Modeling Longer-term Longitudinal Pesticide Exposures to Workers: Seasonal and Lifetime Exposures

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Presented at
The Society for Risk Analysis Annual Meeting
December, 2003
Topics

• Findings of the recent ILSI RSI workshop on Probabilistic Methods to Assess Worker Exposure to Agricultural Pesticides.
• Recommendations for the collection of data
• Example of longitudinal analysis using payroll data
What is Longitudinal Exposure?

- Exposure that occurs to the same worker over multiple consecutive days
- Also called intra individual variability
- Tracking of doses received on each individual day and averaging the daily doses to determine subchronic and chronic doses
- Must rely on exposure modeling
Findings of the ILSI Workshop

• General conclusion
  – Current data collection (CAL PUR and BEAD) do not support longitudinal
  – We need to do more to quantify inter- and intra-individual variability in general
  – Need to bring time dependencies into the models for proper understanding of
    • Toxicity data
    • Absorption, metabolism, and elimination

• Additional efforts will be required to achieve trustworthy modeling results
Longitudinal Exposures and Toxicity

- Typically a subchronic health benchmark is applied to a one day exposure
- No evaluation of variation in chronic exposure and the implication for longer term endpoints
- Failure to go beyond one day will prevent the proper consideration of the role of duration in characterizing risks
Understanding Temporal Processes Requires Longitudinal Modeling

- Dermal absorption may extend beyond one day
- Accumulation of pesticide and pesticide metabolites in workers
- Duration of processes associated with a health endpoint
  - Time interval to cellular damage
  - Time interval to observed effect
  - Time to recovery
Tailoring an Exposure Assessment to a Health Endpoint Duration

• It is relatively easy to tailor the duration of a longitudinal exposure assessment to the duration of the animal study
• Modeling each day as a separate event and using techniques such as rolling averages allows:
  – Matching the duration of the animal study
  – Demonstrating the sensitivity of the risk characterization to a range of durations
Two Sources of Data on Longitudinal Exposures

• Biomonitoring data on workers
  – Can provide a direct measure of longitudinal exposure for pesticides with persistent metabolites
  – Can be used to calibrate models and independently evaluate model predications

• Data collected for other purposes such as financial or insurance
Ongoing and Future Data Collection Efforts

- Existing data collection efforts could support longitudinal exposure assessments
  - It’s critical to collect data at the individual level rather then at the farm or county level
  - Collection of data on the characteristics of the worker and the event
- Determination of the events that trigger the exposure event
- Specialized studies:
  - Investigate the stability of exposure related behaviors in workers (the dirty worker hypothesis)
  - Studies of specific populations (German worker study)
Illustration of Longitudinal Modeling of Pesticide Exposures in Workers

- Data collected for 47 workers at a pesticide application company (soil fumigation)
- Soil fumigation performed year round
- Data consists of:
  - Acres treated in a given month for each of 47 workers over a 12-month period
  - Variation in air concentrations associated with the tasks that make up the standard workday, and
  - Typical duration for the tasks during a work day.
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Longitudinal Exposure in Soil Fumigators

- Using these data, the number of days worked per month per worker can be estimated
Figure 1. Days Worked Each Month by Each Worker
Longitudinal Exposure in Soil Fumigators

• Using these data an estimate of the number of days worked per month per worker

• Using the “day per month” data a Monte Carlo model of each workers’ longitudinal exposures over a one year period is prepared.
  – Probability of working on a given day is based on worker’s days worked per month
  – Each day modeled independently
  – Air concentrations sampled independently
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- Exposure is expressed as average air concentration over 24 hours
- Data on individual days averaged using a rolling average approach
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  - Probability of working on a given day is based on worker’s days worked per month
  - Each day modeled independently
  - Air concentrations sampled independently
- Exposure is expressed as average air concentration over 24 hours
- Data on individual days averaged using a rolling average approach
- Distributions of 24-hour TWA air concentrations were prepared for 1-, 7-, 30-, 90- and 365-day averaging periods
Figure 2. Cumulative Distribution of Average Daily Exposure

- 1- DAY
- 7- DAY
- 30- DAY
- 90- DAY
- 365- DAY

Cumulative Fraction of Values

ppb

Cumulative Fraction of Values

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Results

• The dose for the median exposed individual ranged from
  – 0.9 ppb for 1-day measurements to
  – 0.01 ppb for 365-day averages.

• The dose at the 95\textsuperscript{th} percentile ranged from
  – 0.2 ppb for 1-day measurements to
  – 0.03 ppb for 365-day averages
Summary

- Modeling longitudinal exposure will improve the risk assessment process.
- The collection of different types of data will be required to support such assessments.
- Modeling will play a large role in the process.