



Overview of C5 Honeysweet Plum Risk Assessment



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Background

The EPA Office of Pesticides regulates the sale, distribution, and use of all **pesticides** in the U.S. in order to protect human health and the environment.

Including: GE Plant-Incorporated Protectants (PIPs), such as the plum pox resistant plum tree



Plum Pox Virus (PPV)

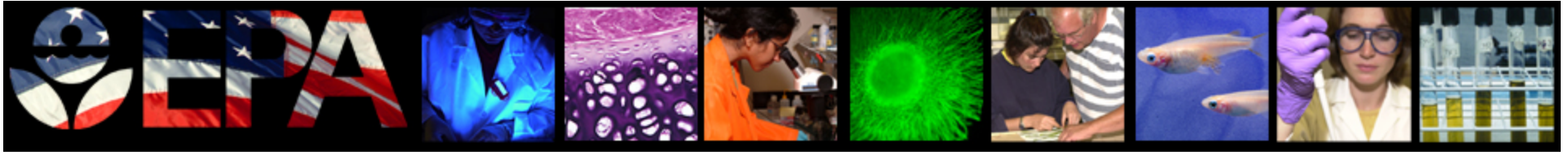
- **Virus infecting stone fruits (*Prunus*) and several other dicotyledonous plants**
 - Host range varies with strain type
- **Detected in Bulgaria 1915, Chile in 1992, then in Pennsylvania in 1998; Canada 1999, then NY and MI; China 2005.**
- **Aphid transmitted (*Myzus, Brachycaudus*)**



PPV on Apricot

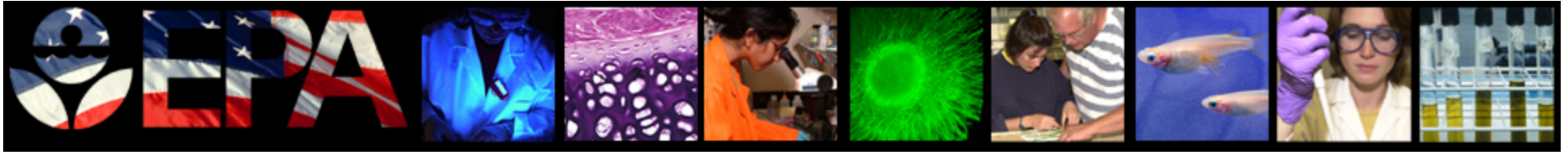
- Leaf symptoms on plum





EPA Regulation of PIPs

- EPA regulates the gene and its product
- Inert ingredients are also considered
- EPA does not regulate the plant itself
- Regulation continues as long as the product is in commerce (**licensing**)
- Food / feed safety and environmental assessments are performed for all PIPs



C5 Honeysweet Plum

- *Prunus domestica* var. *domestica*
- *Agrobacterium*-mediated transformation
- DNA sequences from vcp gene of PPV
- RNAi based mechanism; no protein
- Most of our toxicity studies are based upon a protein as the active ingredient
- Waiver granted for acute oral tox and allergenicity testing



PPV-CP Plum

- **35S promoter – PPV-CP gene inserts**
- **β -lactamase with cos insert – non-fxn1**
- **pBR322 sequences – non-coding**
- **Short TMV sequence – non-coding**
- **β -D-glucuronidase gene – marker**
- ***nptII* gene for antibiotic selection**
- **PTGS through dsRNA product**



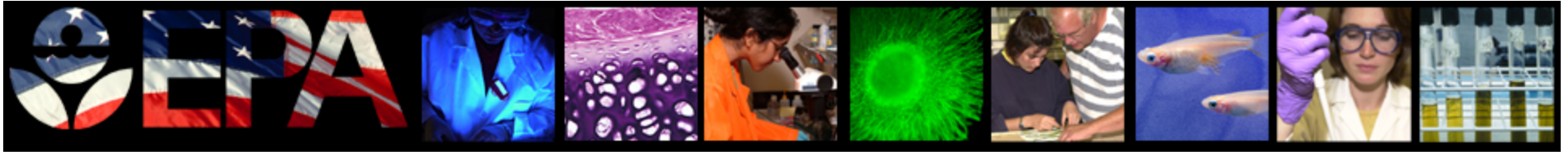
Regulatory Considerations

- Long history of plant virus consumption
- Putative CP protein has no homology with known toxins or allergens
- Food tolerance exemption for RNA / DNA, GUS and NPT II proteins
- No infectious viral particles produced
- No gene flow issues based upon ploidy differences with native / introduced species.



Environmental Assessment Tests Waived

- **Wild mammal toxicity**
- **Aquatic invertebrate toxicity**
- **Freshwater fish toxicity**
- **Non-target arthropod toxicity**
- **Honeybee toxicity**
- **Estuarine / Marine organism toxicity**



Other EPA Regulatory Considerations

- **Conditional FIFRA Registration 3(c)(7)(C)**
 - **Validated analytical method required**
 - **1 year registration prior to review**
- **Requirement to report hypersensitivity incidents and adverse effects – FIFRA**
- **Aggregate exposure - FFDCA 408(b)(2)(D)(vi), all *vcp* pesticides**



Coat Protein Gene of Plum Pox Virus
 Biopesticides Registration Action Document
 May 07, 2010

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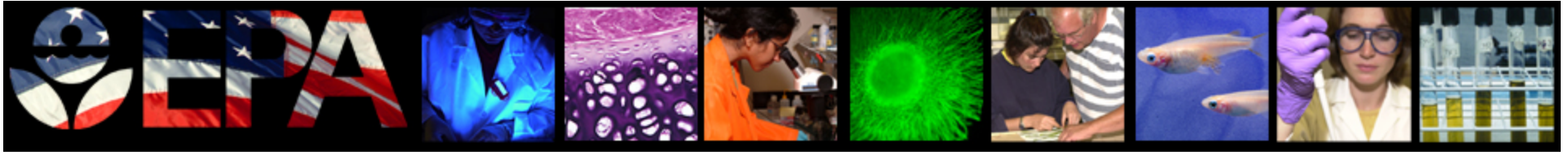
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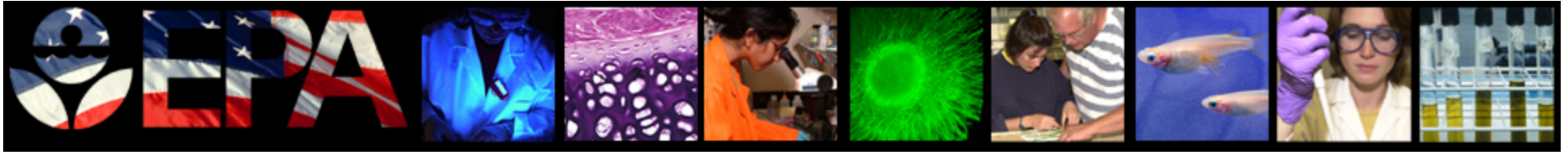
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Timeline

- **June 2007 submission**
- **30-day comment period / 62 comments**
- **May 7, 2010 – FIFRA registration**
- **Independent laboratory validation of the applicant's analytical method**
- **Current consideration of FIFRA exemption**



Food for Thought

- **Communicate with the Agency early and often, even in the development stage**
- **Consider the overall costs and whether / when tech transfer may be appropriate**
- **Regulations are dynamic, not static**
- **Trade issues need to be considered when your product may go international**



Useful websites

- <http://www.epa.gov/oppbppd1/biopesticides/pips/index.htm>
- http://www.epa.gov/pesticides/biopesticides/reg_of_biotech/eparegofbiotech.htm
- http://www.epa.gov/oppbppd1/biopesticides/ingredients/tech_docs/brad_006354.pdf