

# **Risk Assessment (including FQPA assessment) and Risk Mitigation**

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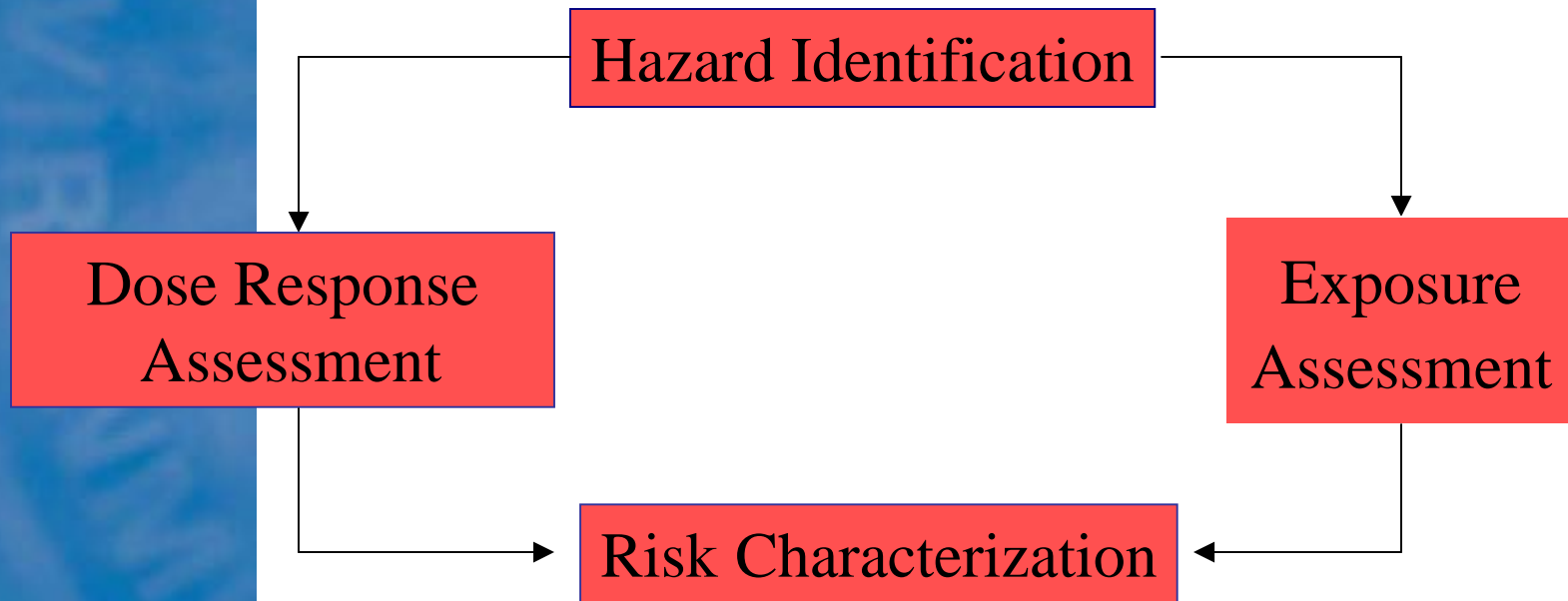
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# The Risk Assessment Paradigm: The "Red Book"



\*From the National Research Council's *Risk Assessment in the Federal Government: Managing the Process*, 1983.

<http://books.nap.edu/books/030904894X/html/1.html>

# What is Risk?

$$\text{RISK} = \text{HAZARD} \times \text{EXPOSURE}$$

- **Hazard Assessment**
  - EPA determines the toxicity of the chemical based primarily on toxicological studies using laboratory animals. These studies address many adverse health effects, including (but not limited to) reproductive effects, developmental toxicity, toxicity to the nervous system, and carcinogenicity.
  
- **Exposure Assessment**
  - EPA examines exposure to the chemical through the diet (e.g., food and drinking water) and through exposures that occur as a result of pesticide use in residential settings.

# Inert Ingredient Evaluation— Elements of Risk Assessment

- Hazard (What are the toxicological effects?)
- Endpoint of concern (toxicological effects relevant to human risk assessment)
- Dose-response assessment (at what dose level do the effects occur?)
- The most **SENSITIVE ENDPOINT** at the **LOWEST DOSE** in the **MOST SENSITIVE** species.
- Exposure assessment (how much of the inert ingredient is a person exposed to?)
- Risk characterization (combines the hazard, endpoint, dose-response, and exposure information to describe the overall magnitude of the risk)

# Types of Toxicity Data used in Inert Ingredient Risk Assessments

**Acute** -- Is there toxicity after a single dose?

**Subchronic** -- Identifies target organ (e.g., liver, kidney) after several weeks or months of exposure

**Chronic** -- Examines effects after long term exposure

**Developmental** -- Examines the effects on growth and development of fetuses (unborn child)

**Reproduction** -- Examines reproductive changes in parents and toxicity to offspring (pups)

**Neurotoxicity** -- Examines effects on the nervous system

**Carcinogenicity** -- Dose it cause cancer?

**Mutagenicity** -- Changes in the genetic content of cells

**Immunotoxicity** -- Changes in immune response

# Hazard Assessment: Standard Guideline Studies

## OPPTS Guidelines

[http://www.epa.gov/opptsfrs/publications/  
oppts-  
harmonized/870\\_Health\\_Effects\\_test\\_  
Guideline/Series](http://www.epa.gov/opptsfrs/publications/oppts-harmonized/870_Health_Effects_test_Guideline/Series)

OECD guidelines available at

[http://www.oecd.org/document/22/0,3343,en\\_  
2649\\_3437\\_1916054\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/22/0,3343,en_2649_3437_1916054_1_1_1_1,00.html)

# **Dose-response Assessment and Endpoint Selection: Exposure Scenarios**

- **Dietary**
  - **Oral food and water (all ages)**
- **Residential**
  - **Incidental oral ingestion (children, adult swimmers)**
  - **Dermal exposure (all ages)**
  - **Inhalation exposure (adults, children indoors)**
- **Occupational**
  - **Dermal and inhalation exposure (adults)**

# Dose-response Assessment and Endpoint Selection (continued)

Exposure Pathways, Routes, and Duration

Dietary : Acute  
Chronic  
Cancer

Non Dietary: Incidental Oral (Short & Intermediate)  
Dermal (Short, Intermediate & Long term)  
Inhalation (Short, Intermediate & Long term)

Duration: Short Term Exposure (1 – 30 Days)  
Intermediate Term Exposure ( 1 -6 Months)  
Long Term Exposure ( > 6 Months)

Dose & Endpoints selected for 11 Exposure Scenarios

# Inert Ingredient Exposure Assessment

- Based on the chemical's proposed use pattern
- All potential exposure scenarios considered and, as appropriate, assessed
- May involve use of models to estimate dietary exposure, occupational exposure, residential exposure, and environmental fate and transport
- Dietary exposure - Primary component is inert ingredient dietary exposure estimation model
- Residential exposures - estimated using standard OPP residential exposure assessment methodologies

# Dietary Exposure Scenarios

- **Acute**

Dose and endpoint for one exposure

- Two Population Subgroups

- General Population/Infants & Children

- Women of Childbearing Age (13-49 yrs)

- **Chronic**

Dose and endpoint for repeated exposures

# Inert Ingredient Dietary Exposure Estimation Model

- Screening level dietary exposure model for inert ingredients developed by EPA.
- Uses DEEM-FCID™
  - Assumptions in Model:
    - Actual crop-specific residue for a.i.s can be used as surrogate data for inert ingredient residues
    - Inert ingredients are used on all crops and 100% of crops are “treated” with the inert
    - No adjustments are made for amount of inert ingredient in formulation, application rate, or multiple applications of different pesticide formulations
    - Considers only preharvest applications
    - Drinking water exposure estimates utilize drinking water concentrations of 100 ppb.

# Inert Ingredient Dietary Exposure Estimation Model (continued)

- Model Inputs
  - 57 most “significant” active ingredients considered: included insecticides (>1 million lbs/yr), fungicides (>1 million lbs/yr) and herbicides (>5 million lbs/yr)
  - Used on crops that are significant contributors to diet (included “kids” foods)
  - Actual residue monitoring studies

# Inert Ingredient Dietary Exposure Estimation Model (continued)

Population Subgroup	Estimated Exposure mg/kg/day
■ All Infants (<1 year)	■ 0.120
■ U.S. Population (total)	■ 0.245
■ Children (1-2 years)	■ 0.422
■ Children (3-5 years)	■ 0.310
■ Children (6-12 years)	■ 0.174
■ Youth (13-19 years)	■ 0.100
■ Adults (20-49 years)	■ 0.087
■ Adults (50+ years)	■ 0.086
■ Females (13-49 years)	■ 0.087

# Occupational and Residential Exposure Assessment

- Occupational exposures:
  - Handler: Mix, load and apply pesticide (agricultural, commercial, others)
  - Post-application: Reentry after application (e.g., pickers, thinners)
- Considers dermal and inhalation routes of exposure

# Occupational and Residential Exposure Assessment (cont)

- Residential exposures
  - Handler: Homeowner application
  - Post-application: Reentry after application (e.g., playing on lawns), contact with treated surfaces (e.g., child crawling on rug)
- Considers dermal, inhalation, and oral routes of exposure

# Inert Ingredient Exposure Assessment

- Occupational and Residential Exposure
- Three Major Inputs:
  - Application Rate: Label or usage information (lbs. A.I./A)
  - Acres treated: Standard values from data and surveys
  - Unit exposure: exposure per pound of active ingredient handled from the Pesticide Handlers Exposure Database (PHED)

# Inert Ingredient Exposure Assessment

## Pesticide Handlers Exposure Database (PHED)

- Concept: Handler exposure is less dependent on chemical structure, more dependent on the physical processes of mixing and loading, the type of formulation, Personal Protective Equipment (PPE), packaging, application equipment, etc.
- PHED aggregates data for different chemicals into scenarios representative of each activity / formulation type / PPE / unit exposures, etc
- e.g., mix/load dry flowables, apply granules

# Inert Ingredient Environmental Fate Assessment

- Estimates of pesticide inert ingredient concentrations in the environment
  - How fast and by what means does the chemical degrade?
  - What are the breakdown chemicals?
  - How much of the chemical or its breakdown chemicals will travel from the application site?
  - Where will they accumulate in the environment?
- Environmental fate assessment uses actual data or modeled data such as the EPISuite model found at <http://www.epa.gov/oppt/exposure/pubs/episuite.htm>.

# Ecological Hazard Assessment

- Characterizes the impact of the inert ingredient on nontarget plants and animals
- May be performed based on proposed use patterns
- Toxicity to aquatic organisms is determined based on actual data or modeled data (such as ECOSAR)  
<http://www.epa.gov/oppt/newchemicals/tools/21ecosar.htm>
- Toxicity to terrestrial and avian nontarget organisms are considered where data are available

# **FQPA Assessment (Key Information needed)**

- Evidence of increased susceptibility
- Evidence of Neurotoxicity- Need for the DNT study?
- Completeness of the database
- Evidence of Immunotoxicity
- Dietary and Drinking water Assumptions

# Aggregate Exposure / Risk Assessment

FQPA defines “safe” as:

“there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposure and all other exposure for which there is reliable information.”

# Aggregate Exposure / Risk Assessment

## When do you aggregate?

- **Aggregate across pathways (e.g. food, drinking water, residential exposure) when you expect concurrent exposure from different pathways**
- **Aggregate across routes (oral, dermal, inhalation) when the same toxic effects are assumed to occur as a result of exposure by the different routes**

# Aggregate Assessment: Useful links

OPP's Guidance for conducting aggregate risk assessments can be found at:

<http://www.epa.gov/EPA-PEST/1999/November/Day-10/6043.pdf>

# Cumulative Risk

- Combined aggregate risks from all chemicals which have a common mode of action

-or-

- Combined risks from food, drinking water, and residential exposure, for all pesticides which have common toxic effects produced in the same way

# Cumulative Risk: Useful Links

Guidance on Cumulative Risk Assessment  
of Pesticide Chemicals that Have a  
Common Mechanism of Toxicity

[http://www.epa.gov/pesticides/trac/science/cumulative\\_guidance.pdf](http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf)

# Use of Inert Ingredient Risk Assessment

- If the assessment demonstrates that the inert ingredient does not cause unreasonable adverse effects to the environment and (in the case of food use inert ingredients) demonstrates that the inert ingredient meets the “reasonable certainty of no harm” standard, the request/petition can be granted
- Inert ingredients with unacceptable risks are not approved

# Risk Mitigation Options

## Options that might satisfy the “reasonable certainty of no harm” finding:

- Limiting use of inert with only certain active ingredients
- Limiting use of inert to only certain crops
- Limiting application timing (before crop emerges from the soil, before edible parts form)
- Limiting application methods (nonfoliar applications only)
- Limiting the percentage of the inert in end-use pesticide formulation
- Limiting application rates