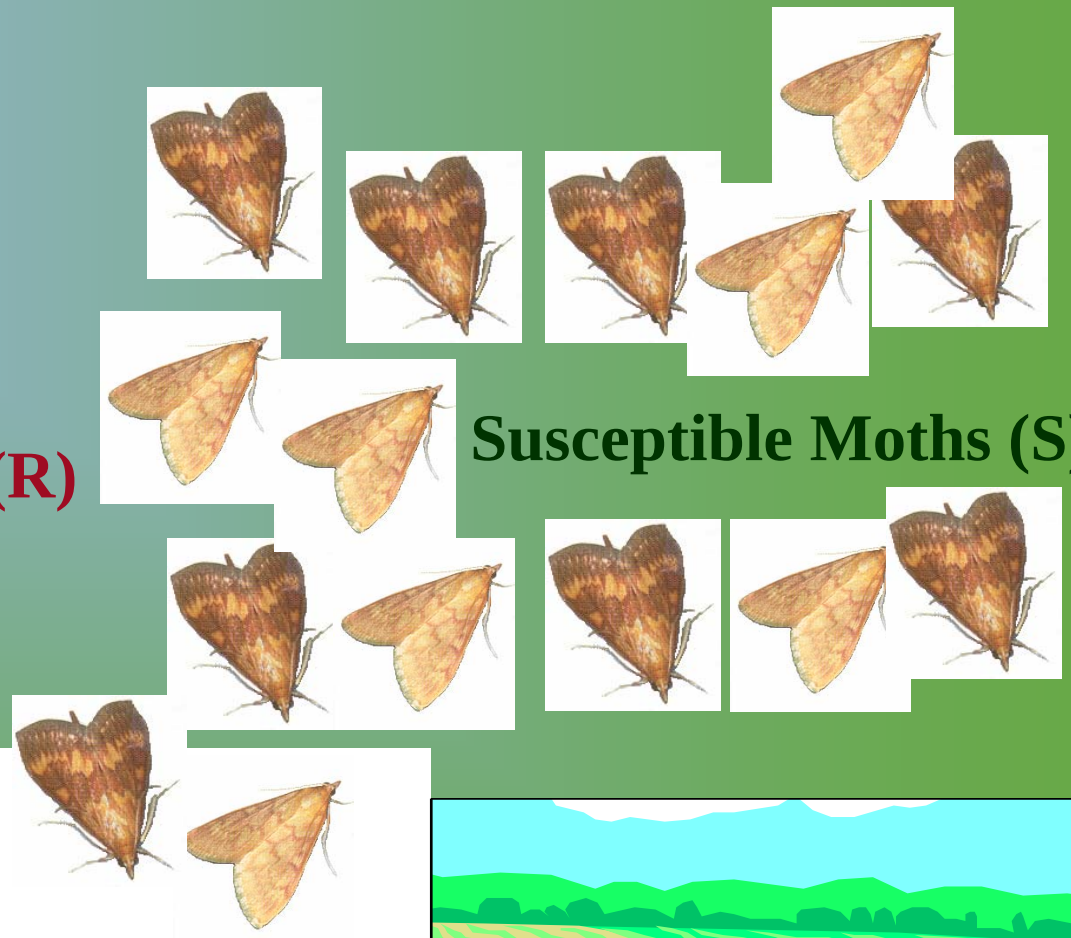
Public Review of IRM Program

- Pesticide Program Dialogue Committee (1996, 1999)
- Public hearings (2 in 1997)
- Scientific Advisory Panels (1995, 1998, 2000, 2002)
- Public workshops (1999, 2001)
- Scientific meetings (ESA, Beltwide)
- USDA research committees (NC205, NCR46)
- Public comments
- Seminars, speeches, published papers

Refuge Strategy

Resistant Moths (R)

Susceptible Moths (S)



TARGET = 500 susceptible to 1 resistant

Bt Crop

Non-Bt Crop

High Dose/Refuge Assumptions

- Single or major resistance gene (R).
  - RRs are rare.
- Susceptible is dominant (S). Resistance is a recessive trait.
  - Refuge supplies SS
- Random mating or preferential mating –
  - RR x RS
  - RR x SS
- RSs will be fully susceptible to Bt PIP
  - High dose = >95% RS will be killed and >99.9% of the SS will be killed]

Resistance Risk Assessment

- Pest Adaptation Factors
  - Operational Factors
    - Dose
    - Toxin, stacks
  - Biological Factor
    - Adult dispersal
    - Larval dispersal
    - Alternate hosts
  - Genetic Factors
- Models

Models

- Predict likelihood of resistance (adaptivity) under certain assumptions.
- Important tool to evaluate and compare IRM options – Aid decision-makers
- Focus monitoring efforts, data needs
- Best tool in absence of field resistance
- Can’t fully validate models without

Risk Management

- Models
- IRM requirements
- Time-limited registrations
  - Bt corn PIPs – October 2008
  - Newer Bt corn PIPs (Cry34Ab1, etc.) – September 2010

2001 Bt PIP Reassessment: IRM Program Required Elements

- Refuge
- Grower agreements (contracts)
- Grower education program
- Grower compliance program
- Monitoring for insect resistance
- Remedial action plans
- Annual reports

Bt Corn Lepidopteran (ECB, SWCB, CEW) Refuge

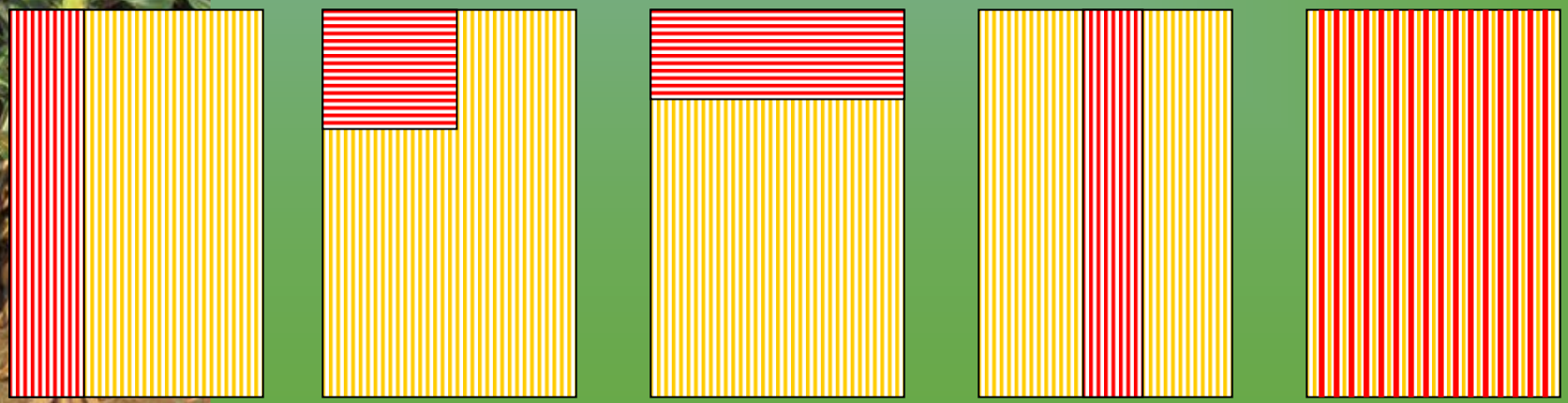
- Field Corn
  - Corn Growing Areas: 80% Bt, 20% Non
    - Deployment:
      - External blocks
      - Borders
      - In-field strips (≥ 4 rows wide, ≥ 6 preferable)
      - Seed mix NOT allowed
- Sweet Corn (Cry1Ab-Attribute) – Expires 10/2008
  - No refuge; destruction of crop residue

Rootworm Bt Corn Refuge

- YieldGard RW (Cry3Bb)
- YieldGard Plus (Cry3Bb + Cry1Ab)
- Expire in 2006
- Newer products expire in 2
- IRM Requirements:
  - 20 % refuge
  - Refuge may be treated for CRW larvae if rest of field is as well
  - Refuge planted as strips (>6 rows, preferably 12) or adjacent blocks

Insect Resistance Management Plans (IRMs)

- Must be planted within ½ mile of Bt field, preferably ¼ mile
- Must be adjacent to Bt fields
- If economic threshold is met, may apply insecticides to non-Bt crop ONLY if Bt crop is treated as well
- Cannot use Bt microbial products
- Read bag or bag tag



Trends in Corn PIPs

- Stacked traits – combining more than one event in a single crop plant
  - PIP + Other trait (i.e. herbicide tolerance)
  - PIP + PIP
- New stack targeting European corn borer/corn earworm & Corn rootworm will accelerate adoption of technology
- Two IRM options for Bt stacks
  - Common refugia
  - Separate refugia for each pest
  - Must always maintain 20% non-resistant to a given target pest

Resistance Monitoring

- Agency requires a basic resistance monitoring program
- Grower reports and laboratory bioassays
- Early warning system – detect significant changes in susceptibility
- Several techniques are available, but they differ in sensitivity (e.g., F2 screen, DNA markers In-field screen)

Remedial Action Plan

- Response measures if resistance develops
- Goal: Contain or slow spread of resistance
- Agency mandates a basic remedial action plan

Elements of Remedial Action Plan

(If resistance confirmed)

- Inform EPA
- Educate growers, consultants etc.
- Implement alternative controls
- Increased resistance monitoring
- Sales suspensions
- Investigate cause of resistance

Grower Education and Compliance Assurance Requirements

- Grower education programs
- Compliance assurance programs
  - Grower agreements/contracts w/annual affirmation
  - 3rd party grower surveys
  - Random visits
  - Threat of losing transgenic seed

For More Information

- EPA Office of Pesticide Programs:
  - www.epa.gov/pesticides/
- EPA Region 5 Pesticides Program:
  - www.epa.gov/region5/
- My e-mail address:
  - vantil.barbara@epa.gov

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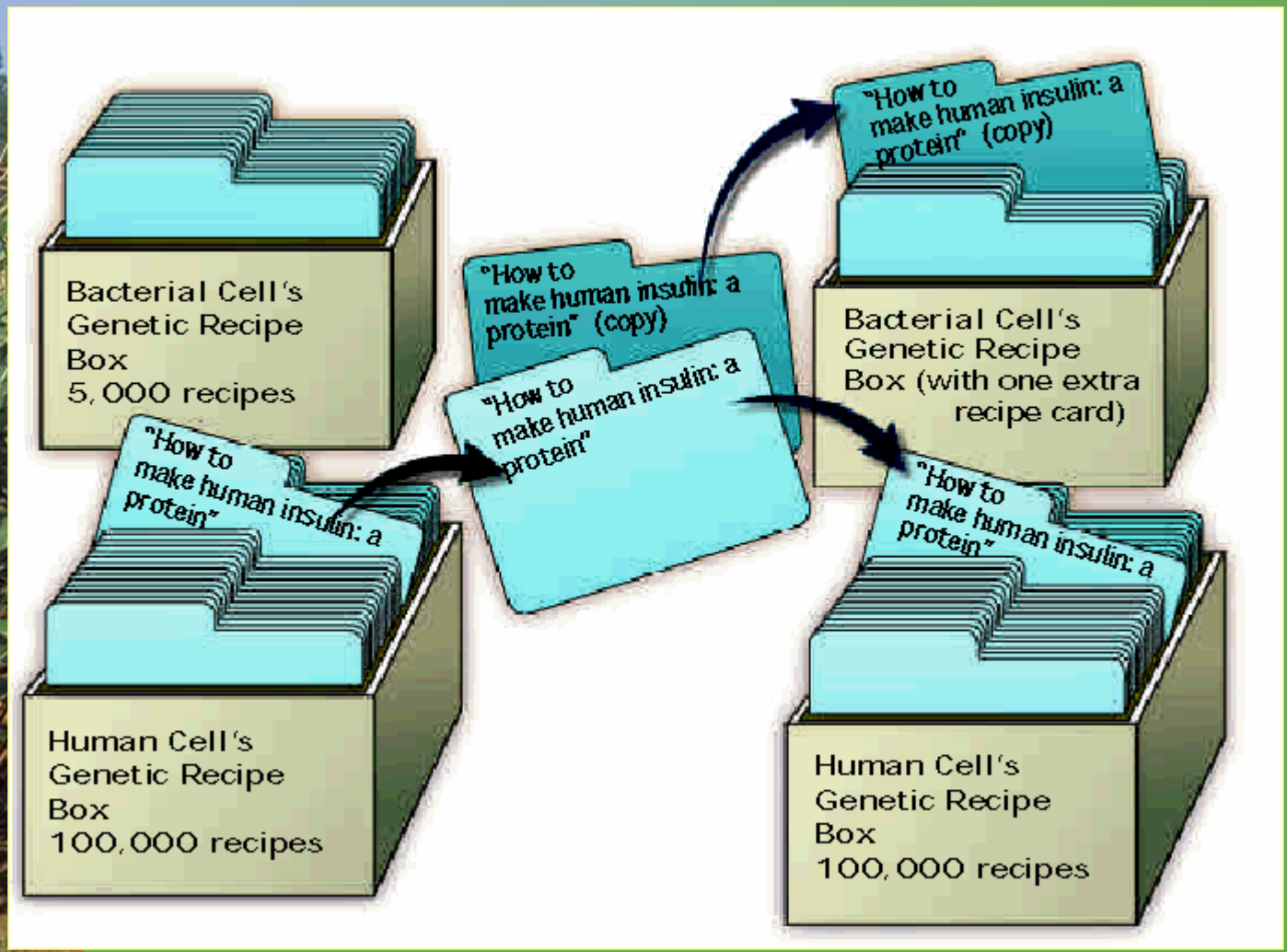
How Do You Make a Biotech Product?

- Identify a source of the gene of interest
- Locate and clone the gene
- Create artificial gene for insertion into new host
  - Must have elements that will allow it to “work” in new host
- Insert the gene
- Check to see if gene was inserted
- Study the modification for safety, etc.

Locate the Genetic Recipe Needed

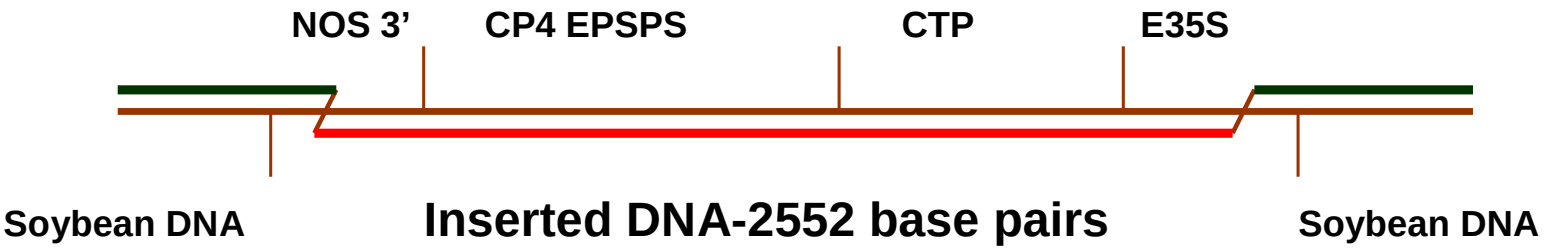


Case Study: Engineering Tolerance to Roundup™ in Soybeans

- Roundup™ destroys a plant's ability to synthesize some of the amino acids necessary for protein building, leading to death
- Foreign genes from a bacterium serve as a backup system in Roundup Ready plants, allowing them to make these amino acids

Modification of Soybeans for Resistance to Roundup™

Roundup Ready Gene



Active Gene-CP4 EPSPS: Enolpyruvyl shikimate phosphate synthase gene from *Agrobacterium* sp. CP4

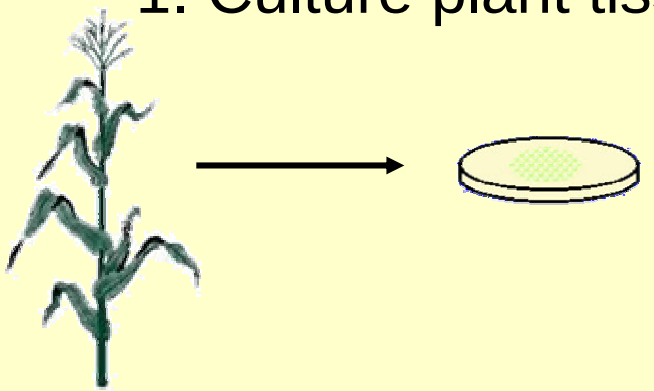
Other Genetic Elements-CTP: Chloroplast transit peptide from *Petunia hybrida*

Promoter-E35S: Cauliflower mosaic virus

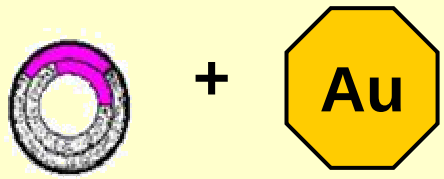
Terminator-NOS 3: Bacterial nopaline synthase gen

Transformation of Crop Plants

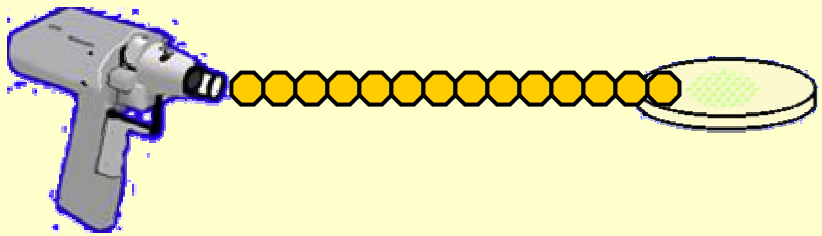
1. Culture plant tissue



2. Coat gene onto Gold



3. Insert gene into DNA



4. Grow into plants.
   Check for transformation