Testing, Toxicity and Exposure: How Safe is “No Unreasonable Risk”? 

Southeast Herbicide Applicator Conference 
Panama City Beach 
October 5, 2011 

Donna R. Farmer, Ph.D. 
Monsanto Company 
St. Louis, MO
Outline

- Pesticide Regulations
- Risk Assessments
  - Hazard Assessments
  - Exposure Assessments
- Summary
Mutual Goals

- Unwanted pests must be managed
- Conflicts about the techniques rather than the goals
- Control technique options:
  - Biological
  - Mechanical
  - Pesticidal
Pesticides and Regulations

- Pesticides are regulated by government agencies
  - Registered both by EPA and the state before distribution
- EPA was established in 1970
  - Federal Insecticide, Fungicide, and Rotenticide Act (FIFRA), 1947
  - States are authorized to regulate pesticides under FIFRA and under state pesticide laws
- The Food Quality Protection Act (FQPA) of 1996 amended FIFRA
  - Fundamentally changed the way EPA regulates pesticides
Required EPA to:

- re-assess all pesticides/uses
- consider exposure from all non-occupational sources (diet, water, residential use) - aggregate risk assessment
- consider exposure to chemicals with common mechanism of toxicity - cumulative risk assessment
- enhance protection of infants & children
- evaluate potential for endocrine disruption
- ensure the product is “safe” when used according to label directions...when used according to its label will not cause "unreasonable risks to human health or the environment" and that there is "a reasonable certainty that no harm will result from aggregate exposure"
How Do We Know When a Technology is Safe/Will Not Pose Unreasonable Risks?

- Will pesticide use harm me?
- Pesticides (including herbicides, insecticides, rodenticides, fungicides, etc.) cannot be categorized simply as “dangerous” just because they are classified as substances that kill pests.
- Likewise, no chemical, either natural (made by plants or other organisms; found in nature) or synthetic (made by man), can be determined to be completely “safe”.
Depends on the perspective - facts, beliefs and experiences....

- Accidental inhalation can kill you
- Primary contributor to erosion
- Drinking large quantities can lead to death
- Has been found in tumors of terminal cancer patients
- Prolonged exposure to its solid form causes severe tissue damage
- It is colorless, odorless, tasteless and kills uncounted thousands of people every year
- Kills 40,000 people a year
- Causes major pollution
- Contains a chemical that causes cancer in laboratory animals
- Produces toxic gases
- Causes major air pollution problems
- Causes billions of dollars in property damage every year
- Requires tremendous resources for production

*MONSANTO imagine*
Uncertainty is inevitable …

- **Absolute safety cannot be proven**

- **However……**
  - There is a logical process by which we can judge the likelihood of harm
  - Decide if a specific technology will accomplish mutual goals with a **reasonable certainty of no harm**

- **Risk Assessment**
  - Science – based process of quantifying and characterizing risk…estimating the likelihood of occurrence, the nature and the magnitude of potential adverse effects
Risk Assessment – 4 elements

**Toxicity** of the pesticide – potential hazards result in adverse effects to human health

- **HAZARD**
- **EXPOSURE**
- **RISK ASSESSMENT**
- **RISK MANAGEMENT**

*Exposure* is by any route including occupational, food, air and water; estimated or measured
## Hazard Assessment

### Standard Battery of Studies

<table>
<thead>
<tr>
<th>Category</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Properties</td>
<td></td>
</tr>
<tr>
<td>Residue Chemistry</td>
<td></td>
</tr>
<tr>
<td>Environmental fate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General fate</td>
</tr>
<tr>
<td></td>
<td>Degradation/Metabolism</td>
</tr>
<tr>
<td></td>
<td>Mobility</td>
</tr>
<tr>
<td></td>
<td>Accumulation</td>
</tr>
<tr>
<td>Spray Drift</td>
<td></td>
</tr>
<tr>
<td>Non-Target Organisms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
</tr>
<tr>
<td>Product Performance</td>
<td></td>
</tr>
<tr>
<td>Applicator and Re-entry</td>
<td></td>
</tr>
<tr>
<td>Humans/Domestic Animals:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute oral, dermal &amp; inhalation</td>
</tr>
<tr>
<td></td>
<td>Eye &amp; skin irritation</td>
</tr>
<tr>
<td></td>
<td>Dermal sensitization</td>
</tr>
<tr>
<td></td>
<td>21-day dermal</td>
</tr>
<tr>
<td></td>
<td>90-day rat, mouse &amp; dog</td>
</tr>
<tr>
<td></td>
<td>1-year dog chronic</td>
</tr>
<tr>
<td></td>
<td>2-year rat chronic</td>
</tr>
<tr>
<td></td>
<td>Oncogenicity</td>
</tr>
<tr>
<td></td>
<td>21-day dermal</td>
</tr>
<tr>
<td></td>
<td>21-day rat chronic</td>
</tr>
<tr>
<td></td>
<td>Oncogenicity</td>
</tr>
<tr>
<td></td>
<td>Genetic toxicity</td>
</tr>
<tr>
<td></td>
<td>Developmental toxicity (rat &amp; rabbit)</td>
</tr>
<tr>
<td></td>
<td>2-Gen. rat reproduction</td>
</tr>
<tr>
<td></td>
<td>Acute neurotoxicity</td>
</tr>
<tr>
<td></td>
<td>Subchronic neurotoxicity</td>
</tr>
<tr>
<td></td>
<td>Developmental neurotoxicity</td>
</tr>
<tr>
<td></td>
<td>Immunotoxicity</td>
</tr>
<tr>
<td>Rat ADME</td>
<td></td>
</tr>
</tbody>
</table>

$200$ million and $10$ years
Nature of the Hazard?

- Is there an effect worth talking about?
- Is it adverse?
- High dose to low dose extrapolation
  - Adverse effect result of high dose testing
- Identify the underlying biochemical/physiological processes and/or metabolic pathway responsible for producing the adverse effect
- Understand species differences - relevance for humans
- Understand the relationship between toxicity and exposure
  - Real world exposures
Exposure Assessment
What are the routes and levels of human exposure?

**General Public**
- Dietary
- Water
- Residential

**Occupational**
- Pesticide handlers (mixer/loader/applicator, re-entry workers, etc.)

Aggregate exposure

Estimated or measured
Occupational Exposure Assessment

- **Exposure scenarios**
  - Mixers, Loaders, Applicators, Flaggers
  - Re-entry - treated fields or greenhouses
  - Harvest/process treated crop (crushing, grinding, etc.)
  - End-user special use (fertilizer granule coating)

- **Application method & practices**
  - Aerial, tractor boom, backpack, mist blower, hand spread
  - Clothing, PPE, equipment (open transfer), wind, etc.
  - Use rate, number of acres, type of formulation (dry, EC)

- **Usually, occupational exposure > dietary, water, residential**
Where Does the Data Come From and How is it Used?

- Regulatory agencies require pesticide manufacturers to generate and submit the data.
- Regulatory scientists and analysts review the data and using conclusions of a risk assessment determine whether to:
  - register a pesticide product or a use
  - whether specific restrictions are necessary
- The most common way the EPA manages the potential risks of a pesticide is through the label directions.
Label Directions – examples of controlling exposure....

- Required PPE
  - Directed by Signal Word – Caution, Warning, Danger

- Restrict use to CPAs

- Limit method of application (e.g. no aerial)

- Use closed-system transfer (pump) and/or bulk shuttles for large acreage applications

- Buffer Zones (safe-guard against surface run-off & subsequent surface water contamination)

- Prohibit use on specific crops or entire use pattern
Risk Assessment – 4 elements

The toxicity of the pesticide – potential hazards result in adverse effects to human health

HAZARD

RISK ASSESSMENT

RISK MANAGEMENT

EXPOSURE

Exposure is by any route including occupational, food, air and water; estimated or measured
Monsanto’s Roundup Causes Birth Defects
Monsanto's Roundup Herbicide Killing Off Frogs Worldwide
Separating High Quality Data from “Headline” Science in the News

Testing, Toxicity and Exposure: How Safe is “No Unreasonable Risk”?

"Best available" loses reliability as it sheds its components of quality

**FIFRA Guideline Data**: Has its utility defined by FIFRA testing guidelines; has its consistency defined by EPA review; has its quantity defined by FIFRA data requirements; has its objectivity, transparency and integrity assured by GLP requirements.

**Repeated Peer Reviewed Publications or Findings**: Has consistency defined by replication; demonstrates quantity based on the statistical design of the studies; has its objectivity from peer review; has utility to the extent it supports risk assessment, but loses its integrity and transparency because methods are not documented to the degree GLP’s require.

**Single Peer Reviewed Publications or Findings**: Has limited objectivity depending on the level of peer review but has its utility defined by one circumstance and may not have been designed for purposes of risk assessment; and loses its transparency because methods are not documented to the degree GLP’s require, loses its quantity by its isolation and is of unknown consistency.

**Hypothetical Association**: Has virtually no utility; loses its objectivity to subjective speculation; has no transparency in methodological scientific application; is not supported by any quantity of data; and has no measure for consistency.
Know where you are in the process of determining no unreasonable risks to human health and the environment!

Experimentation
(measurement, data analysis)

Risk Assessment

Risk Management

Scientific

Socio-political

Economic
Donna Farmer – Chemistry Stewardship Lead

314-694-8860

donna.r.farmer@monsanto.com