Level I Quality Assurance Project Plan (QAPP)

For

The Stochastic Human Exposure and Dose Simulation Model for Multimedia, Multipathway Chemicals (SHEDS-Multimedia)

USEPA, Office of Research and Development
National Exposure Research Laboratory
Human Exposure & Atmospheric Sciences Division

Work Assignments #3-12 and 4-03
Contract No. EP-D-05-065

Prepared by:
Alion Science and Technology
Research Triangle Park, NC 27709

A Project Management

A1 Title and Approvals

NERL's Stochastic Human Exposure and Dose Simulation Model for Multimedia, Multipathway Chemicals (SHEDS-Multimedia)

Approvals:

EPA		Alion	
Valerie Zartarian *EPA Principal Investigator and Work Assignment COR*	6/22/10 Date	Luther Smith *Technical Supervisor, Alion*	6/23/10 Date
Andrew Geller *Branch Chief, EMRB*	6/23/10 Date	Hunter Daughtrey *Program Manager, Alion*	6/23/10 Date
Elizabeth Betz *QA Manager, HEASD*	6/23/10 Date	Paulette Yongue *QA Manager, Alion*	6/23/2010 Date

Prepared for:
National Exposure Research Laboratory
Human Exposure & Atmospheric Sciences Division

Prepared by:
Alion Science and Technology
Research Triangle Park, NC 27709

A2 Table of Contents

A3 Distribution List

EPA

Valerie Zartarian, SHEDS-Multimedia PI and WA COR

Jianping Xue, SHEDS-Multimedia co-PI and Alternate WA COR

Andrew Geller, EMRB Branch Chief

Elizabeth Betz, HEASD QA manager

Rebecca Clausen, COR

John Southerland, CO

Alion Science & Technology

Graham Glen, Principal Investigator

Luther Smith, Technical Supervisor

Hunter Daughtrey, Program Manager

Paulette Yongue, QA Manager

Casson Stallings

Kristin King Isaacs

Melissa Nysewander

Mariko Porter

A4 Project Organization

The organization chart below presents the roles and lines of communication among the SHEDS-Multimedia project participants (EPA and its contractor Alion Science and Technology):

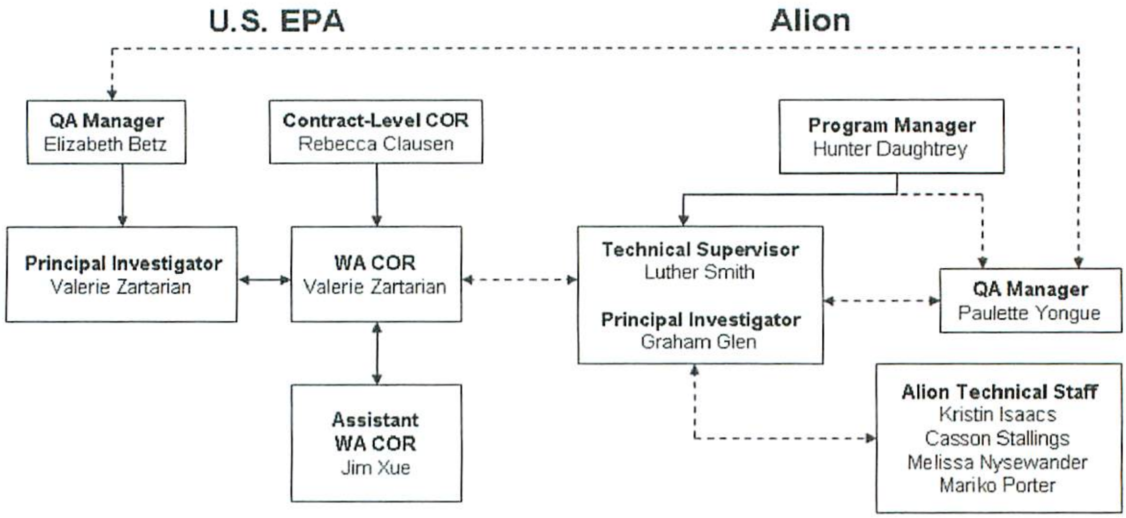


Figure A-1: SHEDS-Multimedia Project Organizational Chart

The EPA project QA manager is Elizabeth Betz, the EPA Contract-Level COR is Rebecca Clausen, the EPA WA COR is Dr. Valerie Zartarian, and the alternate EPA WA COR is Dr. Jianping (Jim) Xue. Drs. Zartarian and Xue are the EPA principal investigators and task leads for SHEDS-Multimedia research. Hunter Daughtrey is the Alion Program Manager. Dr. Luther Smith is the Alion technical supervisor of the project work assignments who performs technical oversight as well as management, including cost tracking, monthly reviews and performance reports. Dr. Graham Glen is the Alion principal investigator and lead programmer. Coding of SHEDS-Multimedia will be conducted both by NERL researchers and by extramural contractors at Alion Science and Technology.

The expected users of the model are primarily ORD and EPA Program Offices (e.g., Office of Pesticide Programs) scientists who will apply the model for research and regulatory purposes. The results of case-study applications of the models will be published in the scientific peer-reviewed literature. Exposure scientists from other government agencies, industry, and academia may also be users of SHEDS-Multimedia and its applications.

Table A-1 summarizes the positions and qualifications of the Alion contractor staff who have been involved in SHEDS development and application.

Table A-1: Alion Contractor Staff Selected to Conduct SHEDS-Multimedia Modeling

Staff Member	Responsibilities	Qualifications
Hunter Daughtrey	Overall contract management	PhD, chemistry Trace analysis and methods development using mass spectrometric, chromatographic, and optical methods Supervision and management of a staff of 30, with annual budgets to $5 million
Luther Smith	Model development and evaluation Analysis and interpretation of results Technical writing and technical support Managerial oversight	PhD, Biomathematics Statistical analysis in a wide variety of applications, primarily using SAS Mathematical modeling -- stochastic and deterministic, and including input development, evaluation, and output analysis (10 years experience with SHEDS) 11 years experience with CHAD diary data 9 years supervisory experience
Graham Glen	Primary role in model development, programming, and evaluation Analysis and interpretation of results Technical writing and technical support	PhD, Physics Mathematical modeling -- stochastic and deterministic, and including input development, evaluation, output analysis, and sensitivity analysis (10 years experience with SHEDS) Data analysis 11 years experience with CHAD diary data
Casson Stallings	Primary role in graphical user interface (GUI) development Technical writing and technical support Document assembly	PhD, Forestry Applications development with a variety of software 6 years experience with SHEDS GUI 8 years experience with CHAD Application of GIS techniques Data analysis

Staff Member	Responsibilities	Qualifications
Kristin Isaacs	Assistance in model development Assistance in model/GUI evaluation Document assembly	PhD, Biomedical engineering Mathematical modeling -- stochastic and deterministic, and including input development, evaluation, output analysis, and sensitivity analysis; particular expertise in respiration (4 years experience with SHEDS and CHAD) Data analysis
Melissa Nysewander	Assistance in model development Assistance in model evaluation GUI evaluation Document assembly	PhD, Physics and astronomy Mathematical modeling Data analysis
Mariko Porter	Input preparation/programming support GUI evaluation Document assembly	MS, Applied mathematics Data review, database preparation, and statistical programming
Paulette Yongue	Review and approve QA documentation	BS, chemistry QA activities such as audits, reporting, and QAPP development

A5 Project Definition and Background

The goal of NERL's Stochastic Human Exposure and Dose Simulation (SHEDS)-Multimedia model development research is to provide better estimates of human exposure and dose to environmental chemicals to improve human health risk estimates. SHEDS-Multimedia (previously SHEDS-Pesticides) was developed in response to the Food Quality Protection Act of 1996, which required a complete reassessment of existing pesticide guidelines. This act required that pesticide regulatory decisions depend upon aggregate human exposure. The primary objective of the model is to provide a modeling tool for exposure assessors, risk assessors, and risk managers that can help address questions including the following:

1. What is the variability in exposures to environmental chemicals across populations of interest?
2. How uncertain are the estimates of population variability?
3. What are the contributions to total exposures from multiple sources, routes, pathways and other factors for a single chemical (aggregate exposure)?
4. What are the contributions to total exposures from co-occurrence of scenarios and chemicals with similar toxicological endpoints (cumulative health effects/risk)?

5. What are the intensity, duration, frequency, and time series of exposures?
6. Where can better data be most effective in reducing the uncertainty in estimates of exposure?
7. How can human exposure study designs be improved to provide data that reduces the uncertainty in modeled exposures?
8. How can exposures be most effectively reduced?

To accomplish the stated objective and help answer the above research questions, the SHEDS-Multimedia model should:

- provide population distributions of exposure and dose using simulated individuals that demographically represent the populations of interest;
- estimate the time series of event-based exposure and dose for each simulated individual using real-world human activity databases and other data;
- quantify exposure and dose for multiple routes and pathways separately for each simulated individual (inhalation, ingestion, and dermal);
- utilize input data that quantitatively represents the variability and uncertainty separately across the populations of interest;
- provide estimates of the uncertainty in the model results; and
- provide estimates that compare well to real-world data.

These performance criteria are the drivers for the model development, and determine the appropriate structure of the model, the algorithms required, the input data needed, and the form of the model outputs.

SHEDS-Multimedia utilizes a 2-stage probabilistic model structure that incorporates random sampling of data to separately characterize population variability and uncertainty. With each model input parameter are associated probability distributions that represent the variability and uncertainty for that parameter. In addition, physically-based algorithms are required to reflect sound scientific relationships within the exposure and dose calculations. Available outputs from the model need to include estimates of population distributions of exposure and dose, as well as appropriate summary statistics and plots for populations and individuals.

Outputs include: (a) detailed model inputs employed; (b) exposure time series, and summary information for individuals simulated; (c) exposure and dose summary statistics from variability analyses; (d) variability and uncertainty in population exposure and dose distributions (e.g., cumulative distribution functions (CDFs)).

A6 Project and Task Description and Schedule

SHEDS-Multimedia is a physically-based probabilistic model (Sexton and Ryan 1988). That is, it uses mechanistic equations to describe physical processes, but rather than using point estimates, it samples from probability distributions for model inputs to characterize variability between individuals and within individuals for the population of interest. SHEDS-Multimedia Version 3 has been peer reviewed by EPA's Office of Pesticide Programs Scientific Advisory Panel (SAP) and is available on the EPA website:

(http://www.epa.gov/heasd/risk/projects/c1b_exposure_models_development.htm). SHEDS-Multimedia Version 4 (cumulative version that combines dietary and residential modules) is in development, and a Scientific Advisory Panel review of that version is anticipated for 2010.

A6.1 Model Design

SHEDS-Multimedia has been developed to assess population exposures to a wide variety of environmental chemicals using a probabilistic approach. The following describes the general structure of the SHEDS methodology (see Figure A-2):

- Simulated individuals are randomly selected to represent the population of interest according to user defined demographic representations/characteristics.
- Each individual is randomly assigned appropriate human activity and in some cases food intake diaries according to demographic characteristics (e.g., age, gender, etc.).
- Values for input parameters are randomly sampled from distributions and are assigned for use in exposure algorithms.
- Chemical concentrations for each microenvironment and medium contacted for the simulated exposure scenario are entered or modeled; individuals' locations and activities are based on Consolidated Human Activity Database (CHAD; McCurdy et al., 2000) diaries.
- An individual's time series of exposure and dose for each route is estimated.
- Results for the simulated individuals are combined using Monte Carlo sampling to produce population distributions of exposure and dose.

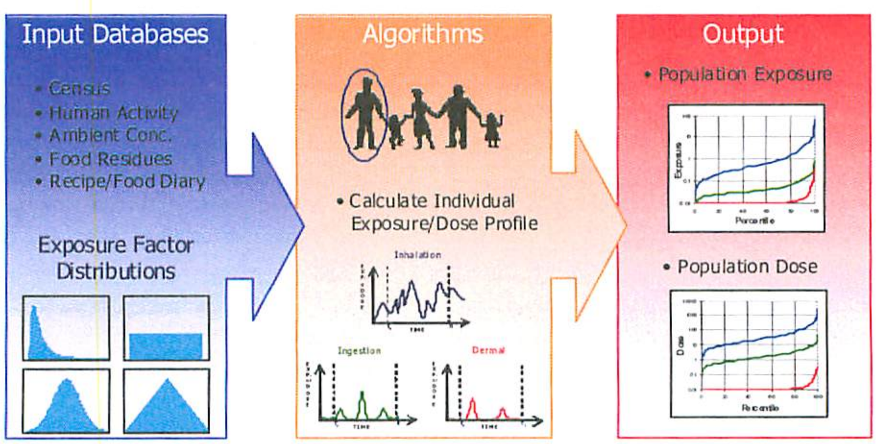


Figure A-2. General structure of SHEDS model

A6.2 Methods and Techniques

A number of different techniques are utilized in SHEDS-Multimedia to support the probabilistic features for characterizing population variability in pollutant exposures, as well as the uncertainty associated with the model predictions.

The SHEDS methodology incorporates a two-stage Monte Carlo simulation technique to produce population distributions of exposure and dose that characterize both the variability and the uncertainty in the exposure and dose estimates (Figure A-3). As stated above, distributions for each input parameter are randomly sampled for each simulated individual. In addition, distributions of the uncertainty associated with each statistical parameter of a variability distribution are also required and randomly sampled to define new variability distributions for each iteration of a model run. Multiple iterations of the model are conducted, with each iteration producing a different population distribution due to the different variability distributions. Using this technique, the exposure and dose distributions generated as output by the model characterize both the uncertainty and variability associated with the input parameters.

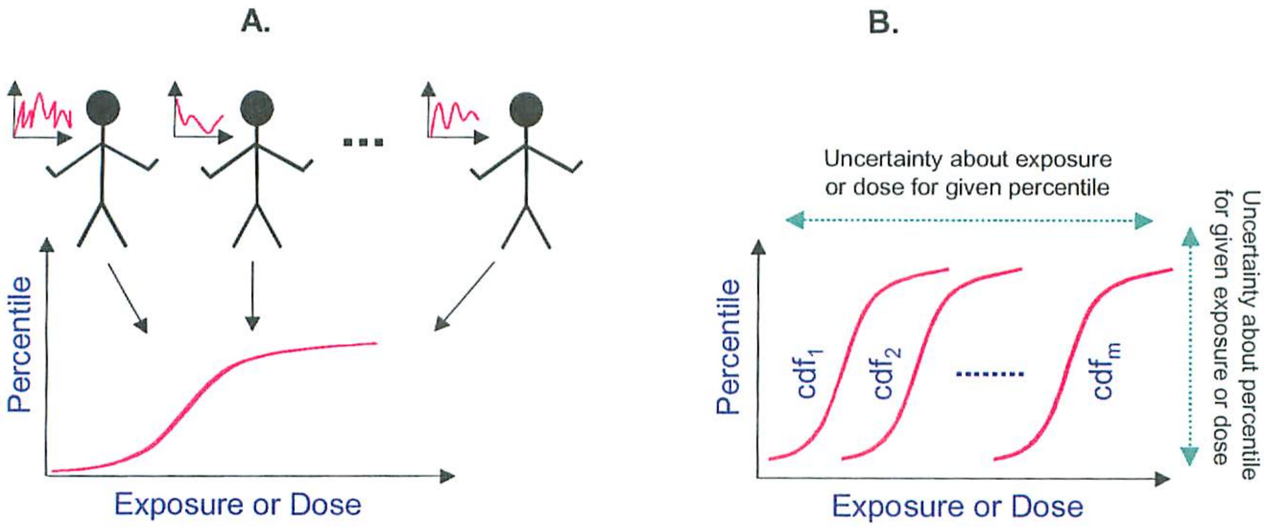


Figure A-3. SHEDS 2-stage Monte Carlo sampling technique: A. Variability distribution for one model iteration; B. Multiple model iterations for characterizing uncertainty.

A6.3 Development of Input Distributions

Variability distributions are fit using the following approach: where few data are available, simplified distributions (e.g., uniform, triangle) are used based on professional judgment and expert solicitation; beta distributions are generally used when values are restricted between 0 and 1; where more data are available, distributions such as Weibull or lognormal are fit using method of moments or maximum likelihood estimation.

To assign uncertainty distributions to SHEDS inputs, a bootstrap method reviewed by EPA/OPP's Scientific Advisory Panel (Zartarian et al. 2005) will be employed. Other methods (e.g., a Bayesian approach) may be developed later. The bootstrap is implemented as follows:

1. Fit a variability distribution (the Aparent distribution@), with parameters *v1* and *v2* (e.g., geometric mean and geometric standard deviation) to all data from the original *N* studies containing relevant data.
2. Fit a variability distribution (using the shape of the parent distribution) to data in each of the

original *N* studies and examine a scatter plot of the *N* *v1* and *v2* values, to get a sense of the scale of uncertainty.

3. Sample *B* data points from the parent distribution *M* different times (*B* is the bootstrap sample size; *M* is the number of parameter pairs to be saved for the uncertainty runs).
4. For each of those *M* sets of *B* data points, fit the parent distribution and compute the parameter values of interest. This gives *M* (*v1*, *v2*) pairs.
5. Overlay the scatter plot of the *M* (*v1*, *v2*) pairs with the *N* (*v1*, *v2*) pairs obtained in step 2.
6. Repeat steps 3-5 with different values of *B*, until the scatter plot from step 4 satisfactorily matches the spread seen in the scatter plot from step 2.
7. At the start of an uncertainty iteration, one of the *M* parameter pairs is randomly selected for each input. The selected (*v1*,*v2*) pairs define the variability distributions to be used for this iteration.

A6.4 Generation of Simulation Population

The primary input databases (US Census demographic data and CHAD human activity pattern data) are used to generate a simulation population for each model run based on user-selected options for the model run scenario. The age and gender of each individual in the simulation population is randomly selected from the appropriate US Census demographic proportions supplied as input to produce a demographically representative set of individuals for the model run. Additional characteristics of the simulated individuals are also randomly assigned based on US Census data, such as housing type and employment status, and/or other demographic proportion data such as pesticide use data.

The human activity diary data in CHAD are then categorized by age, gender, or any other user-specified criteria to obtain a group of appropriate CHAD diaries available for each simulated individual. For each individual, diaries are drawn from the appropriate group(s) and linked together to represent that individual's time series of activities and locations for the model run (lasting one day to a year or more as specified by the user). Each individual is also randomly assigned a time series of values, or for some parameters a single value, from each of the input distributions needed for estimating environmental media concentrations and exposure factors.

A6.5 Estimation of Individual Exposure Profiles

The time series of exposure and dose for each simulated individual is estimated using an event-based approach. Each CHAD diary consists of a series of events from 1 to 60 minutes in length. Each event identifies the location and activity being performed by the person. For each diary event, chemical concentrations in the appropriate environmental media (e.g., air, soil) are assigned based either on values selected from user-specified concentration distributions or time series, or from equations calculating concentrations. The corresponding activity in the CHAD diary is used to estimate physical activity level and thus breathing rate. The time series of exposure and dose are calculated separately for each exposure route and pathway (inhalation, ingestion, dermal) using pathway-specific equations (Zartarian et al., 2008). Two-stage Monte Carlo probabilistic simulation is used to produce distributions of exposure for various cohorts (e.g., age/gender groups) that reflect both the uncertainty and variability in the input parameters (MacIntosh et al., 1995).

A6.6 Analysis of Results

The program provides the user the ability to summarize and display the model results. A variety of tabular and graphical analysis functions are needed to condense the model output. The ability to subset the population for the analysis by gender, age, and other characteristics is also needed.

Summary statistics for characterizing the population distribution for each of the model outputs (exposure and dose) are calculated using the model results for each simulated individual. The following types of graphical output are also used to meet the goals and performance criteria specified in Section 2.3

- Population cumulative distribution functions (CDFs) describing the population variability for exposure or dose.
- Pie charts displaying the relative importance of pollutant exposure and dose by route (e.g., dermal, inhalation, ingestion), microenvironment, or source.
- Time series plots of exposure or dose for an individual over time.
- Compilations of multiple population CDFs for the different uncertainty runs to characterize uncertainty in the model outputs.

Additional methods and techniques for post-processing of the model results include sensitivity analysis such as screening type sensitivity analyses using local or scaling analysis (nominal sensitivity analysis) and correlation type analyses (e.g., Spearman correlation, Pearson correlation). Stepwise regression techniques can also be used. In addition, other techniques such as Sobol's method may be applied. These methods address sensitivity analysis under 1-stage (variability only) and 2-stage sampling. The sensitivity analyses help fulfill several model goals such as identifying areas most in need of additional research. The sensitivity analyses also assist in model development and assessment and are appropriate for either variability or uncertainty simulations.

A7 Quality Objectives and Criteria for Model Inputs/Outputs

As described above, SHEDS-Multimedia requires data for characterizing the population of interest, the concentrations of chemicals in various environmental media (e.g., air, water, food, soil), and the factors that influence human contact and uptake of the chemicals from the various media. These data are either obtained directly from existing publicly available databases or are compiled into distributions based on available data gathered from published data sources such as scientific journals and technical reports. All data used in the SHEDS model will be of the highest quality possible. Publicly available databases used for the model shall provide relevant data and be thoroughly evaluated. Thorough reviews of the published literature sources shall be conducted so that all relevant data are examined in the development of appropriate data distributions.

The relevance and quality of new data will be critically assessed to prevent inappropriate use of the data and to evaluate parameter uncertainty. Assessment of potential SHEDS input data will be performed considering the following acceptance criteria:

- *Data reasonableness:* consideration of the applicability of data to the intended use of the data in the model.
- *Data completeness:* consideration as to whether data are sufficient in sample size.
- *Data representativeness:* spatial and temporal considerations for data will be evaluated for appropriate predictions.
- *Data accuracy and precision:* consideration of the analytical or measurement quality of the data.

SHEDS-Multimedia utilizes a variety of data in different ways, and *how a particular data set is to be used will impact the level of quality control required.* One strength of the SHEDS-Multimedia model is its versatility. However, because of this, the data quality objectives will depend upon the usage of the model on a case-by-case basis. It is important for the users of the model to assess the required accuracy of the input data given the type and quality of output data desired.

Data used as input to the model include publicly available databases (e.g., US Census data, CHAD), data obtained from publications in the peer-reviewed literature, and raw data produced or obtained by EPA under contract or assistance agreement. These different types of data have received different levels of quality assurance and quality control and therefore require different quality control procedures for assuring the quality of data used in the model.

Prior to being used for the SHEDS model, all data will be subjected to procedures to evaluate data quality as follows:

- *Publicly available databases*: Data obtained from publicly available databases will be evaluated using the documentation available for these databases. Information provided in the documentation on the level of quality assurance performed prior to public release of these databases will be reviewed. Quality flags provided with the database will be used to identify data records for additional review. Data from these databases will also be analyzed to evaluate the quality of each type of data to be used from the database (e.g., number of missing data points).

- *Data from peer-reviewed publications*: Data obtained from peer-reviewed journal articles, books, reports, or other peer-reviewed publications that contain descriptions of methods/procedures used for quality assurance of the data may be used without further quality control. When these publications do not contain sufficient information on quality assurance procedures used by the originators of the data, further evaluation of the data will be conducted.

- *Raw data produced or obtained by EPA under contract or assistance agreement*: Data generated by EPA will have been produced using EPA approved QAPPs. Quality assurance reports for raw data will be reviewed and information provided in this documentation will be used to determine whether further evaluation of the data quality is needed. Quality flags for the data will be used. Information such as analytical detection limits will be used to evaluate the quality of the data if appropriate.

- *Other sources of data*: Other sources of data for which the level of quality control is not as well documented will be subjected to a more stringent review of data quality.

When available data for input to the SHEDS model have been obtained and reviewed as described above, quality control procedures will be implemented that are appropriate for the intended use of the data in the model. For example, the main concerns with use of data from quality-controlled public databases (e.g., US Census, USDA Continuing Survey of Food Intakes by Individuals (CSFII)) are whether 1) its use is appropriate for the project, 2) data were extracted correctly, and 3) data were manipulated correctly for model use. The methods that will be used to ensure correct application and evaluation of the data are visual and internal computing checks, comparison to published summaries, and maintaining auditable processing procedures.

Outputs from the model must meet the requirements for their intended use. The quality of the model outputs will be evaluated through comparisons of the model outputs against available measurements data (e.g., personal exposure data, biomonitoring data) and/or against output from other models intended for a similar purpose. The necessary degree of agreement between SHEDS model results when compared to other data sources will depend on the application of interest. In general, SHEDS model predictions at different percentiles including uncertainty bounds should capture available measurement data or predictions of other similar models. Any discrepancies should be investigated and documented where appropriate. These comparisons will be documented through the quality assurance procedures described in detail for validation and usability of model results in Section D of this document.

A8 Special Training Requirements/Certification

SHEDS developers require skill in the programming languages used to create the model, expert knowledge of the statistical techniques implemented by the program, and an understanding of the scientific basis of the decisions made. No specific certifications are required.

A9 Documentation and Records

Documentation and record keeping efforts are one of the most important elements in model development for ensuring the quality of the model produced and for defending the model results. Documentation of the model development procedures will be created in electronic form and archived on CD-ROM. Documentation of the development of model inputs will include raw data files (in spreadsheet or database format such as Microsoft[7] Excel or Access, ASCII, or SAS[7] (Statistical Analysis Software, SAS Institute, Cary NC) datasets) and a technical report summarizing the quality control procedures performed. The SHEDS model code will be archived on CD-ROM when each new version has been completed, along with the supporting documentation on the quality control procedures (code verification, calibration testing, and model assessment), the peer reviews and audits, and the model validation testing procedures (design verification, beta-testing, acceptance testing) performed. All records shall be archived by the project manager upon completion of the project.

Configuration management for SHEDS-Multimedia is conducted through code documentation, assignment of version numbers to the model code, and routine archiving of previous versions of model code. Each time the model code is modified, the following information will be included in the code header: date, name of individual making change(s), sections of code changed, and code version number. Major versions of the code (i.e., Version 1, 2, 3, ...) will be defined by model developers based on major alterations to the model. Sub-versions (e.g., Version 1.1, 1.2, 1.3, and so on) are defined by the model programmers and described clearly in the code headers typically pertaining to algorithm code modifications or additions. Each new version of the code will be saved on the hard drive and on disk and maintained by the primary SHEDS model developer(s). Regular backups will be conducted.

B Measurement/Data Acquisition

Section 3 focuses on the methods to calibrate the model, details the methods used to generate and acquire data, and provides an overview of the data management techniques. Note that sections B1 – B6 and B8 are not applicable to modeling projects and are therefore not included in this document.

B7 Model Calibration

Calibration testing will be performed routinely whenever existing model code is modified or new model code is developed and added to the SHEDS model.

B7.1 Calibration testing guidelines

A standardized set of calibration inputs will be used to test that new or modified code produces the expected result. The calibration run will also have a defined set of outputs to create, compare, and archive. Because SHEDS is a stochastic model that involves random sampling techniques, testing of the distribution sampling will be conducted using sufficient iterations to adequately characterize the distribution tails (minimum = 1000 iterations). Testing may be carried out on the model as a whole or only on the directly affected module.

Each major module within the SHEDS models will be tested as follows:

1. The simulated population generated will be compared with the input demographics.
2. Assignment of appropriate CHAD diaries will be checked by comparing demographic characteristics of simulated individuals with those of CHAD individuals and diary date information.
3. Assignment of values from the various input distributions (e.g., environmental media concentrations, equation parameters for estimating environmental media concentrations, exposure factors for contact and uptake from the media) will be tested by comparing against original distribution parameters.
4. The actual sampling rate of parameters will be calculated and compared with the expected sampling rate.
5. Intermediate values and summaries will be compared with anticipated values (e.g., average hours worked per week, frequency of bathing, maximum PAI, total of by route values).
6. Results of SHEDS algorithms and equations will be compared with available data.

This process will be iterative, with each calibration test potentially identifying modifications that are needed to the model code. Following corrective action, the process will be repeated for each step related to the change and documented.

B7.2 Visual and Internal Computing Checks

Where time and resources are available, data entered by hand will receive a 100% check against the source by someone other than the person who entered the data. When a 100% check is not feasible, then a random spot check of a documented size will be done independently. If the results are favorable, the data will be accepted. If the spot checks prove unacceptable, then one of three actions will be taken: 1) the data will not be used; 2) an attempt to procure resources for a complete check and correction of the data will be made; 3) alternative input data will substituted. In the event that no available data meet established criteria, existing data will be used and the problems identified in the QA will be documented. The hand-entered data will be maintained for later auditing, regardless of the QA results.

Electronic data sets received from less reliable sources will be treated with more caution. In addition to the checks mentioned in the previous paragraph, an attempt will be made to verify that the records are individually consistent. The specific methods will necessarily depend on the individual data set.

Several types of checks will be built into the data processing to increase the likelihood that all steps are carried out correctly. Such checks include: ensuring the correct number of records were read and produced; independently checking calculations (e.g., ensuring that probabilities add to 1.0) or comparing to other values from the same database (e.g., check sums against other sums provided in the data set); checking the type (integer, real, character) of values read and produced. Additionally, spot checks against hand calculations and examination of data summaries for the resulting values can be done.

B7.3 Published Summary Comparisons

Processed data will be checked against publicly available summaries based on the same data set. Data documentation and summary statistics will be reviewed to judge the appropriateness of the data and previous quality assurance. The exact summaries of interest will vary by data set. Typical summaries may include: checking the minimum, maximum, and several of the extreme values; checking for the number of observations near, at, or below a procedural detection limit; looking for the percentage of missing values and any relevant patterns in the missing values. Sometimes this requires that intermediate values be checked or that processed data be subset or additionally processed. For example, a desired summary of Census data can be produced based on those to be used as model inputs, and this summary compared to one produced by the Census Bureau.

Quality control procedures for creation of input distributions that represent population variability (e.g., environmental media concentrations, exposure factors) include comparison of the different data sources, the number of measurements from each source, and the variety of locations from which the measurements were obtained. Where data are of sufficient quantity, goodness-of-fit tests (e.g., Kolmogorov-Smirnov, Cramer-von Mises, Anderson-Darling and chi-square) and probability plots will be done to assess agreement with the proposed input distribution. Comparability of data sets originating from multiple unique sources will be assessed (e.g., distribution types, descriptive statistic comparison) before merging such data to fit a single distribution. Where data are of insufficient quantity for developing distributions or employment of reasonable test statistics, professional judgment within the bounds of the scientific literature will be employed and documented by the model developers.

B9 Non-direct Measurements (Data Acquisition Requirements)

The types of information needed by the SHEDS model include:

- Population demographic data from the US Census
- Human activity pattern data from CHAD daily diary records
- Food and water intake data from daily diary records (e.g., CSFII; NHANES)
- Environmental concentration data (measured or modeled)
- Data on exposure factors relating the transfer of environmental chemicals from environmental media to individuals.

These types of information are described below.

Population Demographic

SHEDS-Multimedia utilizes population demographics data from the 2000 US Census. Age and gender data are typically used to generate a simulation population that demographically represents the population of interest. The US Census data is publically available and has highly detailed documentation. Therefore, use of the US Census data in the SHEDS model should be guided by the limitations of the data as stated in the documentation. Documentation on the Census SF1 (US Census Bureau, 2001), SF3 (US Census Bureau, 2002), and PUMS (US Census Bureau, 2003) data sets provide extensive information on collection and quality assurance methods used, in addition to methods employed to calculate standard errors and other statistics for specific quantities derived from the data.

Human Time Location Activity Patterns

SHEDS-Multimedia also uses EPA's Consolidated Human Activity Database (CHAD) to simulate the activity patterns of individuals in the simulation population (McCurdy et al., 2000). CHAD contains over 30,000 diary records (i.e., person days) from 17 separate studies that collected human activity data. The diary data includes the time individuals spent in various locations during a day and the various activities performed while in each location. Documentation is available for the CHAD database and a number of analyses of the data have been published in peer-reviewed journals. The database continues to be maintained and improved. The use of the CHAD database in the SHEDS model shall consider the limitations of the database, as well as the results of published analyses.

Food/Water Consumption Patterns

Where food is a significant route for the pollutant, dietary consumption data are taken from the USDA Agricultural Research Service Continuing Survey of Food Intake for Individuals (CSFII) 1994-96, 1998 (USDA ARS, 2000). These data contain about 40,000 daily food diaries. Each diary gives the amount and type of food and water intake at different times throughout the day. Ancillary data give information about the individuals (e.g., age, gender, weight) and about the likely components of the food and source of the water (e.g., well, municipal system). This data does not provide any information about chemicals in the food or water.

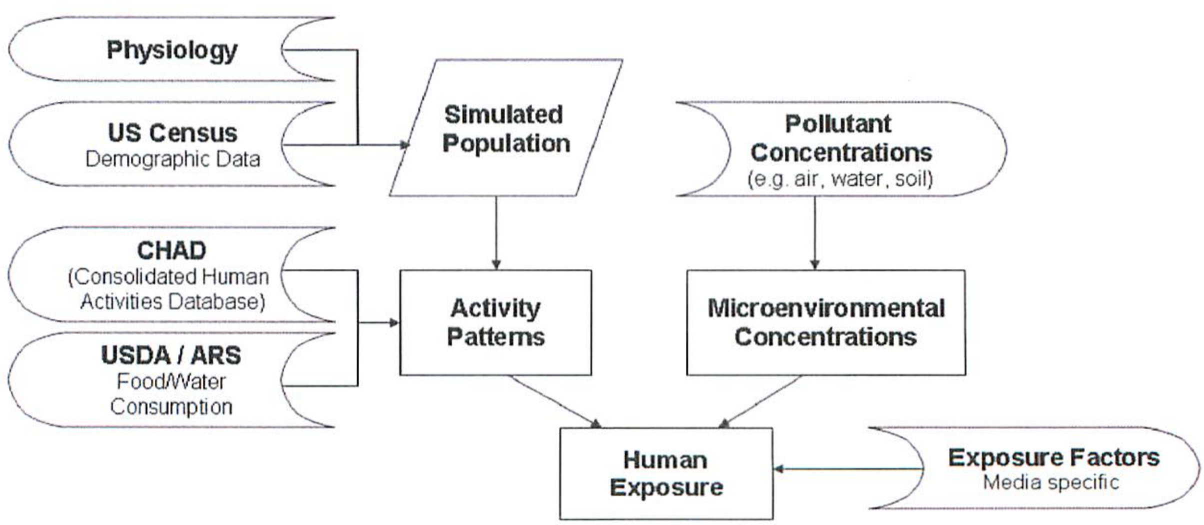
Multimedia Contact Rates and Residues
Data on the concentrations of chemicals in different environmental media (e.g., air, water, food, soil) may also be required input for SHEDS-Multimedia. For any particular chemical, concentration data for each of the relevant environmental media may be obtained from an existing database, model output, or from a number of different data sources combined into a distribution. The use of available concentration data shall be guided by the acceptance criteria below to ensure that the data are both appropriate for use in the SHEDS model and of acceptable quality.

Other Exposure Factors
Data for the media-specific factors that influence exposure and uptake are also required as inputs to SHEDS. These data come from a variety of sources, many of which are already quality assured, including EPA's Exposure Factors handbooks (US EPA 1997, 2002c), as well as published peer-reviewed literature and technical reports. For many of the chemicals of interest to the Agency, the availability of data on exposure factors is the most limited of all the SHEDS model inputs. The use of what data are available shall be guided by the acceptance criteria below to ensure that the data are both appropriate for use in the SHEDS model and of acceptable quality. Where necessary, data are to be qualified and documented when insufficient in quantity.

B10 Data Management and Hardware/Software Configuration

B10.1 Data Management

The flow chart below presents the general data management procedures in SHEDS Multimedia, including data entry, tracking and manipulation:



To maintain auditability of the data extraction and processing of large data sets, every effort will be made to write and maintain code that reads directly from the data set or a standard extraction of the data set. Additional code will process the data until it is in the form required for use in the model. All of this pre-processing code will be maintained and archived with the model code. This will provide an audit trail for methods used to process input datasets.

A technical report for the model application will be written, including a description of all literature sources used for model inputs and documentation on how variability and uncertainty distributions were obtained or produced. The data sources used and excluded, and reasoning behind their utilization or exclusion, and the effect of potential selection bias will be addressed in the documentation. Where data, data distributions, or parameter estimates appear to be less than ideal, a qualification will be noted in the documentation.

B10.2 Hardware/Software Configuration

SHEDS-Multimedia is being developed for PCs with Microsoft Windows operating systems to allow for the broadest usability of the model. Model development will occur within EPA's standard PC environments. Any differences in functionality due to operating systems will be described in Release Notes.

The model is stochastic and requires many iterations of model code sections; therefore, hardware configuration is an important issue. In general, the computer hardware necessary to ensure model simulations are performed according to code requirements will be determined and provided as information in model documentation. Model run times will be evaluated using different hardware configurations to determine whether the processing is CPU, IO, or memory limited. This will help define an optimal configuration as well as the minimum requirements for processor and disk speed, RAM, and hard disk space. Recommendations based on the model run time evaluations will be provided in user documentation.

SHEDS-Multimedia model development was initiated using the SAS software system. SAS is an internationally recognized statistical analysis software package and as such its wide usage and acceptance indicates an inherent high level of quality. Development of the model will be performed using the most recent version of the SAS software supported by EPA (currently SAS version 9.1). The SAS BASE, STAT, and GRAPH modules are required to run SHEDS. When software version updates are supported by EPA, the model functionality will be evaluated in the new version of the software. The use of SAS to code the SHEDS model requires that a user of the model have a SAS software license covering the appropriate SAS modules.

Versions of SHEDS-Multimedia provided to the EPA as a product will be packaged as self-installing programs that load the model code and input files for the user and provide standardized program set-up using a tool such as Wise for Windows Installer.

C Assessment and Oversight

Assessment of the SHEDS model results will be conducted using a number of techniques to address the goals, performance criteria, potential error sources, and evaluation of the model outputs. These techniques help to assure that the model is functioning as expected and is providing outputs that meet user needs.

C1 Assessment and Response Actions

C1.1 Model Code Assessment

A number of routes will be pursued to assess the quality of the SHEDS-Multimedia model code:

GUI Evaluation and Assessment
Two basic methods will be used to ensure the GUI is functioning properly. The first will be to implement a series of use cases that test the response of the GUI to normal use scenarios and aberrant input. The second will permit members internal to the project and external beta testers to comment on its design and point out any malfunctions found.

Evaluation of Graphical and Tabular Output
Tabular output will be checked by comparison with model data sets generated, accounting for any subsetting applied before the table was produced. The graphical output will be evaluated to ensure that the graphical features and text features are correct. The graphical features will be compared to the data from which they were created. The text will be checked to ensure correct spelling, proper variable description, and that titles, labels, and legends are appropriate, correct, and readable.

Reasonableness Checks
Reasonableness checks of the SHEDS model results will be routinely conducted as part of the quality control procedures. SHEDS-generated population distributions will be examined to evaluate how the average, upper tail and lower tail percentiles compare to anticipated or measured values and other modeled estimates (using deterministic and/or probabilistic models).

Because the SHEDS models can preserve detailed information at the individual level, extreme high and low exposure and dose profiles (e.g., the 1st and 99th percentiles) will be examined to understand what drives the extreme values and to assess whether they are reasonable. Sample sizes for simulations will take into account both computational time considerations as well as stability in the upper tails of the distribution.

A nominal range sensitivity analysis, also called local or scaling sensitivity analysis, will be carried out to ensure that the model responds appropriately to each input distribution. This helps ensure that the model was formulated correctly. The method to be used first makes a model run holding all input parameters at a central value (e.g., their median). Then separate runs are made for each input variable by varying it over a large section of its range. This may be in terms of percentiles for variables represented as distributions or percent changes for other variables (e.g., plus or minus 50%). Except for the variable being manipulated, all variables are kept at their central value. The results of the runs are combined and the magnitude and direction each input influences the output of interest is calculated.

The optional production of scatter plots relating individual model inputs to model outputs can provide additional information. Scatter plots can ensure that the inputs influence the model outputs in the expected manner. Additionally, they can identify nonlinear relationships, saturation values, and threshold values for the inputs. These last quantities can help the researcher pick appropriate sensitivity analysis methods during the later stages of analysis.

Variability Analyses
Measurement and understanding of the variability assists in achieving a few of the model goals and assessment criteria. One goal of the SHEDS model is to identify methods to reduce human exposure to chemicals. This can be done by identifying input variables that are both important to determining the model output and that are controllable (i.e., the variable represents a human behavior or other factor which can be modified). The controllable inputs can be identified by model users. The importance of a variable can be determined through sensitivity analysis.

Additional benefits of sensitivity analysis can include identification of unimportant variables and identification of variables or specific values that lead to high or low exposures (Mokhtari and Frey, 2004). The identification of unimportant variables can reduce the effort required in later analysis by identifying which variables do not need to be investigated.

Nominal range sensitivity analysis, also known as local or scaling sensitivity analysis, is one of these methods and was described earlier. Additionally, the correlation of inputs and an output of interest can be calculated using Spearman or Pearson correlation coefficients. The importance of the input variables can then be estimated by their strength of correlation with the output variable.

Additional methods of sensitivity analyses may be conducted to allow inputs to be varied simultaneously, run 2-stage analyses, or accommodate qualitative or categorical inputs. Two common approaches for this are stepwise regression and analysis of variance (ANOVA). A researcher could apply one or two of the screening sensitivity analyses on a model to determine the most important variables and then follow up with one of the additional techniques. Sobol's method of sensitivity analysis may also be a useful tool.

Uncertainty Analyses
Uncertainty analyses (2-stage model runs) can be used to achieve a number of goals.

1. Identify methods of reducing human exposure (taking into account the uncertainty of the inputs).
2. Directly address the usability of the model results by forming bounds on the population output, thus quantifying the spread among the variability distributions at specific percentiles.
3. Address the need to identify the inputs which introduce the greatest uncertainty into the model and therefore should receive additional study.

To conduct uncertainty analyses, SHEDS will be run for the simulation time frame using two-stage Monte Carlo probabilistic sampling, with M uncertainty runs each consisting of N simulated individuals (Xue et al., 2006). For the 2-stage Monte Carlo model runs, the SHEDS results for specific individuals will typically not be retained. Instead, on each iteration of the uncertainty loop, the results for each exposure or dose variable will be summarized by selected statistics before proceeding to the next iteration. Additionally, the specific values for each of the input parameters subject to uncertainty will be noted. At the end of the model run, the relationship between input parameters and the output statistics will be examined using correlation and/or multivariate statistical methods.

The 2-stage Monte Carlo runs produce *M* population variability distributions, along with *M* sets of input variable distributions. Collectively, these may be used to address two related issues. The first is the extent of spread among the variability distributions. This is often expressed as a range for given percentiles of the variability distribution. The second issue is to ascertain the relative influence of the various model inputs subject to uncertainty.

The results from the uncertainty runs may be analyzed as follows. To determine which model inputs contributed the most to uncertainty, a measure of central tendency for each input variable is computed, along with the corresponding statistic for absorbed dose, for each of the *M* uncertainty runs. Spearman and Pearson correlation coefficients will be computed between the dependent variable and each input variable; these will then be ranked to identify the most important contributors to uncertainty. In applying stepwise regression, the *M* numbers for each input and exposure or dose estimate will be used. The inputs are ranked in order of relative importance by their partial R^2 correlation coefficients.

The graphical analysis of uncertainty will take two forms. One involves displaying three complete variability distributions (CDFs), namely the variability distributions corresponding to the 5^{th}, 50^{th}, and 95^{th} percentile as ranked by their medians. The horizontal axis represents percentiles of the population variability. The vertical distances between the three curves represent uncertainty in each percentile of the variability distribution. The second type of graph displays three selected variability percentiles (the 5^{th}, 50^{th}, and 95^{th}) from each of the *M* uncertainty runs. Here the horizontal axis represents percentiles of the uncertainty distribution, while the vertical separation between the curves measures variability.

C1.2 Hardware/Software Assessments

Code will be independently checked and tested for each module by individuals other than the original programmer. These code checks will minimize coding and logic mistakes in the final model. Internal testing of SHEDS modules will include the following:

1) Either an independent read through or a group walk through will check that:
   a) the module matches the model design
   b) the module is significantly independent of other modules, where possible
   c) the module does not contain any logic errors
2) It will be verified that the comments:
   d) are clear
   e) describe the code in sufficient detail at the module level
   f) identify input parameters
   g) identify, at least by description, global variables expected or generated.

3) Where appropriate, the module will be tested with typical or specially designed datasets to insure proper functioning. This may often be in the context of a separate testing program that displays or evaluates the results.
4) The routine containing the implementation of the basic exposure equations will be confirmed by comparing the events output file with hand calculations for representative records, verifying exposure calculations under an appropriate range of conditions. SHEDS-Multimedia can maintain the detailed sequential data used for calculations so that these basic calculations can be evaluated.

Occasionally algorithms that are difficult to implement in one programming language may be programmed in another language to verify that the code is executing properly. When this is done model results will be verified using the two model codes.

C1.3 Hardware/Software Configuration Tests

Model beta-testing is used to verify that the model or model output satisfies the baseline requirements established prior to development of the model code and any requirements resulting from changes that have occurred over the life cycle of the code development. When a version of SHEDS that is intended to be used by a customer(s) is completed, the executable code will be given to the customer(s) and/or an independent contractor along with documentation, default input (test case) files, and example output for results comparison. The customer will also be asked to verify the model performance, provide input on the interface, record any problems setting up and running the model, and complete a brief questionnaire to assist model developers in finalizing the version to meet customer needs.

C1.4 Plans for Science and Product Peer Review

External review may occur in the forms of beta testing, formal scientific advisory panels, and peer review for scientific journal articles. These reviews will concentrate on the conceptual basis, model structure, data sources, and application of the model to specific case studies. Summary reports of the findings from external peer reviews will be supplied upon completion of these reviews for the current and future model development.

SHEDS-Multimedia version 4 is currently expected to undergo review at a Scientific Advisory Panel (SAP) in 2010. Past peer reviews of earlier versions of the model include assessments of the model algorithms by the NERL University Partnership Agreements peer consultation panel and an SAP review of Version 3 with the interface and documentation (http://www.epa.gov/heasd/risk/projects/c1b_exposure_models_development.htm; Zartarian et al., 2008; Stallings et al., 2008). Peer-reviewed journal articles will be published for chemical case-studies using the model.

C2 Reports to Management

- To provide essential feedback to management on the progress of the QA program, any pertinent QA/QC activities will be reported to the WA COR in the weekly meetings. The following issues will be addressed:

- Status of any major QA activities
- Corrective actions taken during the period
- Performance and systems audit results
- Significant changes in facilities, personnel, procedures, data processing, or reporting

D Data Validation and Usability

This section describes the steps needed to verify that SHEDS-Multimedia has been developed to meet the performance requirements through evaluation, testing, and corrective actions if needed.

D1 Departures from Validation Criteria

To verify that the model code meets its intended requirements and that the model design has been implemented correctly, independent checks will be conducted by scientists other than the SHEDS model developers and programmers. These independent reviewers will be informed of the intention of model algorithms and code through annotation within the SHEDS code as well as accompanying documentation.

Internal review and verification of SHEDS code will be conducted by the principal investigators as each new module is developed. Internal branch and division level audits of SHEDS-Multimedia will be conducted in accordance with the requirements in NERL's IIQMP. Additionally, this QAPP will be reviewed annually by the SHEDS PI to assure that it is current. This annual review will be documented by either new versions of the QAPP or a memo to the Division Quality Assurance Manager stating the current version of the QAPP has been reviewed and needs no update.

Checks will be performed on each method used in SHEDS described above: distribution fitting for input variables; sequential calculations of exposure for random individuals; probabilistic sampling to generate population estimates; sensitivity analyses; and uncertainty analyses.

D2 Validation Methods

SHEDS model results will be evaluated to the extent possible using available measurements data and predictions from other models. Where possible, individual components or modules of SHEDS will be compared to available measured or modeled data (e.g., dermal exposure estimates compared to dermal wipe measurements; modeled dietary estimates compared to duplicate diet measurements). Available biomonitoring data (e.g., metabolite excreted in urine) will be compared against the corresponding model predictions to evaluate aggregate or cumulative model estimates.

The output from SHEDS-Multimedia will be primarily characterized by the nature of the input parameters. If the inputs to the model are known values, the output data set from the model can be cross-checked with the output from the test run data to see if they match. On the other hand, if the input parameters are chosen from a probability distribution, then an exact match between model output data and the test run data is not expected. In such situations, a statistical match between the output data and the test data sets is the best possible outcome. Rather, comparisons between central tendency values, various percentiles, dispersion measures, and CDFs will be used to assess acceptability of the results. These tests can help explain the observed variations between the output and measured data.

D3 Reconciliation with User Requirements

The final step in quality assurance is acceptance testing. Following beta-testing of the model, modifications to the model may be needed to address user identified problems or comments/ suggestions. When these modifications have been completed and no further beta-testing is required, a final review of the inputs, functionality, and outputs of the model will be performed. A formal testing procedure will be developed that includes verification of all aspects of the model requirements. A model evaluation will be performed documenting that the model performs appropriately for all of the specified requirements and test procedures. All deviations from the requirements will be documented and corrected.

Any corrective actions required following the various testing steps described above will be documented as part of each testing procedure. Model developers will use this documentation and explore options for modifying the SHEDS model code to address each problem. If solutions are found and implemented, appropriate quality control procedures for code verification, calibration testing, model assessment, and configuration management will be performed on the revised model. If a solution is not implemented, then the problem will be documented in the model Release Notes.

E References

MacIntosh DL, Xue J, Ozkaynak H, Spengler JD, Ryan PB. 1995. A population-based exposure model for benzene. *J Exp Anal Environ Epidemiol* 5(3): 375-403.

McCurdy T, Glen G, Smith L, and Lakkadi Y. 2000. The National Exposure Research Laboratory's Consolidated Human Activity Database. *J Exp Anal Environ Epidem.* 10: 566-578.

Mokhtari A, and Frey HC. 2004. Evaluation of classification and regression trees for sensitivity analysis: case study for the E. Coli Food Safety Process Risk Model. Submitted to *International Journal of Food Microbiology.*

Sexton K and Ryan PB. 1998. Assessment of human exposure to air pollution: methods, measurements, and models, In: Air Pollution, the Automobile, and Public Health. National Academy Press, Washington, DC.

Stallings C., Zartarian V. G., Glen G.. (2008). SHEDS-Multimedia Model Version 3 User Guide. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/118.

US Census Bureau. 2001. Census 2000 Summary File 1, Technical Documentation.

US Census Bureau. 2002. Census 2000 Summary File 3, Technical Documentation.

US Census Bureau. 2003. Census 2000, Public Use Microdata Sample, (PUMS), United States. Technical Documentation.

US Department of Agriculture, Agricultural Research Service. 2000. Continuing Survey of Food Intakes by Individuals 1994-96, 1998. CD-ROM. (Available from USDA web site or NTIS)

US EPA. 1997. Exposure Factors Handbook. USEPA Office of Research and Development, National Center for Environmental Assessment, Washington Office, Washington, DC, EPA/600/P-95/002Fa.

US EPA. 2002a. Guidance for Quality Assurance Project Plans for Modeling. Document Control Number EPA/240/R-02/007. Office of Environmental Information, Washington, DC.

US EPA. 2002b. Integrated Information and Quality Management Plan (IIQMP) for the National Exposure Research Laboratory. Document Control Number NERL IIQMP No. 1. Research Triangle Park, NC.

US EPA. 2002c. Child-Specific Exposure Factors Handbook (Interim Report). USEPA Office of Research and Development, National Center for Environmental Assessment, Washington Office, Washington, DC, EPA-600-P-00-002B.

Xue J., Zartarian V., Ozkaynak H., Dang W., Glen G., Smith L., Stallings C., 2006. A Probabilistic Arsenic Exposure Assessment for Children Who Contact CCA-Treated Playsets and Decks, Part 2: Sensitivity and Uncertainty Analyses. *Risk Analysis* , 26(2): 533-541.

Zartarian VG, H Özkaynak, JM Burke, MJ Zufall, ML Rigas, and EJ Furtaw Jr. 2000. A modeling framework for estimating children's residential exposure and dose to chlorpyrifos via dermal residue contact and nondietary ingestion. *Environ Health Persp.* 108: 505-514.

Zartarian V.G., Xue J., Ozkaynak H.A., Dang W., Glen G., Smith L., Stallings C., 2005. "A Probabilistic Exposure Assessment for Children Who Contact CCA-treated Playsets and Decks Using the Stochastic Human Exposure and Dose Simulation Model for the Wood Preservative Scenario (SHEDS-WOOD)" Final Report. U.S. EPA. Washington, DC, EPA/600/X-05/009.

Zartarian, V. G., Glen G., Smith L., and Xue J. (2008). SHEDS-Multimedia Model Version 3 Technical Manual. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/118.