bpia 2024 Annual Meeting

Regulatory Panel: EPA Pesticide Registration Overview

Conventional, Biochemical, and Microbial Pesticide Registration: What's the Difference?

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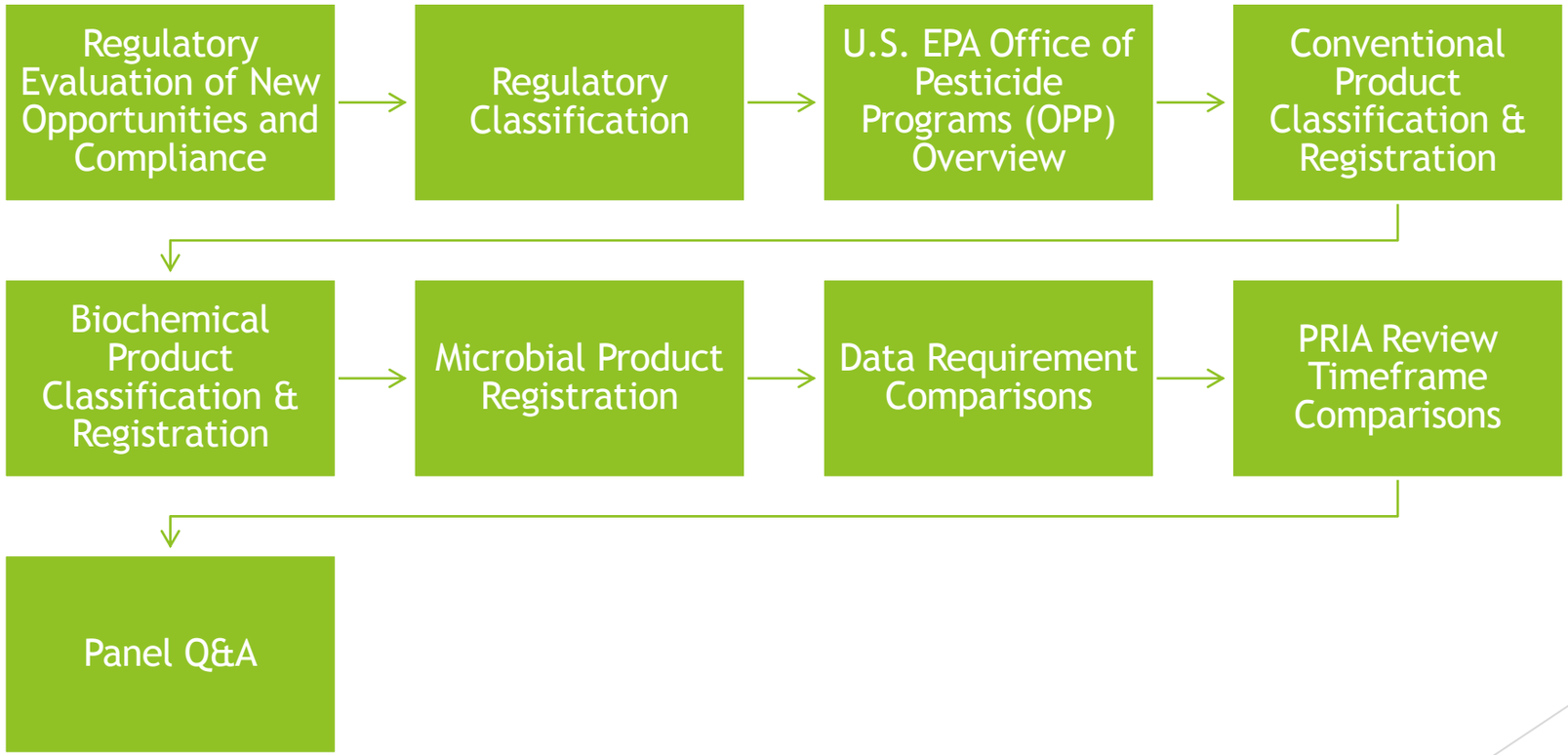
Agenda Topics



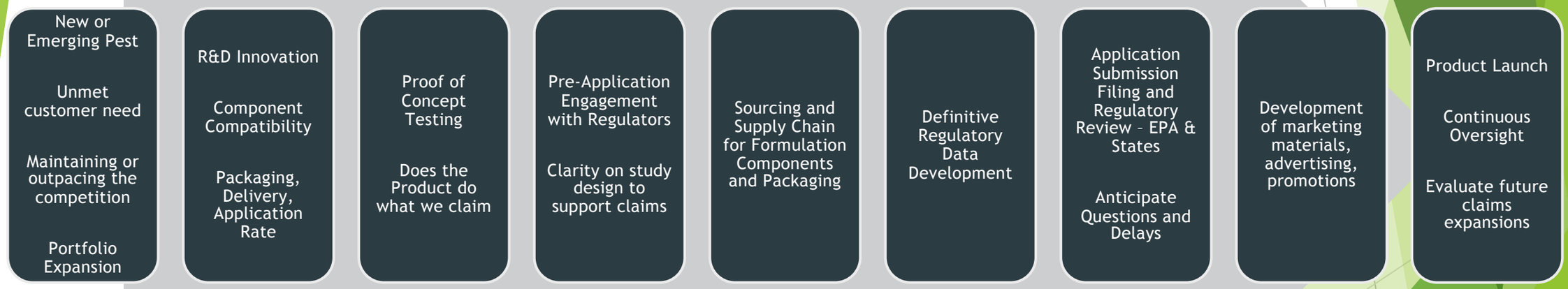
Regulatory Evaluation of New Opportunities and Compliance

What is a pesticide?

"Pesticide" is defined in FIFRA § 2(u), 40 CFR § 152.3.

- This definition includes:
  - Any (1) substance of mixture (2) intended for preventing, destroying, repelling, or mitigating (3) any pest;
  - Any substance or mixture intended for use as a plant regulator, defoliant, or desiccant;
  - Any nitrogen stabilizer (in FIFRA only, can be excluded from FIFRA regulation if certain criteria are met)
- This definition excludes:
  - New animal drugs
  - Animal feed containing a new animal drug
  - Liquid chemical sterilants for devices that enter the human body or contact mucous membranes

Pesticide Product Development Timeline



Regulatory Classification

FIFRA Pesticide Definition - "Intent Test"

A substance is a pesticide requiring registration if:

- The distributor or seller claims, states, or implies (by labeling or otherwise) that the substance
  - Can be used as a pesticide or,
  - Contains an active ingredient and can be used to manufacture a pesticide
- The substance contains one or more active ingredients and has no significant commercially valuable use as distributed or sold other than
  - Use for pesticidal purposes
  - Use for manufacture of a pesticide
- The distributor or seller has actual or constructive knowledge that the substance will be used, or is intended to be used, for a pesticidal purpose

- Reference: 40 CFR § 152.15

Products Excluded from FIFRA

- Liquid chemical sterilants, nitrogen stabilizers (meeting certain criteria), human/animal drugs and animal feeds, Vitamin Hormone products (if criteria are met), products intended to aid desirable plant growth (40 CFR 152.6)
- Products that are not for use against “pests” (i.e. fertilizers) (40 CFR 152.8)
- Products not intended for pesticidal purpose (cleaners, deodorizers, bleaches, attractants used for pest survey/detection, barrier products) (40 CFR 152.10)

Pesticides Exempt from FIFRA

- **Products adequately regulated by another Federal agency (40 CFR 152.20)**
  - Living plants intended for use as biological control agents, exception of plant-incorporated protectants; Certain non-liquid chemical sterilants, including ethylene oxide
- **Of a character not requiring regulation (40 CFR 152.25)**
  - Treated articles, Pheromones and pheromone traps; Preservatives for biological specimens; Foods containing no active ingredients and used to attract pests; Natural, untreated cedar with non-tick arthropod or mildew claims
  - Minimum Risk Pesticides (aka FIFRA 25(b) products), which fit the 6 conditions
- **Devices (defined in FIFRA § 2(h))**

What does FIFRA regulate? What's in and what's out?

- **Regulated by FIFRA (registration required):**
  - Herbicides, fungicides, rodenticides, insecticides, nematicides
  - Insect repellents, biochemicals, microbial pesticides, plant growth regulators
  - Other emerging technologies meeting the "intent test" (use & claims)
- **Excluded from FIFRA:**
  - Fertilizers, soil amendments, plant nutrients, plant inoculants, vitamin hormones, adjuvants
  - Products not intended for use against pests and not intended for a pesticidal purpose
- **Somewhere in the in-between:**
  - Minimum risk pesticides (exempt from regulation if meeting all criteria)
  - Devices (exempted from registration requirements)
  - Pheromones (depending on use pattern)
  - Plant Incorporated Protectants (new exemption criteria exist)
  - Biostimulants (depending upon claims and formulation)

Biostimulants

- Popular category of products containing naturally-occurring substances and/or microbial inoculants used to stimulate plant growth, enhance resistance to plant pests, improve the plant's use of nutrients, and reduce abiotic stress.
- However, since one of the FIFRA "intent triggers" is claims, some claims for a product as a biostimulant can easily be misinterpreted as a plant growth regulator claim which then makes the product subject to FIFRA regulation.
- **No Federal definition of plant biostimulants exists today.**
- Draft Plant Biostimulant Act (advocating for inclusion in the next Farm Bill)
  - "Not later than 18 months after date of enactment of this Act, Administrator of EPA shall issue a final rule to define the term "plant biostimulant" and exempt from requirement of regulation under FIFRA"
- EPA has previously published **draft** guidance on plant biostimulants
  - Has NOT been finalized
  - Draft EPA guidance November 2020
- American Association of Plant Food Control Officials (AAPFCO) has approved a Beneficial Substances Model Bill.
  - Definition: Plant Biostimulant means a substance(s), microorganism(s), or mixtures thereof, that, when applied to seeds, plants, the rhizosphere, soil or other growth media, act to support a plant's natural nutrition processes independently of the biostimulant's nutrient content. The plant biostimulant thereby improves nutrient availability, uptake, or use efficiency, tolerance to abiotic stress, and consequent growth, development, quality or yield.

PRIA M009 – Formal Regulatory Classification

Non-FIFRA Regulated Determination

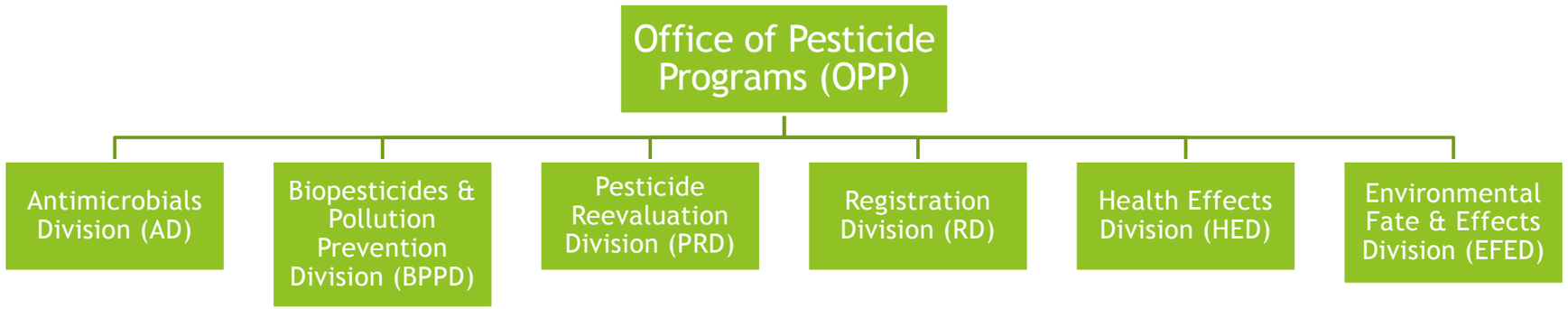
- Request for Agency determination of whether FIFRA registration is required for a proposed product. Included, but not limited to, treated articles exemptions, 25b minimum risk pesticides, and devices.
- Agency reviews product formulation, labeling, and marketing/advertising materials for a proposed product and determines whether FIFRA regulation applies.
- Determinations are NOT publicly published as classifications are product-specific.
- Good approach…may help with state registrations and definitive conclusion.
- Bad approach…buyer beware; cannot put the cat back in the bag.

Miscellaneous PRIA Actions

Action Code	Description	FY'22-FY'23 Fee	Decision Time (months)
M009	Non-FIFRA Regulated Determination: Applicant initiated, per product.	$2,607	4

U.S. EPA Office of Pesticide Programs (OPP) Overview

EPA Office of Pesticide Programs Organization – Regulatory & Science Divisions



*Biological & Economic Analysis Division (BEAD) omitted for space

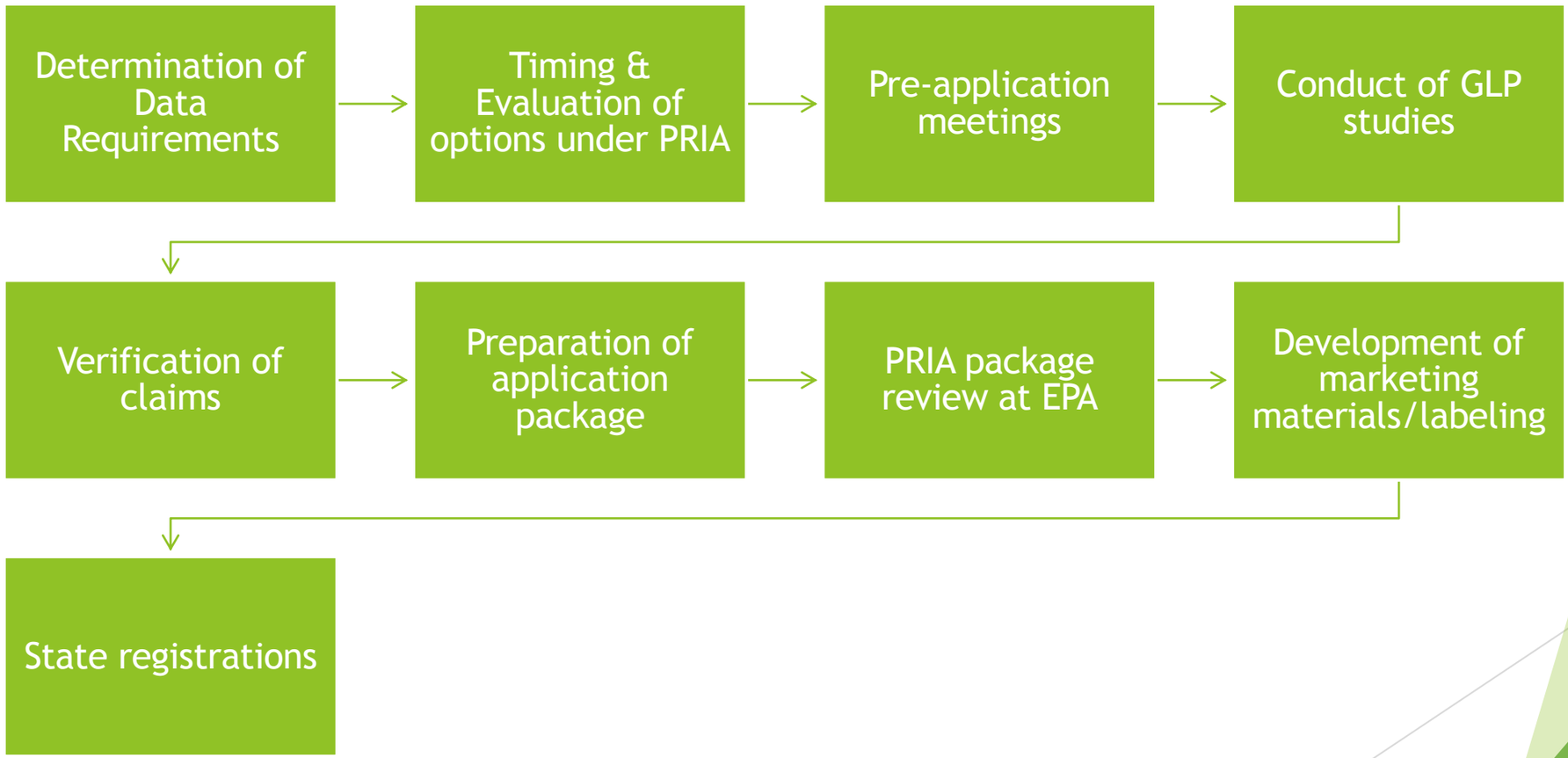
Types of Pesticide Registrations

- **Technical Grade Active Ingredient (TGAI) -** substance in a pesticide product responsible for pesticidal activity.
- **Manufacturing Use Product (MUP)** - product that contains one or more active ingredients solely for the manufacture of end-use products
- **End Use Product (EP)**
  - New end-use product
  - 100% repack
  - "Me-Too" or Substantially Similar
  - Supplemental Distribution
- **Restricted Use Product (RUP)**
- **Inert Ingredients**
- **Special Local Need (SLN), Section 24(c)**
- **Emergency Exemption, Section 18**

Common Pesticide Submissions

- New Active Ingredient
- New Use (first food use, first outdoor use)
- New Product Form
- Amendment requiring review in science division
- New End Use Product
- Label Amendment/Minor Formulation Amendment
- Label Notification/CSF Notification
- "Me-Too" registrations
- 100% repack registrations
- Sub-registration – Supplemental Distribution
- FIFRA Regulatory Determination (device, 25b, adjuvant)
- Pre-application waiver/justification review

Registration Process Summary



Registration Application In-take & Review

- All registration filings and amendments undergo in-take through Information Services Branch (ISB) of the Registration Division
- Content screens and payment confirmations verified before actions are routed to regulatory divisions
- PRIA timeframe starts and (45-day/90-day) technical review screen initiated
- Application deficiencies can be identified in results of technical screen or during science review thereafter
- If application determined sufficient to review, data routed to EFED/HED for conventionals and RAB for biochemicals/microbials
- Data reviewed and risk assessments performed
- Risk management decisions made in conjunction with label review
- Stamped-accepted labeling concludes a registration or amendment action

Conventional Product Classification & Registration

Conventional Classification & Registration

Type of Pesticide:

- **Conventional**
- Biochemical
- Microbial

Definition

Data Requirements

Registration

PRIA Timelines & Fees

What is a "Conventional" Product?

- All pesticide active ingredients that do NOT meet the definitions of a biochemical pesticides (i.e., not a naturally derived product or synthetic equivalent thereof), are NOT an antimicrobial pesticide, and that are NOT microbial pesticides.
- Generally produced synthetically
- Considered the traditional chemical-based active ingredients:
  - Herbicides
  - Fungicides
  - Rodenticides
  - Nematicides
  - Fumigants
  - Insecticides, Insect Repellents, Insect Growth Regulators

Data Requirements for Conventional Active Ingredients

Product Chemistry (OCSPP 830)	Environmental Fate (OCSPP 835)	Toxicology (OCSPP 870)
• Identity, composition, manufacturing process, and analysis • Physical and chemical characteristics	• Degradation & transformation (hydrolysis, photolysis, metabolism) • Mobility (leaching, adsorption/desorption, dissipation, volatility)	• Acute toxicity • Subchronic & chronic toxicity • Special studies (developmental, reproductive, neurotoxicity, immunotoxicity) • Mutagenicity

Ecological Effects (OCSPP 850)	Residue Chemistry (OCSPP 860)	Exposure (OCSPP 875)
• Avian studies • Aquatic studies • Non-target plants and insects (including bees) • Acute and chronic studies • Freshwater & Estuarine/Marine	• Nature and magnitude of the residue • Plant and/or animal tissues • Processed commodities • Residue analytical methods • Storage Stability	• Occupational/applicator, post-application, bystander • Dislodgeable Foliar Residue (DFR), Turf Transferable Residue (TRR) studies • Food contact residue studies

Data requirements for pesticides can be found in 40 CFR § 158

Data Requirements for Conventional End-Use Products

Product Chemistry (OCSPP 830)	Toxicology (OCSPP 870)	Special Toxicology (OCSPP 870)

• Identity, composition, manufacturing process, and analysis
• Physical and chemical characteristics
	• Acute toxicity
	  • Acute Oral
	  • Acute Dermal
	  • Acute Inhalation
	  • Eye Irritation
	  • Skin Irritation
	  • Dermal Sensitization
		• Companion animal safety
		• Dermal penetration

Efficacy (OCSPP 810)	Child-Resistant Packaging	Exposure (OCSPP 875)
• Invertebrate control agents against pests of public health concern (i.e., tick, mosquito, flies, roaches) • Structural treatments (i.e., wood-boring insects, termites) • Data to be "available" for non-public health pests	• If applicable	• Mixer/loader/applicator, post-application, if needed

Data requirements for pesticides can be found in 40 CFR § 158

Data Requirements for Conventional Active Ingredients – Nuances

- Pesticide data requirements can be found in 40 CFR § 158
  - Since data requirements can vary, important to pay close attention to data tables and test notes in this section
- Data requirements for active ingredients is driven by the intended use pattern (i.e., less data burden for indoor or non-food uses)
- Various consortia/industry task forces formed to address exposure data requirements (AHETF, ARTF, ORETF, AEATF, REJV, NDETF, etc. depending on exposure pattern) for indoor and outdoor inhalation and dermal exposures. Consider when product's intended use may create new exposure scenario.
- Tolerance petitions or exemption petition/notice of filing (food use could trigger new use!)
- Each class of active ingredients (conventional, biochemical, microbial, antimicrobial) have various nuances in data requirement needs
  - Biochemical and microbial active ingredients have tiered testing approach for toxicology and environmental fate/non-target organism toxicity and often reduced data requirements compared to conventionals

Conventional Registration Strategy Considerations

- Where the product is to be used/what's the impact
  - Residential vs. Commercial, Indoor vs. Outdoor, Food Use vs. Non-Food Use Sites
  - Each represents significant data development and exposure assessment options
- Formula – Ingredient Assessment
  - Use of a Registered source vs. an Unregistered Source
  - Is the Registered Source of AI approved for the intended uses?
- Product Profile
  - Safety/Hazard, Packaging, Concentrate vs. ready-to-use, Refills
- Where Product is sold/what's the intended market

Conventional PRIA 5 Fees & Review Time

EPA No.	New CR No.	Action	Decision Review Time (Months) [1]	FY'23 - FY'24 Fees ($)
R010	1	New Active Ingredient, Food use. [2] [3]	36	1,079,356
R020	2	New Active Ingredient, Food use; reduced risk. [2] [3]	27	899,464
R040	3	New Active Ingredient, Food use; Experimental Use Permit application; establish temporary tolerance; submitted before application for registration; credit 45% of fee toward new active ingredient application that follows. [3] [4]	18	662,883
R060	4	New Active Ingredient, Non-food use; outdoor. [2] [3]	30	749,886
R070	5	New Active Ingredient, Non-food use; outdoor; reduced risk. [2] [3]	24	624,905
R110	7	New Active Ingredient, Non-food use; indoor. [2] [3] [4]	20	417,069
R120	8	New Active Ingredient, Non-food use; indoor; reduced risk. [2] [3] [4]	14	347,556

Biochemical Product Classification & Registration

Biochemical Classification & Registration

Type of Pesticide:

- Conventional
- **Biochemical**
- Microbial

Definition

Classification

Registration

Data Requirements

PRIA Timelines & Fees

Biochemicals

Naturally occurring substances that control pests by non-toxic mechanisms.

Include substances that interfere with mating, such as insect sex pheromones, as well as various scented plant extracts that attract insect pests to traps.

It is sometimes difficult to determine whether a substance meets the criteria for classification as a biochemical pesticide, EPA has established a special committee to make such decisions.

Biochemical Classification

Biochemical Classification Committee

- BiochemicalClassification@epa.gov
- Reviews applications to ensure substance meets criteria.
- Consists of approx. 13 voting members across EPA OPP.
- Representation includes science and regulatory divisions.
- Applications are considered CBI.

BPPD PRIA 'Other Actions'

PA No.	New CR No.	Action	Decision Review Time (Months) (1)	FY'23 - FY'24 Fees ($)
B617*	158 (new)	**Pre-application**; biochemical classification determination.	5	4,715

*Optional, registrant initiated

Criteria for Classification

- Evidence of natural occurrence, or evidence that the compounds are structurally-similar and functionally identical to naturally-occurring compounds.
- Evidence for a **non-toxic mode of action** against the target pest.
  - This is the **MOST** important criterion.
- Evidence for a history of safe exposure to humans and the environment.
  - Must be quantitative in nature.
  - Must be supported by references.

Information to Support a Classification

- Product chemistry
- Rate and timing of application
- Use pattern
- Toxicity/Mutagenicity/Carcinogenicity
- Efficacy data

Biochemical Registration

Contents of an Application (40 CFR Part 152.5)

- Application Form (8570-1)
- Draft Labeling 40 CFR Part 156
- Confidential Statement of Formula*
- Data requirements 40 CFR Part 158
- (*if food use*) Tolerance Exemption or Tolerance for Residues 40 CFR Part 180
- (*if relevant*) Child Resistant Packaging 40 CFR Part 157
- PRIA 5 Fees
- Cover Letter

Biochemical Data Requirements

40 CFR Part 158

- Different set of Data Requirements
- Subpart U*: Biochemical Pesticides 158.2000

*Biopesticides Confidential Statement of Formula | US EPA

*eCFR :: 40 CFR Part 158 -- Data Requirements for Pesticides

Subpart U Biochemical Pesticides

- The determination of data requirements including required (R), conditionally required (CR), or not required (NR) are driven by your proposed use pattern.
- The test substance that is required to be tested typically includes either or both the TGAI, MP, and EP.
- Data requirements are organized by tiers with higher tiers 'triggered' when adverse effects are seen in lowered tiered studies.
- Guideline Series 880 is intended to meet requirements for chemical composition and toxicity of biochemicals.
- Residue data requirements are determined by use pattern. All food use applications for a new biochemical active ingredient must be supported by a petition to establish an exemption and/or tolerance for residues of the active ingredient in or on all food commodities.

Series 880: Biochemical Test Guidelines

Product Analysis (Group A)	Toxicology (Group B)	Non-target Organisms (Group C)
• Identity, composition, manufacturing process, and analysis • *(Relevant)* Physical and chemical characteristics • (*Relevant)* Impurities	• (Relevant) Acute 6-pack • Immunotoxicity (when required) • Immune Response (if relevant, Tier II)	• Nontarget Insect (if relevant, Tier I) • Dispenser Water Leaching (only if relevant to packaging)
Additional studies may be triggered based on results of Tier I testing.		

Series 880 - Biochemicals Test Guidelines | US EPA

Biochemical Data Requirements

Series No.	Series Name	FOR ALL USE PATTERNS*	TEST SUBSTANCE
880	Product Identify & Composition Biochemicals	R	TGAI, MP, AND EP
830	Product Properties	R, CR	TGAI, MP, AND EP
835	Fate, Transport, and Transformation	CR	TGAI
850/880	Ecological Effects	Tier I: R Tier II-III: CR	TGAI, EP
860	Residue Chemistry	CR	TGAI, RESIDUE OF CONCERN
870	Human Health / Toxicology	Tier I: R Tier II-III: CR	TGAI, MP, AND EP
875/880	Occupational and Residential Exposure	CR	TGAI, MP, AND EP

*R=Required, CR=Conditionally Required

R or CR depends on use patterns and use sites.

eCFR : 40 CFR Part 158 -- Data Requirements for Pesticides

PRIA Fees & Review Timelines

BPPD New Active Ingredient

EPA No.	New CR No.	Action	Decision Review Time (Months) [1]	FY'23 - FY'24 Fees ($)
B580	123	New active ingredient: petition to establish tolerance. [2] [3] [4]	22	73,173
B590	124	New active ingredient: petition to establish a tolerance exemption. [2] [3] [4]	20	45,737
B600	125	New active ingredient: no change to a permanent tolerance or tolerance exemption (includes non-food uses). [2] [3] [4]	15	27,443

RD New Active Ingredient

EPA No.	New CR No.	Action	Decision Review Time (Months) [1]	FY'23 - FY'24 Fees ($)
R010	1	New Active Ingredient, Food use. [2] [3]	36	1,079,356
R020	2	New Active Ingredient, Food use; reduced risk. [2] [3]	27	899,464

Microbial Product Classification & Registration

Microbial Classification & Registration

Type of Pesticide:

- Conventional
- Biochemical
- **Microbial**

Definition

Classification

Registration

Data Requirements

PRIA Timelines & Fees

Microbial Pesticide: Definition

Microbial agent intended to prevent, destroy, repel, mitigate any pest or plant regulator, defoliant, desiccant.

Includes (but not limited to) eucaryotes, procaryotes, and viruses

Relatively simple to classify if your product falls into this definition if your desired product is included in the groups above and based on intent.

Note that each new isolate/ strain of a species is considered a new active ingredient that must be registered independently.

Microbial pesticide: experimental use differences

- 10 acre FIFRA exemption for experimental field applications per year may not apply

Native isolates

USDA APHIS PPQ Unit has jurisdiction over potential microbial biocontrol agents: permits for isolation, containment, and release

Non-native to U.S. isolates

May require EPA Experimental Use Permit for any field release

OR

USDA APHIS PPQ Permit for **import,** containment, and field release

Genetically engineered isolates

USDA Biotechnology Regulatory Service (BRS) Unit has jurisdiction over genetically modified microbes- containment facilities and field trial permits

EPA TSCA also has jurisdiction over “new” microbes

Microbial Registration

All Applications Include

- Application Form (8570-1)
- Draft Labeling 40 CFR Part 156
- Confidential Statement of Formula*
- Data requirements 40 CFR Part 158
- *(If food use)* Tolerance Exemption or Tolerance for Residues 40 CFR Part 180
- *(If relevant)* Child Resistant Packaging 40 CFR Part 157
- PRIA 5 Fees
- Cover letter

Microbial Applications

- Different set of Data Requirements

*see guidance specifically for preparing a biopesticides-csf

Microbial Data Requirements

Always have a presubmission consultation with EPA before finalizing data generation plans!

Series No.	Series Name	FOR ALL USE PATTERNS	TEST SUBSTANCE
885	Product Analysis (microbials)	R	TGAI, MP, and EP
830	Product Properties	R	TGAI, MP, and EP
885	Residue	**CR**[1]	TGAI, EP
885/ 870	Tiered Toxicology	Tier I: R Tier II-III: CR[2]	TGAI; MP and EP
885/ 850	Tiered Nontarget organisms and e-fate	Tier 1: R, **CR**[3] Tier II-IV: CR	TGAI, EP

[1] Required when toxicology testing indicates potential cause of adverse human health effects or potential for mammalian toxin; and food or feed residues may be present
[2] Required only if significant mammalian toxicity and/or pathogenicity and/or persistence in host; or presence of harmful contaminants
[3] Required studies differ depending on use patterns and use sites.

Data Requirements for Microbial (TGAI/ MP/ EP) Products

Product Analysis (OCSPP 885 & 830)	Non-target Organisms and Fate (OCSPP 885 & 850)	Toxicology (OCSPP 885 & 870)

• Identity, composition, manufacturing process, and analysis
• *(Relevant)* Physical and chemical characteristics
• Storage Stability *(can be a condition of registration)*
	Requirements depend on use patterns
	
	Tier I:
	• Avian, aquatic, non-target plant and insect (+bees), freshwater studies
	Higher tier studies conditionally required if Tier I demonstrates potential hazard
		Tier I:
		• Acute toxicity
		  • Acute Oral
		  • *Acute Dermal*
		  • Acute Inhalation
		  • Eye Irritation
		  • Skin Irritation
		• Toxicity/ pathogenicity 21-day studies
		Higher tier studies conditionally required if Tier I demonstrates potential hazard

Efficacy (OCSPP 810)	Residue (OCSPP 885)	Child-Resistant Packaging
• Must be available/ provided upon request for non-public health hazard • Public health hazard: required	• ***Conditionally Required****: if toxicologically significant residues are anticipated on food or feed crops*	• *If applicable*

Data requirements for pesticides can be found in 40 CFR § 158

PRIA 5 Fees & Review Timelines

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RD New Active Ingredient

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R010	1	New Active Ingredient, Food use. [2] [3]	36	1,079,356
R020	2	New Active Ingredient, Food use; reduced risk. [2] [3]	27	899,464

Review

Data Requirement Comparison

Conventional*	Biochemical	Microbial
Product Identity (830)	Product Identity (880)	Product Identity (885)
Phys/Chem (830)	Less Phys/Chem	Even Less Phys/Chem
Toxicology (870) – no tiers	Toxicology (870/880) – T1**	Toxicology (870/885) – T1**
EcoTox (850) – no tiers	EcoTox (850/880) – T1**	EcoTox (885) – T1**
Environmental Fate		
Residue Data (860)	Residue Data (860)***	Residue Data (885)***
Spray Drift		
Human Exposure		

*Conventional data requirements established on the basis of intended use pattern rather than tiered into levels.
**Higher Tiered testing required only if triggered by results of Tier 1 testing.
***Often, biochemicals and microbials have favorable tox profiles and can successfully argue for an exemption from the requirement of a tolerance; in this case, residue data are not required.

New Active Ingredient Data Comparison

- Conventional
  - $10,000,000 +
- Biochemical
  - $1,500,000 - $2,000,000
- Microbial
  - $500,000 - $1,000,000

PRIA Filing Fee Comparisons

Conventional/RD PRIA Categories		Biochemical/Microbial BPPD PRIA Cat.	
R010: New AI, Food Use*	$1,079,356 36 months	B590: New AI, petition for tolerance exemption	$45,737 20 months
R020: New AI, Nonfood Use	$749,886 30 months	B600: New AI, Nonfood Use	$27,443 15 months
R150: First Food Use	$454,490 23 months	B640: First Food Use, tolerance exemption	$27,443 19 months
R310: New End-Use Product, registered source	$10,466 7 months	B670: New End-Use Product, registered source	$7,322 9 months
R333: New Product, unregistered source	$28,434 11 months	B672: New Product, unregistered source	$13,069 15 months

*Code presumes establishing various crop tolerances

Thank you!

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Q & A