

CARES Training

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Overview

- What is an aggregate and cumulative risk assessment and how are they performed theoretically?
- What models are currently accepted by EPA?
- What models are currently used by EPA in-house assessors.

Background

- David Hrdy, Chemistry and Exposure Branch in the Health Effects Division of OPP/ EPA
- Responsibilities include:
 - Models and their inputs
 - Risk Assessments including OP and NMC CRAs
 - Measures and Indicators

Brief History of Aggregate and Cumulative Assessment in OPP

- Food Quality Protection Act, 1996
 - Aggregate assessment
 - Cumulative assessment
- Requires EPA to take into account when setting pesticide tolerances
- “available evidence concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity.”

Aggregate Risk

- Residential
 - Includes dermal, inhalation, and oral hand to mouth
- Food
- Water

- ...this does not include occupational

Key Concepts in Aggregate Assessment

- Important to “integrate” or combine these route specific estimated exposures in an internally consistent manner to develop a total risk picture
 - Integrated (or Combined) Exposure = “Total MOE”
 - “Appropriate Matching and Combining”

$$\text{MOE}_{\text{dermal}} = \frac{\text{PoD}}{\text{Exposure}_{\text{dermal}}}$$

$$\text{MOE}_{\text{oral}} = \frac{\text{PoD}}{\text{Exposure}_{\text{oral}}}$$

$$\text{MOE}_{\text{inhalation}} = \frac{\text{PoD}}{\text{Exposure}_{\text{inhalation}}}$$

$$\text{MOE}_{\text{total}} = \frac{1}{\frac{1}{\text{MOE}_{\text{dermal}}} + \frac{1}{\text{MOE}_{\text{oral}}} + \frac{1}{\text{MOE}_{\text{inhalation}}}}$$

Basic Steps in a Cumulative Risk Assessment

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



Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, D.C. 20460

January 14, 2002

- Identify common mechanism group (CMG)
- Determine relevant exposure scenarios/pathways
- Identify cumulative assessment group (CAG)
- Consider appropriate method(s) & data sources
- Conduct assessment
 - Characterize & select common mechanism endpoint(s), determine chemical potency & select index chemical
 - Convert pesticide residues to equivalents of the index chemical
 - Combine/integrate food, water, & residential exposures on an internally consistent manner which incorporates demographic & temporal-spatial factors

A multi-chemical/multi-route/multi-pathway assessment:

- Multiple chemicals with common mechanism of toxicity
- Multiple routes of exposure
 - Oral, dermal, inhalation
- Multiple pathways of exposure
 - e.g., food, drinking water, indoor surfaces, air

STEPS in Cumulative Risk Assessment (abbreviated version)

- Grouping chemicals by common mechanism
- Estimate toxic potencies of common effect for each chemical
- Select index chemical
- Use index chemical to calculate RPFs

STEPS in Cumulative Risk Assessment (abbreviate version) (cont'd)

- Convert residues in food to cumulative basis (“index chemical-equivalents”)
- Do same for water and residential exposures
- Combine/integrate food, water, and residential exposures on an internally consistent manner which incorporates temporo-spatial factors

Cumulative Risk

- Common Mechanism Group (CMG)
- Cumulative Assessment Group (CAG)
- Exposure from either, and/or – food, water, residential routes of exposure
- Sum across a CAG

Multi-Pathway Analysis

- OPP now has several models to estimate cumulative risk and is using them per the SAP's recommendations
 - Calendex, CARES, LifeLine, SHEDS
- Cumulative RA include:
 - Several percentiles
 - Common percentiles are 95th , 99th , and 99.9th
 - All subpopulations
 - Represents regional and temporal variations
- Calculations by OPP can provide information from exposure estimates on the primary contributor to total risk
 - Oral exposure can be contributed from all three pathways, hand to mouth, drinking water and food

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Populations Groups Assessed

- Separate assessments are based on survey information including the following age groups:
 - Children 1-2 years old
 - Children 3-5 years old
 - Adults 20-49
 - Adults 50+
- For Cumulative Risk Assessment the remaining age groups are included

Example Outputs

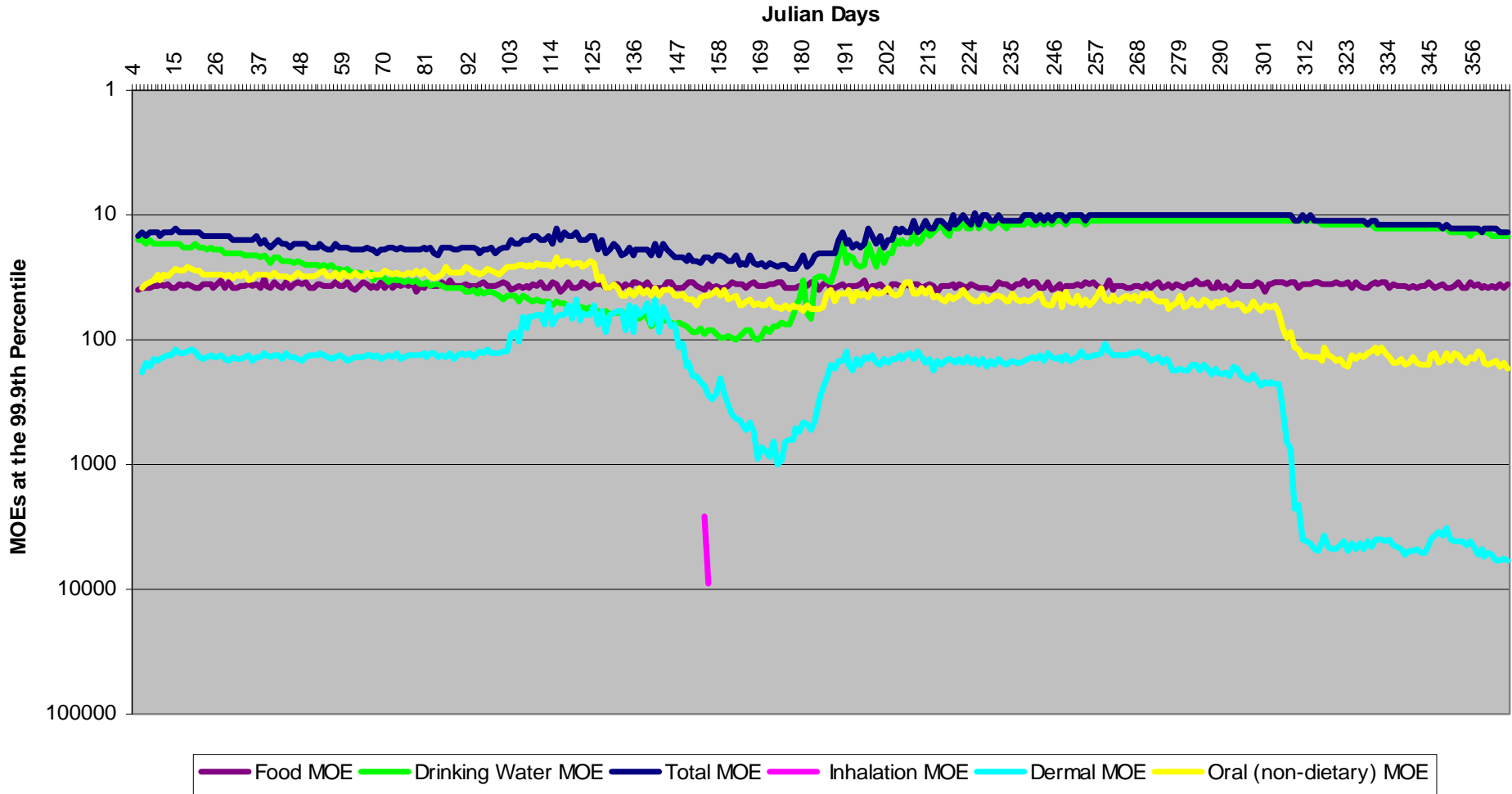
“MOE Profile Graphs”

- The following graphs represent the Florida Central Ridge area from a previous assessment
 - Additional graphs can be found in Appendix II.F.1-2 of NMC CRA Preliminary
<http://www.epa.gov/scipoly/sap/meetings/2005/index.htm#august>
- Each line in the graph represents a separate pathway of risk in MOEs
 - Expressed in terms of MOE for index chemical
 - Example subpopulation presented here is Children 1-2 years old

Cumulating MOEs

- This series of daily MOE distributions is arrayed as distribution across time (one year)
- The MOEs developed such that the exposures from NMCs in foods, drinking water and from residential uses are all calculated simultaneously for each individual.
- Preliminary risk assessment focuses on regional locations which are believed to represent higher end exposure potential due to usage, pest pressures, and other environmental factors.
 - Exposures in drinking water from the remaining parts of the country are expected to be substantially lower than from these sites

Cumulative MOEs for Children 1-2 in FL Central Ridge using Ground Water in a Daily Analysis



Example Outputs

“MOE Profile Graphs”

- For the examples given here:
 - Relative Risk by Pathway
 - Calendex was used to estimate risks through each of the three pathways
 - *In this example the following order is seen. This order is assessment dependent.*
 - $\text{Risks}_{\text{oral}} > \text{Risks}_{\text{dermal}} > \text{Risks}_{\text{inhalation}}$

Models Accepted by EPA

Must be...

- Able to Conform to EPA Guidance
- Publically available
- Peer Reviewed

Models Used by EPA in OPP

- CARES
- LIFELINE
- SHEDS (internally developed by EPA)
- DEEM/Calendex

Similarities Include

- Estimate of Exposure in mg/kg/day
- Daily Acute and Long Term Chronic scenarios
- Use CSFII and FCID consumption database
- Allow for residue distribution inputs and provide distributional outputs
- Able to compare to an endpoint (i.e., POD) for a risk calculation

EPA Uses All Models

- DEEM/Calendex historically most frequently used
 - Still the only model entirely based on the empirical consumption data
- Lifeline was included in the OP CRA 2006 update.

EPA Uses All Models

- CARES used for cumulative assessments and most recently is being used in residential risk assessments helping in our SOP updates
- SHEDS continues to be used for cutting edge work in exposure assessment in OPP
 - ½ life analyses, eating occasion, etc..

Model Comparison Framework

Model Design Components	DEEM-FCID	CARES	Lifeline
Reference Population	CSFII Survey (2 Day)	Census (PUMS)	Nativity (NCHS)
Binning Methodology	Random (2 Day Diaries)	Gower Dissimilarity Index	Random (Age, Season)
Reference Population Bodyweight	CSFII normalized	CSFII normalized	Lifeline (NHANES)
Model Weight	CSFII Sampling Weights	CARES (Stratified)	Equal Weights (Random)
Modeled Population	US Population	US Population	US Population (Nativity, Mortality)

Conclusion

- Aggregate exposure is the sum total of the inhalation, dermal, oral (hand to mouth), dietary food and water exposures
- Cumulative exposure is the sum total of aggregate exposures from a cumulative assessment group chemicals that have been classified as having a common mechanism
 - Multi-chemical, multi-pathway, multi-route assessment

Conclusion cont...

- EPA uses all software available provided it meets certain standards
 - Publicly available
 - Peer reviewed

The End

Helpful links:

<http://www.epa.gov/pesticides/>

<https://www.epa.gov/pesticides/cumulative/>

<http://www.epa.gov/pesticides/trac/science/>