EPA Updates

Proposed Data Requirements for Plant-Incorporated Protectants (PIPs)

Progress on STAR Grants

NAFTA Regulators Meeting

September 16, 2010

Outreach for PIP Rule

- Pre-rule
  - Updates at meetings w/ EPA Regions, other federal agencies, stakeholders
  - Focus is on announcing that rule is coming
- Post-rule
  - Plan to hold a public meeting, announced in FR, to answer questions about the rule during comment period

TIP: Copies of pre-rule outreach the Agency has done on this rule will be available to the public through http://www.regulations.gov by mid-October by visiting docket EPA-HQ-OPP-2009-0499.

Overview – Proposed PIP Rule and Test Guidelines

- Proposed rule is under development
- Guidelines presented at the SAP are undergoing revision
- Proposed rule and test guidelines will be available for public comment later this year
- Intra-Agency review continues regarding the content of the rule and clarifications

Data Requirements for PIPs – Proposed Rule

- **EPA is preparing to propose a data requirements rule for Plant-Incorporated Protectants (PIPs)**
  - Will reflect the data and information necessary to support a regulatory decision on experimental use permits and commercial registrations for PIPs
  - This proposal is part of a larger effort to update and improve all of the data requirements for pesticide regulatory purposes

- **This rule will mostly codify existing data requirements that are currently applied on a case-by-case basis**
  - Will reflect current scientific knowledge and understanding and are also being written broadly enough to consider what may be needed to assess a non-protein based PIP, such as RNAi-based mechanisms
  - As new types of PIPs emerge in the future, the Agency will revisit these data requirements to make any necessary revisions

Schedule

- A proposed rule is expected in late 2010
- There will be a public comment period
- Final rule will be published approximately 2 years later (don’t ask me why)

TIP: Check the Unified Agenda (also known as Semiannual Regulatory Agenda) for schedule updates every six months

– http://www.gpoaccess.gov/ua/index.html

Overview of Rule

- New data requirements
  - Most are “newly codified” – i.e., have been applied on a case-by-case basis, but are not in the CFR
  - 8 are “new” – i.e., never before imposed on any registrant
    - Biology of the plant
    - Toxicity of substances other than proteins
    - Specific serum binding test
    - 90-day oral toxicity
    - Soil microbial community testing
    - 2 gene flow data requirements: gene flow when interbreeding with compatible relative and horizontal gene transfer of genetic material to other organisms
    - Weediness of PIP expressing plant

Notes about Table

- Data requirements and test guidelines
  - These are two different things
    - Data requirements: what will be proposed in the rule
    - Test guidelines: guidance documents that will be shared for public comment separately
- Use pattern and test substance may trigger different data requirement

PIP Test Guidelines & SAP

- BPPD is concurrently developing test guidelines that will go with the PIP data requirements
  - These guidelines will follow international conventions/ agreements, such as OECD and Codex
  - Some will also be based on existing EPA OPPTS harmonized guidelines as appropriate
  - These are not mandates – only guidance
  - Maintain case-by-case approach to satisfy data requirements
- Feb 2009 SAP – scientific issues on PIPs which EPA hadn't brought to the advisory panel before
  - Questions highlight new data which EPA is thinking about requiring for future registrations (e.g., gene flow)
  - Four draft guidelines were shared at this SAP

Scientific Issues Brought to February 2009 SAP

- **Product Characterization**
  - **Gene Nomenclature**
- **Human Health**
  - **Bioinformatics - allergenicity**
- **Synergism of Pesticidal Substances**
- **Microbial Soil Community Testing**
- **Environmental Impacts of Gene Flow**

TIP: More information on this SAP (including SAP report):

- http://www.epa.gov/scipoly/sap/meetings/2009/022509meeting.htm
- http://www.epa.gov/scipoly/sap/meetings/2009/february/022526finalreport.pdf

Overview of Rule

- Data requirement tables will address:
  - Product characterization
  - Human health
  - Nontarget organisms (biodiversity)
  - Environmental fate and effects of gene flow
  - Resistance management
- Tables will include elements similar in format to other existing pesticide data tables
  - Reference to guideline, use pattern, test substance, table note(s)

Cisgenic Exemption

- The Agency is also considering including a provision for a cisgenic PIP exemption.

- This provision would exempt from registration a PIP created by moving cisgenic genetic material between plants that can naturally interbreed.

- Cisgenic PIP = Transfer of genetic material using bioengineering technology but represents a transfer that could occur naturally

Resistance Management

- Data are required when there is a potential mechanism in the target organism to develop resistance to a pesticidal substance of a PIP.
- Data on each target organism must be submitted for each pesticidal substance. For combination PIPs, dose expression must be provided for each pesticidal substance and the combination of pesticidal substances.
- The plan must contain a monitoring strategy on each target organism for each pesticidal substance of the PIP.

P-VCPs - Exemptions

- Viral Coat Protein-based Resistance
- Squash – ZYMV, WMV, CMV
- Papaya – PRSV
- Potato - PVY
- Plum - PPV

Synergistic Effects of Multiple PIPs in a Plant

- EPA is considering the potential for synergistic activity (toxicity) from combined trait PIPs and is developing test requirements dealing with multiple pesticidal substances.
- The June 8-9 2004 SAP agreed with the Agency that “combined oral toxicity studies for multiple proteins is not necessary if each protein had been previously independently tested, unless such testing would be intended to detect any effects produced by interactions between the proteins.”

Soil Microbial Community Test

- EPA is considering to conditionally require soil microbial community toxicity tests for plants that are modified to inhibit microbial growth (e.g., a gene is inserted into a plant that exhibits a microbicidal mode of action against a plant pathogen).
- To that end, soil would be analyzed for NH_3 and NO_3 content to establish possible adverse effects on ammonification and nitrification processes, and for CO_2 efflux as an indication of microbial respiration and carbon balance.

Evaluation of Environmental Impacts of Gene Flow Between Sexually Compatible Plants

- EPA is considering that assessing risk of the potential impacts of transgene movement to sexually compatible wild relatives would require data / information on geographic distributions, non-target, population, and community effects, as well as genetic information on introgression and stability.
- Greenhouse, confined field / cage and field testing may be required to ascertain the potential for adverse effects from a gene flow event.

Summary – Upcoming PIP Proposed Rule and Test Guidelines

- Proposed rule is under development
- Guidelines presented at the SAP in Feb 2009 are undergoing revision
- Proposed rule and test guidelines will be available for public comment later this year

Questions

- Do you have any questions about the process outlined?
- Do you have any ideas or issues you would like EPA to consider as we prepare this rule?
- What kind of PIPs do you predict we will be seeing in the future?

Contact Information

- Cameo Smoot – Smoot.Cameo@epa.gov
  - Rule process related questions
- Chris Wozniak – Wozniak.Chris@epa.gov
  - Guidelines / technical questions

STAR Grants
Food Allergenicity

- Science to Achieve Results-Office of Research and Development's National Center for Environmental Research
- Funded a number of grants intended to be cooperative and goal oriented since 2005
- In 2007 a cooperative RFP with the NIH-NIAID- Exploratory Investigations in Food Allergy

STAR Grants
Food Allergenicity

- Continued support and development of Structural Database of Allergenic Proteins
- Examination of Cross-Reactive Epitopes in the context of specific serum screening as described by Codex
- Several Animal Models for addressing potential food allergenicity by isolated proteins.

STAR Grants
Food Allergenicity

- Recommend looking at proposals at the National Center for Environmental Research website for more details:

- http://www.epa.gov/ncer/

- Look at grants under “Food Allergy/Genetically Engineereed Foods”