Introduction to the U.S. Pesticide Registration Process

AAPCO Laboratory Committee

Jake Vukich
Manager – US Registration & Regulatory Affairs
DuPont Crop Protection
March 6, 2017
OVERVIEW

- Definition of a Pesticide
- Federal Pesticide Laws
- Data Required for Pesticide Registration
- Types of Pesticide Registrations
- Timelines and Costs to Registration
- The EPA Registration Process
- Pesticide Tolerances (MRLs)
- Registration Review
- Ongoing Registration Activities
Definition of a Pesticide – FIFRA Section 2

- Any substance or mixture of substances intended for preventing, destroying, repelling or mitigating any pest

- Any substance or mixture of substances intended for use as a plant growth regulator, defoliament or desiccant

FIFRA defines “pesticide” not in terms on inherent characteristics of a particular substances, but rather in terms of “intent” underlying the use of a substance.
Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) - requires all pesticides sold or distributed in the United States (including imported pesticides) to be registered by EPA.

Federal Food, Drug and Cosmetic Act (FFDCA) - requires EPA to set pesticide tolerances for all pesticides used in or on food. A tolerance (MRL) is the maximum permissible level for pesticide residues allowed in or on commodities for human food and animal feed.

EPA will register a pesticide after determining that it will perform its intended function without unreasonable adverse effects on human health or the environment when used according to label directions.
§3 **Federal Registration Actions:** EPA can register pesticides for use throughout the United States.

§5 **Experimental Use Permits (EUPs):** EPA can allow manufacturers to field test unregistered pesticides/uses when conducting field tests on >10 acres.

§18 **Emergency Exemptions:** EPA can allow state agencies to permit the unregistered use of a pesticide in a specific geographic area for a limited time if emergency pest conditions exist and there is no registered alternative available.

§24(c) **State-Specific Registrations:** States can issue a registration for a federally-registered product for an additional use, as long as there is both a demonstrated "special local need," and a tolerance, or exemption from a tolerance. EPA can disapprove a State's special local need registration.
Data Requirements that must be satisfied to support a food-use registration:

- Product Chemistry
- Toxicology
- Environmental Fate
- Ecological Effects
- Residue Chemistry
Product Chemistry

- What are the ingredients?
- Are the inert ingredients cleared for use in formulations to be applied to food crops?
- How are the active ingredient and end-use product(s) produced?
- What are the impurities?
- What are the physical properties of the active ingredient and end-use products?
Toxicology

- What are the short-term hazards to humans and animals?
- What are the toxic effects that could result from long-term exposure?
- Can exposure cause reproductive or birth defects, cancer, gene mutations, effect the nervous system or the immune system?
- What label precautions should be required to protect workers?
Environmental Fate

- How rapidly does the product degrade in the environment?
- What is the potential for the product to move off-target through drift, runoff, volatility or leaching?
- What are the degradation products?
- Can the active ingredient or its degradation products accumulate in the environment?
What are the acute hazards and potential long-term effects on birds, fish, aquatic invertebrates, mammals, non-target insects and non-target plants?

Are special restrictions required to protect non-target organisms?
What is the nature of the residue in plants and animals?

What are the maximum residues that may result in food and feed?

What are the analytical methods to measure these residues?
Cost and Time to Registration for a New Crop Protection Product (2010 – 2014 Data*)

- **Cost** of Development and Registration - $286 million

- **Number of Compounds** Processed Leading to a Successful Launch
  
  Research 159,500 → Development 1.5 → Registration 1

- **Number of Years** Between the First Synthesis and First Sale of the Product – 11.3

* Phillips McDougall – March 2016
Pesticide Registration
Application for Food/Feed Use

- Petition for Tolerance

- Required Test Data
  - Product Chemistry
  - Human and environmental assessment for food safety
  - Tolerance information - information about pesticide residues on food

- Proposed Label
  - Precautionary statements
  - Worker protection requirements
  - Directions for use
  - Other appropriate warnings (e.g., environmental hazards, spray drift)

- Application fees
  - Per PRIA fee schedule (Pesticide Registration Improvement Act)
## Table 1

<table>
<thead>
<tr>
<th>EPA No.</th>
<th>New CR No.</th>
<th>Action</th>
<th>Decision Review Time (Months)</th>
<th>FY'16/17 Registration Service Fee ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R010</td>
<td>1</td>
<td>New Active Ingredient, Food use</td>
<td>24</td>
<td>627,568</td>
</tr>
<tr>
<td>R020</td>
<td>2</td>
<td>New Active Ingredient, Food use; reduced risk</td>
<td>18</td>
<td>627,568</td>
</tr>
<tr>
<td>R040</td>
<td>3</td>
<td>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</td>
<td>18</td>
<td>462,502</td>
</tr>
<tr>
<td>R060</td>
<td>4</td>
<td>New Active Ingredient, Non-food use; outdoor</td>
<td>21</td>
<td>436,004</td>
</tr>
<tr>
<td>R070</td>
<td>5</td>
<td>New Active Ingredient, Non-food use; outdoor; reduced risk</td>
<td>16</td>
<td>436,004</td>
</tr>
<tr>
<td>R090</td>
<td>6</td>
<td>New Active Ingredient, Non-food use; outdoor; Experimental Use Permit application; submitted before application for registration; credit 45% of fee toward new active ingredient application that follows</td>
<td>16</td>
<td>323,690</td>
</tr>
<tr>
<td>R110</td>
<td>7</td>
<td>New Active Ingredient, Non-food use; indoor</td>
<td>20</td>
<td>242,495</td>
</tr>
<tr>
<td>R120</td>
<td>8</td>
<td>New Active Ingredient, Non-food use; indoor; reduced risk</td>
<td>14</td>
<td>242,495</td>
</tr>
<tr>
<td>R121</td>
<td>9</td>
<td>New Active Ingredient, Non-food use; indoor; Experimental Use Permit application; submitted before application for registration; credit 45% of fee toward new active ingredient application that follows</td>
<td>18</td>
<td>182,327</td>
</tr>
</tbody>
</table>
Office of Pesticide Programs (OPP) reviews the application for completeness, assigns the application to the appropriate OPP divisions for review, and publishes a notice of filing in the Federal Register, including a detailed summary of the application.

OPP evaluates human health, dietary, occupational and environmental risks and compiles all of the scientific data on the pesticide product into a comprehensive health and environmental risk assessment.

OPP determines if the data support the conclusion that the registration will not result in unreasonable adverse effects on human health or the environment, and if the proposed tolerance meets the statutory food safety standard of a reasonable certainty of no harm to consumers.

EPA approves registration, **establishes tolerance level** if pesticide is used on food crops, and publishes notice in Federal Register. The newly established tolerance is codified in the Code of Federal Registrations and notification is sent to the World Trade Organization.

The application or petition is withdrawn, amended, or denied.
Food/Feed Tolerances (MRL’s)

Tolerance = amount of a pesticide residue allowed by regulatory authority to remain in or on a raw agricultural commodity (also referred to as the Maximum Residue Level, or MRL)

A tolerance is also established on processed commodities, animal feeds and on consumable animal items

EPA may grant exemption from tolerance

Enforcement is responsibility of FDA

- A raw agricultural commodity or a processed food or feed is deemed to be adulterated and subject to FDA enforcement action if it contains either:
  - A pesticide residue at a level greater than that specified by a tolerance or food additive regulation; or
  - A pesticide residue for which there is no tolerance, tolerance exemption, or food additive regulation.

- Pesticide residues in imported commodities must be in conformity with a tolerance
Aggregate exposure is determined from 3 main routes:

1. Dietary exposure estimated using DEEM (Dietary Exposure Evaluation Model)
   - Food consumption data from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2008
   - Exposure to residues in water estimated from modeling or measured
   - Residues from plant residue studies
   - Residues from animal feeding studies (cow, chicken)

2. Residential exposure

3. Worker exposure

“Risk Cup” = level of exposure to a pesticide that a person could receive over a 70-year lifetime without significant risk of long term or chronic health effects
Registration Review was initiated in 2006

- The focus is on new data requirements and areas of concern
- Transparent process with multiple opportunities for public comment
- Timelines based on individual chemical requirements.
- EPA is required to review all active ingredients every 15 years.
  - The plan is to complete the review of all actives by 2022
  - EPA will try to cluster the review of similar chemistries.
- Endangered species assessments are conducted during Registration Review
State Registrations

Registrations Required In:

- All 50 States
- The District of Columbia
- Puerto Rico
Ongoing Registration Activities

- Compliance with FIFRA 6(a)(2) Adverse Effects rules and regulations

- Label Amendments – Registrant and/or EPA initiated

- Label Expansion – New uses and additional crops

- Registration Review

- Registration Renewals (Yearly at the State and/or Federal level)
Thank You.