Pesticide Risk Assessment--
Dietary Exposure

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Mandates of the FQPA

- All tolerances are safe
  - Reasonable certainty of no harm from single
    or lifetime exposure to residues from all
    sources of exposure (aggregate risk)
  - Consider multiple residues if same mode of
    toxic action
  - Consider special sensitivity of children
  - Consider effects on endocrine system
  - Consider carcinogenic potential

Mandate of FIFRA

- No registration without tolerance
  - Tolerance may be waived, but same degree
    of risk assessment scrutiny
- How is tolerance developed?
  - Pre-FQPA
    • Tolerances only consider food sources of
      exposure
  - Post-FQPA
    • Tolerances consider aggregate exposure
    • Must consider children’s health
    • Must consider cumulative exposure

Tolerance

- Legal limit of residues on food
  - Mechanism of satisfying the mandates of the
    Federal Food Drug and Cosmetic Act
    (FFDCA), which is risk oriented, and Federal
    Insecticide, Fungicide, and Rodenticide Act,
    which is benefits oriented
  - NOT a safety standard
- Expression of pesticide residues on food
  - ppm
  - mg/kg
  - µg/g

FQPA Mandate

- FQPA amendments made pesticide law
  risk oriented;
  - i.e., tolerances must be safe;
  - No consideration of benefits of pesticide use
    with several exceptions;
    • Applies to consumers only;
    • Benefits can be considered for ecological risk and
      worker risk
    • If compound is non-threshold, i.e., EPA deems it
      is carcinogenic, benefits may be considered if
      pesticide found necessary to ensure safe food
      supply and alternatives not available

How Tolerance is Developed

- Manufacturer proposes tolerance
  - Based on field studies of residues on
    commodity in major growing regions parts of
    the country
    • Tolerance always a little higher than the highest
      residues to hedge bets against exceeding it
- EPA validates tolerance
  - Risk assessment
  - TMRC (Total Maximum Residue Contribution)
    analysis
Risk Assessment

- Hazard Identification
- Dose-Response Characterization
- Exposure Assessment
- Risk Characterization

TMRC

- Tolerances are residues
- Toxicological endpoints are doses relative to an effect and body weight
- The sum of all exposures to residues at the tolerance level cannot exceed the Reference Dose, the “safe” level by policy design
  - Pre-FQPA: considered food residues only
  - Post-FQPA: tolerance would have to account for aggregate exposures

The Risk Cup Metaphor

- “Old” Risk Cup
- FQPA Risk Cup
- FQPA Risk Cup w/ Child Endocrine, Cancer Hazard
- Home & Lawn
- Water
- Food

Field Residue Studies

- Recommended application rates and one or two levels higher
- Harvest at the recommended or desired Pre-Harvest Interval (PHI)
- Normally samples are composited
  - But for many fresh fruits, a single unit (single serving) contributes to acute exposure

TMRC--Basic Procedure

- Applicable to new registrations
  - Screening tool when tolerances are used as the exposure residue
  - Can use field residues (higher tier or refined analysis)
  - Modify residues by % Crop Treated
- Need food consumption information
  - USDA Continuing Survey of Food Intake by Individuals
- Multiply residue tolerance by food consumption of that food to give exposure
- Sum all exposure possibilities
- Total exposure cannot exceed RID

Example

- Tolerance (old) for chlorpyrifos on apples at 1.5 ppm
- Tolerance for chlorpyrifos on wheat at 0.5 ppm
- Average male eats 100 g/day wheat and 75 g/day apples

\[
\text{Sum} = (1.5 \mu g/g \times 75 \text{ g/day}) + (0.5 \mu g/g \times 100 \text{ g/day}) = 162.5 \mu g/day \times 0.1625 \mu g/day
\]

\[
\text{Daily Exposure} = (162.5 \mu g/day) / 70 \text{ kg bw} = 2.32 \mu g/kg \text{ bw/day} = 0.000232 \text{ mg/kg}
\]
Example (con’td)
- The RfD for chlorpyrifos is 0.0003 mg/kg/day for chronic exposure
- Thus, just from the two commodities alone, the RfD is exceeded for an adult
- Note that average consumption based on the FDA Total Diet Study is only 0.000015 mg/kg/day (for an infant of 10 kg)

Modern Day Dietary Exposure Assessment
- Chronic Exposure
  - 70 year lifetime of daily exposure
  - Must meet standards of the chronic RfD
  - Use average residues
  - Use average food consumption data
- Acute Exposure
  - 24-hour time frame of exposure
  - Must meet acute RfD
  - Considers exposures at 99.9th percentile

Dietary Exposure Assessment
- DEEM (Dietary Exposure Evaluation Model)
  - Contains USDA CFSII database
    - Three-day record of consumption for about 15,000 people
    - Divided by population subgroup
    - Foods are deconvoluted
      - Pizza is tomatoes, wheat, cheese, and other vegetables as appropriate
      - French fries are potatoes, spices, and vegetable soils
- Residues
  - Tolerances (TMRC)
  - Maximum residues in field trials
  - Field residues at 95th percentile
  - Average residues from field
  - Government surveillance and dietary monitoring programs
    - FDA
    - USDA PDP
  - Industry generated market basket surveys

Real Residue Data Advantages
Wright ‘99 (DowAgro)

Acute Dietary Exposure
- Probabilistic assessment employing Monte Carlo analysis
  - The entire distribution of food consumption and food residue data are used
  - Essentially, the two distributions are multiplied together to yield a distribution of exposures
- Chronic exposure assessment is deterministic
  - Point estimates of food consumption and residues are used
### Food Consumption Matrix (kg/day)

<table>
<thead>
<tr>
<th>Food matrix</th>
<th>Person 1 Day 1</th>
<th>Person 1 Day 2</th>
<th>Person 1 Day 3</th>
<th>Person 1 Day 4</th>
<th>Person 2 Day 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>0.10</td>
<td>0.15</td>
<td>0.00</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Peach</td>
<td>0.02</td>
<td>0.10</td>
<td>0.00</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Raisins</td>
<td>0.03</td>
<td>0.05</td>
<td>0.01</td>
<td>0.00</td>
<td></td>
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<tr>
<td>Corn flakes</td>
<td>0.00</td>
<td>0.75</td>
<td>0.04</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Pizza</td>
<td>0.06</td>
<td>0.00</td>
<td>0.05</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Cookies</td>
<td>0.04</td>
<td>0.06</td>
<td>0.04</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Granola Bar</td>
<td>0.02</td>
<td>0.03</td>
<td>0.06</td>
<td>0.02</td>
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</tr>
<tr>
<td>Hot Dog</td>
<td>0.08</td>
<td>0.08</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>French Fries</td>
<td>0.06</td>
<td>0.04</td>
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<tr>
<td>Milk</td>
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<td>0.10</td>
<td>0.03</td>
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### Residue Data Matrix (mg/kg)

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<tbody>
<tr>
<td>Apple</td>
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<td>0.05</td>
<td>0.02</td>
<td>0.00</td>
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### Monte Carlo Technique

- The Monte Carlo program randomly selects a food consumption value for each type of food and matches it to a randomly selected residue value for that food
  - The food consumption and residue value are multiplied together to yield the exposure
- For every food consumption and residue selection, the process is repeated hundreds or thousands of time to obtain a stable distribution of exposures

### Probabilistic Exposure Assessment

- All exposures are summed together to obtain an overall dietary exposure
- All the exposures are ranked by percentile to find the 99.9th percentile of exposure
  - The exposure level greater than 99.9% of all other exposures
  - Or, the exposure level only exceeded by 0.1% of the population
Estimated Exposure to Chlorpyrifos in Strawberries Using a Monte Carlo Analysis (1-6 year old)

<table>
<thead>
<tr>
<th>Toxicity Parameter</th>
<th>mg/kg/day</th>
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<tbody>
<tr>
<td>Acute Oral LD50</td>
<td>4.5</td>
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<tr>
<td>Acute Dermal LD50</td>
<td>2000 Rabbit 200 Rat</td>
</tr>
<tr>
<td>Acute NOEL</td>
<td>0.3</td>
</tr>
<tr>
<td>Chronic NOEL</td>
<td>0.149</td>
</tr>
</tbody>
</table>

Acknowledgments of Estimation of Exposure to Chlorpyrifos in Strawberries

Chaisson et al. 1999