Presentation entitled "Modeling Children's Exposure to Pesticides: Issues and Challenges" by Dr. Halûk Özkaynak

Modeling Children's Exposure to Pesticides: Issues and Challenges

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RTP, NC

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Human Exposure Source-to-Dose Modeling

Major Components

Source-Concentration Relationships | Personal & Population Exposures | Exposure-Dose Relationships | Model Evaluation & Uncertainty | Modeling Framework

Contributors

Program Offices

OPP, OPPT, OAQPS
OAR, OSWER, OW

States/Regions

EPA/ORD

NERL
NRMRL
NHEERL
NCEA
NCCT

Universities & Children's Centers

Other Private & Public Groups

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Exposure Modeling Steps

- **Evaluate potential exposure scenarios to single or multiple pesticides (what, where, when, why and by whom)**
- **Select and apply appropriate aggregate or cumulative exposure/dose model (s) for the scenario (s) of interest**
- **Evaluate conditions (subjects, locations, sources, pathways) that result in typical and high-end exposures to pesticides of concern**
- **Determine the intensity, duration, frequency, route and timing of exposures**
- **Evaluate the health significance of modeled exposures and dose**

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Elements of Modeling Analysis

- Identify population groups/ages and microenvironments of concern
- Estimate exposure factors
  - Time-activity data by age, gender, region, etc.
  - Contact/transfer/uptake/PBPK rates or parameters
- Estimate physical factors
  - Source use and emissions
  - Penetration, Infiltration, re-suspension, track-in, volatilization, decay and migration rates
- Application of data and algorithms using a selected modeling structure

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Exposure Model Types

	Mechanistic	Empirical
Deterministic	Mathematical constructs of physical/chemical processes that predict fixed outputs for a fixed set of inputs	Statistical models based on measured input and output values (e.g., regression models that relate air concentrations and blood levels of a chemical or ambient pollutant concentrations with personal exposures)
Stochastic	Mathematical constructs of physical/chemical processes that predict the range and probability density distribution of an exposure model outcome (e.g., predicted distribution of personal exposures within a study population)	Regression-based models, where model variables and coefficients are represented by probability distributions, representing variability and/or uncertainty in the model inputs and parameters.

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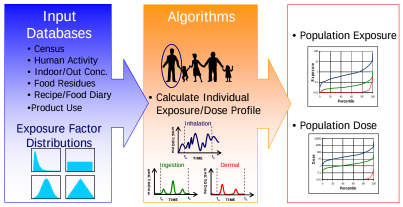
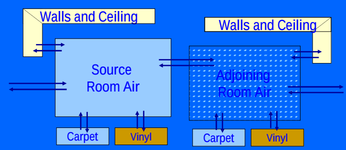
Typical Microenvironments

- **Indoors**
  - **Home, office, school, day care centers, public buildings, etc.**
- **Outdoors**
  - **residential lawn/yard, near home, school, day care centers, recreation grounds, etc.**
- **In-Vehicle**
  - **car, bus, subway/train, etc.**

SHEDS Model Structure



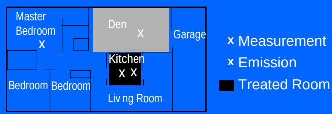
Fugacity Model Compartments



Chlorpyrifos Case Study

EPA applied a crack and crevice application to their test house

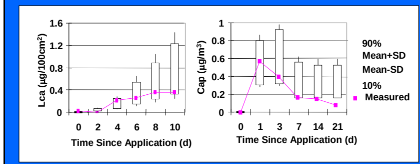
We considered a treated and an untreated region



Uncertainty Analysis

250 Monte Carlo Simulations carried from Crystal Ball in Excel to Matlab

Appears that we are overestimating source



Pyrethroids of Concern

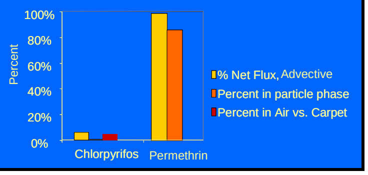
Allethrin	Ortho Flying Insect Killer Hot Shot Flying Insect Killer
Cyfluthrin	Raid Ant and Roach
Cypermethrin	Raid Ant and Roach Fogger
Esfenvalerate	Ortho Roach, Ant, and Spider Killer
Permethrin	Raid Fumigator; Ant Killer Hot Shot Flying Insect; Fogger Spectracide BugStop
Tralomethrin	Raid Wasp, Hot Shot Insect, Spectracide BugStop Fogger

Note Chlorpyrifos and diazinon (OP pesticides) were phased out of indoor uses after 2000

Indoor Fugacity Model: Chlorpyrifos vs. Permethrin

After 5 days, permethrin concentration in air is much less than chlorpyrifos concentration

For permethrin, dust movement plays an important role in transport



Number of applications for 16 pyrethroids in 1217 household with 12 month REJV survey data

chem	Total No. of Applications	Number of Homes applied	Average number of applications/home/year
allethrin	2741	437	6.3
bifenthrin	563	99	5.7
cyfluthrin	219	46	4.8
cyhalothrin	7	4	1.8
cypermethrin	1319	163	8.1
deltamethrin	131	22	6.0
esvenvalerate	91	25	3.6
fenvalerate	130	37	3.5
permethrin	3461	518	6.7
phenothrin	1805	293	6.2
piperonyl_butoxide	2759	461	6.0
prallethrin	59	13	4.5
pyrethrin_I_II	2447	472	5.2
resmethrin	355	106	3.3
tetramethrin	2141	342	6.3
tralomethrin	1356	279	4.9

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Table 0: Jacksonville Study: Detection Frequencies in the 9 homes

Outdoor Air	% homes (n=9)	Indoor Air	% homes (n=9)	Surface wipes	% wipe (n=46)
total Permethrin	100.0%	total Permethrin	88.9%	Total_Permethrin	91%
total Cypermethrin	22.2%	total Tetramethrin	55.6%	Total_Cypermethrin	80%
total Tetramethrin	22.2%	Pyrethrin I	44.4%	Esfenvalerate	30%
total Allethrin	0.0%	total Allethrin	33.3%	Total_Allethrin	22%
Bifenthrin	0.0%	total Cypermethrin	22.2%	Bifenthrin	20%
total Cyfluthrin	0.0%	Sumithrin	22.2%	Total_Cyfluthrin	20%
lamda-Cyhalothrin	0.0%	Bifenthrin	11.1%	Delta_Tralomethrin	15%
Delta/Tralomethrin	0.0%	total Cyfluthrin	11.1%	Total_Tetramethrin	13%
Esfenvalerate	0.0%	Esfenvalerate	11.1%	lamda_Cyhalothrin	9%
Pyrethrin I	0.0%	Pyrethrin II	11.1%	Sumithrin	4%
Pyrethrin II	0.0%	lamda-Cyhalothrin	0.0%	Pyrethrin_II	2%
Resmethrin	0	Delta/Tralomethrin	0.0%	Pyrethrin_I	0%
Sumithrin	0.0%	Resmethrin	0	Resmethrin	0%

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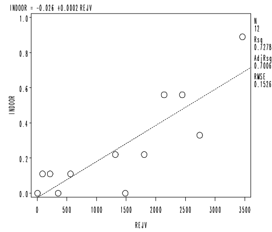
Fig 2. REVJ-2 (total number of applications) *vs.* Indoor Air detection frequency (R2=0.73, p<0.01, n=12)



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Major food items contributing to predicted permethrin intake

Food items	Average food consumption per day (g)	Average permethrin intake per day (ug)
Lettuce, raw	8.05	0.73
Spinach, cooked, from canned, fat not added in cooking	0.24	0.32
Apple juice	13.60	0.20
Tomatoes, raw	8.54	0.19
Spinach, cooked, from fresh, fat not added in cooking	0.15	0.19
Apple juice, with added vitamin C	11.11	0.17
Spinach, raw	0.13	0.16
Spinach, cooked, from frozen, fat not added in cooking	0.21	0.14
Cucumber, raw	2.25	0.09
Apple, raw	14.68	0.08
Spinach, cooked, NS as to form, fat not added in cooking	0.03	0.04
Celery, raw	0.58	0.03
Pear, raw	2.14	0.03
Carrots, raw	2.41	0.03
Spinach, cooked, from canned, fat added in cooking	0.04	0.03

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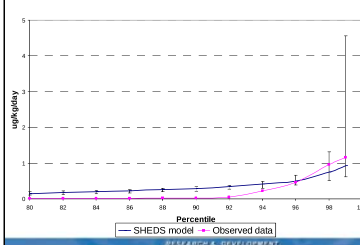
Comparison of Predicted vs. Observed Dietary Permethrin Intake: SHEDS results vs. CTEPP, OH



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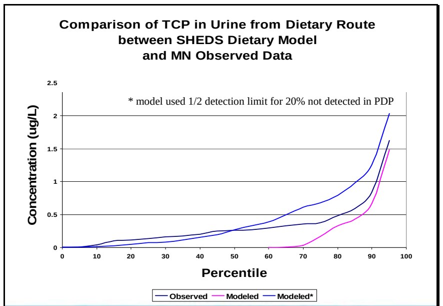


Opportunities for Reducing Model and Input Uncertainty*

- Pesticide usage information
  - *What, where, when, how often*
- Human activity patterns
  - *microactivities (e.g.,videography info) for infants and toddlers*
  - *transfer coefficients for body parts other than hands*
  - proximities of subjects to applied surfaces
  - longitudinal time-location-activity and food consumption diaries

*Note: text in bold italics indicate special value of field data for model refinement

Opportunities for Reducing Model and Input Uncertainty (Cont.)*

- Pesticide concentrations and residues
  - *pesticide concentrations in non-home environments*
  - *pesticide concentrations due to track-in and pets*
  - *phase changes of pesticides over time*
  - *distribution of pesticides indoors after an application*
  - measure both concentrations rather and mass loading at skin surface
  - residues by: different types of surfaces, post-application times, proximities to application
  - *pesticide residues and their transformation products in environmental samples and in food and beverages*
    - *Need reliable approaches for dealing with non-detects in residue data*

*Note: text in bold italics indicate special value of field data for model refinement

Opportunities for Reducing Model and Input Uncertainty (Cont'd)*

- Exposure Factors
  - *TC vs. TE and differences between studies*
    - *Pooled analysis of all available data to fit more robust variability distributions to TC and TE estimates*
    - *Analyze statistically study-to-study differences to fit uncertainty distributions to TC and TE values*
  - *transfer efficiency, dermal absorption as a function of pesticide residue type/composition*
  - surface area contact fraction
  - factors affecting surface-to-skin (e.g., # contacts) and skin-to-surface residue transfer (off-loading) efficiency
  - saliva and water removal efficiency as a function of contact duration

*Note: text in bold italics indicate special value of field data for model refinement

Opportunities for Reducing Model and Input Uncertainty (Cont'd)*

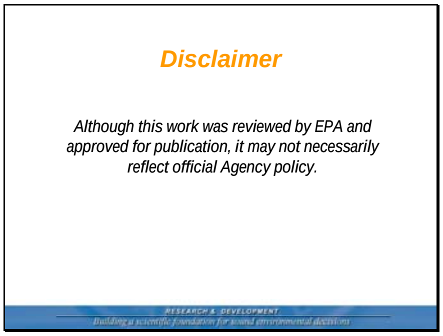
- Refined Concentration and Exposure Algorithms
  - develop, test and implement indoor fugacity based source-concentrations models
  - incorporate environmental metabolite ingestion pathway in models
  - *more accurate dermal exposure models (e.g., clothing, evaporation, deposition, skin-to-surface transfer)*
  - methods to extrapolate cross-sectional to longitudinal estimates
  - *co-occurrence algorithms based on multiple pesticide use (field study data and IREJV survey)*
  - new techniques for sensitivity analysis (e.g., SOBOL method)
  - develop and incorporate more complex and physiologically based PK/PBPK modules

*Note: text in bold italics indicate special value of field data for model refinement

Opportunities for Reducing Model and Input Uncertainty (Cont'd)*

- Model Evaluation
  - *Compare modeled dose predictions against biomarker measurements (e.g., urine, blood, hair, saliva, nail, etc.)*
  - *Compare hand/body loading estimates to field measurements*
  - *Compare inhalation exposure estimates to personal air measurements*
  - *Individually evaluate each model component (inhalation, ingestion, dermal)*
  - Contrast results to alternative model predictions

*Note: text in bold italics indicate special value of field data for model refinement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