The EPA's Stochastic Human Exposure and Dose Simulation (SHEDS) - Dietary Model

USDA Office of Risk Assessment and Cost-Benefit Analysis
ORACBA Risk Forum

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1:00-2:30 pm

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- Alion Science and Technology, Inc. contractors

Presentation Outline

- Background (goals, features, applications)
- SHEDS-Dietary module overview (inputs, methodology, outputs)
- SHEDS-Dietary results
- Q&A
- SHEDS-Dietary demo

What is SHEDS-Dietary?

- SHEDS-Dietary is a probabilistic, population-based dietary exposure assessment model that simulates individual exposures to chemicals in food and drinking water over different time periods (e.g., daily, yearly)
  - can produce population percentiles of dietary exposure by source and age-gender group; quantify contribution to total exposure by food, commodity, and chemical; and be used for eating occasion, sensitivity, uncertainty analyses
  - can use either USDA's CSFII (1994-96, 1998) or NHANES/WWEIA dietary consumption data (1999-2006), along with EPA/USDA recipe translation files (Food Commodity Intake Database), and available food and water conc. data
- *SHEDS-Dietary is a module (along with residential) of NERL's more comprehensive human exposure model, SHEDS-Multimedia, which can simulate aggregate or cumulative exposures over time via multiple routes of exposure (dietary & non-dietary) for multiple types of chemicals & scenarios*

Background

- Since the passage of FQPA, the EPA has primarily conducted three types of dietary risk assessments: (i) acute, (ii) chronic, and (iii) cancer
- For higher-tier acute dietary risk assessments, Monte Carlo simulations are performed by OPP to estimate total daily dietary exposure to a pesticide
- SHEDS-Dietary and SHEDS-Multimedia represent an advancement in science over existing models, but peer review is necessary for broad regulatory applications
  - Conceptual review of model by August 2007 FIFRA Scientific Advisory Panel (SAP)
  - Upcoming July 2010 FIFRA SAP meeting will formally review these models with a permethrin case study

Background (cont'd)

- SHEDS modeling research program focusing on enhancing the science of probabilistic dietary exposure assessments
  - provides additional analyses for pesticides
  - quantifies uncertainty in acute dietary risk assessments (QUA)
  - future: enhance chronic and cumulative risk assessments

- OPP collaboration on model development has considered criteria for regulatory use
  - peer-reviewed / transparent (algorithms)
  - publicly available (free or nominal cost)
  - consistent with EPA/OPP policy/guidelines

- SHEDS-Dietary can be applied to other chemicals as well as pesticides, and may be useful to other Program Offices and Agencies (e.g., USDA, FDA)

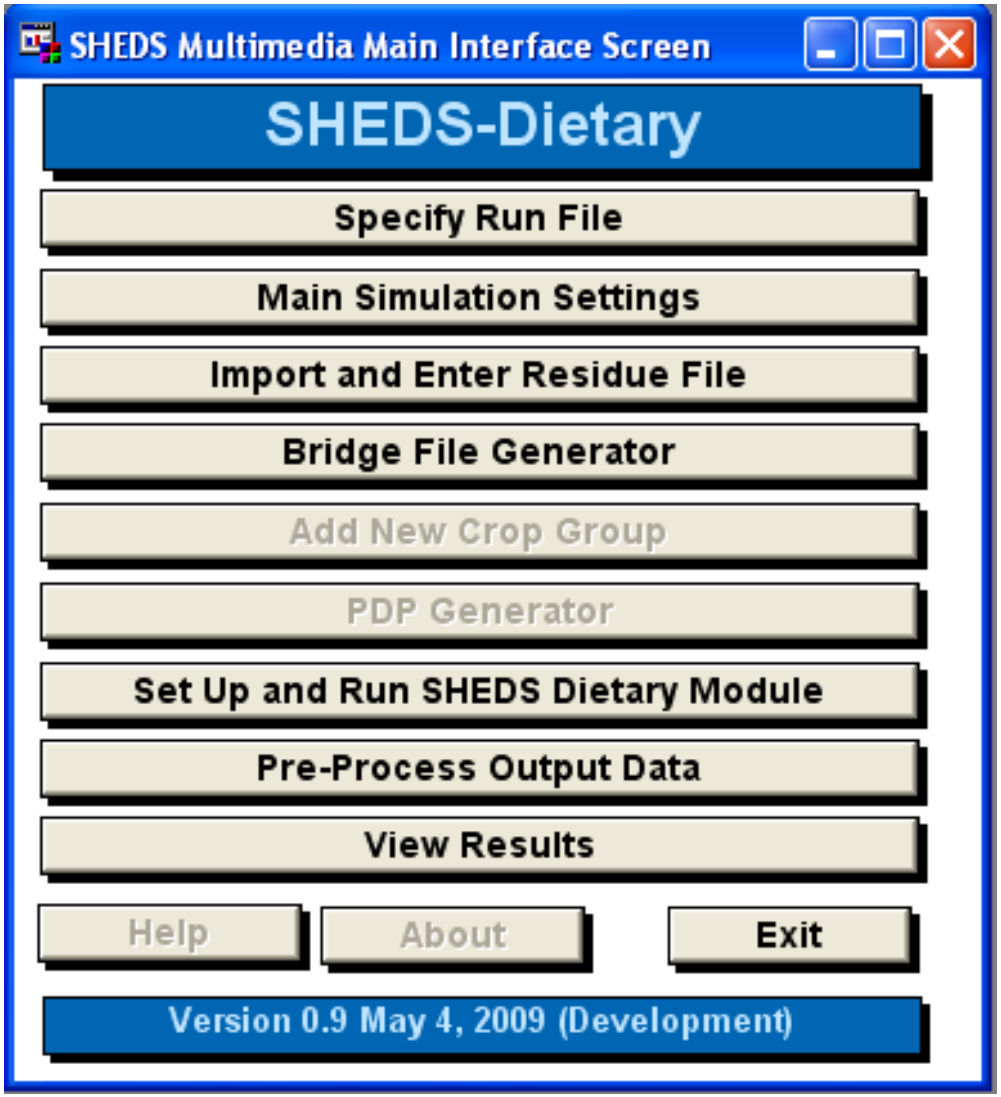
Key Features

- Develop/apply new methods for sensitivity and uncertainty analyses
- Uses CSFII (1994-1996, 1998) or NHANES/WWEIA (1999-2006) food consumption data
- Can link to PBPK models for evaluating model predictions against biomarker data
- Provides enhanced capability to conduct dietary 'Eating Occasions' analyses
  - contributions by food type, chemical, for age-gender groups
  - longitudinal and half-life analyses ("persisting effects" for OPs)
    - 3 options: Cross-Sectional or 2-diary, 8-diary, Diary Assembly

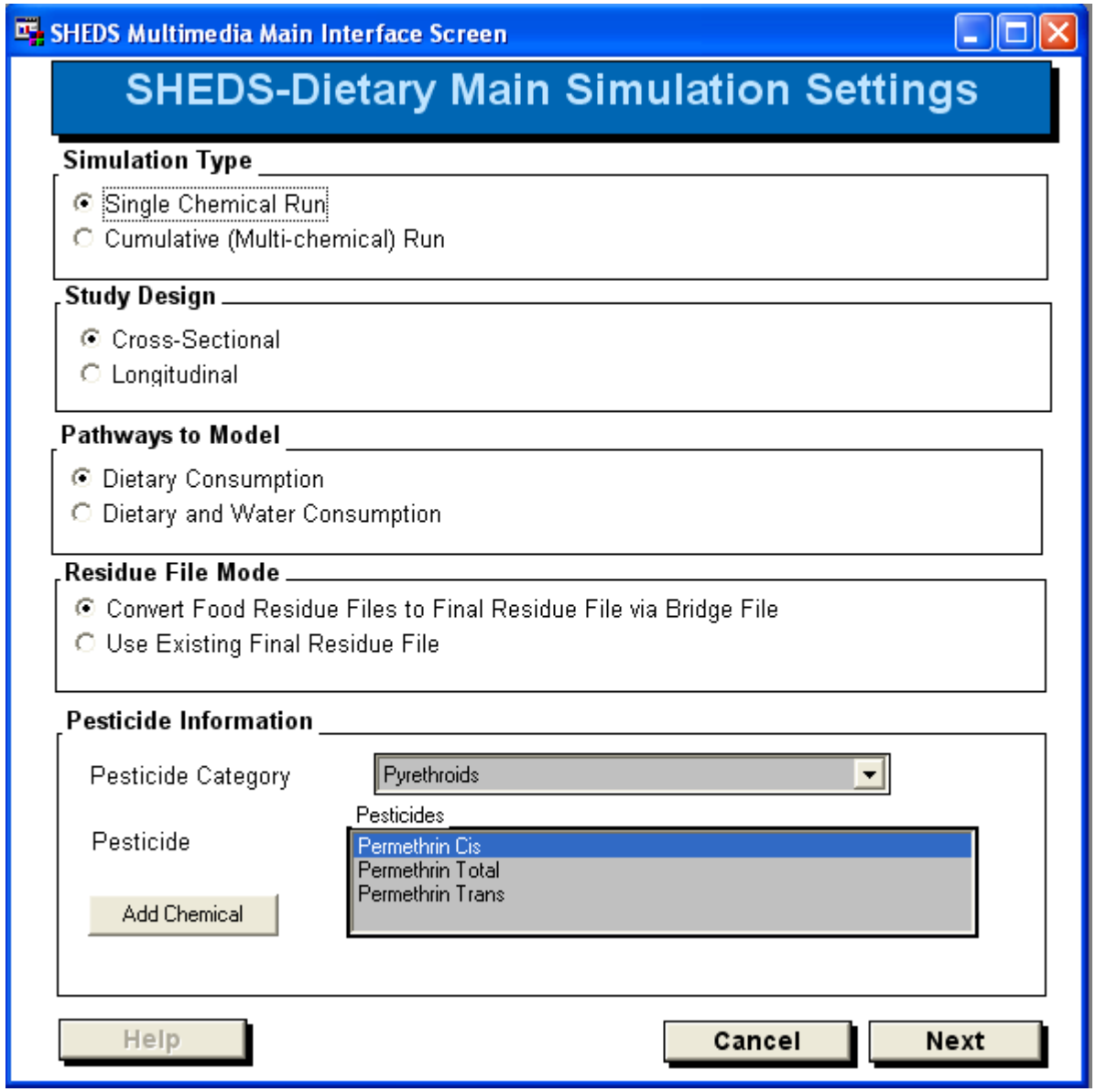
Key Features (cont'd)

- Multi-chemical ability (NMC CRA, OP CRA, next: pyrethroid CRA)
- SAS Platform (requires SAS license)
  - facilitates viewing, querying, analyzing, updating underlying databases (e.g., consumption, recipes, residues)
  - facilitates development of alternate exposure modeling assumptions (e.g., stochastic assumption on residues, by eating occasion or day)
  - provides flexibility to develop alternate contribution analyses
  - facilitates linkage with PBPK models
- Publicly available and transparent

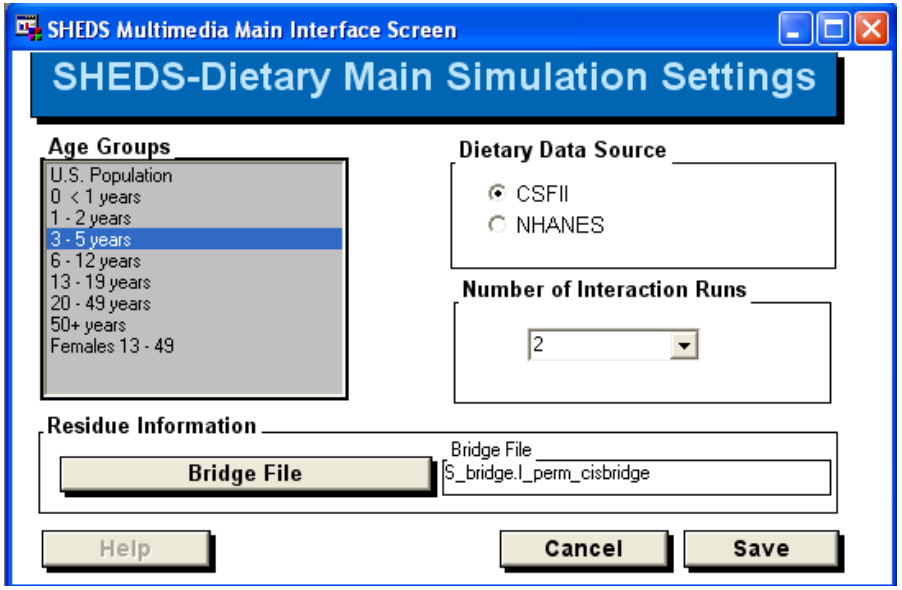
Main Dietary Interface Screen



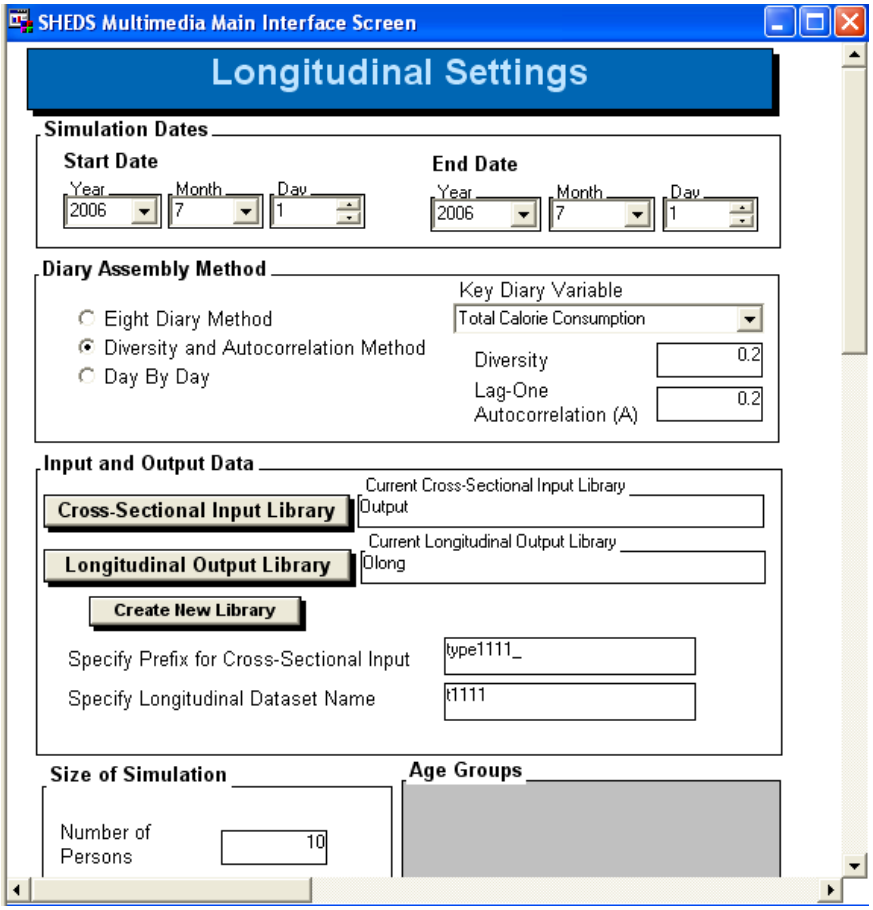
Main Simulation Settings: Screen 1



Main Simulation Settings: Screen 2



Single chemical run, cross-sectional, converting using Bridge file



Single chemical run, longitudinal

Check Other Variables

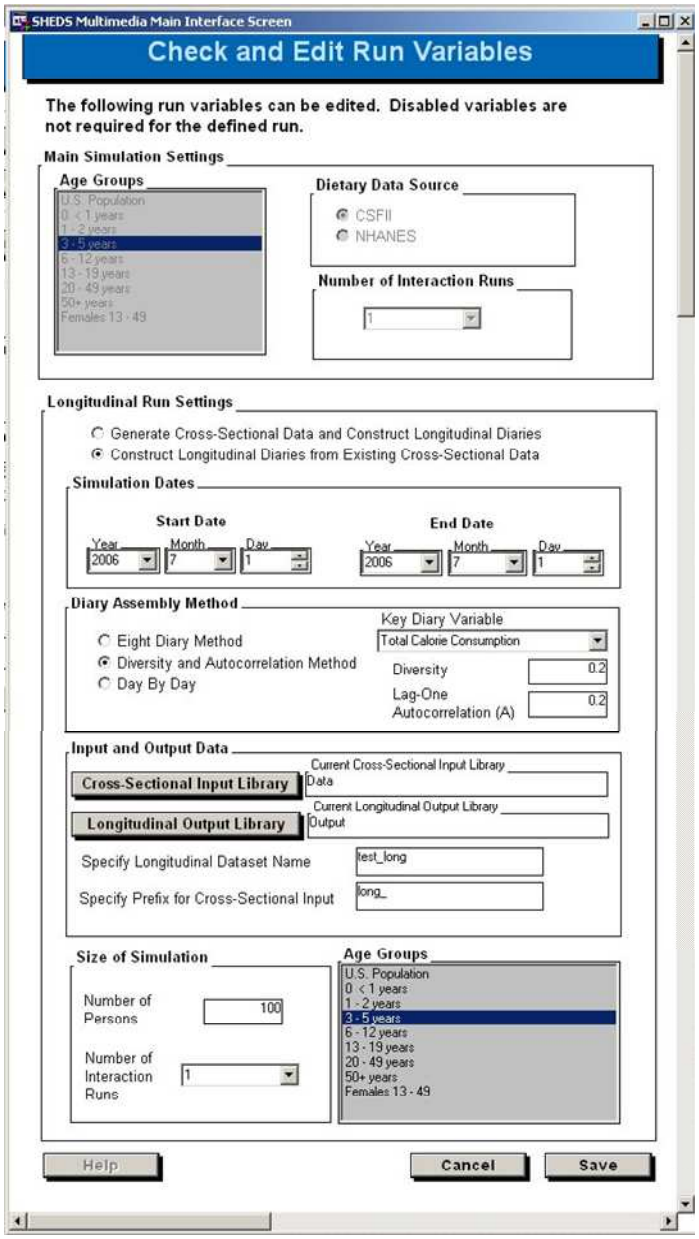
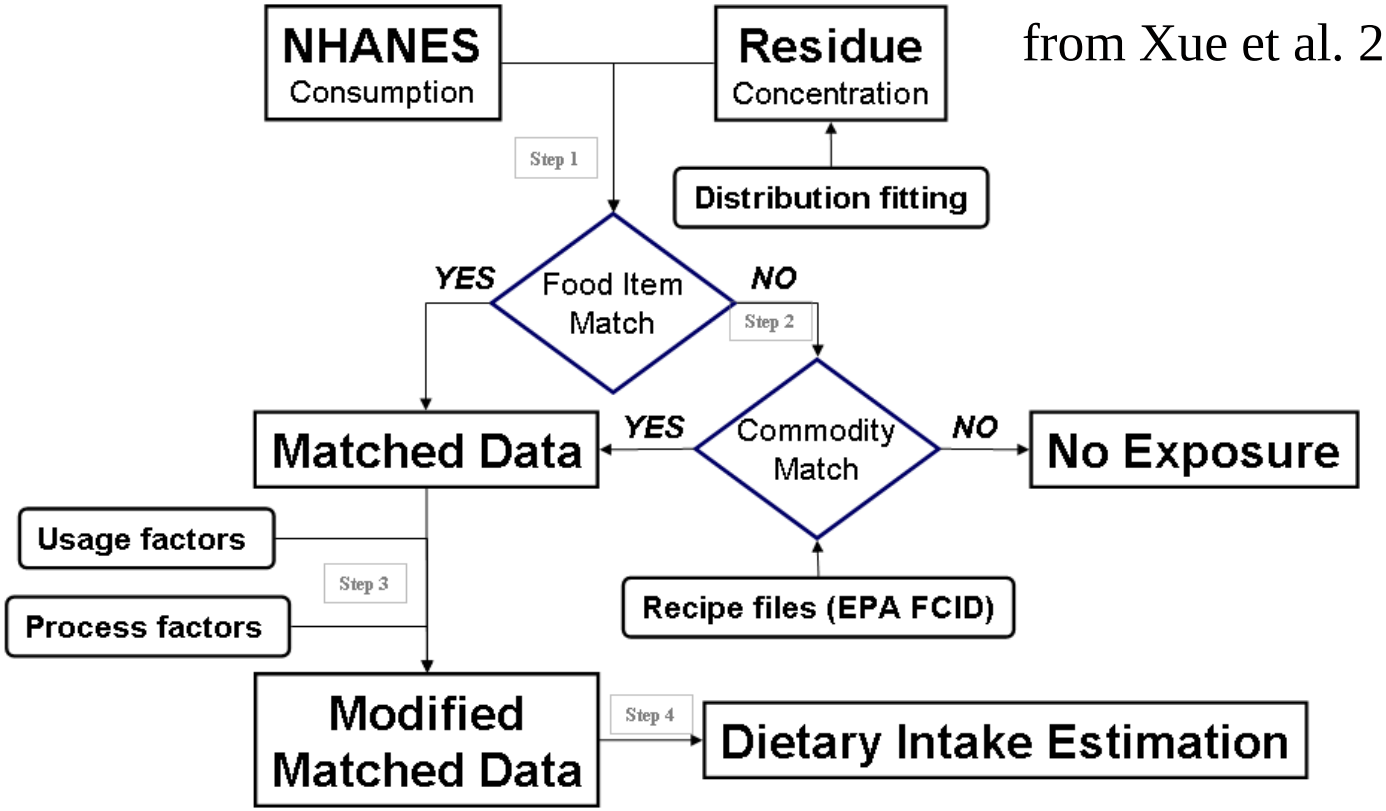


Figure 1 SHEDS Dietary Module Overview



from Xue et al. 2010, *EHP*

NHANES Consumption: Food consumption data from NHANES/WWEIA
Residue Concentration: Residue concentration data by food item or commodity from TDS
Distribution fitting: fittings of residue data into suitable statistical distribution
Food Item: food products people in the survey consumed such pizza, raw apple
Commodity: raw agriculture commodity (RAC)
Usage factors: Pesticide usage percentages by RAC from USDA.
Process factors: concentration or dilution factors due to processes of food from RAC into food products.
Recipe files (EPA FCID): data base for percents of various RACs for the food products.

SHEDS-Dietary Model Overview (cont'd)

- A person's exposure for each commodity is calculated by multiplying total daily consumption with the corresponding residue:

$$\text{Exposure} = \sum \{\text{amount of food item consumed [grams]} \times \text{concentration in the food item[ppm]}\}$$

- Summation of exposures for each commodity over all an individual's eating occasions within a day yields the individual's total daily exposure.

- This process is repeated for each food consumption diary (simulated person-days) via Monte Carlo sampling to generate population estimates of dietary exposure

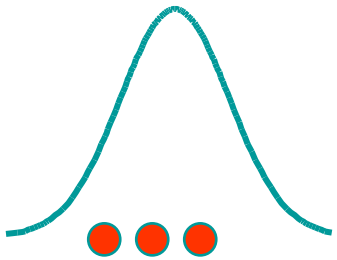
Consumption (g food/kg bw) **x Residue** (mg pesticide/gram food) **=**

Exposure (mg pesticide/kg bw)

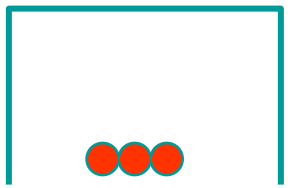
MONTE CARLO SIMULATION

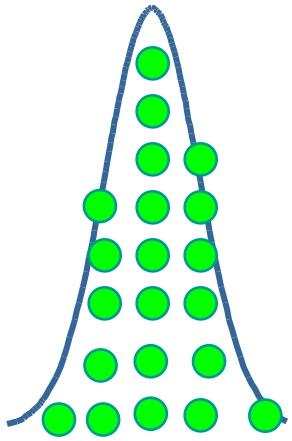
each MC trial is an iteration => simulated exposure event
a series of trials => simulated distribution of exposures

Normal



Uniform





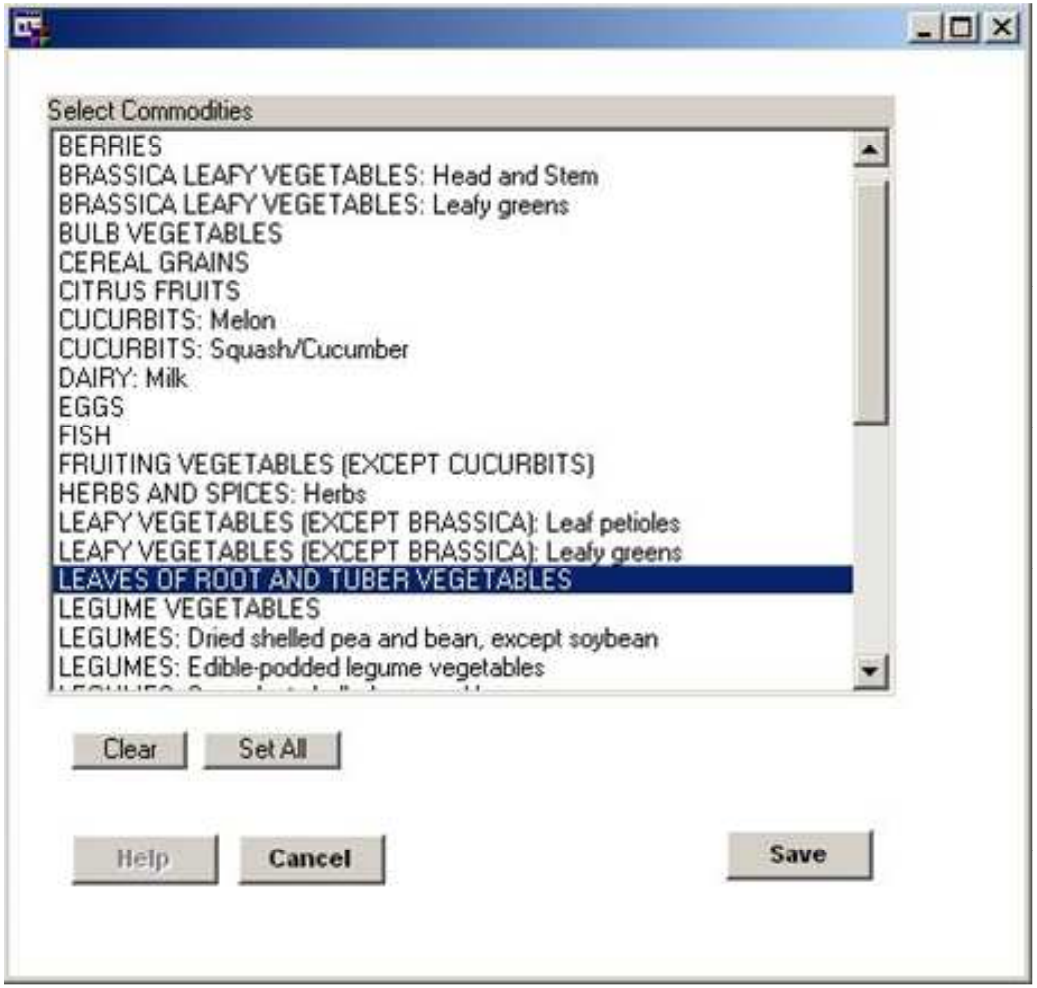
Exposure Outcomes

Exposure distribution

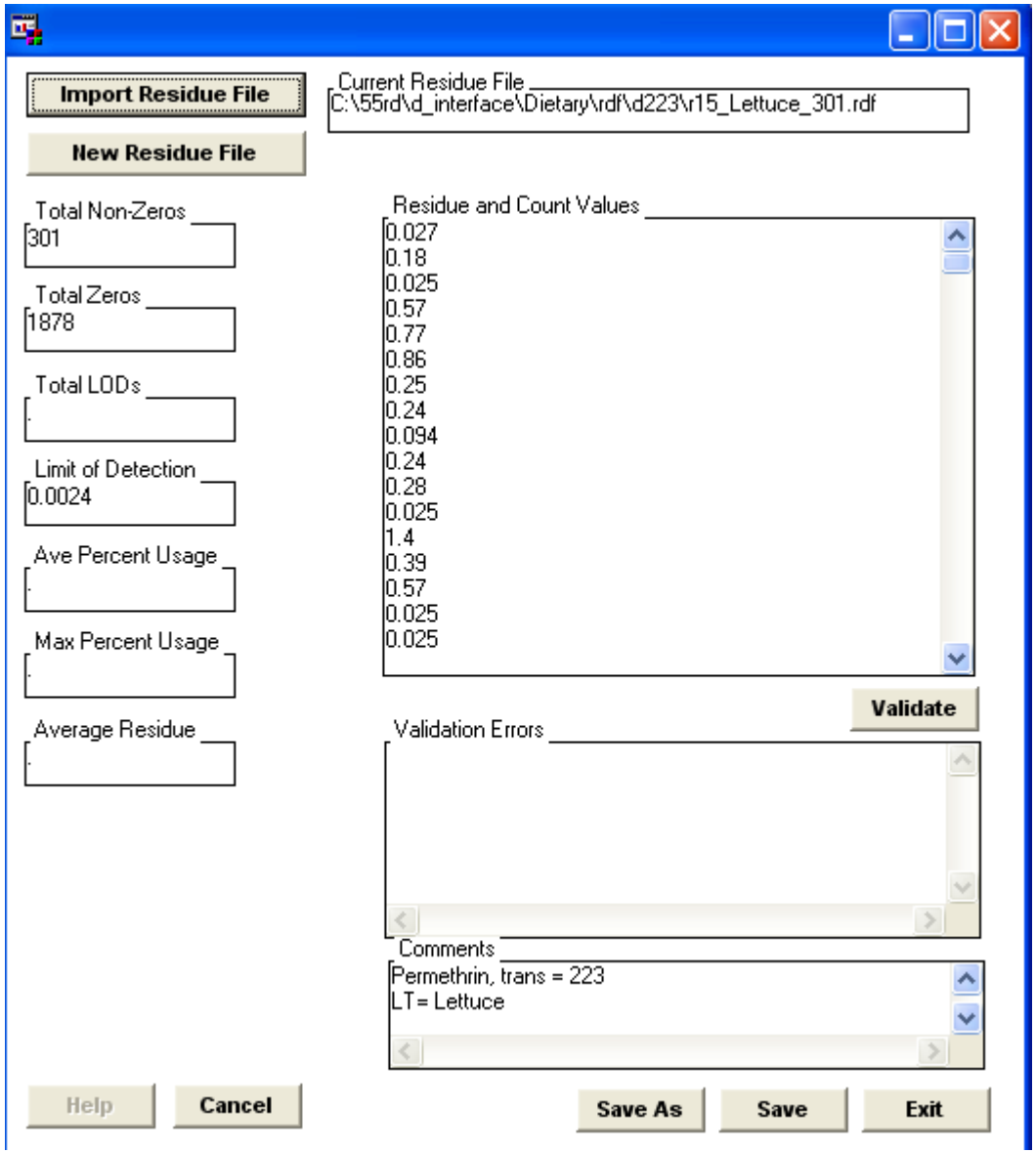
SHEDS-Dietary Inputs

- Food and Indirect Water Consumption
  - USDA CSFII 1994-96, 1998 *OR*
  - NHANES/WWEIA 1999-2006
- Direct Water Consumption Data
  - SHEDS currently distributes total direct water consumption in 6 equal amounts at 6 fixed times (6 am, 9, 12, 3, 6, 9)
- Food Residues & Drinking Water Concentrations
  - Point estimate or empirical distributions
  - Field Trials, USDA/PDP, FDA/TDS; PRZM-EXAMS, etc.

Select Crop Groups



Import and Enter Residue File



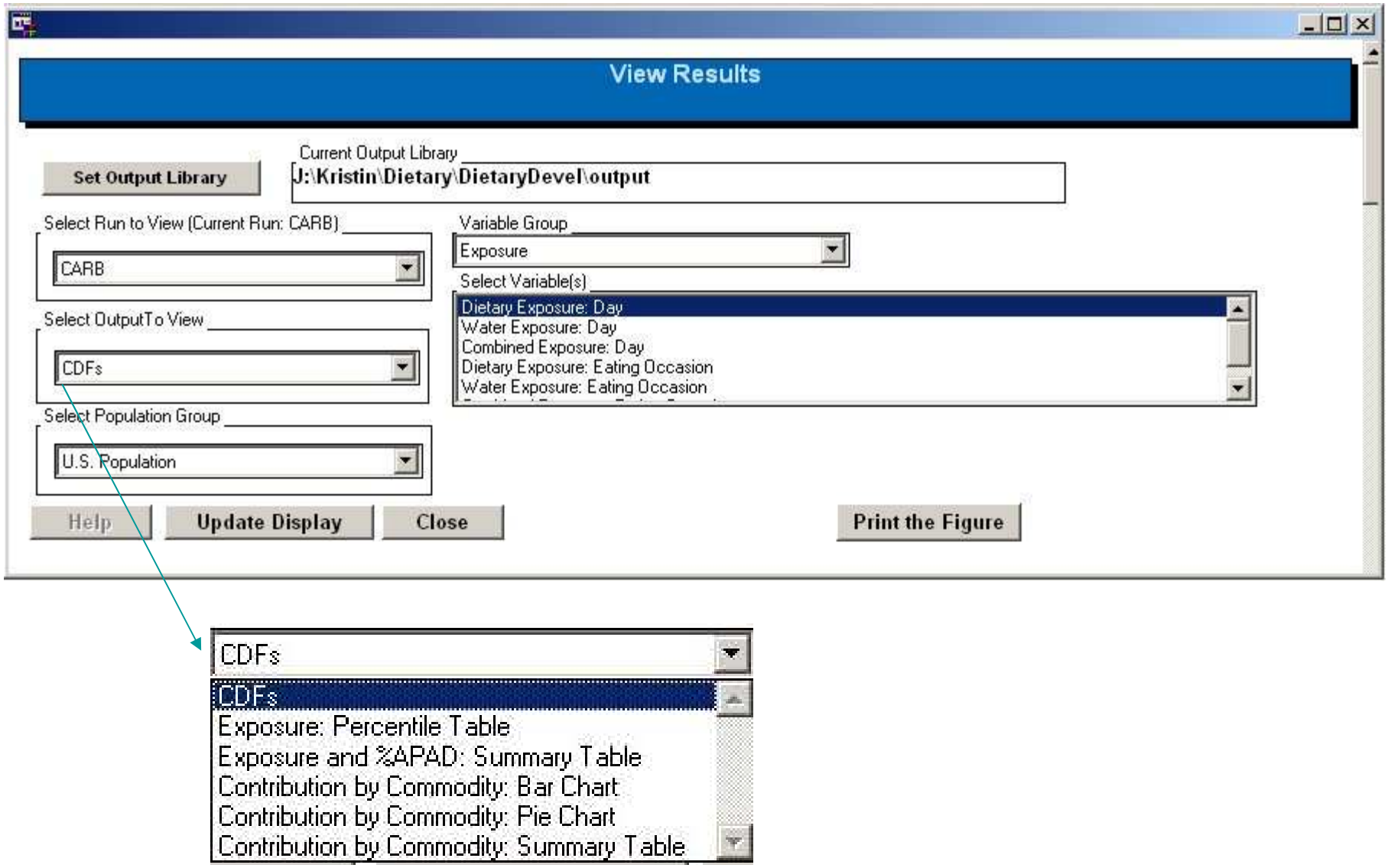
SHEDS-Dietary Inputs (cont'd)

- Recipe Files
  - EPA Food Consumption Intake Database (FCID) contain recipes for each food item recorded in the CSFII diaries
  - FCID recipes convert foods into 553 raw agricultural commodities (RAC)
  - Recipes are being developed by OPP for new NHANES/WWEIA food items
- Pesticide Use (Percent of Crop Treated)
  - USDA National Agricultural Statistics Service
- Processing Factors (concentration or dilution factors due to cooking, food processing, etc.)
  - Registrant submission
  - Peer reviewed literature

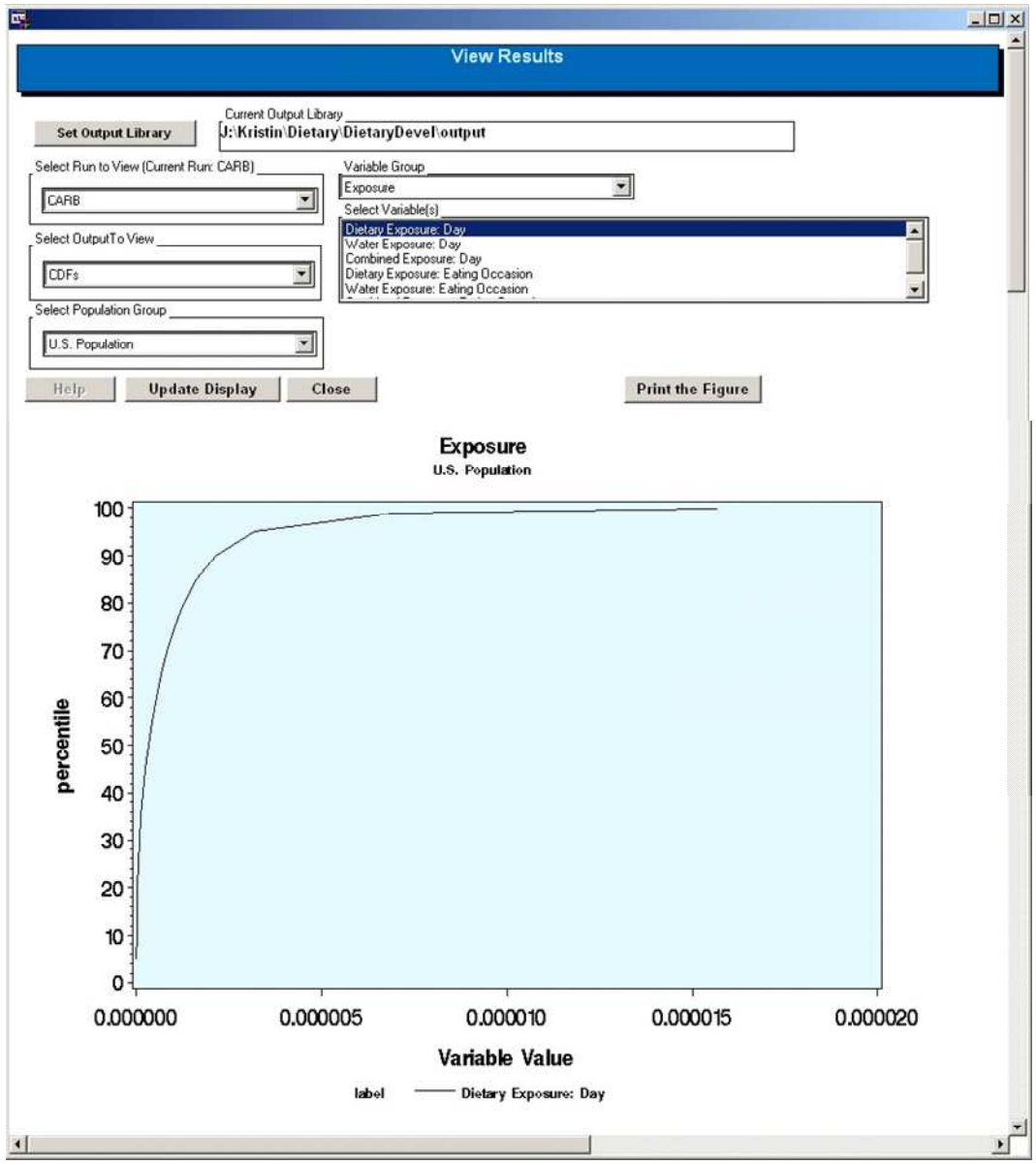
SHEDS-Dietary: Outputs/Results

- Aggregate Dietary Exposure at different percentiles, by source (food, water, food+water), age-gender group
- CDFs of dietary exposures for populations of interests
- Pie/bar charts showing contribution to total exposure in upper %iles (e.g., 99.9-100th), by food, commodity, commodity-chemical (multi-chemicals)
- Sensitivity analyses
  - NHANES/WWEIA (1999-2006) vs. CSFII (1994-1996, 1998)
  - impact on exposure of removing commodities
  - half-life analyses
  - eating occasion analyses
- Uncertainty analyses
  - assess impact of residues vs. consumption, and sample sizes
  - assess impact of number of exposure days before dose results stable

View Results



View Results: Example



View Results Example: Exposure and %aPAD Summary Table

Exposure Type	Exposure Category	Age Group	sample size	95th exposure mg/kg/day	99th exposure mg/kg/day	99.9th exposure mg/kg/day	95th %APAD mg/kg/day	99th %APAD mg/kg/day	99.9th %APAD mg/kg/day
Combined	Daily	U.S. Population	82428	3.8E-04	1.2E-03	3.5E-03	188.08	591.20	1732.73
Combined	Daily	0 < 1 years	5944	7.0E-04	2.4E-03	8.3E-03	935.06	3206.39	11021.64
Combined	Daily	1 - 2 years	8384	5.3E-04	1.9E-03	4.6E-03	711.17	2483.24	6117.40
Combined	Daily	3 - 5 years	17564	5.8E-04	1.8E-03	5.5E-03	771.49	2338.60	7385.55
Combined	Daily	6 - 12 years	8356	3.9E-04	1.3E-03	4.2E-03	518.65	1708.70	5556.37
Combined	Daily	13 - 19 years	4888	3.3E-04	1.1E-03	3.1E-03	163.26	552.84	1544.33
Combined	Daily	20 - 49 years	18708	3.5E-04	1.1E-03	3.1E-03	172.85	534.16	1548.17
Combined	Daily	50+ years	18584	3.7E-04	1.1E-03	3.1E-03	184.38	572.09	1562.46
Combined	Daily	Females 13 - 49	11752	3.6E-04	1.1E-03	3.0E-03	181.46	558.08	1520.58

View Results Example: Contribution by Commodity Summary Table

Age Group	Food Commodity	FCID_Code	Percent of Food Consumed	Percent of Pesticide Consumed
6 - 12 years	Milk, water	27022240	56.31	50.57
6 - 12 years	Banana	95000230	13.97	25.75
6 - 12 years	Potato, tuber, w/o peel	1033000	4.32	9.62
6 - 12 years	Sunflower, seed	20003640	0.48	3.31
6 - 12 years	Potato, tuber, w/peel	1032990	0.78	1.84
6 - 12 years	Potato, dry (granules/ flakes)	1032970	0.39	1.36
6 - 12 years	Corn, field, meal	15001210	4.14	1.12
6 - 12 years	Pumpkin	9023080	0.10	1.11
6 - 12 years	Sugarcane, sugar	95003620	8.71	1.07
6 - 12 years	Milk, nonfat solids	27012230	1.27	0.94
6 - 12 years	Banana, dried	95000240	0.10	0.75
6 - 12 years	Corn, field, flour	15001200	2.63	0.71
6 - 12 years	Plantain	95002830	0.34	0.61
6 - 12 years	Milk, fat	27002220	0.57	0.39
6 - 12 years	Pumpkin, seed	9023090	0.28	0.23
6 - 12 years	Corn, field, starch	15001230	0.74	0.20
6 - 12 years	Coffee, roasted bean	95001150	0.01	0.14
6 - 12 years	Rice, white	15003230	2.51	0.11
6 - 12 years	Potato, chips	1032960	1.10	0.09
6 - 12 years	Rice, flour	15003250	1.06	0.05
6 - 12 years	Coffee, instant	95001160	0.00	0.03
6 - 12 years	Rice, brown	15003240	0.11	0.00
6 - 12 years	Sugarcane, molasses	95003630	0.04	0.00
6 - 12 years	Potato, flour	1032980	0.03	0.00
6 - 12 years	Corn, field, bran	15001220	0.00	0.00
6 - 12 years	Rice, bran	15003260	0.00	0.00

SHEDS-Dietary Applications to Date

United States Environmental Protection Agency

- Aldicarb (2006)
  - development/testing of eating occasion analyses
  - allowed comparison to DEEM-based analyses
  - applied Bayer DWCS data (little difference) for direct water intake
- Carbaryl (2007)
  - explored longitudinal (multi-day) eating occasion analyses (DW-infants, 5+ hrs)
- N-Methyl Carbamate CRA (2007)
  - supported contention that not significantly overestimating risk by not accounting for recovery (food-only)
    - maximum exposure, by eating occasion, provides best case scenario for recovery
- Organophosphates CRA (2009-2011)
  - updating the 2006 OP Cumulative Risk Assessment
  - SHEDS longitudinal eating occasion analysis used to consider persisting effects (carry-over) on AChE inhibition using chemical-specific recovery (half-life) rates
  - SHEDS contribution analyses allowed assessing effects of mitigation options on the population 99.9th percentile

SHEDS-Dietary Applications to Date (cont'd)

- Arsenic (As)
  - Xue et al., 2010 *EHP* paper provides SHEDS-Dietary model evaluation
  - Inorganic As exposure from food more important than drinking water for U.S.
    - Major food contributors to iAs exposure include rice, vegetables, fruit juices/fruits
    - Major food contributor for tAS exposure is fish (contributing 60% of exposure)

- Mercury (Hg)
  - NERL/HEASD draft journal manuscript (in progress) comparing fish consumption exposures for high risk populations using NHANES/WWEIA and FDA TDS
  - for Asians, Native Americans, and Pacific Islanders, major contributors for MeHg are tuna, fresh water fish–other, seawater fish–other
  - exposure estimates for MeHg in fish can explain the high level of MeHg in blood for populations with higher fish consumption

- Permethrin: in progress to support OPP's pyrethroids CRA
  - exposure ranges and age-specific results
  - most important commodities contributing to exposure
  - sensitivity and uncertainty analyses
  - comparison of model predictions against duplicate diet data
  - linkage with residential scenarios and PBPK modeling

SHEDS-Dietary: As Application (Xue et al., "Probabilistic Modeling of Dietary Arsenic Exposure and Dose And Evaluation," *EHP* 2010)

- BACKGROUND
  - Dietary exposure from food to toxic inorganic arsenic (iAs) in the general US population has not been well studied.
- OBJECTIVES
  - This research quantifies dietary As exposure, and analyzes the major contributors to total As (tAs) and iAs.
  - Another objective was to compare model predictions to observed data.
- METHODS
  - Probabilistic exposure modeling for dietary As was conducted with the SHEDS-Dietary model, using NHANES/WWEIA consumption data and TDS residue data.
  - The dose modeling was conducted by combining the SHEDS-Dietary model with EOSHI's MENTOR-3P system.
  - Model evaluation was conducted via comparing exposure and dose modeling predictions against NHEXAS duplicate diet data and NHANES biomarker measurements, respectively, for the same individuals.

SHEDS-Dietary: As Application (Xue et al., *EHP* 2010) – cont'd

- RESULTS
  - Mean modeled tAs exposure from food is 0.38 ug/kg/day, ~14 times higher than the mean As exposures from the drinking water.
    - Fish contribute 60% of tAs exposure.
  - Mean iAs exposure from food is 0.05 ug/kg/day (1.96 ug/day), ~2 times higher than the mean iAs exposures from the drinking water.
    - Major food contributors to iAs exposure were vegetables, fruit juices, and fruits; rice; beer and wine; and flour, corn, and wheat.
  - SHEDS modeled exposure and dose estimates matched well with the duplicate diet data and measured As biomarkers.
  - Approximately 10% of tAs exposure from foods is the toxic iAs form.

- CONCLUSIONS
  - The general US population may be exposed to tAs and iAs more from eating some foods than from drinking water.
  - This model evaluation effort provides more confidence in the exposure assessment tools used.

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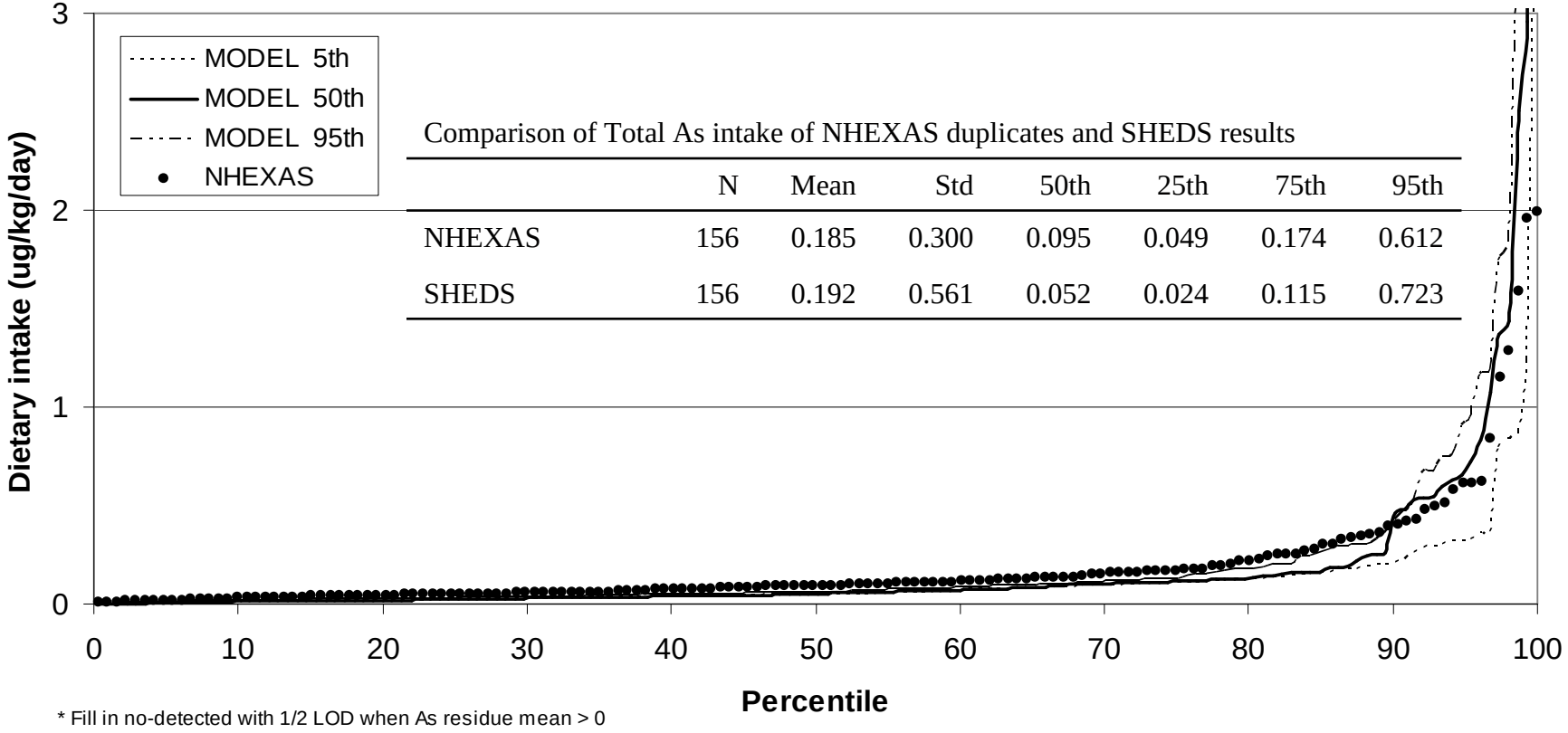
Figure 3. SHEDS Dietary Exposure Model Evaluation with Duplicate Food Survey*



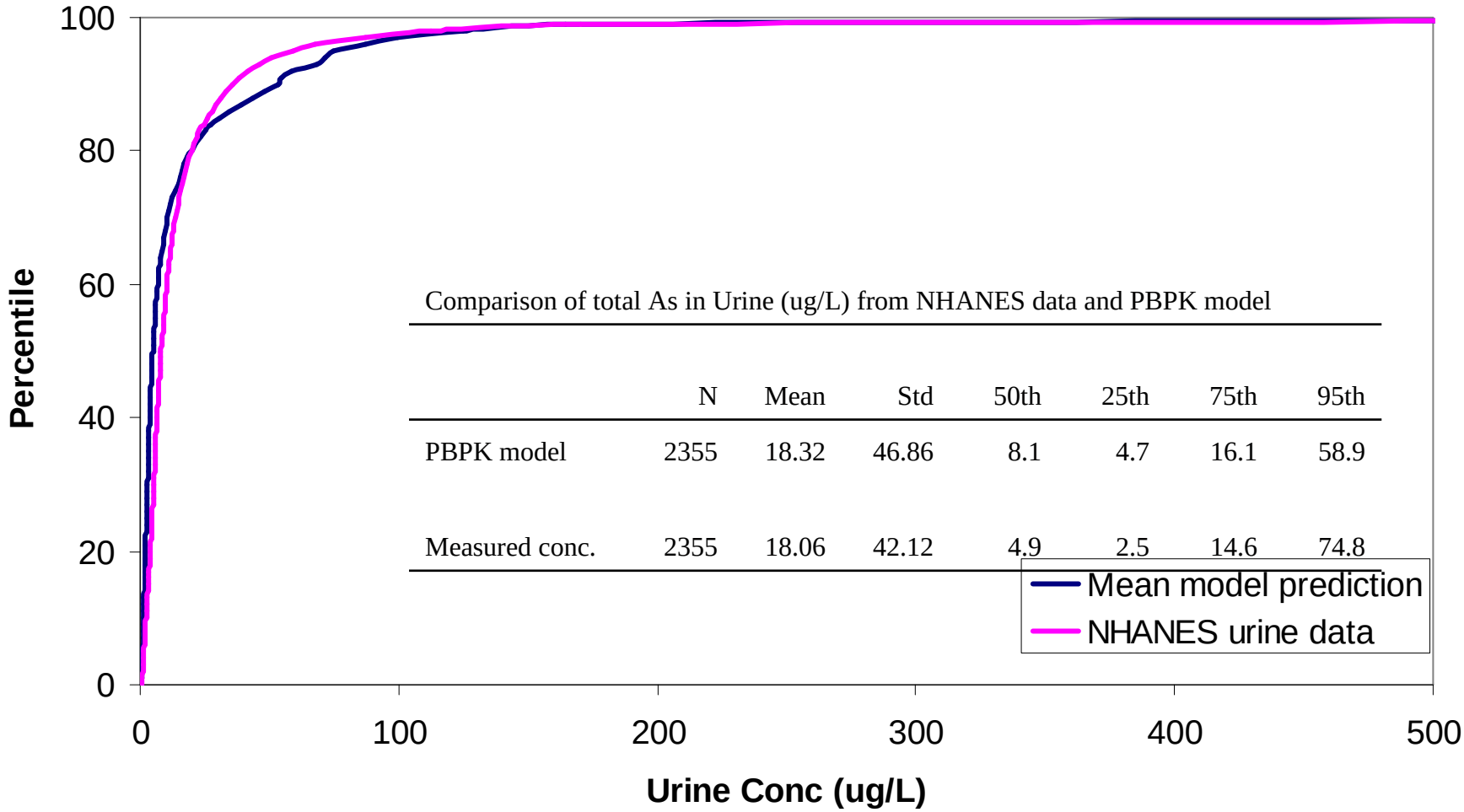
Comparison of Total As intake of NHEXAS duplicates and SHEDS results

	N	Mean	Std	50th	25th	75th	95th
NHEXAS	156	0.185	0.300	0.095	0.049	0.174	0.612
SHEDS	156	0.192	0.561	0.052	0.024	0.115	0.723

* Fill in no-detected with 1/2 LOD when As residue mean > 0

Source: Xue et al., *EHP* 2010

Figure 4. Total Arsenic Model Evaluation for SHEDS and MENTOR PBPK with NHANES Urine data

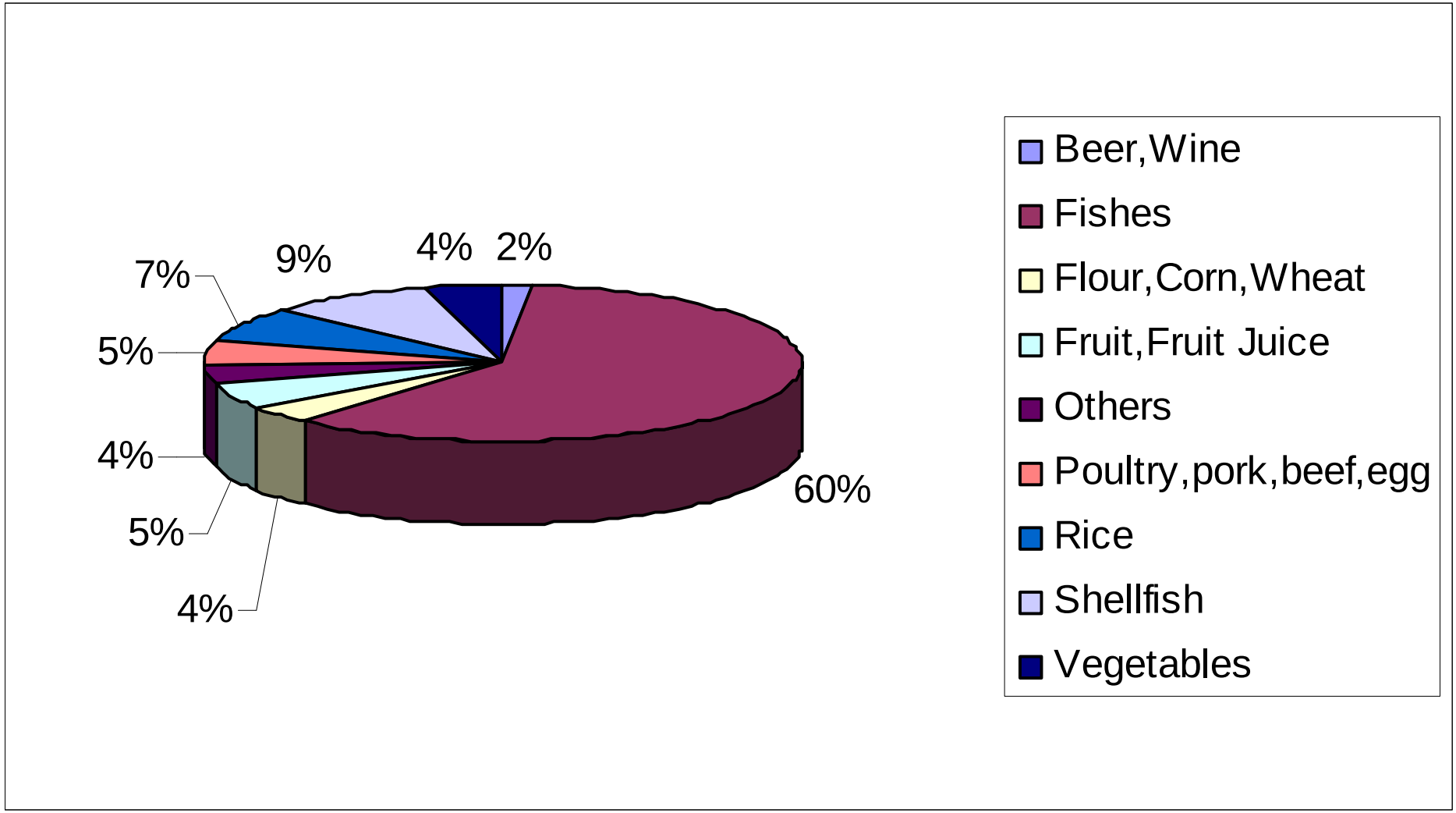


Comparison of total As in Urine (ug/L) from NHANES data and PBPK model

	N	Mean	Std	50th	25th	75th	95th
PBPK model	2355	18.32	46.86	8.1	4.7	16.1	58.9
Measured conc.	2355	18.06	42.12	4.9	2.5	14.6	74.8

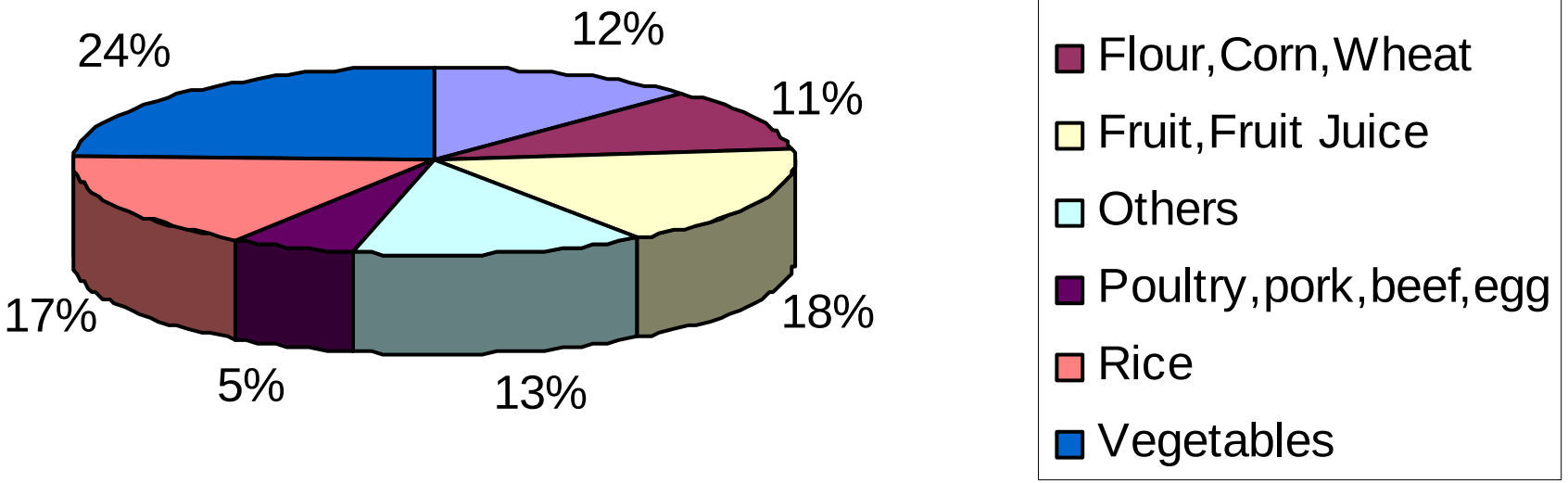
Source: Xue et al., *EHP* 2010

Figure 5 Contributions of Total Arsenic Intake by Foods



Source: Xue et al., *EHP* 2010

Figure 6 Contributions of Inorganic Arsenic Intake by Foods

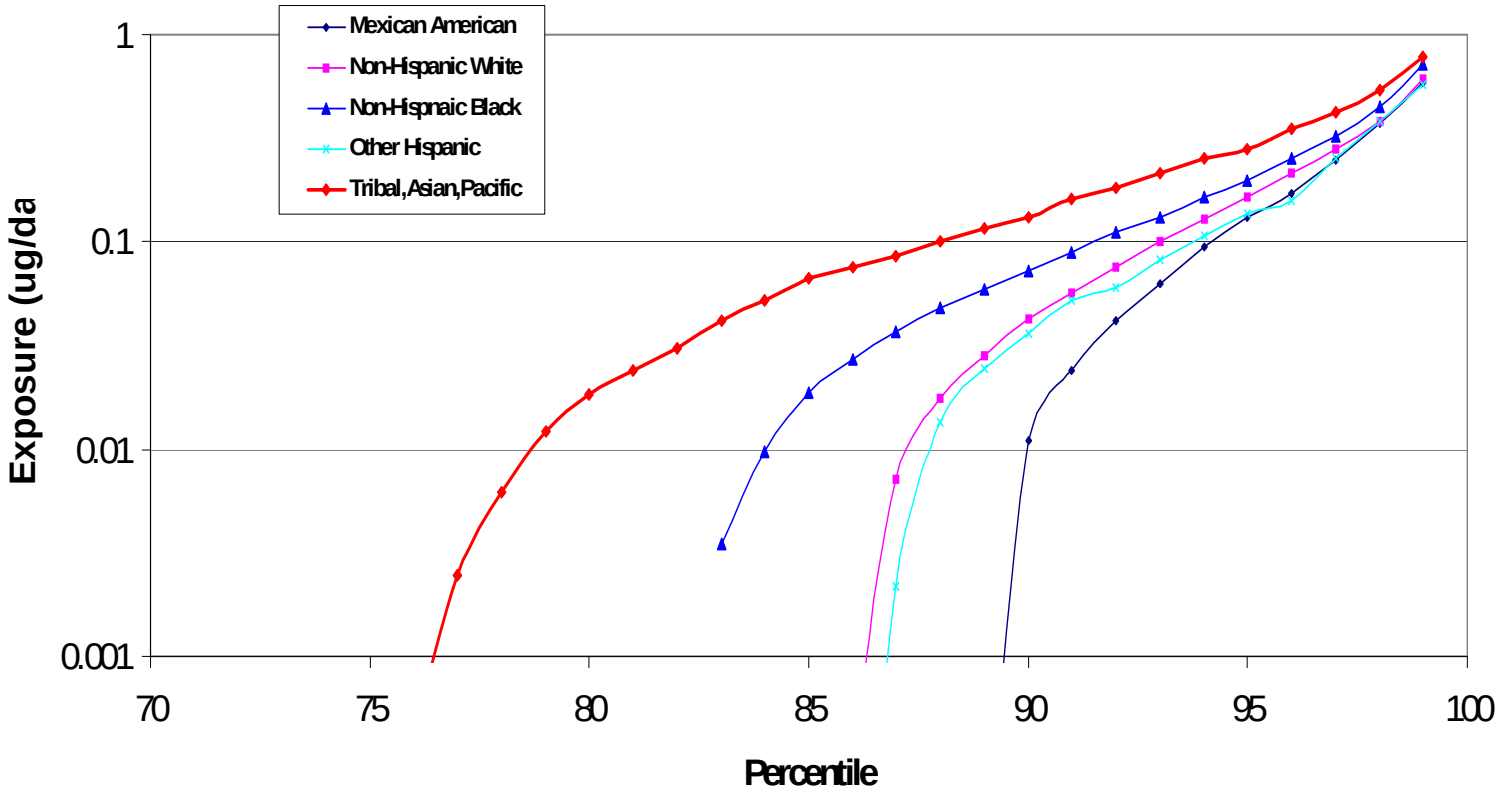


Source: Xue et al., *EHP* 2010

SHEDS-Dietary: Hg Application
draft manuscript in progress

- BACKGROUND
  - Asians, Native Americans, and Pacific Islanders (A/N/P) have shown higher levels of MeHg in previous NHANES; reasons have not been well studied.
- OBJECTIVES
  - Examine dietary exposures to MeHg through fish consumption in different racial/ethnic groups, and extend previous NHANES blood level analyses.
- METHODS
  - Probabilistic exposure modeling for dietary MeHg was conducted with SHEDS-Dietary, using NHANES/WWEIA fish consumption data and FDA TDS fish residue data.
  - MeHg exposures by race/ethnicity, age group, and food type analyzed.
  - Statistical analyses of blood MeHg levels by race/ethnicity from 1999-2006 compared against previous published results for 1999-2002 data (6 times larger sample size).

SHEDS-Dietary MeHg exposure by ethnicity using 1999-2006 NHANES data



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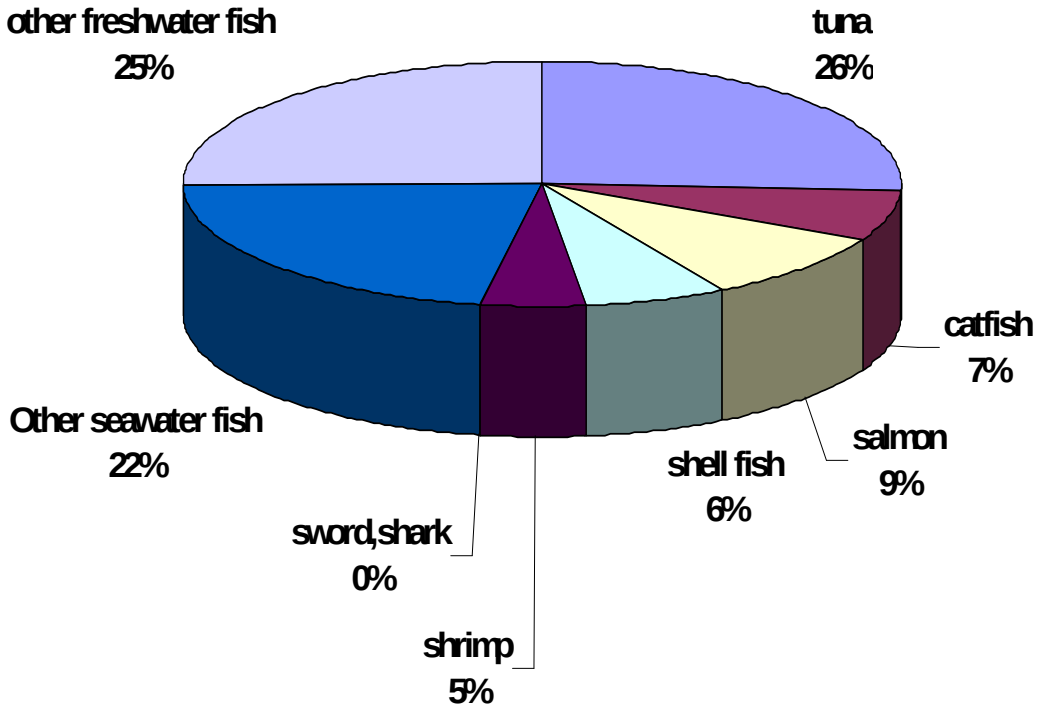
Contribution of MeHg exposure from different fish types for Asians, Native Americans, Pacific Islanders



SHEDS-Dietary: Hg Application
draft manuscript in progress

United States Environmental Protection Agency

- ADDITIONAL RESULTS
  - SHEDS exposure predictions correlate well with NHANES blood biomarker levels in terms of age, gender, and ethnicity.
  - Percentage of MeHg blood levels higher than critical health-based concentrations is higher (up to 8x) for A/N/P compared to other racial/ethnic groups.
  - 1-2 yr-olds, A/N/P have highest ratio of SHEDS modeled MeHg exposure and NHANES MeHg blood levels.

- CONCLUSIONS
  - This research extends and is consistent with findings from previous studies focusing on higher blood levels in A/N/P populations, by examining dietary exposures to MeHg from fish consumption.
  - A/N/P populations are exposed to higher levels of MeHg from fish consumption than the general US population and other ethnicity groups.
  - SHEDS-Dietary modeling allows identification of Hg intakes by age, gender, ethnicity, and type of fish.
  - Correlations of modeled dietary exposure predictions with NHANES blood biomarker levels suggest that fish consumption is a key exposure pathway for these populations.

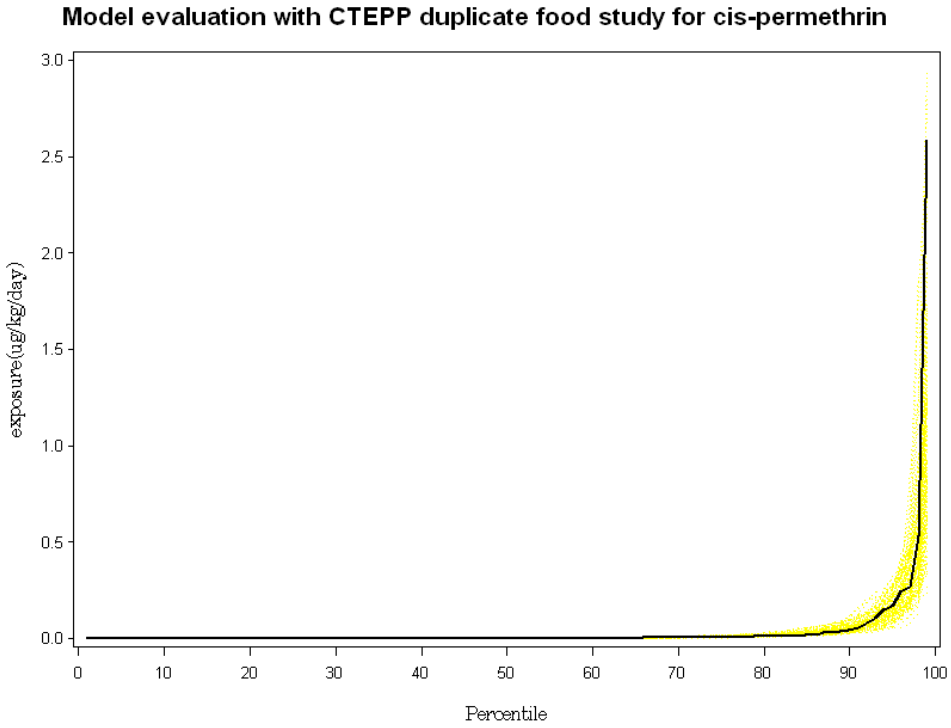
Activities in Progress/Next Steps:
SHEDS-Dietary Permethrin FIFRA SAP (July 2010)

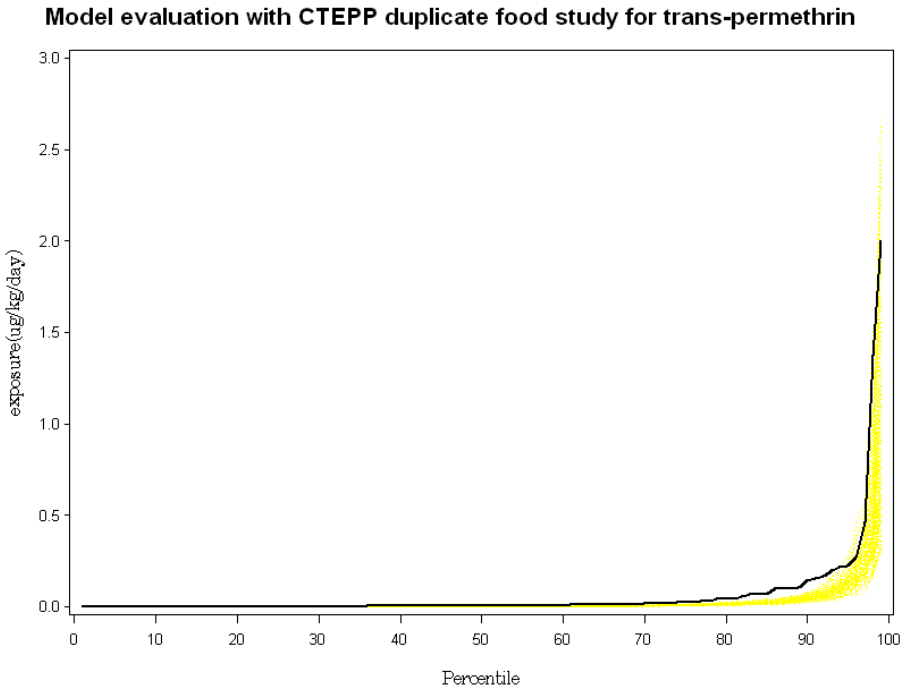
United States Environmental Protection Agency

- **BACKGROUND**
  - Need permethrin dietary estimates for 2010 SAP case study, and to support OPP's PYR CRA
- **OBJECTIVES**
  - Quantify dietary permethrin exposure, and identify the major contributors
  - Compare SHEDS-Dietary model predictions to observed data using CTEPP duplicate diet data and NHANES biomonitoring data
- **METHODS**
  - Use CSFII 1994-1996,1998 consumption data and PDP data for residues
  - Evaluate model predictions against CTEPP duplicate food data for cis- and trans-permethrin (matched SHEDS and CTEPP data by age and gender)
  - Apply bootstrap to assess uncertainty and relative importance of dietary consumption vs. residue data
  - Link to PBPK models and compare results to NHANES biomonitoring data

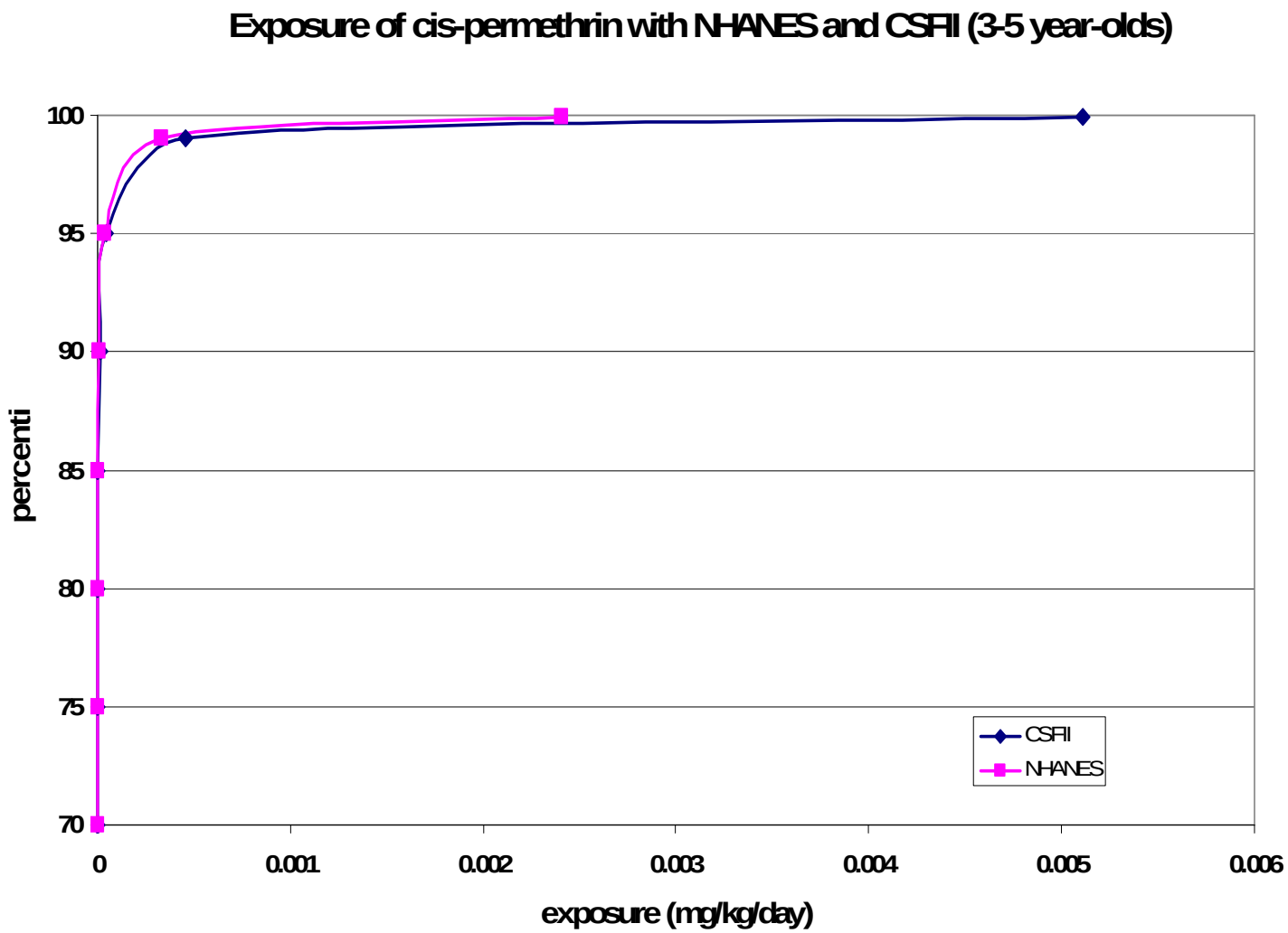
Activities in Progress/Next Steps: SHEDS-Dietary Permethrin FIFRA SAP (July 2010)

Comparison of SHEDS-Dietary Estimates Against CTEPP Duplicate Diet Exposure Data for cis- and trans-permethrin





Activities in Progress/Next Steps: SHEDS-Dietary Permethrin FIFRA SAP (July 2010)



Activities in Progress/Next Steps:
SHEDS-Dietary Permethrin FIFRA SAP (July 2010)

- **EXPECTED RESULTS**
  - SHEDS-Dietary will be applied to assess population exposures
  - Key factors and contributors will be identified
  - Uncertainty analyses will show importance of consumption data
  - More research needed with PBPK linkage and model evaluation

Additional Plans/Future Research Needs for SHEDS-Dietary

- Apply to other case studies with PBPK linkage, sensitivity and uncertainty analyses, model evaluation
- Expand model applications to local/community scale for different chemicals
- Refine longitudinal algorithms based on available data
- Match dietary & residential module (food consumption and activity diaries)
- Analyze impact of different residue sampling: same vs. different residues within a day for same foods eaten by an individual
- Possible refinements to drinking water allocations
- Explore enhancements to uncertainty analyses

"Take Away Message"

- SHEDS-Dietary is being applied in EPA for research and regulatory purposes
- SHEDS-Dietary has capabilities in which USDA and FDA may be interested
- SHEDS-Dietary can use either CSFII or NHANES/WWEIA food consumption diaries to simulate individuals' ingestion exposures on separate eating occasions
- SHEDS-Dietary has been published in the peer reviewed literature with an As model evaluation case study (*Environmental Health Perspectives, 2010*)
- SHEDS-Dietary will undergo external peer review by the FIFRA SAP July 2010 (with a permethrin case study), after beta testing by OPP
  - Conceptual basis presented to SAP for peer consult in August 2007
- SHEDS-Dietary will be transparent and available for potential broad use within EPA and by other Agencies

Disclaimer

Although this work was reviewed by EPA and approved for presentation, it may not necessarily reflect official Agency policy.