

OPP Human Health Risk Assessment Overview



Briefing For PPDC
May 2020



EPA Roadmap

- Basis
- Risk Assessment
 - Hazard
 - Exposure
 - Characterization



Legislative Basis

FIFRA (Risk/Benefit Standard)

- Occupational Risk Assessment
- Ecological Risk Assessment

FFDCA/FQPA (Risk-Only Standard)

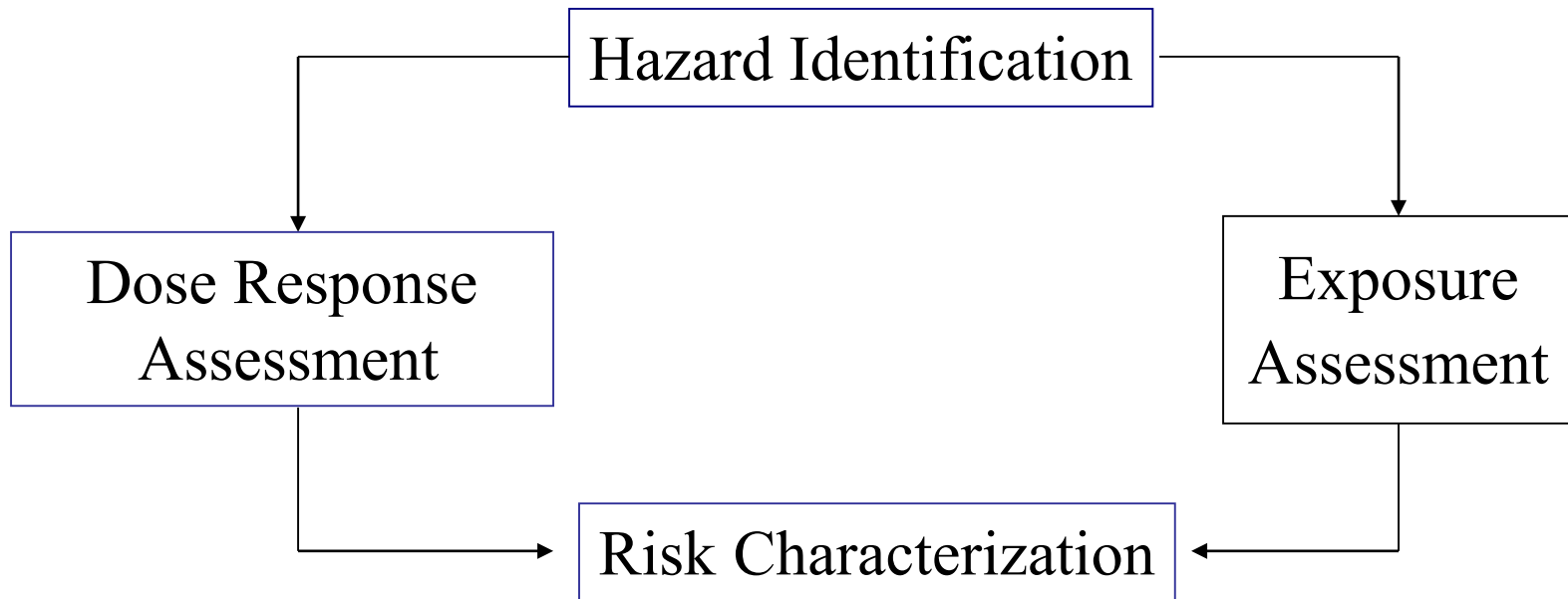
- Human Health Risk Assessment
 - Dietary Exposure
 - Residential Exposure

Food Quality Protection Act

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



Basic Construct



*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>



How Risk Is Expressed

Dietary Risks: % of acute (aPAD) & chronic (cPAD)

$$\text{PAD} = \frac{\text{Point of Departure (e.g., NOAEL)}}{\text{Uncertainty Factors (includes FQPA)}} \quad \% \text{PAD} = \frac{\text{Exposure}}{\text{PAD}} \times 100$$

Occupational/Residential Risks: MOE or Margin of Exposure

$$\text{MOE} = \frac{\text{Point of Departure (e.g., NOAEL)}}{\text{Exposure}} \quad \text{Target MOE} = \text{Uncertainty Factors (Residential Includes FQPA)}$$

Cancer risks are expressed as population based estimate

Barolo Memo, typically a range of results



Scientific Rigor

- Well established guidelines and GLP criteria are basis of methods
- Key approaches and data sources have undergone extensive external scientific peer review
- Risk assessments are vetted in public participation process
- Many methods are broadly accepted on an international level
- Leaders in cutting edge science policy development



Key Definitions

- **Endpoint:** The adverse effect upon which the risk assessment is based
- **Lowest Observed Adverse Effect Level (LOAEL):** Lowest dose from a study at which adverse effects are observed
- **No Observed Adverse Effects Level (NOAEL):** The dose at which no adverse effects are observed
- **Point of Departure (POD):** The dose level used to quantify risk (generic)
- **Control:** Background response with dosing (dose = zero)



Hazard Identification

- Battery of toxicology studies are required
<https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines>
- Data intended to identify variety of potential adverse effects
 - e.g., neurotoxicity, reproduction and developmental toxicity, cancer, immunotoxicity
- Studies are conducted in a variety of species e.g., mice, rats, rabbits, dogs
- Treatments range from single (acute) exposure to repeated longer term exposures (up to 2 yrs)
- Non-guideline data important too ((comparative cholinesterase (CCA) and comparative thyroid (CTA))
- Fit for Purpose approaches being used as appropriate – e.g., HASPOC/data waiver process



Hazard Identification

- Process of identifying the potential health effects as a result of various types of chemical exposure
- Output is “Points of Departure” or POD
- Goal is to match route & duration of exposure

Typical Scenarios & Durations	Oral	Dermal	Inhalation
Acute (1 Day)	✓ Dietary		
Short-Term (up to 1 Month)	✓ Incidental	✓	✓
Intermediate-Term (up to 6 Months)	✓ Incidental	✓	✓
Chronic (> 6 Months)	✓ Dietary		



Uncertainty/Safety Factors

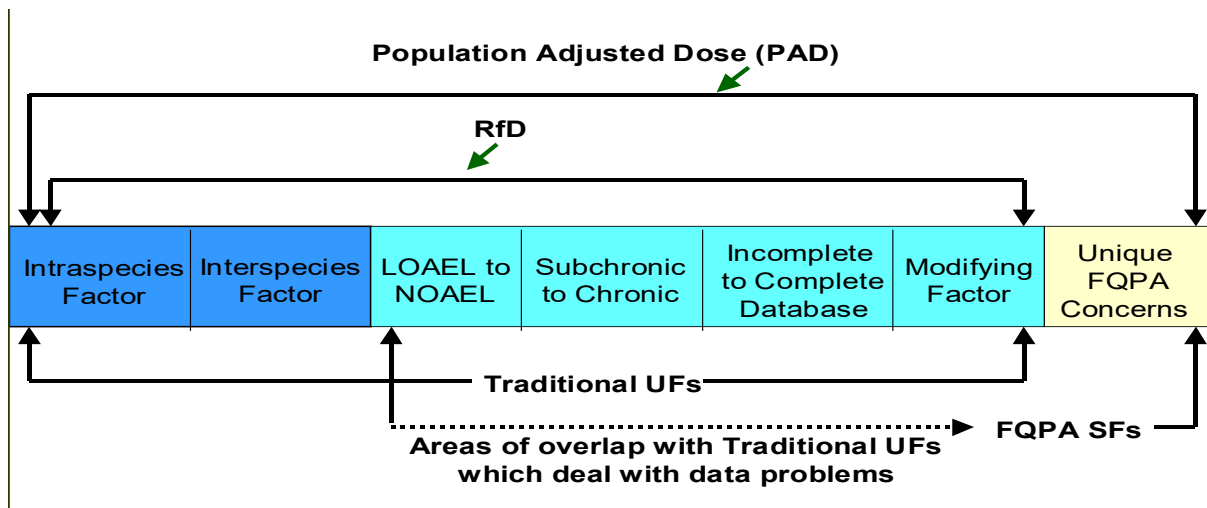
- **Intraspecies – variability among humans**
- **Interspecies – extrapolating animal data to humans**
- **Extrapolating from less-than-lifetime to lifetime exposures**
- **LOAEL to NOAEL**
- **Incomplete data base**
- **Increased concern for susceptibility of infants and children not addressed by other safety factors**

FQPA Safety Factor

Generally 10X unless:

- A smaller factor can be shown to be protective, or

Maximum = 3000



Example of factor application to develop PAD for dietary risk assessment



Exposure Types

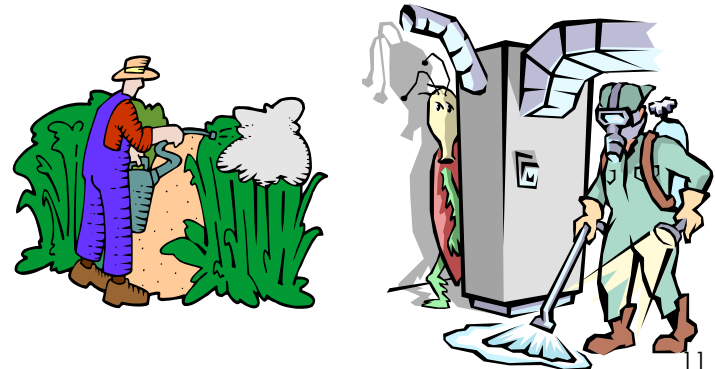
Dietary Exposure



Residential Exposure
(General Public)



Occupational Exposure





Key Factors In Exposure Assessment



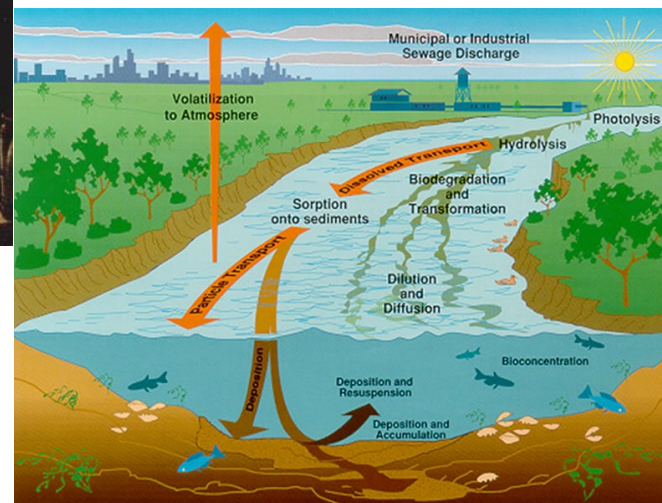
Use Information
(rate, type, & crop)



Chemistry



Human Behaviors



Fate & Transport₁₂



Dietary Exposure



Food Consumption
(WWEIA)



Food Recipe
Database
(FCID)

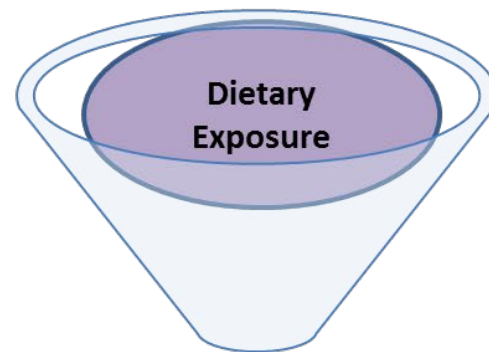
Raw Agricultural
Commodity (RAC)
Consumption

X

Pesticide Residue



=



Acceptable Level
aPAD, cPAD, ssPAD, etc.



Dietary Exposure

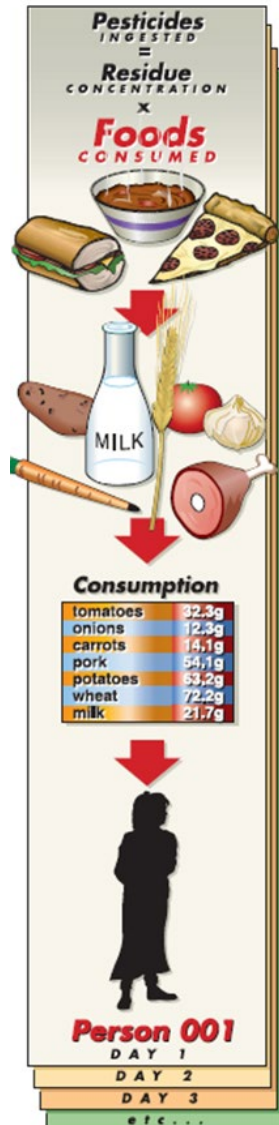
Consumption

X

Residue

=

Dietary
Exposure



- Assessments range from simple to complex, but based on same general exposure algorithm.
- OPP uses a data-driven approach
 - USDA's What We Eat In America (WWEIA) Survey**
Nationally representative food consumption survey
 - U.S. EPA's Food Commodity Intake Database (FCID)**
Recipe database that links WWEIA foods to residue data
 - Residue Data**
Sources vary depending on level of refinement



Refinement Approach

No refinements: Tolerance-level residues and 100%CT

- % Crop Treated
- Field trial data
- PDP/FDA monitoring data
- Processing studies
- Cooking Factors
- Bridging studies
- Residue degradation/decline studies
- Market basket data

residue refinements

A large red arrow pointing downwards, indicating the direction of the refinement process from the initial state to the final state.

highly refined residues



Tolerances & MRLs

- Is a label-compliance tool and not a health-based standard
- Tolerances set on food or feed crops (maximum residue levels)
 - Amount of pesticide that can legally remain in or on foods
- Based on results from field trials designed to identify the highest concentrations expected on crops
 - Use maximum application rates
 - Maximum number of applications
 - Shortest application to harvest interval
- Generally, actual measured residues in food are 10-100 times lower than tolerances
 - Due to degradation during distribution, storage or washing



Residential Exposure

- Exposure from uses
 - In and around homes
 - Athletic fields and golf courses
 - Public areas

- Exposure scenario based pathways
 - Handlers
 - Post-application
 - Index lifestages considered

- Routes of exposure
 - Dermal (application and post-application)
 - Inhalation (application and post-application)
 - Oral (post-application; children only)

- Key tool – *SOPs For Residential Exposure Assessment*





Residential Handlers

$$\frac{\text{lb ChemX}}{\text{Area}} \times \frac{\text{Area}}{\text{day}} \times \frac{\text{mg ChemX Exposure}}{\text{lb ChemX Handled}} \div \text{kg BW} = \text{Exposure (mg/kg/d)}$$

MOE = Point of Departure (e.g., NOAEL)/Exposure (mg/kg/day)

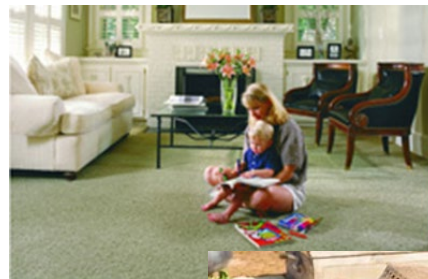
■ Key Inputs/Factors

- Label/Use Directions
 - e.g., application rate
- Activity/Amount per day
- Unit Exposure (dermal and inhalation)
 - Exposure per amount of product handled
 - Use pattern specific values
- Dermal Absorption
- Body Weight



Post-Application Residential Exposure

- Complex compared to handler assessments
- Exposure source characterization
 - e.g., Turf-Transferrable Residue (TTR)
- Behavioral based approaches
 - Index lifestage
 - Dermal contact levels
 - Mouthing rates
 - Breathing Rates
 - Frequency/Duration of Behaviors
 - Types of behavior & how to address





Post-Application Residential Exposure

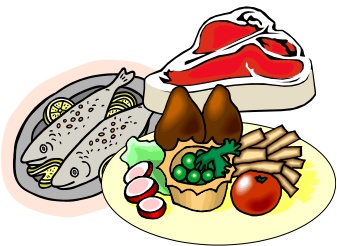
$$\frac{\mu g \text{ chemX}}{cm^2} \times \frac{TC - cm^2}{hour} \times \frac{hours \text{ of activity}}{day} \div kg \text{ BW} = \text{Exposure (mg/kg/d)}$$

MOE = Point of Departure (e.g., NOAEL)/Exposure (mg/kg/day)

- Key Inputs/Factors
 - Label/use directions
 - Residue level
 - Deposition on area basis & dissipation kinetics
 - Activity which defines:
 - TC or Transfer Coefficient (dermal rate of contact)
 - Index lifestage (determines if mouthing behavior considered)
 - Exposure Time
 - Dermal Absorption
 - Body Weight



EPA Aggregate Exposure





Aggregate Exposure

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.”

- Combine Routes of Exposure
 - Generally a single compound
 - Common effects across routes
 - Reliable estimates of exposure
 - Avoid overestimate + overestimate + overestimate
- Does not include occupational exposure



Aggregate Scenarios

- **Acute (≤ 1 -day)**
 - usually dietary food and DW only, occasionally includes refined residential exposures
- **Short-term (1-30 days)**
 - food, DW, residential - only done when residential scenarios exist
- **Intermediate-term (1-6 months)**
 - food, DW, residential - only done when residential scenarios exist
- **Chronic (6 months - lifetime)**
 - usually dietary food and DW, occasionally includes residential exposures
- **Cancer**
 - food, DW, residential

Occupational Exposure

- Handlers: those who may be exposed while mixing, loading, and/or applying pesticides
- Post-application workers: those who enter previously treated areas to tend/harvest crops that have been previously treated



Scenario Based Approach





Occupational Handlers

$$\text{Exposure (mg/day)} = \frac{\text{Application Rate}}{\text{Rate}} \times \frac{\text{Area Treated}}{\text{Treated}} \times \frac{\text{Unit Exposure}}{\text{Exposure}}$$

- Key Inputs

- Application Rate:

- based on the label or usage information (lb ai/Acre)

- Acres treated:

- standard values from data and surveys (Acres or gallons per day)

- Unit exposure:

- Exposure per pound of active ingredient handled (e.g., mg/lb ai)
 - Distinct values based on task and level of personal protection
 - Extensive library of values developed through a collaborative multi-governmental and industry effort

Occup. Post-application

- Exposure occurs from contact with treated areas and crops
 - Varies by type of crop and activity being performed
 - >7000 crop/activity combinations identified





Occup. Post-application

$$\text{Exposure (mg/day)} = \text{DFR or TTR } (\mu\text{g/cm}^2) \times \text{TC } (\text{cm}^2/\text{hr}) \times \text{ET } (\text{hrs/day})$$

- Key Inputs
 - Dislodgeable Foliar Residue (DFR) or Turf Transferable Residue (TTR):
 - Residue on foliage that can transfer to a worker's skin
 - Transfer Coefficient (TC)
 - Measure of contact with foliage while performing a specific activity
 - Exposure Time (ET)
 - Amount of time spent performing activity per day
- Risk estimates used to define Restricted Entry Intervals or REIs are key output
 - i.e., time-based exclusions from fields until residues dissipate



Risk Characterization

Risk Assessment gives you a number.

Risk Characterization tells what that number means.

We routinely consider (among other factors):

- Data Quality
- Distributional Data
- Interdependencies Between Variables
- Co-Occurrence of Exposure

We also follow EPA Risk Characterization Guidance

Back Pocket Slides



EPA Antimicrobial Pesticides

- Assessments follow same framework as conventional pesticides.
 - Antimicrobials are defined by claims. If the product label makes antimicrobial claims, the active ingredient is considered an antimicrobial pesticide.
 - Many high production volume (HPV) compounds and/or overlap jurisdiction with FDA and other parts of EPA such as Offices of Air and Water.
 - Supporting data may be from open literature and not from guideline studies.

EPA Antimicrobial Pesticides

- Occupational and residential exposure scenarios are unique.
 - Janitors, factory and processing facility workers, health care personnel, painters.
 - Task forces such as AEJV and AEATF support AD assessments
 - Cannot mitigate risk by PPE for many occupational and residential uses.
 - End use products for material preservatives don't have pesticide labels informing users of potential exposures.

EPA Antimicrobial Pesticides

- Dietary exposures:
 - Direct dietary exposures from postharvest and processing rinses.
 - Indirect dietary exposures from transfer from items such as food packaging, countertops and cutting boards.
 - Major issue is the assumption that Potable Water Rinses do not remove 100% of residues.
 - AD is using new models developed with ACC such as Indirect Dietary Residential Exposure Assessment Model (IDREAM) and Food Contact Sanitizing Solutions Model (FCSSM).



Biopesticides

- Biochemical, Microbial and PIPs
 - Biochemical assessments similar to conventional pesticides with reduced and tiered testing requirements
 - Microbial assessments based on pathogenicity and infectivity hazard endpoint in addition to toxicity
 - Plant-Incorporated Protectants assessment for proteins and nucleic acids expressed in plants using bioinformatics and reduced testing requirements



PPE Types





Engineering Controls



Closed Loading

Closed Cab Sprayer





Unit Exposure Example

USEPA / Office of Pesticide Programs / Health Effects Division Occupational Pesticide Handler Unit Exposure Surrogate Reference Table					
Scenario	Exposure Route	Personal Protective Equipment (PPE) Level ¹	Data Source ²	Statistic	Unit Exposure (µg/lb ai)
Mixing / Loading Dry Flowable	Dermal	Single layer, no gloves (A)	AHETF	Mean	227
		Single layer, gloves	AHETF	Mean	51.6
		Double layer, gloves (B)	AHETF	Mean	41.2
		Engineering control (water-soluble packaging)	PHED	"Best fit"	9.8
	Inhalation	No Respirator	AHETF	Mean	8.96
		PF5 (C)	AHETF	Mean	1.79
		PF10 (D)	AHETF	Mean	0.90
		Engineering control (water-soluble packaging)	PHED	"Best fit"	0.24
Applicator, Open Cab Groundboom	Dermal	Single layer, no gloves (A)	AHETF	Mean	78.6
		Single layer, gloves	AHETF	Mean	16.1
		Double layer, gloves (B)	AHETF	Mean	12.6
		Engineering control (Enclosed Cab)	PHED	"Best fit"	5.1
	Inhalation	No Respirator	AHETF	Mean	0.34
		PF5 (C)	AHETF	Mean	0.07
		PF10 (D)	AHETF	Mean	0.03
		Engineering control (Enclosed Cab)	PHED	"Best fit"	0.043



Transfer Coefficient Examples

Crop/Activity Combinations and Recommended TCs						Source Study	
Crop Group	Crop	Crop Height	Foliage Density	Activity	TC	Crop	activity
Field/row crop, tall	Sweet corn	High	Full	Irrigation	1,900	Potato	irrigation
Field/row crop, tall	Sweet corn	High	Full	Scouting	210	Cotton and Tomato	Scouting
Field/row crop, tall	Sweet corn	High	Full	Detasseling, hand harvesting	17,600	Sweet corn	Hand harvesting
Vegetable, "root"	Sweet potato	Low	Full	Irrigation	1,900	Potato	Irrigation
Vegetable, "root"	Sweet potato	Low	Full	Mechanical weeding and harvesting	0	No TC	No TC
Vegetable, "root"	Sweet potato	Low	Full	Hand weeding	70	Cotton	Hand weeding