

Mehrfachrückstände von
Pflanzenschutzmitteln in
Lebensmitteln

Teil III
Internationale Bewertungskonzepte
für Mehrfachrückstände
10.11.2005

**Cumulative Risk
Assessment:
Experiences and
Approaches in the USA**

10:30 - 11:00

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EPA, Washington

Cumulative Risk Assessment: Experiences and Approaches in the USA

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Presented to:

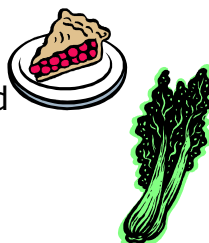
*2nd BfR Forum For Consumer Protection
"Multiple Residues in Foods"
November 9-10, 2005
Berlin, GERMANY*

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Overview of Presentation

- ❖ History/General Background of CRA in U.S.
- ❖ Steps in Cumulative Risk Assessment
- ❖ Key Data inputs into CRA
 - Consumption
 - Residue
 - Relative Potency Factors
- ❖ Overall Experiences/Lessons Learned
- ❖ Future Directions
- ❖ Information Sources



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Background: *The Statutes*

- ❖ Two Statutes:
 - The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
 - The Federal Food Drug and Cosmetic Act (FFDCA)
- ❖ In 1996, both were amended by:
 - The Food Quality Protection Act (FQPA)
 - “aggregation” across pathways
 - “cumulation” across chemicals
 - “reasonable certainty of no harm” standard

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Brief History of Cumulative Assessment in OPP

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

"available evidence concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity."

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A Multi-Chemical/Multi-Route/Multi-Pathway Assessment:

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

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A Multi-Chemical/Multi-Route/Multi-Pathway Assessment:

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

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Scenarios and the Range of Exposure Assessments

Toxic Concern	Exposure Route	Assessment Type
Single Chemical	Single Food	--
	Multiple foods	Aggregate dietary
	Multiple media	Aggregate
Multiple chemicals with the same mechanism of action	Single food	--
	Multiple foods	Cumulative dietary
	Multiple media	Cumulative

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Cumulative Assessment Represents New "Paradigm"

- ❖ Clearly not just a compilation of individual chemical risks
- ❖ Different way of looking at risk
 - Different questions
 - Different methods
 - Different risk management considerations

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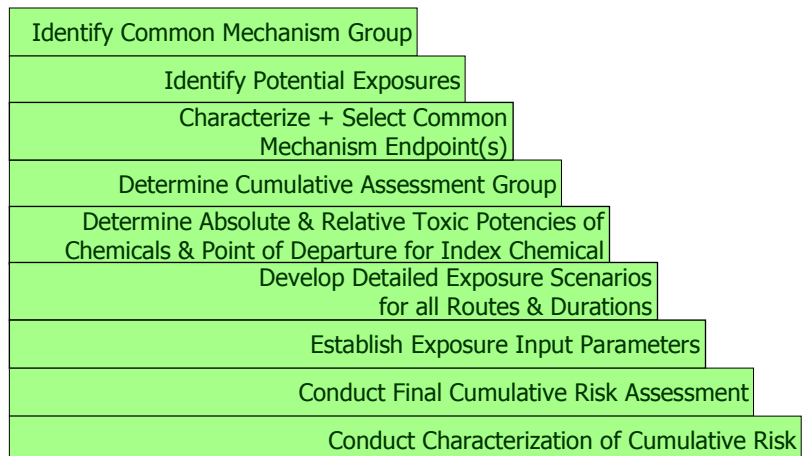
Ongoing Cumulative Risk Assessments at US EPA

- ❖ Organophosphorus pesticides (update)
 - http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#op
- ❖ N-methyl carbamates
 - http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#carbamate
- ❖ Triazines
- ❖ Chloroacetanilides

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Steps for Conducting a Cumulative Risk Assessment



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STEPS in Cumulative Risk Assessment for Food (*abbreviated version*)

- ❖ **Identify chemicals by common mechanism**
 - Common Mechanism Group (CMG)
- ❖ **Estimate toxic potencies of common effect for each chemical**
- ❖ **Determine Cumulative Assessment Group (CAG)**
- ❖ **Select index chemical**
- ❖ **Use index chemical to calculate RPFs**
 - RPF = Relative Potency Factor

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STEPS in Cumulative Risk Assessment for Food (*abbreviated version*)

- ❖ **Convert residues in food to cumulative basis ("index chemical-equivalents")**
- ❖ **Combine/integrate food exposures on an internally consistent manner which incorporates appropriate demographic and other factors**

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Three Key Inputs for Dietary Cumulative Assessments:

- ❖ Food Consumption Data
 - USDA's Continuing Survey of Food Intake by Individuals (CSFII), 1994-96/1998
- ❖ Pesticide Residues in Food
 - Various federal & specialized pesticide monitoring programs
- ❖ Relative Potency Factors

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Cumulative Dietary Exposure

$$\text{Exposure} = \sum_{\text{All Foods}} \sum_{\text{All CAG Foods}} \text{Residue} \times \text{Consumption} \times \text{RPF}$$

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Consumption Data: USDA's CSFII

- ❖ CSFII = USDA's Continuing Survey of Food Intake by Individuals, 1994-96/1998
- ❖ 21,662 individual participants interviewed over the period
- ❖ **Nationally Representative/Statistically-Based**
 - Intakes of individuals residing in 50 states and D.C.
- ❖ **2 non-consecutive days using in-person 24 hour recalls**
- ❖ Total of ca 6000 different "as eaten" foods

<http://www.barc.usda.gov/bhnrc/foodsurvey/home.htm>

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Residue Data : USDA's PDP Program

- ❖ PDP = USDA's Pesticide Data Program
- ❖ **GOAL:** to provide EPA with high-quality nationally-representative data on residues in food for use in dietary risk assessment
 - Standardized and uniform sampling techniques
 - Common Standard Operating Procedures
 - Similar Analytical methodologies
 - Low limits of detection

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Residue Data : USDA's PDP Program

- ❖ Program began in 1991
- ❖ PDP has tested more than 50 different commodities for ca. 300 pesticides/ metabolites
- ❖ Statistically designed for use in dietary risk assessment and be representative of residue concentrations in U.S.
- ❖ Children's foods are targeted
- ❖ Samples collected near point of consumption
 - terminal markets and distribution centers
- ❖ Samples Prepared as if for consumption

<http://www.ams.usda.gov/science/pdp/>

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PDP Food Types

Fruits and Vegetables

Fresh
Frozen
Canned
Processed

Fruit Juices

Ready-to-Drink
Frozen
Concentrate

Grains

Whole

Dairy

Milk
Butter

Beef/Poultry/Pork

Fat
Liver
Muscle

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Example PDP Foods

Apples	Green Beans	Potatoes
Apple Juice	Grapes	Bell Peppers
Bananas	Grape Juice	Strawberries
Broccoli	Lettuce	Sweet Potatoes
Celery	Milk	Soybean
Cantaloupe	Oats	Spinach
Carrots	Oranges	Sweet Peas
Sweet Corn	Orange Juice	Tomatoes
Cucumbers	Peaches	Wheat
Corn Syrup	Pears	Winter Squash
Cherries	Nectarines	Poultry
Rice	Pineapple	Peanut Butter



Relative Potency Factor (RPF) Method of Estimating Cumulative Residues in Foods

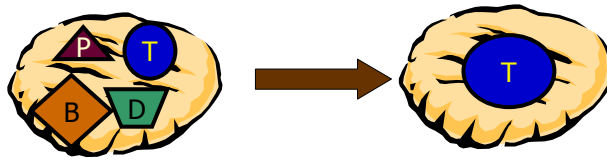
Converts chemical specific residues on food samples to a common residue

Index Equivalent Residue (Residue_{IE})



Example of RPF Approach

Converts chemical specific residues (B,D,P,T) on a food sample to a common residue (T)

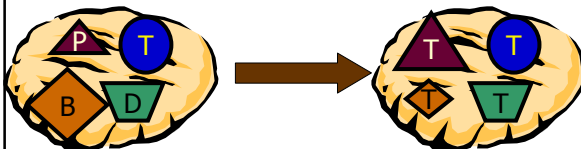


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Two Steps Needed to Derive Cumulative Residue_{IE}

$\text{Residue}_{IE} = \text{Residue} \times \text{Processing Factor} \times \text{Relative Potency Factor}$



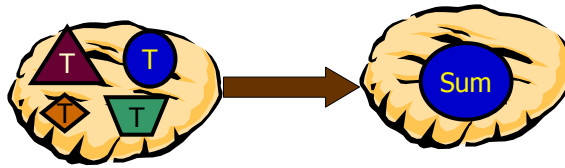
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Two Steps Needed to Derive Cumulative Residue_{IE}

$$\text{Residue}_{IE} = \text{Residue} \times \text{Processing Factor} \times \text{Relative Potency Factor}$$

$$\text{Cumulative Residue}_{IE} = \Sigma \text{Residue}_{IE} \text{ (per PDP sample)}$$



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Relative Potency Factor Method

Chemical	RPF	Conc. (ppm)	PF	Exposure Equivalents of Index (ppm)
(index)	1	15	1	15
D	1	10	0.5	5
B	0.5	20	1	10
P	3	10	1	30
Total Exposure Equivalents of Index Chemical =				60

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Lesson Learned:

Need for Involving Public and Stakeholders in the Decision Process

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Public Participation

- ❖ CARAT/PPDC Workgroups
- ❖ Technical Briefings
- ❖ Scientific Advisory Panel Presentations
 - Consultations
 - Case Studies
 - Preliminary CRA
 - Revised CRA
- ❖ Web sites
- ❖ Other Federal Agencies

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Lesson Learned:

Need for Representative Data

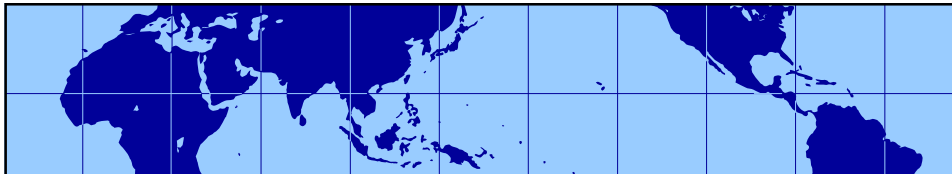
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Representative Data

- ❖ Consumption Data
 - USDA's Continuing Survey of Food Intakes by Individuals (CSFII)
 - <http://www.barc.usda.gov/bhnrc/foodsurvey/>
- ❖ Residue Data
 - USDA Pesticide Data Program (PDP)
 - <http://www.ams.usda.gov/science/pdp>
 - FDA Center for Food Safety & Applied Nutrition
 - Pesticide Residue Monitoring Program
 - Total Diet Study (TDS)
 - <http://www.cfsan.fda.gov/~lrd/pestadd.html>
 - Co-occurrence of Residues

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Lesson Learned:

Need for Probabilistic Methods

(and to avoid compounding conservatisms)

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Need for Probabilistic Methods

- ❖ Traditional Methods
 - Produce high-end or bounding estimates at the extremes of exposure
- ❖ Probabilistic (Monte Carlo) methods
 - Permit the use of the entire distribution of residue levels in crops to be combined with the distribution of food consumption
 - ...and allow us to more accurately estimate the complete distribution of exposures and assess their associated probabilities



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Lesson Learned:

Ability to “Trackback” Sources of Exposures

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“Trackback”

- ❖ Ability to identify major contributors to exposure at high-end exposure tails
 - Pesticide
 - Crop
 - Pesticide/Crop Combination

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"Trackback"

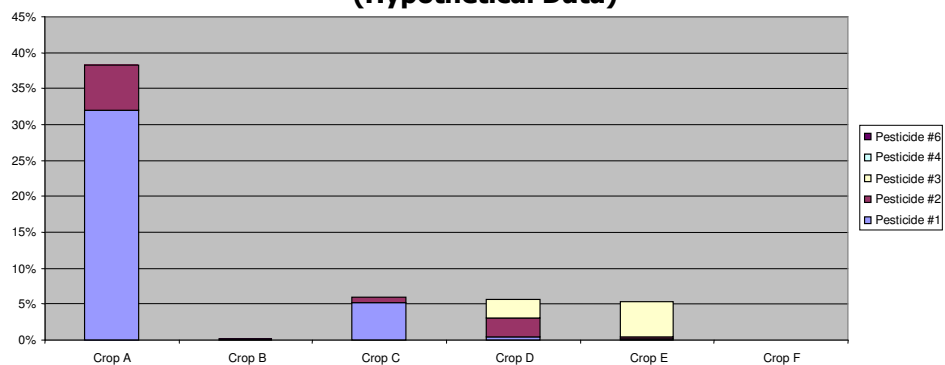
❖ Commodity Exposure Contribution List

- Ability to (semi)quantitatively rank the "risk drivers"
 - Can be used to focus refinements of exposure estimates, sensitivity analyses, and risk mitigation activities on those commodities which contribute most significantly to risk

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Relative Contribution of Crop/Chemical Pairs to Top 99.8+ Percentile (Hypothetical Data)



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“Trackback”

❖ Sensitivity analyses

- Subtract out specific pesticides, specific crops, and specific pesticide/crop combinations
- Examine impact of removal of a given pesticide from all forms of each of these foods from the cumulative assessment
- Examine impact of removal of given pesticide from certain foods/food forms

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Impact of Foods A, B, & C on Assessment

Hypothetical MOEs at Selected Points in the Exposure Distribution

	50 th	95 th	99 th	99.5 th	99.9 th
Full Assessment	16606	457	160	110	52
Minus Food A	47676	651	222	149	70
Minus Food B	19920	495	178	115	55
Minus Food C	60737	652	192	126	60
Minus A & B	57494	727	255	174	75
Minus A,B,& C	149770	1666	428	268	105



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Lesson Learned:

Need for Characterization of Exposure and Risk Estimates

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Characterization of Exposure and Risk Estimates

- ❖ Kinds and quality of data available
- ❖ Key assumptions and their potential impact on the outcome of the assessment
- ❖ Strengths, limitations, and uncertainties inherent in data and analysis
- ❖ Magnitude and direction of likely bias and the impact on the final assessment
- ❖ Identification of risk contributors
- ❖ Sensitivity analyses

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Future Directions

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**Additional
Information/References**

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EPA: Pesticides - Assessing Pesticide Cumulative Risk - Microsoft Internet Explorer

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

U.S. Environmental Protection Agency

Pesticides: Health and Safety

Recent Additions | Contact Us | Print Version Search: **GO**

EPA Home > Pesticides > Health and Safety > Human Health Issues > Assessing Pesticide Cumulative Risk

Assessing Pesticide Cumulative Risk

This website provides information on EPA's

- process for conducting pesticide [cumulative risk](#) assessments,
- cumulative risk assessment [methods and tools](#), including several exposure assessment models, and
- cumulative risk assessments for four [groups](#) of pesticides,
 - [Organophosphates \(OPs\)](#)
 - [N-methyl carbamates](#)
 - [Triazines](#)
 - [Chloroacetanilides](#)

Through the [pesticide reregistration](#) program, EPA evaluates the risks of individual, older pesticides to human health and the environment. Under the Food Quality Protection Act (FQPA), the Agency also must assess the cumulative risks of pesticides that share a [common mechanism of toxicity](#), or act the same way in the body.

Contents

- [Assessing Pesticide Cumulative Risk](#)
- [Cumulative Risk Assessment Methods and Tools](#)
 - [Guidance Documents](#)
 - [Exposure Assessment Models](#)
- [Common Mechanism Groups](#)
 - [Organophosphates](#)
 - [N-methyl carbamates](#)
 - [Triazines](#)
 - [Chloroacetanilides](#)

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A Good Place to Start:

- ❖ EPA's Cumulative Website:
 - <http://www.epa.gov/pesticides/cumulative/>
- ❖ Introductory Background Information on Data Sources:
 - *Available Information for Assessing Exposure to Pesticides in Foods: A Users Guide*
 - <http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf>

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Aggregate and Cumulative

- ❖ U.S. EPA (2001). General Principles For Performing Aggregate Exposure And Risk Assessments
 - <http://www.epa.gov/pesticides/trac/science/aggregate.pdf>

- ❖ **GUIDANCE FOR IDENTIFYING PESTICIDE CHEMICALS AND OTHER SUBSTANCES THAT HAVE A COMMON MECHANISM OF TOXICITY**
 - <http://www.epa.gov/fedrgstr/EPA-PEST/1999/February/Day-05/6055.pdf>

- ❖ U.S. EPA (2002). 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

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Useful Science Policy Documents

Topic	Document	Web Address
The "Zero Issue"/Censored Data	Assigning Values to Nondetected / Nonquantified Pesticide Residues in Human Health Dietary Exposure Assessments; March 23, 2000	http://www.epa.gov/pesticides/trac/science/trac3b012.pdf
99.9 Policy	Choosing a Percentile of Acute Dietary Exposure as a Threshold of Regulatory; March 16, 2000	http://www.epa.gov/pesticides/trac/science/trac2b054.pdf
Anticipated Residue Refinement	Guidance for Refining Anticipated Residue Estimates for Use in Acute Probabilistic Dietary Risk Assessments; June 15, 2000	http://www.epa.gov/pesticides/trac/science/residues.pdf

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Or Contact...

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