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Design of the Comprehensive Chemical Exposure Framework for American Chemistry Council

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Abstract

The purpose of this research is twofold: design an overarching framework that is comprehensive, logical, and useful for industrial needs; and within that framework identify research needs based on gap and sensitivity analyses. The overarching framework, called the Comprehensive Chemical Exposure Framework, will be used to house models, algorithms, and databases associated with micro-environmental exposure modeling. The research needs are defined for

representative high volume compounds that could be involved in home and work exposure scenarios defined specifically for this study. These exposure scenarios were used to guide the types of models, algorithms, and databases required to evaluate each scenario. Model and process flow diagrams were developed for each exposure scenario, and research gaps were identified based on publicly available information. Once the gap analysis was completed for the source, transport, exposure, and health impact components of each scenario, a qualitative sensitivity of the entire system was conducted. The Gap Analysis focused on reviewing the process flow diagrams that had been developed to properly evaluate each of the four example exposure scenarios to identify models, algorithms, and databases that were missing or unknown. This was done for the Source, Transport, Exposure, and Impacts components of the exposure scenarios. In some cases, models existed, but they were determined to be too simplistic or conservative and were considered a research gap. In these cases, alternative paths were explored to determine the type of model or algorithm required to fill the research gap. A qualitative Sensitivity Analysis was also performed on the models and algorithms identified for the various compounds and exposure scenarios.

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Comprehensive Chemical Exposure Framework

1.0 INTRODUCTION

There is a growing awareness in recent years that a person's exposure to particular chemicals occurs via multiple routes from multiple sources. To adequately evaluate such exposures, the scientific community requires models that can predict the occurrence of exposures for each potential combination of pathways and sources, and then accumulate these exposures over time. Ideally, the models will account for variations in people's activity patterns that are influenced by age, gender, occupation, and other demographic factors. These activity patterns should realistically simulate the movements of representative people through zones defined by geographic location and micro-environment.

Recently, the Food Quality Protection Act mandated that the exposure assessment community address the limitations of existing models and provide improved models that can be used to estimate exposures to agricultural-related compounds. Although exposure modeling on agricultural pesticides is clearly moving forward, there is also a pressing need for improved models to assess exposures to non-agricultural compounds. To this end, the American Chemistry Council has requested the design of a Comprehensive Chemical Exposure Framework (CCEF), which is intended to inform and advise the American Chemistry Council in its effort to identify, facilitate, and communicate generic research that will characterize people's exposure to chemicals, especially non-agricultural chemicals, and raise the confidence and lower the uncertainty for quantitative estimates of exposure associated with potential human health effect to chemicals.

The American Chemistry Council's Human Health Exposure Assessment Technical Implementaiton Panel funded this research, and Battelle Pacific Northwest Division and Battelle Columbus Operations staff conducted the work. This technical report is a final product of this research and is property of the American Chemistry Council. This report documents the design of the CCEF, research gaps in exposure modeling, algorithms, and data, and sensitivity of exposure results to specific models, processes, algorithms, and data.

1.1 Modeling and Framework Terminology

The overall design of the CCEF consists of developing framework requirements, architecture design, and data exchange protocols using a modular approach that allows users the flexibility to construct, combine, and couple attributes that meet their specific modeling needs. This allows a variety of models and databases to work within a single construct. There are various terms that need to be defined to help the reader understand the overall design of the CCEF documented in this report.

Framework

A *framework* typically consists of a set of modules that have been specified by the client, an associated *framework* user interface, and data exchange protocols. The purpose of a the framework is to:

- Minimize data-exchange requirements between modules in the *framework*
- Allow relatively easy inclusion of additional modules and models into the framework

- Allow for unlimited access to data
- Address linkage concerns for a variety of models.

The *framework* typically includes a user-friendly interface to enable the user to access these capabilities easily. Other terms that are often used in place of *framework* are 'system' and 'overarching architecture.'

Object

An object, in the context of this study, is a module, model, database, or algorithm that is associated with the CCEF. The Framework treats all these the same, as objects. An object reads data from other objects, processes that data, and writes out that data to other objects. In the case of a database, the data may not necessarily be processed. From the Framework's point of view, these objects are all the same and must follow the data exchange protocols associated with them.

Module

A *module* potentially contains three components: the user interface, the scientific model, and, for those frameworks that incorporate legacy models, pre-and/or post-processors. Examples of *modules* include source term releases, vadose zone transport, saturated zone transport, surface water transport, air transport, exposure pathway analysis, dose estimates, health impacts, and sensitivity/uncertainty support tools.

Model

A *model* is the set of scientific algorithms, calculations, and databases that define a particular module. Several models have been developed over the past 10 years by researchers focusing on developing fully integrated, multi-media, multi-pathway, multi-route modules that allow a more transparent connection between individual medium-specific *models*. The grouping of these models takes a holistic approach to environmental assessment of potential contaminant impacts as they simulate:

1. Release of contaminants into the environment
2. Transport and fate through various environmental media (i.e., groundwater, surface water, air, and overland surfaces)
3. Resultant exposures and impacts to an organism
4. Support tools such as sensitivity, uncertainty, graphical interface systems, and displaying results.

Module User Interface

The purpose of the module user interface is to make it easy for the user to collect the data necessary to run the model. Besides gathering the necessary data, the *module user interface* often provides online help to the user, reference storage options for collected data, flexible unit inputs, and other user support functions.

Module Pre/Post-Processors

As mentioned earlier, time and cost are saved if models can be integrated into a framework intact. Legacy models that have been tested and reviewed can be preserved and integrated by the addition of *pre- and/or post-processors* to the module. These processors transfer reorganized data into the specified format of the overall framework, thus allowing the inclusion of models that were initially created for a media-specific analysis to be used in this more holistic approach to multiple media assessments. Whether a *pre/post-processor* is used depends on the needs of the scientific model and the data exchange protocols of the framework. Models that have been created or modified with the data exchange protocols predefined will likely not need *pre/post-processors* before integration.

Overall Design of Comprehensive Chemical Exposure Framework (CCEF)

Framework attributes for micro-environmental exposure modeling vary depending on the needs of the research area. The problem set and client needs will define the requirements, design, and data exchange protocols for a framework. This section will provide a brief definition and purpose of the framework requirements, design, and data exchange protocols.

Framework Requirements

A project starts with the definition of the research needs. What problem or problems must be solved? What kinds of information are needed? Who are the ultimate users and how can the framework best meet their needs? This definition begins with the analysis of the needs, a definition of the functional components of hardware and software, and packaging of the information. The requirements analysis is based on communication with the client and needs of the research area of interest and produces a set of requirements for the framework that describe what the software should do.

The information in the requirements package should, at a minimum, answer the following questions:

- Which capabilities have been discussed with the client and research area of interest?
- What additional capabilities are necessary to produce a quality product?
- What specific restrictions have been noted?
- What potential difficulties have been identified?
- What compatibilities are necessary for usability?

Specific requirements for a framework include:

- Data exchange protocol needs
- Mathematical algorithms and formulations
- Necessary help information
- Identification of ways to ensure a consistent look and feel with related interfaces
- Expected deliverables for the task.

Framework Design

If the requirements of a framework describe what the software should do, the framework design describes how the software will implement the stated requirements. Design of a framework cannot start until a set of requirements has been developed. Usually an initial set of requirements is developed and then a design is implemented based on those requirements. In almost all cases, issues will arise during the design process that will require changes to the requirements. In this way the definition of requirements and design is an iterative process. In many cases, design will include prototyping of software to provide an early look at the software and its functionality.

Data Exchange Protocols

Before a framework is designed, the appropriate databases and the file structures of the input and output for the framework and modules must be defined. Module file structure should be consistent with the framework's *data exchange protocols*. Pre/post-processors may be used to aid in the conversion of legacy code file formats not already meeting those *data exchange protocols*. All file formats should be designed to ensure readability and compatibility with most spreadsheet programs, and to incorporate necessary information to communicate the use and purpose of each file.

1.2 Modeling Background

Within this document, the term "model" will refer to the software codes inside the Framework, and the Framework will represent the overall structure linking the models and databases to allow for a seamless transfer of data between components.

To meet the current and future intent of the CCEF, as stated by the requirements, six development goals will be considered when formulating the design of the CCEF:

1. *Provide a platform that allows "objects" to access information generated/produced by other "objects."* For example, a model or database produces a set of data for consumption by another model. The downstream model accesses the information it needs and expects from the upstream model or database, but it does not

have to accept all of the information. There is no requirement on the consuming model to utilize all of the information that is made available to it. A consuming model should not have to consume information that it does not use.

2. *Keep it simple, not simplistic.* By definition, simple means "easy to understand, deal with, use, etc" (Barnhart 1970). Simplistic refers to "making complex problems unrealistically simple" (Guralnik 1976). One of the major problems associated with other frameworks that never became deployable is that they could not capture the essence of the problem that they were trying to solve. The elegance of a simple design is that it captures the essence of the problem without burdening the user with unnecessary extraneous information or components.

3. *Make it understandable (shared responsibility).* A simple design allows for the developers and users to understand the design and structure of the framework. Not only that, but to maximize the ability for two disparate components to seamlessly communicate, each component must share in the responsibility for communication. For example, who should be charged with transferring information from a database to a model: the database owner (i.e., information producer) or the model owner (information consumer)? It is not the responsibility of the model owner to understand the structure of the database; likewise, it is not the database owner's responsibility to understand the model that is consuming the data. Therefore, each owner must share some of the burden to ensure that the appropriate data are transferred to the model in a form that the model understands. This philosophy is applicable for communication between all types of components (e.g., models, databases, and other frameworks).

4. *Develop consistent and repeatable protocols.* By developing a conceptual consistency in the design of the system, the design of the framework is more easily understood by those who use it. For example, all databases should link to models in the same manner. In addition, since models, databases, and other frameworks can be considered "objects" in this system, the conceptual philosophy for linking any object should be similar. By developing repeatable protocols, software developed for one aspect of the system can by reused to support other aspects of the system. Reusing the same software results in a simpler QA/QC program, easier maintenance, and more universal trouble shooting, as one fix corrects many problems.

5. *Identify the MINIMUM linkage information.* All models have been developed to solve specific problems in certain way, regardless of how generic the models are. As such, each model requires "typical" and "unique" data. Typical data include information expected from an upstream model or from a database. Unique data tends to be user supplied and tends to be unique to that model. For example, an atmospheric model may expect emission rates from a source-term model, joint frequency distributions, and the number and types of surface disturbances from the user. When linking to an upstream model, a minimum set of information is traditionally expected to be made available by that upstream model. If the two models want to communicate, they must agree as to what that minimum set is because neither model wants to have to produce or consume unnecessary information that is irrelevant to its design. Focusing on the truly relevant data requirements helps to ensure a higher probability that two models will be able to communicate.

6. *Recognize that this is an iterative process to meet these goals.* A well-designed framework will have the ability to solve today's problems, yet contain the flexibility and robustness to be modified to address future problems. This is not to say that the framework needs to include unnecessary components, but the design should contain the structure to allow it to be modified to account for new models, new data, new parameters, etc., yet maintain backward compatibility for the components existing in the system. Each problem requires a unique solution; therefore, the framework needs a design that expects change.

1.3 Framework Background

The world is traditionally compartmentalized with the flow of information from compartment to compartment. The basic conceptualization of the problem begins with a flow of information from beginning to end. If this happens to be over the "life cycle" of a 1) a person (e.g., conception to death), 2) a process (e.g., production life cycle), 3) an activity (e.g., certain job type), and 4) a compound (e.g., traditional U.S. Environmental Protection Agency risk assessment), a beginning and end can be defined, and, hence, a flow diagram can be constructed to link the individual components. Each of the "life cycles" listed above represents, in effect, types of frameworks. To capture the structural relationship among the principle components required in estimating human exposure to chemicals, multiple frameworks, representing existing legacy software, may need to be linked to provide the most scientifically defensible picture of the impacts to non-agricultural chemical exposure. Because the real world is compartmentalized, each of these life cycles are also compartmentalized, meaning that the

various life cycles can be linked to address the demanding questions associated with the identification, facilitation, and communication of generic research that will characterize people's exposure to chemicals and raise the confidence and lower the uncertainty for quantitative estimates of exposure associated with potential human effects to chemicals.

An abstract view of these various life-cycle "ribbons" is illustrated in Figure 1.3. Each of these framework ribbons represents a flow of information from the beginning to the end of an assessment. The Life-Form ribbon could represent micro-environmental modeling. The Compound ribbons could represent the standard U.S. Environmental Protection Agency fate & transport risk assessment paradigm for two different compounds, and where the Compound ribbons cross the life-form ribbon (i.e., black dots), data are transferred. When there is no intersection and no data are transferred between ribbons, then black dots do not appear at the interaction points. A similar case can be made for the Activity and Process framework ribbons, if applicable.

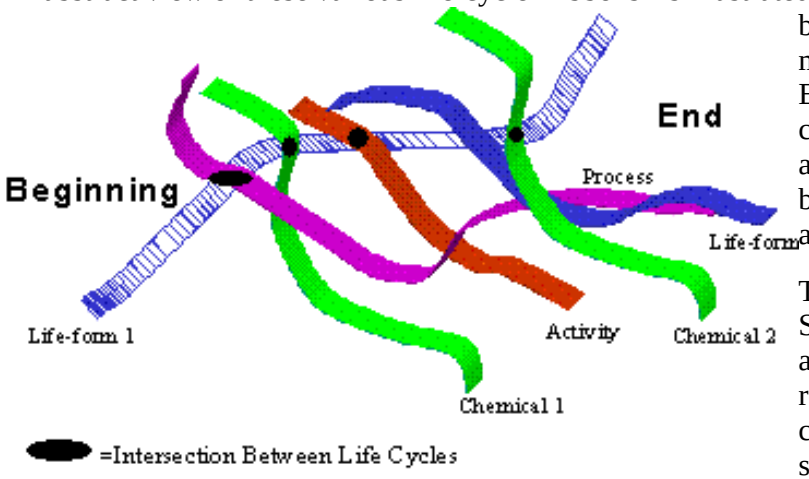


Figure 1.3 Abstract Example of the Linkage Between Different Types of Framework Life- Cycle Ribbons

To meet this requirement for current and future situations, the CCEF design needs to have a System User Interface that is flexible enough to capture not only the current linkages of models and databases but also other frameworks (i.e., ribbons in figure) that provide the essence of relationships in general. These linkages need to be visual so the analyst can immediately construct and understand the problem. A visual interface is also very effective in conveying simulation results to various stakeholders.

A software framework integrates the different components of a modeling system to provide a consistent and efficient architecture to conduct scientific research and analyses. The components of a framework are 1) a user interface, 2) module and model types, and 3) system databases. This section will discuss the different aspect of these framework components.

1.3.1 System User Interface

The conceptualization of the problem is the conceptual site model, which represents the analyst's understanding of the problem, problem components, spatial relationships, and flow of information among components. The real world is very complicated and the traditional way to approximate the real world is to simplify and compartmentalize it into more manageable "pieces." These generally represent what we understand, tending to group all of the things that we do not know or understand into a selected group of parameters; hence, our conceptualization of the real world tends to be a function of what we know and understand. The intent of the CCEF is to design a framework that allows this conceptualization to change and grow more sophisticated as our understanding of the real world grows, so we may more accurately estimate the impacts associated with our anthropogenic activities.

The most effective interfaces, which are currently being used to help construct a conceptual site model, use a drag & drop approach on a workspace. Drag & drop is where a user double clicks on icons contained in an icon pallet, the selected icons appear on the work space, icons are rearranged and connected according to the flow of information (i.e., lines with arrows, indicating the direction of data flow), and the user chooses the most appropriate model from a list of models that represent the icon. This type of approach is fairly common and used by a number of successful frameworks (e.g., Stella, FRAMES, MMS, ARAMS, and GoldSim). The following figure illustrates the drag & drop work space for FRAMES (Whelan and Nicholson 2001).

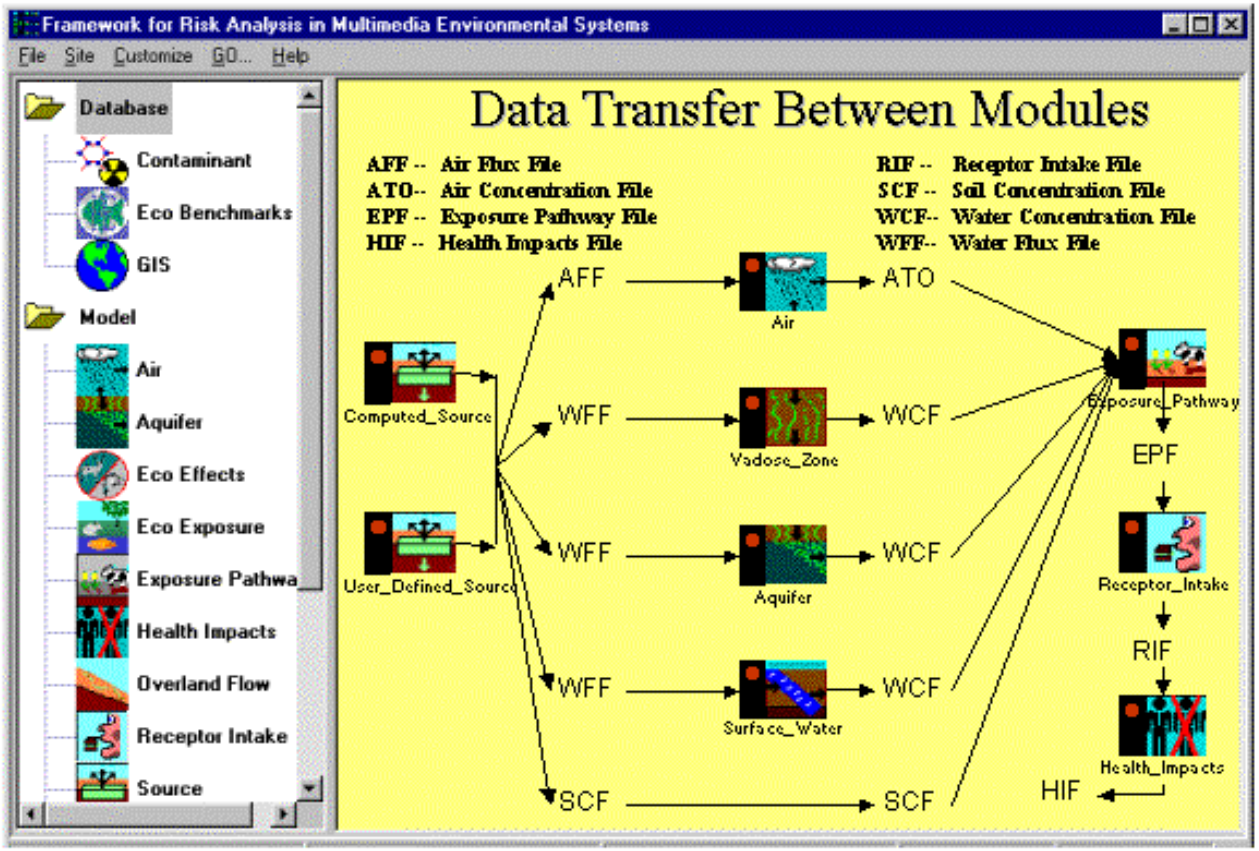


Figure 1.3.1 Schematic Illustrating the Linkage of Models in FRAMES, Using Its Drag & Drop System User Interface

With the Drag & Drop feature, the user will have an icon pallet from which to choose their modeling categories, which contain the choice of models. The user will have the ability to expand the icon pallet to include new types of models, databases, system supported software, or unique categories. The icon pallet will also be tiered, so intricate divisions in simulations can be captured. For example in transport and fate, surface water modeling can be divided into rivers, lakes, reservoirs, estuaries, bays, oceans, etc. Exposure route modeling can be divided into inhalation, oral, and dermal contact. The icons and icon categories can be changed to meet whatever need is identified. Typical icon categories for the standard EPA risk assessment paradigm is presented in Table 1.3.1 (pdf format). Micro-environmental modeling would have a separate Domain associated with it, as such it would have its own Classes, Groups, and SubGroups.

1.3.2Model vs. Module

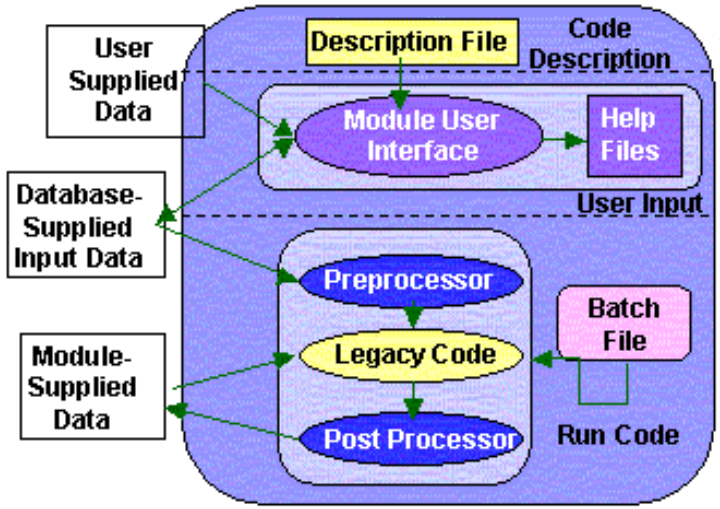
A model or code is the mathematical representation of a process, device, or concept (Sippl and Sippl 1980) coded into a computer language for execution on a computer, which is consistent with current preconceived notions of what a model is intended to represent.

A module consists of a model description, module user interface (i.e., input), and the execution code (i.e., run model), which contains pre- and post-processors for converting the models input/output for recognition by the model/system. The following figure illustrates these three basic components of a module.

The code description provides what the model is, who you should contact for questions, what information it consumes and produces, the connection schemes with other models that it allows, how the model fits into the system and how it should be perceived of by the system.

Figure 1.3.2 shows that the Module User Interface, input files, and executable are separate from each other. By separating these, any Module User Interface

Figure 1.3.2 Design of a Module



associated with a legacy code can remain unchanged, so the user will see no change from expectations developed when they used the original code outside of the framework. The input may come from the user, which is traditionally associated with the Module User Interface, database(s), and upstream models supplying boundary conditions. By distinctly separating the input from the executable, sensitivity/uncertainty analyses on the input data is possible. As such, batch files can be established for multiple runs. Finally, the execution code is represented by the legacy code and its pre- and post-processors. The pre-processor converts the input data that the system recognizes into a format that the model recognizes, while the post-processor converts the model output into the standardized system format.

1.3.3 System Databases

Specific databases would be available for user choice, as multiple databases may be required to meet the needs of a model. Upstream data are accessed by down stream connections in the conceptual site model (i.e., an inherent priority is built into the system), and all of the linkage protocols establish procedures to "access" executables and files containing data. Because the conceptual site model is only a vehicle for communication, the modules require information to complete datasets, which may be fulfilled by multiple databases; as such, the icons are linked to databases to complete a dataset, although the dataset may only be partially completed with the available databases.

The user would have the option of listing modules by alphabetical order or by conceptual site model sequencing. For example, under the Chemical Life Cycle paradigm, the modules are sequenced and grouped by source, fate and transport, and human exposure/intake/effects, which follows the intuitive conceptual site model development structure. Also, when viewing the conceptual site model, the user would have the option of hiding the connections between the Database icons and Simulation Modules, to help reduce the number of connecting lines that would be on the conceptual site model screen. The connections would still be there, only the user could choose to not show them.

2.0 CCEF Literature Review

This section provides a description of how the literature search was conducted and its results, as well as a discussion of how the specific compounds were selected for the exposure scenarios. This literature review was not meant to be exhaustive but to be a general search of current research and models in this area. The review was done mainly via the Internet, and only publicly available items were included. The focus was on Frameworks, Models, Algorithms, and Databases. Where ever possible, hyperlinks are provided, along with a purpose and description of the object being reviewed.

2.1 Models and Databases Lists and Descriptions

This section provides a general review of models, databases, and algorithms that are readily available via the Internet. The review included all types of models, databases, and algorithms required for detailed micro-environmental modeling. The following section (Section 2.2 - Exposure and Impact Review) provides a detailed review of Models and Databases associated with Exposure and Impact Components of the CCEF.

The list of Models and Databases considered for the four scenarios is found below.

Models

Table 2.1.1 Framework Risk Assessment and Methods					
3MRA	APAC	ARAMS	CEAM	ChemScreen	DIAS
FRAMES	GoldSim	HWIR	LifeLine	MENTOR	MIMS
MMS	Multi-domain Framework for Integrating Models and Measurements of Multimedia Environmental Contaminants				
SEDSS	SHEDs	TEAHRS	THERdbASE	TNRCC	TRIM

Table 2.1.2 Source, Fate & Transport					
ADORA	CALMET	CALPUFF	CARES	CFAST	COMIS
CONSEXPO	CONTAMW	E-FAST	EPI Suite	EXAMS	FIRIN/FIRAC
GASFLOW	GEMS	GENII	HARVARD VI	HGSYSTEM	IA-NBC-HMAS
IAQX	INPUFF	MCCEM	MEPAS	MMSOILS	Models-3/CMAQ
OBODM	pNEM	PRESTO	PROMISE	RESRAD	RISK
SCIPUFF	SES	WPEM			

Table 2.1.3 Exposure and Impacts (including toxicity models)					
BDBR models (numerous)	CalTOX	ChemSTEER	Cleek and Bunge	CPIEM	E-FAST
GEMS	GENII	HPV	IA-NBC-HMAS	IEUBK	MEPAS
MMSOILS	Modeling Benzene Exposures and Absorbed Dose		Modeling Dietary Exposures to Heavy Metals and Pesticides		MTHEM
PBPD (numerous)	PBPK (numerous chemical and route specific models)		QSAR models	ReachScan	REHEX - II
RESRAD	RISC	RISK	TEM	Thongsinthusak	UCSS

Databases

Table 2.1.4 Databases					
AHS	ATW	CARB	CHAD	Cohne Hubal, et al. (children's exposure and microenvironment data)	CPDB
CSFII	DEPM	EPA's Child-Specific Exposure Factors Handbook		EPA's Exposure Factors Handbook	HazDat
ITER	IRIS	NCHS data (e.g., birth records)		NHANES NHAPS	NHEXAS
NHGPUS	OEHHA Toxicity Criteria Database	RAIS		RTECS® SRD	
Superfund resource center	TOMES	TOXNET (includes several toxicity databases)		US Census	USEPA

Descriptions of Models and Databases listed in ACC Project Scope of Work

Framework Risk Assessment and Methods

3MRA - Multimedia, Multi-pathway, Multi-receptor Exposure and Risk Assessment:
A risk-based strategy was developed to generate constituent-specific exemption levels for low- risk solid wastes as part of USEPA's Hazardous Waste Identification Rule (HWIR). The 3MRA framework is designed to perform multiple site-based risk assessments by considering the various types of land-based waste management units as the source of contaminants and computes the exposures and the resulting national-scale statistical distributions of human and ecological risks. The regional site-based risk assessments are conducted with an Ni ^ Nf realizations of exposure scenarios, where Ni is the number of Monte-Carlo iterations and Nf is the number of sampled facilities associated with that type of waste management unit.

In each Monte-Carlo realization, fate-and-transport and exposure-and-risk analyses are conducted for the human and ecological receptors at a given site. For a given chemical and a given waste management unit type, the process is repeated for a number of concentrations in the waste of the chemical within the possible chemical concentration range. The methodology is an extension of a regional site-based approach, which accounts directly for correlations between model parameters and utilizes data from actual waste sites across the U.S. The methodology is highly flexible and allows the aggregation of nationwide distributions of risks and the uncertainty in the risks. The querying of risk results yields the regulatory exemption levels based on several types of protection criteria.

A two-dimensional Monte-Carlo simulation procedure is utilized which allows the separation of variability and uncertainty in the risk assessment and the quantification of uncertainty associated with the estimates of protection measures. The results of the Monte-Carlo simulations are compiled in the forms of risk matrices that are queried to determine regulatory exemption levels that meet specified protection levels with specified levels of confidence. Preliminary risk calculations based on a selected pathway (groundwater) are discussed. (Saleem, et al., 1999)
http://www.epa.gov/

APAC, a DOE sponsored program, developed a very detailed analysis of the technical strengths/weaknesses of computer models for the following 6 areas of consequence assessment: chemical & radiological source term generation, fire analysis (inside and outside), in-facility transport, ex-facility chemical transport, ex-facility radiological transport, and energetic events (e.g. explosions, deflagrations, etc.). Many of these groups, including ex-facility chemical, evaluated and compared the codes against test problems. Hundreds of chemical dispersion codes were screened and 23 were evaluated with 13 of the codes involved in test problem evaluation (CALPUFF and INPUFF included).

ARAMS - Army Risk Assessment Modeling System:

ARAMS is based on a widely accepted risk paradigm that integrates exposure and effects assessments to characterize risk. ARAMS is a computer-based decision support system that integrates multimedia fate/transport, exposure, intake/uptake, and the effect of military relevant compounds, explosives, and depleted uranium to assess human and ecological probabilistic risks. ARAMS incorporates various existing databases and models for exposure, intake/update, and effects (health impacts) into a conceptual site modeling framework. With ARAMS, the user has the flexibility to visually specify, through objects, multimedia pathways and risk scenarios. Also, the user can choose which particular model or database to use for each object. Thus, the heart of ARAMS is the object-oriented Conceptual Site Model (CSM). The CSM is based on the Framework for Risk Analysis in Multimedia Environmental Systems (FRAMES) developed by Pacific Northwest National Laboratory (PNNL) of the U.S. Department of Energy (DOE) in cooperation with the U.S. Environmental Protection Agency (EPA).
http://www.wes.army.mil/el/arams/intro.html

CEAM:
Environmental Protection Agency's (EPA) Center for Exposure Assessment Modeling **(CEAM)** (part of Office of Research and Development) CEAM distributes environmental simulation models and databases for urban and rural nonpoint sources, conventional and toxic pollution of streams, lakes and estuaries, tidal hydrodynamics, geochemical equilibrium, and aquatic food chain bioaccumulation. The most relevant models for exposure work are:

- Exposure Analysis Modeling System **(EXAMS)**: evaluates the fate, transport, and exposure concentrations of synthetic organic chemicals.
- Framework for Risk Analysis in Multimedia Environmental Systems **(FRAMES)**, Hazardous Waste Identification Rule **(HWIR)** model: screening-level risk-based assessment of potential human and ecological health risks resulting from long term (chronic) exposure to HWIR chemicals released from land-based waste management units (WMUs) containing currently listed waste streams.
- Multimedia Contaminant Fate, Transport, and Exposure Model (**MMSOILS**) estimates the human exposure and health risk associated with releases of contamination from hazardous waste sites.

http://www.epa.gov/ceampubl/
EPA National Exposure Research Laboratory, Atmospheric Science Modeling Division .
http://www.epa.gov/asmdnerl/modeling.html

DIAS - Dynamic Information Architecture System:
DIAS is a software framework intended to facilitate the holistic management of information processes, including the construction of federation simulations from component models according to a user-supplied context. These processes are modeled in DIAS as interrelated actions caused by and affecting the collection of diverse objects - which may range from abstract concepts represented by a simulation, through data sets to real world objects, and to input from simulators. The domain of DIAS is flexible, determined by the objects available within DIAS and by the collection of models and other data processing applications which have been gathered by users to address specific information processing concerns.
http://www.dis.anl.gov/DEEM/DIAS/diaswp.html

FRAMES - Framework for Risk Analysis in Multimedia Environmental Systems:
The FRAMES software was created with many features to aid the user in conducting assessments. These features serve to enhance the user's interaction with the underlying scientific models used in many assessments. Included in these features are items such as a pictorial depiction of the Conceptual Site Model to ensure the transfer of the user's idea of the analysis flow of contamination to the modeling scenario correctly. The drag-and-drop environment enables the user to quickly diagram a contaminant flow and, therefore, communicate that image to others (i.e. stakeholders, clients, and other assessment team members). Another timesaving feature is the use of online help. FRAMES has the ability to encompass many different environmental models.

A feature designed to aid in quick results assessment and document preparation is the ability to graphically view data at multiple points throughout the analysis. The FRAMES software has been modularized based on media to allow users to view data before and after each media of interest. The FRAMES platform is a key tool that can be used effectively to analyze environmental contaminant scenarios, benchmark models, and communicate scenarios and results to decision-makers, regulators, and the public. (Gelston, et al., 1998)
http://mepas.pnl.gov:2080/earth/

GoldSim:
GoldSim is a powerful and flexible platform for visualizing and dynamically simulating nearly any kind of physical, financial or organizational system. This software offers the power, flexibility and usability necessary to efficiently deal with the complex issues associated with real-world systems. In this sense, real world systems a) involve multiple interacting components and sub-systems, b) are uncertain, and c) include both continuous (gradual) processes and discrete (sudden) events.

The unique capabilities of GoldSim make it an ideal simulation tool for a wide variety of real-world applications such as Strategic Planning, Portfolio Management, Program Planning, Risk Management, Supply Chain Management, Environmental Modeling, and Engineered Systems Modeling.
http://www.goldsim.com/home/home.asp

HWIR - Hazardous Waste Identification Rule:
The Framework for Risk Analysis in Multimedia Environmental Systems (FRAMES), Hazardous Waste Identification Rule (HWIR) technology provides the ability to conduct screening-level risk-based assessment of potential human and ecological health risks resulting from long term (chronic) exposure to HWIR chemicals released from land-based waste management units (WMUs) containing currently listed waste streams. The FRAMES-HWIR model system consists of a series of components within a system framework.

LifeLine ™, Risk*Assessment, Risk*Works:
Three software packages that model exposures to a defined person as they travel through various microenvironments, accounting for 100% of a set determined timeframe. Developed by The LifeLine Group, LifeLine™ is used to determine the aggregate and cumulative doses occurring from agricultural exposures in the home and yard (emphasis on pesticides).
http://www.hrilifeline.org/

MENTOR:
Modeling Environment for Total Risk studies is a framework for the conceptual/theoretical formulation for exposure and dose assessments presented by Georgopoulos and Lioy (1994), and built on EDMAS (Exposure and Dose Modeling and Analysis System) developed at EOHSI.
http://eohsi.rutgers.edu/decm/EMA/

MIMS - Multimedia Integrated Modeling System:
The MIMS project is a problem solving software framework to support ecosystem modeling and environmental health assessment.
http://www.epa.gov/asmdnerl/mims/
http://www.epa.gov/asmdnerl/models3/

MMS - Modular Modeling System:
A Modeling Framework for Multidisciplinary Research and Operational Applications, MMS is developed to enable a user to selectively couple the most appropriate process algorithms from applicable models to create an "optimal" model for the desired application. Where existing algorithms are not appropriate, new algorithms can be developed and easily added to the system. This modular approach to model development and application provides a flexible method for identifying the most appropriate modeling approaches given a specific set of user needs and constraints.
http://wwwbrr.cr.usgs.gov/projects/SW_precip_runoff/mms/

Multi-domain Framework for Integrating Models and Measurements of Multimedia Environmental Contaminants:
Multi-domain Framework for Integrating Models and Measurements of Multimedia Environmental Contaminants is a LBNL work, EPA sponsored. The goal of this project is to develop and apply models to provide a more complete picture of both how human exposure comes about and how precisely it can be quantified for a number of important pollutants. These efforts are being organized around two research components: (1) an indoor/outdoor model for total human exposure to particulate matter (PM); and (2) the development and evaluation of source-to-dose models for persistent pollutants. (T.E. McKone , W.J. Fisk, A.T. Hodgson, R.G. Sextro)

SEDSS - Sandia Environmental Decision Support System:
SEDSS is a tool for decision-makers that provides a basis for quantitative analyses in support of qualitative questions such as "Is the monitor well network adequate?", "How many samples are enough?" etc.
http://www.nwer.sandia.gov/sedss/smeth.html

SHEDs - Stochastic Human Exposure and Dose Simulation:
A physically based stochastic model, SHEDS has been developed to estimate pesticide exposure and dose to children via dermal residue contact and non-dietary ingestion. Time-location-activity data are sampled from national survey results to generate a population of simulated children. For each child, a sequence of 5 second object contact events is generated probabilistically for every location-activity combination, yielding sequential micro-level activity profiles. These profiles are combined with probability distributions for surface concentrations and exposure factors (e.g., pesticide transfer and removal efficiency, skin surface area contacted) to yield daily time profiles for dermal loading, body burden, and eliminated pesticide metabolite. Population estimates are then generated via Monte Carlo sampling. The SHEDS model has been applied for children aged 0-4 and 5-9 years for six chlorpyrifos application scenarios: broadcast and crack and crevice methods; <1 day, 1-7 day, and 8-30 days post-application. Diary data for 1096 children from the National Human Activity Pattern Survey were combined with videotaped activity data and probability distributions for measured concentrations and exposure factors (based on a literature review). For each application scenario and age group, population estimates of daily eliminated 3,5,6-trichloro-2-pyridinol (TCP), the urinary metabolite of chlorpyrifos, were generated. These modeled results are comparable to measured results from EPA's National Human Exposure Assessment Survey and other studies following broadcast and crack and crevice applications of chlorpyrifos.
http://www.riskworld.com/Abstract/1999/SRAam99/ab9ab373.htm

TEAHRS:
The aim of the TEAHRS project is to develop and assess methodologies to determine the acute toxicity of inhalation of fluctuating concentrations of hazardous substances as a contribution to the improvement of quantitative risk assessment.
http://www.risoe.dk/rispubl/SYS/ris-r-1208.htm

THERdbASE - Total Human Exposure Risk database and Advanced Simulation Environment:
The THERdbASE is an integrated database and analytical/modeling software system for use in exposure assessment calculations and studies. THERdbASE was developed to provide a collection of frequently used databases and models related to human exposure assessment all in a single software system. Models are conveniently linked to databases, or queried subsets of data, on human activity patterns, U.S. Census data, and related human exposure databases so that an assessment or analysis can be conveniently run.
http://www.epa.gov/nerlesd1/therd/therd-home.htm

TNRCC:
Texas Natural Resources Conservation Commission (TNRCC) model guidelines.
http://www.tnrcc.state.tx.us/permitting/trrp.htm

TRIM - Total Risk Integrated Methodology:
EPA project to develop models and data for assessing the multimedia residual health and ecological risk from pollutants released to air sheds.
http://www.pestlaw.com/calendar/1998/EPA-19980407A.html

Source, Fate & Transport

ADORA is a unique source characterization and dispersion model for extremely hazardous chemicals in the atmosphere. Existing atmospheric dispersion models do not treat the chemical reactions and thermodynamics satisfactorily. In ADORA, the source characterization for various release scenarios, reacting puff spreading, lift-off and rise, and transient dispersion under practical meteorological conditions are modeled based on engineering principles. The complex interactions of buoyant/heavy cloud turbulent dynamics, multi-phase thermodynamics, and multi-step chemical reactions for various pollutants are included. The accurate treatment of these processes allows the application of the model to realistic release scenarios without being too conservative.

CALMET:
The CALPUFF Modeling System is composed of three basic components: CALMET, CALPUFF, and CALPOST. CALMET includes a diagnostic wind field model containing objective analyses and parameterized treatments of slope flows, valley flows, terrain blocking effects, and kinematic terrain effects, lake and sea breeze circulations, and a divergence minimization procedure. An energy-balance scheme is used to compute sensible and latent heat fluxes and turbulence parameters over land surfaces. A profile method is used over water. CALMET contains interfaces to prognostic meteorological models such as the Penn State/NCAR Mesoscale Model. CALMET was modified to enable use of vertical profiles of wind and temperature as characterized by the MM4-FDDA (Mesoscale Model-4 with Four-Dimensional Data Assimilation) meteorological model.

CALPUFF:
CALPUFF is a multi-layer, multi-species non-steady-state puff dispersion modeling that simulates the effects of time-and space-varying meteorological conditions on pollutant transport, transformation, and removal. CALPUFF is intended for use on scales from tens of meters from a source to hundreds of kilometers. It includes algorithms for near-field effects such as building downwash, transitional buoyant and momentum plume rise, partial plume penetration, subgrid scale terrain and coastal interactions effects, and terrain impingement, as well as longer-range effects such as pollutant removal due to wet scavenging and dry deposition, chemical transformation, vertical wind shear, over-water transport, plume fumigation, and visibility effects of particulate matter concentrations.

CALPUFF is appropriate for long-range transport (source-receptor distances of 50km to 200km) of emissions from point, volume, area, and line sources. The meteorological input data should be fully characterized with time-and-space-varying three dimensional wind and meteorological conditions using CALMET. The meteorological fields used by CALPUFF are produced by the CALMET meteorological model.

The CALPUFF modeling system has 3 main components: CALMET (a diagnostic 3-D meteorological model), CALPUFF (the transport and dispersion model), and CALPOST (a postprocessing package). Each of these programs has a graphical user interface (GUI). In addition to these components, there are several other processors that may be used to prepare geophysical (land use and terrain) data in many standard formats, meteorological data (surface, upper air, precipitation, and buoy data), and interfaces to other models such as the Penn State/NCAR Mesoscale Model (MM5).

CalTOX - Soil Model:
CalTOX is an innovative spreadsheet model that relates the concentration of an organic chemical in soil to the risk of an adverse health effect for a person living or working on or near the contaminated soil. It computes site-specific health-based soil clean-up concentrations given target risk levels or human health risks given soil concentrations at the site.
http://www.ntis.gov/fcpc/cpn6462.htm

CARES™:
Residential exposure assessment module currently under development by the American Crop Protection Association and infoscientific.com, Inc. with input from a variety of stakeholders. Cumulative and Aggregate Risk Evaluation System (CARES™) will be developed and deployed through a cooperative effort of stakeholders, including government, industry, and environmental groups. CARES™ will utilize currently accepted and other relevant databases to evaluate potential risk from dietary, drinking water, and residential sources. Risks will be calculated deterministically for Tier 1 screening and probabilistically using Monte-Carlo simulation of individuals for higher tier analyses. CARES will allow users to estimate doses and risks from acute, short term, intermediate duration, and lifetime exposures.

http://infoscientific.com/files/concept.pdf
http://alphacares.org/index.htm

CFAST:
CFAST is a zone model capable of predicting the environment in a multi-compartment structure subjected to a fire. It calculates the time-evolving distribution of smoke and fire gases and the temperature throughout a building during a user-specified fire. CFAST is the result of a merger of ideas that came out of the FAST and the CCFM.VENTS development projects at NIST. The organization of the CFAST suite of programs is thus a combination of the two models. Details of the models including algorithm structure, the physics-based equations, assumptions, and variables descriptions are provided in such a way as to permit modification and tailoring of the program to indoor chemical exposure assessment. With this level of detail, researchers not intimately involved in the development of CFAST should be able to add to the model in a straightforward manner. Independent or cooperative efforts to enhance the capabilities of the model are encouraged. Model developers can use this version of the model for open or proprietary additions to the model or as the basis for new models. CFAST is a member of a class of models referred to as zone or finite element models. This means that each room is divided into a small number of volumes (called layers), each of which is assumed to be internally uniform. CFAST is based on solving a set of equations that predict state variables (pressure, temperature and so on) based on the enthalpy and mass flux over small increments of time. These equations are derived from the conservation equations for energy mass, and momentum, and the ideal gas law. Although it may not be all-inclusive, CFAST has demonstrated the ability to make reasonably good predictions. Also, it has been subject to close scrutiny to insure its correctness. Thus it forms a prototype for what constitutes a reasonable approach to modeling fire growth and the spread of smoke and toxic gases.
http://fast.nist.gov/

ChemScreen:
ChemScreen Risk Assessment Software is based on the US Environmental Protection Agency's RMP Offsite Consequence Analysis Guidance document, dated 24 May 1996. The objective of the program is to provide the user with an initial assessment of offsite consequences resulting from the worst-case release of 40 CFR Part 68 specified chemicals.

Cleek and Bunge:
Cleek and Bunge (1993) developed a model to estimate dermal absorption from infinite dose aqueous solutions; very simplified mathematical model with some QSAR capabilities. (White Paper HHEA-3)

COMIS:
COMIS models the air flow and contaminant distributions in buildings. The program can simulate several key components influencing air flow: cracks, ducts, duct fittings, fans, flow controllers, vertical large openings (windows and/or doors), kitchen hoods, passive stacks, and "user-defined components."

COMIS allows the user to define schedules describing changes in the indoor temperature distribution, fan operation, pollutant concentration in the zones, pollutant sources and sinks, opening of windows and doors, and the weather data. The flexible time step implemented in COMIS enables the modeling of events independent of the frequency with which the weather data are provided.

The COMIS air flow calculation is based on the assumption that indoor air flows reach steady-state at each time step. The contaminant transport is based on a dynamic model and has its own time step, based on the time constant of the most critical zone. The two models are coupled. Results for air flows and contaminant levels are reported in terms of tables by COMIS and in graphical form by some of the user-interfaces.

CONSEXPO - CONSumer EXPOsure Model:
CONSEXPO-3 is a multi-route, single-chemical modeling tool for assessing human exposure to chemicals emitted from consumer products. It focuses on non-professional indoor use of consumer products. The exposure routes include inhalation, dermal, and oral. Because of the wide range of exposures associated with consumer products, CONSEXPO defines five dermal loading scenarios, plus one scenario to model dermal exposure to airborne compounds. The five dermal loading scenarios are: 1) *Fixed volume scenario* assumes that the product is well mixed, 2) *Diffusion in product scenario* assumes that the product is not well mixed and transport of a chemical compound takes place by means of diffusion, 3) *Migration to skin scenario* assumes that dermal exposure is a result of

migration of product to the skin, 4 and 5) *Transfer coefficient scenario* and *contact rate scenario* are similar to the dermal models used in the EPA's residential SOPs.
http://www.epa.gov/chemrtk/revmodlr.pdf

An Evaluation of the Potential for Use of Existing Exposure Software (or Software Currently Under Development) in a Tiered Approach to the Assessment of Exposures and Risks to Children.

The LifeLine Development Team, 2001. Phase 1 Report: Findings from Literature Search and Review of Modeling Projects Currently Available or Under Development. Prepared for the American Chemistry Council, Comprehensive Chemical Exposure Framework (CCEF) Project (Agreement #1388).

CONTAMW:
CONTAMW is a multi-zone indoor air quality and ventilation analysis computer program designed to help predict airflows, contaminant air concentrations, and personal exposure for buildings.
http://www.bfrl.nist.gov/IAQanalysis/CONTAMWdesc.htm

California Population Indoor Exposure Model (CPIEM):
Developed by GOMET for the California Air Resources Board, CPIEM uses Monte Carlo Simulation to determine distributions of daily time-integrated concentrations of inhalation exposures (and doses) for Californians.

DEPM - Dietary Exposure Potential Model (DEPM):
DEPM is a model and database system that correlates extant food information in a format for estimating dietary exposure. The resident database system includes results from government-sponsored food intake surveys and chemical residue monitoring programs. A special feature of the DEPM is the use of recipes developed specifically for exposure analysis that link consumption survey data for prepared foods to the chemical residue information, which is normally reported for raw food ingredients. Consumption in the model is based on 11 food groups containing approximately 800 exposure core food types, established from over 6500 common food items.

The summary databases are aggregated in a fashion to allow analyst selection of demographic factors such age/sex groups, geographical regions, ethnic groups and economic status. Daily intake is estimated by the model for over 300 pesticides and environmental contaminants. In addition, contributions to total exposure from exposure core food groups and individual exposure core foods can also be estimated.
http://www.epa.gov/nerlcwww/depm.htm

E-FAST - Exposure & Fate Assessment Screening Tool:
E-FAST provides screening-level estimates of the concentrations of chemicals released to air, surface water, landfills, and from consumer products. Estimates provided are potential inhalation, dermal and ingestion dose rates resulting from these releases. Modeled estimates of concentrations and doses are designed to reasonably overestimate exposures for use in screening level assessment.

E-FAST calculates appropriate human potential dose rates for a wide variety of chemical exposure routes. and estimates the number of days per year that an aquatic ecotoxicological concern concentration will be exceeded for organisms in the water column.

EPI Suite:
The EPI (estimation program interface) Suite™ is a Windows® based suite of physical/chemical property and environmental fate estimation models developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). These properties are the building blocks of exposure assessment. EPI Suite™ uses a single input to run the following estimation models: KOWWINTM, AOPWINTM, HENRYWINTM, MPBPWINTM, BIOWINTM, PCKOCWINTM, WSKOWWINTM, BCFWINTM, HYDROWINTM, and STPWINTM, WVOLWINTM, and LEV3EPITM. This suite of models does various fate and transport estimates such as partition coefficients, rat of volatilization, etc..

EXAMS - The Exposure Analysis Modeling System:
EXAMS simulates an aquatic ecosystem tracing the path and behavior of a toxic pollutant. It has a database of toxic substances and a command-driven interface, which allows for the definition of new substances and for modification of the ecosystem definition.

Each water body may be constituted of up to 32 different segments, for each of which the balance of up to 28 different substances may be simulated. The basic phenomena taken into consideration are: accumulation, chemical and biological transformation, and transport. Environmental conditions may be constant (in the short or the long term) or varying monthly. It ma be use to conduct rapid evaluations and error analyses of the probable aquatic fate of synthetic organic chemicals.

EXAMS combines chemical loadings, transport, and transformation into a set of differential equations using the law of conservation of mass as an accounting principle. It accounts for all the chemical mass entering and leaving a system as the algebraic sum of external loadings, transport processes that export the compound from the system, and transformation processes within the system that convert the chemical to daughter products. The program produces output tables and simple graphics describing chemical exposure, fate, and persistence.

FIRIN/FIRAC:
FIRAC estimates radioactive and non-radioactive source terms and predicts fire-induced flows and thermal and material transport within the facilities. It is applicable to any facility with or without ventilation systems. It is a fast-running code with a user-friendly interface and includes source term models for fires.

FIRAC is one of a family of codes designed to provide improved safety analysis methods for the nuclear industry. The basic material transport capability of FIRAC includes estimates of entrainment, convection, deposition, and filtration of material. The interrelated effects of filter plugging, heat transfer, and gas dynamics are also simulated. A ventilation system model includes elements such as filters, dampers, ducts, and blowers connected at nodal points to form networks. A one-dimensional, lumped-parameter zone-type compartment model is incorporated to simulate flow-induced transients within a facility. No spatial distribution of parameters is considered in this approach, but an effect of spatial distribution can be approximated by noding. (Gregory, W.S., et al.,1992)

FIRAC is designed to estimate radioactive and non-radioactive source terms and predict fire-induced flows and thermal and material transport within the facilities. Particular focus is on transport through the ventilation system of these facilities. FIRAC includes a fire compartment module based on the FIRIN computer code, which was developed at Pacific Northwest National Laboratory (PNNL). The FIRIN module calculates fuel mass loss rates and energy generation rates within the fire compartment. It can also calculate the generation rate and size distribution of radioactive particles that become airborne as a result of a fire in a nuclear facility. More recently, a second fire module, based on the CFAST computer code, was added to FIRAC. CFAST was developed by the National Institute of Standards and Technology (NIST) to model fire growth and smoke transport in multi-compartment structures. The new combined code is called FIRAC2.

GASFLOW:
GASFLOW is a computational fluid dynamics model applied to solving internal and external engineering type flows. The code accounts for turbulent mixing, combustion, and chemical kinetics of gases and aerosol species, as well as heat transfer and condensation to walls and structures. It solves the compressible form of the Navier-Stokes conservation equations using the ICED-ALE numerical scheme. It is basically a multi-dimensional (3-D) finite volume field code with the capability to characterize low-speed, buoyancy driven, diffusion-dominated, or chemically reactive and non-reactive flows within a compartment network. It can be used to analyze spatially refined flow phenomena such as circulation patterns; gas stratification; and chemical distribution and kinetics. The code is written in FORTRAN 90 and is configured for UNIX and LINUX workstations.

A technical assessment of building a virtual building model from a core CFD building interior model (such as GASFLOW) is given at the following URL
http://eande.lbl.gov/BTP/papers/43006.pdf

GEMS - Geographical Exposure Modeling System:
GEMS is a modernization of OPPT's older Graphical Exposure Modeling System and PCGEMS tools. GEMS brings together in one system several EPA environmental fate and transport models and some of the environmental data needed to run them. GEMS includes models and data for ambient air, surface water, soil, and ground water and makes the models much easier to use than their stand-alone counterparts. GEMS will have graphics and Geographical Information

System (GIS) capabilities for displaying environmental modeling results.

GEMS will have interactive menus to guide the user in selecting models, selecting and organizing data to be used as input to model runs, executing model runs, and presenting model outputs. The menus will also provide user help. The new system will be modular in design so that EPA can easily add other models to the system in the future. GEMS will also have the capability of retrieving some data from EPA Oracle databases, such as the TRIS data in the EPA Envirofacts Data Warehouse.

GENII:
The GENII computer code was developed at Pacific Northwest National Laboratory (PNNL) to incorporate the internal dosimetry models recommended by the International Commission on Radiological Protection (ICRP) into updated versions of existing environmental pathway analysis models. The resulting second generation of environmental dosimetry computer codes is compiled in the Hanford Environmental Dosimetry System (Generation II or GENII). The GENII system was developed to provide a state-of-the-art, technically peer-reviewed, documented set of programs for calculating radiation doses from radionuclides released to the environment. Although the codes were developed for use at Hanford, they were designed with the flexibility to accommodate input parameters for a wide variety of generic sites.

HARVARD VI:
The WPI/Fire Codes are derived from the Harvard Computer Fire Codes. Harvard VI is a control volume code designed for fire analysis, and can be adapted to chemical transport. It has many of the same modeling capabilities as CFAST and can be extended to multi-compartment facilities. Technical reference: Gahm, J.B., 1983. This info was obtained from www.wpi.edu. The website contains more information on the latest version of this model.

HGSYSTEM:
HGSYSTEM is a suite of programs for assessing dispersion of vapor from gas, liquid or 2 phase releases including multi-component mixtures. HGSYSTEM was first assembled to model the release of Hydrogen Fluoride (HF) and ideal gases (Version 1.0), and then extended to include multicomponent mixtures (version 3.0). HGSYSTEM has been developed by Shell Research Ltd with the support and sponsorship of industry groups. HGSYSTEM/UF6 is a collaborative development of HGSYSTEM by Lockheed Martin Energy Systems and Earth Technology, sponsored by the United States Department of Energy (DOE) to predict the dispersion of the hydrolysis products of Uranium Hexafluoride.HGSYSTEM possesses an advanced near field transport model with a spatial resolution of less than 1 meter. It has modeling options for calculating time-dependent chemical source terms for pressurized liquids and gases, buoyancy-driven flows, and evaporating pools of single or multi-component releases. It is written in FORTRAN 77 and is highly modularized which allows for program modification to address special needs analysis.
http://www.hgsystem.com/hgweb.html

HPV - HPV Exposure Assessment Screening Tool - HPVScreen :
Physical-chemical properties and fate. This component of HPVScreen will define the physical-chemical properties the user will need for use with the models in the other components. This component will also provide the user with the ability to estimate removal of a chemical by wastewater treatment.

Models for screening-level exposure estimates. This component provides modeled screening-level estimates of the concentrations and potential doses of chemicals released to air, surface water, landfills and from consumer products. The estimates are designed to be conservative (i.e. to be on the high end of exposure or even to overestimate exposure).

Multimedia modeling programs. This component of HPVScreen provides the user with easy access to the EQC and Level III programs developed by Trent University. Among other uses, these programs can be used to address the environmental fate and transport endpoint that are part of the U.S. HPV Challenge Program and the OECD SIDS Program.

- A fourth major component, a "Report Generator," will be added over the next year.
- This component will assist the user in completing a standard template for providing exposure information.
- If the user is using one of the models in HPVScreen, many of the data elements in the reporting template will be automatically filled in.

- If the user has monitoring data or exposure estimates from another model, the reporting template will allow the user to use those data as well. In this case, the user will be queried to provide the data needed to complete the template.
- Online guidance for the user will be available.

IA-NBC-HMAS - Indoor Air-Nuclear, Biological and Chemical-Health Modeling and Assessment System:
The Indoor Air Nuclear, Biological and Chemical Health Modeling and Assessment System (HMAS for short) was developed to serve as a health impacts analysis tool for use in addressing these concerns. HMAS is designed to serve as a functional health modeling and assessment system that can be easily tailored to meet specific building analysis needs. IA-NBC-HMAS is a model designed to focus on indoor air (complex buildings). While its original design is to use for counter terrorism and chemical/biological agent attacks, it also has equal applicability for modeling and assessing indoor pollution from natural sources (e.g., building construction materials, process releases, etc.). It is designed to be coupled with both micro and macro ambient models to be able to model both finite indoor concerns and the full picture of ambient and indoor effect from releases either in the building or outside the building that impact indoor air quality.

IAQX - Simulation Tool Kit for Indoor Air Quality and Inhalation EXposure:
IAQX includes a variety of stand-alone simulation programs, including a general-purpose simulation program, VOC emissions from solvent-based indoor coating products, small-scale solvent spills, VOC emissions from diffusion-controlled homogeneous slabs, and indoor particulate matter. IAQX source models can address emission of chemicals from consumer products, building materials, indoor furnishings, and appliances, including dry sources.
http://www.epa.gov/chemrtk/revmodlr.pdf.
An Evaluation of the Potential for Use of Existing Exposure Software (or Software Currently Under Development) in a Tiered Approach to the Assessment of Exposures and Risks to Children.

The LifeLine Development Team, 2001. Phase 1 Report: Findings from Literature Search and Review of Modeling Projects Currently Available or Under Development. Prepared for The American Chemistry Council, Comprehensive Chemical Exposure Framework (CCEF) Project (Agreement #1388).

INPUFF:
INPUFF is a Gaussian puff model, developed by the U.S. EPA. The model is intended for simulating the atmospheric dispersion of neutrally buoyant or buoyant chemical releases. The model allows for a vertically oriented stack (point source) and a release duration that may be either finite or continuous. INPUFF can account for plume rise due to both buoyancy and momentum. In addition, the model can include the effects of stack-tip downwash.

INPUFF allows the user to specify the location and dimension of a receptor grid where concentration estimates will be calculated downwind of the release. To estimate concentrations, the model uses the Pasquill-Gifford dispersion coefficients with modifications to account for initial dispersion and buoyancy-induced dispersion (if applicable) and a user-specified averaging time.

MCCEM:Multi-Chamber Concentration and Exposure Model:
MCCEM estimates average and peak indoor air concentrations of chemicals released from products or materials in houses, apartments, townhouses, or other residences. And it estimates inhalation exposures to these chemicals, calculated as single day doses, chronic average daily doses, or lifetime average daily doses.

MCCEM is a user-friendly software product that estimates indoor air concentrations using a mass balance approach. It maintains a library of residences, containing data on zone or area volumes, interzonal air flows, and whole-house exchange rates and allows its users to tailor their analysis to a particular location, and to model air concentrations in as many as four zones for a given residence. It estimates exposure for periods ranging from 1 hour to 1 year and develops seasonal or annual exposure profiles using a long-term model and offers several different options for dealing with ‘sinks’. A sink is a material (e.g., carpeting, wallboard) that can absorb chemicals from the air; the absorption can be either reversible or irreversible.

MEPAS - Multimedia Environmental Pollutant Assessment System:
The Multimedia Environmental Pollutant Assessment System considers chronic exposure and human health risks resulting from environmental emissions. Physics-based models of contaminant processes in the air, groundwater, and surface water are integrated in a system that considers both chemical and radioactive potential impacts.

The Multimedia Environmental Pollutant Assessment System (MEPAS) software utilizes sophisticated modeling codes to quickly and easily assess risks from activities that could impact human health, such as remediating hazardous waste sites.

The MEPAS software provides physics-based modeling codes for environmental risk assessment. It quickly integrates results from separate models of contaminant behavior in various media (air, soil, ground water, surface water) and for different scenarios, turning a task that could take weeks (or might never be attempted) into a few hours' work.

MEPAS integrates and evaluates transport and exposure pathways for chemical and radioactive releases according to their potential human health impacts (multimedia in this context refers to multiple environmental transport media). MEPAS takes the nontraditional approach of combining all major exposure pathways into a multimedia computational tool for public health impact. MEPAS is a physics-based approach that couples contaminant release, migration and fate for environmental media (groundwater, surface water, air) with exposure routes (inhalation, ingestion, dermal contact, external dose) and risk/health consequences for radiological and non-radiological carcinogens and non-carcinogens.
http://www.epa.gov/asmdnerl/models3/

MMSOILS - The Multimedia Contaminant Fate, Transport, and Exposure Model:
MMSOILS estimates the human exposure and health risk associated with releases of contamination from hazardous waste sites. The methodology consists of a multimedia model that addresses the transport of a chemical in groundwater, surface water, soil erosion, the atmosphere, and accumulation in the food chain. The human exposure pathways considered in the methodology include: soil ingestion, air inhalation of volatiles and particulates, dermal contact, ingestion of drinking water, consumption of fish, consumption of plants grown in contaminated soil, and consumption of animals grazing on contaminated pasture. For multimedia exposures, the methodology provides estimates of human exposure through individual pathways and combined exposure through all pathways considered. The risk associated with the total exposure dose is calculated based on chemical-specific toxicity data.

The methodology is intended for use as a screening tool. It is critical that the results are interpreted in the appropriate framework. The intended use of the exposure assessment tool is for screening and relative comparison of different waste sites, remediation activities, and hazard evaluation. The methodology can be used to provide an estimate of health risks for a specific site. Since the uncertainty of the estimated risk may be quite large (depending on the site characteristics and available data), MMSOILS addresses these uncertainties via Monte-Carlo analysis.

Models-3/CMAQ - Models-3 and Community Multi-scale Air Quality:
CMAQ modeling system represent the air component to EPA’s MIMS framework. The Models-3 release contains three types of environmental modeling systems meteorological, emission, and chemistry transport. It also includes a visualization and analysis system.
http://www.epa.gov/asmdnerl/models3/index.html

OBODM - Open Burn/Open Detonation Model:
OBODM is intended for use in evaluating the potential air quality impacts of the open burning and detonation (OB/OD) of obsolete munitions and solid propellants. OBODM uses cloud/plume rise dispersion, and deposition algorithms taken from existing models for instantaneous and quasi-continuous sources to predict the downwind transport and dispersion of pollutants released by OB/OD operations.

pNEM:
pNEM is an EPA exposure model for particulate matter, adapted and further developed at UBC for use in Canada to estimate population exposure to particulate matter.
http://hajek.stat.ubc.ca/projects/pnem.html

PRESTO - Prediction of Radiological Effects Due to Shallow Trench Operations:
PRESTO is a computer model for evaluating radiation exposure from contaminated soil layers, including waste disposal, soil cleanup, agricultural land application, and land reclamation. The models in PRESTO are designed to calculate the maximum annual committed effective dose to a critical population group and cumulative fatal health effects and genetic effects to the general population in several scenarios:

1. near surface disposal trench containing low-level radioactive waste and/or naturally occurring or accelerator produced radioactive material (NARM)
2. residual radionuclides remaining in soil layers after cleanup
3. agricultural land application of technologically enhanced naturally occurring radioactive materials (TENORM) waste
4. stripped land reclamation with applied TENORM waste

The models simulate the transport of radionuclides in air, surface water, and groundwater pathways, and evaluate exposures through ingestion, inhalation, immersion and external exposure pathways.

PROMISE - PRObabilistic Methodology for Improving Solvent Exposure Assessment:
PROMISE© Version 7 is an ongoing modeling project by Silken, Inc., for the Solvents Council of the American Chemistry Council. The software is designed to evaluate exposures and doses from single and multiple uses of products that contain volatile solvents (e.g., adhesives, paints, floor cleaners, etc.). Appropriate activities for modeling include the use of large volumes of solvents (open drums or open tanks), use of an applied product, or from spills.

The PROMISE©model can be used to investigate products used in the workplace and the home. PROMISE© can calculate multi-route exposures from dermal, inhalation (indoor or outdoors), and/or ingestion routes of solvent exposure. The source models included in the software are labeled constant concentration, source and ventilation, pure-substance evaporation, open-can evaporation, and wall or floor liquid application and evaporation. The program's algorithms model the release of solvent from mixtures that change over time.
http://www.epa.gov/chemrtk/revmodlr.pdf.
An Evaluation of the Potential for Use of Existing Exposure Software (or Software Currently Under Development) in a Tiered Approach to the Assessment of Exposures and Risks to Children.
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ReachScan:

- Estimates surface water chemical concentrations at drinking water utilities downstream from industrial facilities.
- Estimates the populations served by those drinking water utilities.
- Serves as a database for the identification of facilities and utilities.
- Estimates the number of days per year that an aquatic ecotoxicological concern concentration will be exceeded in the subject stream or stream segment. A chemical's aquatic ecotoxicological concern concentration is the estimated concentration at which the chemical may adversely affect aquatic organisms.
- Provides stream flow statistics on a daily average basis.
- Determines the presence of endangered species or critical habitats in the county of the releasing facility. ReachScan operates as an integrated software package, with links to other computer-based programs developed by the U.S. Environmental Protection Agency (EPA), including the Probabilistic Dilution Model (PDM3) and the Endangered Species Data Base and estimates chemical concentrations in single or multiple stream (segments) reaches by simple dilution or using simple fate algorithms.

RISK:
A computer model sponsored by the EPA for calculating individual exposure to indoor air pollutants from sources is presented. The model is designed to calculate exposure due to individual, as opposed to population, activity patterns and source use. The model also provides the capability to calculate risk due to the calculated exposure. RISK is the third in a series of indoor air quality (IAQ) models developed by the Indoor Environment Management Branch of U.S. EPA's National Risk Management Research Laboratory.

The model uses data on source emissions, room-to-room air flows, air exchange with the outdoors, and indoor sinks to predict concentration-time profiles for all rooms. The concentration-time profiles are then combined with individual activity patterns to estimate exposure. Risk is calculated using a risk calculation framework developed by Naugle and Pierson (1991). The model allows analysis of the effects of air cleaners located in either/or both the central air circulating

system or individual rooms on IAQ and exposure. The model allows simulation of a wide range of sources including long term steady state sources, on/off sources, and decaying sources. Several sources are allowed in each room. The model allows the analysis of the effects of sinks and sink re-emissions on IAQ. The results of test house experiments are compared with model predictions. The agreement between predicted concentration-time profiles and the test house data is good.
http://www.ntis.gov/fcpc/cpn7493.htm

RESRAD - RESidual RADioactivity:
RESRAD is a computer code developed at Argonne National Laboratory for the U.S. Department of Energy to calculate site-specific RESidual RADioactive material guidelines as well as radiation dose and excess lifetime cancer risk to a chronically exposed on-site resident.

A soil guideline is defined as the radionuclide concentration in soil that is acceptable if the site is to be used without radiological restrictions. Soil is defined as unconsolidated earth material, including rubble and debris that might be present. These guidelines are based on the following principles: (1) the annual radiation dose received by a member of the critical population group from the residual radioactive material - predicted by a realistic but reasonably conservative analysis and calculated as committed effective dose equivalent - should not exceed 100 mrem/yr, and (2) doses should be kept as low as reasonably achievable, a concept commonly known as ALARA.

Nine environmental pathways are considered: direct exposure, inhalation of particulates and radon, and ingestion of plant foods, meat, milk, aquatic foods, water, and soil.

SCIPUFF - Second-order Closure Integrated Puff:
SCIPUFF model is a Lagrangian puff dispersion model developed by Titan's ARAP Group that uses a collection of Gaussian puffs to represent an arbitrary, three-dimensional time-dependent concentration. The turbulent diffusion parameterization is based on turbulence closure theory, providing a direct relationship between the predicted dispersion rate and turbulent velocity statistics of the wind field. In addition to the average concentration value, the closure model also provides a prediction of the statistical variance in the concentration field resulting from the random fluctuations in the wind field. The closure approach also provides a direct representation for the effect of averaging time. SCIPUFF has been incorporated into the Defense Threat Reduction Agency's (DTRA) Hazard Prediction and Assessment Capability (HPAC) software. HPAC is utilized for planning and analysis as well as in the field by military personnel to rapidly determine consequences of dispersing chemical, nuclear and biological agents. SCIPUFF has been validated against a number of laboratory and field experiments, demonstrating its usefulness for non-military applications. It has been recommended as an alternative model by the EPA which can be used on a case-by-case basis for regulatory applications. The publicly available version of SCIPUFF is the same version incorporated in HPAC except that the proprietary and developmental features have been disabled. SCIPUFF runs on a PC with a user-friendly Graphical User Interface (GUI).

SES - Subway Environmental Simulation: Subway Environmental Simulation **(SES)** model developed by Parsons Brinkerhoff for the DOT

WPEM - Wall Paint Exposure Assessment:
The WPEM estimates the potential exposure of consumers and workers to the chemicals emitted from wall paint, which is applied using a roller or a brush. WPEM is a user-friendly, flexible software product that uses mathematical models developed from small chamber data to estimate the emissions of chemicals from oil-based (alkyd) and latex wall paint. This is then combined with detailed use, workload, and occupancy data (e.g., amount of time spent in the painted room, etc,) to estimate exposure.
http://www.epa.gov/opptintr/exposure/docs/wpem.htm

Exposure and Impacts (including toxicity models)

BDBR:
A predictive tool used to estimate potential human health risks by describing and quantifying the key steps in the cellular, tissue and organismal responses as a result of chemical exposure.

ChemSTEER - Chemical Screening Tool For Exposures & Environmental Releases:
Chemical Screening Tool For Exposures & Environmental Releases (ChemSTEER) estimates occupational inhalation and dermal exposure to a chemical during industrial and commercial manufacturing, processing, and use operations involving the chemical. It estimates releases of a chemical to air, water, and land that are associated with industrial and commercial manufacturing, processing, and use of the chemical.

It allows users to select predefined industry-specific or chemical functional use-specific profiles or user-defined manufacturing, processing and use operations. Using these operations and several chemical-specific and case-specific parameters and general models, the ChemSTEER computer program estimates releases and occupational exposures. The methods in ChemSTEER were developed by the EPA Office of Pollution Prevention and Toxics (OPPT); Economics, Exposure, and Technology Division; Chemical Engineering Branch.

E-FAST - Exposure & Fate Assessment Screening Tool:
E-FAST provides screening-level estimates of the concentrations of chemicals released to air, surface water, landfills, and from consumer products. Estimates provided are potential inhalation, dermal and ingestion dose rates resulting from these releases. Modeled estimates of concentrations and doses are designed to reasonably overestimate exposures for use in screening level assessment.

E-FAST calculates appropriate human potential dose rates for a wide variety of chemical exposure routes. and estimates the number of days per year that an aquatic ecotoxicological concern concentration will be exceeded for organisms in the water column.

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IEUBK - Integrated Exposure Uptake Biokinetic Model for Lead in Children:
The Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) attempts to predict blood-lead concentrations (PbBs) for children exposed to lead in their environment. The model allows the user to input relevant absorption parameters (e.g., the fraction of lead absorbed from water) as well as intake and exposure rates. Using these inputs, the IEUBK model rapidly calculates and recalculates a complex set of equations to estimate the potential concentration of lead in the blood for a hypothetical child or population of children (6 months to 7 years of age). The IEUBK model is designed to predict the probable PbB concentrations for children between 6 months and 7 years of age who have been exposed to lead through environmental media (air, water, soil, dust, and diet). Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) is an EPA model circa 1999. (White Paper HHEA-3)

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Modeling Benzene Exposures and Absorbed Dose:
Probabalistic model of benzene exposure and absorbed dose applied to 40 million people represented by EPA Region 5 (MacIntosh, 1995).

Modeling Dietary Exposures to Heavy Metals and Pesticides:
Chronic (1-yr average) dietary exposure to 11 heavy metals and pesticides for a population of approximately 120,000 US adults (MacIntosh, 1996).

MTHEM - Multi-pollutant Total Human Exposure Model:
EPA and Stanford model is mainly modeling patterns of exposure to air pollutants (ozone, PM, carbon dioxide).
http://www.riskworld.com/Abstract/1996/SRAam96/ab6aa368.htm
http://www.riskworld.com/Abstract/1996/SRAam96/ab6aa329.htm

PBPK & PBPD - Physiologically Based PharmacoKinetic (PBPK) & Physiologically Based PharmacoDynamic (PBPD):
A PBPK/PBPD model for humans describes the body as a set of interconnected compartments, or continuous stirred tank reactors. Each compartment can describe either an organ or a tissue. A PBPK/PBPD model is founded on known physiological processes (blood flow rates, tissues volumes, breathing rates, etc.), on chemical-specific processes (partition coefficients, chemical density, metabolic constants, molecular weight, etc.), and on species-dependent processes.
http://www.pnl.gov/eshs/cap/cd/pbpk.html

QSAR Models - Quantitative Structure Activity Relationship:
Quantitative-structure activity-relationships models used to relate chemical structure to the physiochemical parameters that are important to dermal absorption. QSAR studies attempt to model a variety of molecules and predict their activities based upon their structures. Models are built from sets of data referred to as descriptors. Such models, when accurately constructed, allow for the prediction of the activity of other unknown molecules not originally used to construct the model. These methodologies have terrific potential in the field of drug discovery.(White Paper HHEA-3)

REHEX - II:
Regional Human Exposure Model was developed to estimate the population's exposure to PM concentrations.
http://www.eih.uh.edu/publications/99annrep/rifai.htm
http://www.burningissues.org/abstracts/econstdy.htm

RESRAD - RESidual RADioactivity:
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A soil guideline is defined as the radionuclide concentration in soil that is acceptable if the site is to be used without radiological restrictions. Soil is defined as unconsolidated earth material, including rubble and debris that might be present. These guidelines are based on the following principles: (1) the annual radiation dose received by a member of the critical population group from the residual radioactive material - predicted by a realistic but reasonably conservative analysis and calculated as committed effective dose equivalent - should not exceed 100 mrem/yr, and (2) doses should be kept as low as reasonably achievable, a concept commonly known as ALARA.

Nine environmental pathways are considered: direct exposure, inhalation of particulates and radon, and ingestion of plant foods, meat, milk, aquatic foods, water, and soil.

RISC (RISK in webpage): RISC (Risk Assessment Model for Soil and Groundwater Applications):
RISC is relatively widely established in New Zealand among environmental risk assessors. RISC models the fate and transport of contaminants in steady state and transient modes. The model is intuitive to use, and relatively simple.

The present version (3.0) evaluates human health risk only. However the updated RISC model will incorporate both aquatic and terrestrial ecological risk assessment by modeling contaminant concentrations at key receptor areas and comparing these values with specific acceptance criteria. However, in developing the new version, the developers have highlighted particular difficulties associated with modeling the fate and transport of metals in soils.

The main advantages with RISC are that the risk assessment approach (for human health risk assessment) is relatively widely accepted, the model is able to incorporate NZ specific data, and that investigators are relatively familiar with the software.

RISK:
A computer model sponsored by the EPA for calculating individual exposure to indoor air pollutants from sources is presented. The model is designed to calculate exposure due to individual, as opposed to population, activity patterns and source use. The model also provides the capability to calculate risk due to the calculated exposure. RISK is the third in a series of indoor air quality (IAQ) models developed by the Indoor Environment Management Branch of U.S. EPA's National Risk Management Research Laboratory.
The model uses data on source emissions, room-to-room air flows, air exchange with the outdoors, and indoor sinks to predict concentration-time profiles for all rooms. The concentration-time profiles are then combined with individual activity patterns to estimate exposure. Risk is calculated using a risk calculation framework developed by Naugle and Pierson (1991). The model allows analysis of the effects of air cleaners located in either/or both the central air circulating system or individual rooms on IAQ and exposure. The model allows simulation of a wide range of sources including long term steady state sources, on/off sources, and decaying sources. Several sources are allowed in each room. The model allows the analysis of the effects of sinks and sink re-emissions on IAQ. The results of test house experiments are compared with model predictions. The agreement between predicted concentration-time profiles and the test house data is good.
http://www.ntis.gov/fcpc/cpn7493.htm

TEM - Total Exposure Model:
EPA and US Air Force developed The Total Exposure Model (TEM) to estimate population and individual exposure to waterborne contaminants. TEM models the fundamental physical and chemical processes that occur as individuals are exposed to the contaminated water supply. TEM calculates an individual's exposure and dose using finite difference techniques, estimating the mass transfer of the chemicals from the water to the air during water use activities (i.e. showering).

Thongsinthusak:
Thongsinthusak, et al. (1999) exponential saturation model with lag time to estimate dermal absorption; used for pesticide exposure; model derived from experimental data sets. (White Paper HHEA-3)

UCSS - Use Clusters Scoring System:
Use Clusters Scoring System identifies and screens clusters of chemicals ("use clusters") that are used to perform a particular task. A use cluster is a set of chemicals that may be substituted for one another in performing a given task. It identifies clusters of potential concern and provides an initial ranking of chemicals using human and environmental hazard and exposure data from a number of sources.

For each chemical in a cluster, UCSS allows the user to enter data indicating the potential for human and ecological exposure and hazard, and the level of U.S. Environmental Protection Agency (EPA) interest. It calculates health and ecological risk or toxicity rating scores for each chemical within a cluster using the information entered and preprogrammed scoring algorithms. UCSS uses individual chemical scores to calculate an overall cluster score, which is an indicator of potential risk for the use cluster. It contains data on nearly 400 use clusters and 4,700 chemicals.

Databases

AHS:
The major objective of the Adult Health Study (AHS) was to collect information on the health condition of the atomic-bomb survivors, especially those health issues that are not directly related to death. To do this, about 20,000 subjects selected from the RERF Life Span Study sample of atomic-bomb survivors were followed through biennial health examinations since 1958. About 2,400 Life Span Study participants and 1,000 in-utero-exposed persons have been added to the sample since 1978.

http://www.rerf.or.jp/eigo/titles/ahstitle.htm

ATW - Air Toxics Website:
As part of EPA's National Air Toxics Assessment, EPA conducted a national-scale assessment of 33 air pollutants (a subset of 32 air toxics on the Clean Air Act's list of 188 air toxics plus diesel particulate matter (diesel PM)).

The assessment includes four steps that look at the year 1996. As of May 2002, the results posted for all four steps include revisions based on input from scientific peer review.

1. Compiling a national emissions inventory of air toxics emissions from outdoor sources.
2. Estimating ambient concentrations of air toxics across the contiguous United States.
3. Estimating population exposures across the contiguous United States.
4. Characterizing potential public health risk due to inhalation of air toxics including both cancer and noncancerous effects.

The goal of the national-scale assessment is to identify those air toxics which are of greatest potential concern in terms of contribution to population risk. The results will be used to set priorities for the collection of additional air toxics data (e.g., emissions data and ambient monitoring data).
http://www.epa.gov/ttn/atw

CARB - California Air Resources Board:
The California Air Resources Board is a part of the California Environmental Protection Agency, an organization which reports directly to the Governor's Office in the Executive Branch of California State Government.

The mission of CARB is to promote and protect public health, welfare, and ecological resources through the effective and efficient reduction of air pollutants while recognizing and considering the effects on the economy of the state.

CHAD - Consolidated Human Activities Database:
CHAD is a relational database with a graphical user interface that facilitates queries and report generation. It contains databases from previously existing human activity pattern studies, which were incorporated in two forms: (1) as the original raw data and (2) as data modified according to predefined format requirements. The latter involved development of a common activity/location code system, compilation of background questionnaire information, and the application of data quality flags. CHAD is intended to be an input file for exposure/intake dose modeling and/or statistical analysis.
http://www.epa.gov/chadnet1/

Cohne Hubal et al:
Dr. Elaine Cohne Hubal designed studies to evaluate dermal exposure assessment approaches and to collect exposure factor data in support of the Food Quality Protection Act. 1998 - present. Dr. Cohne Hubal worked on the development of a modeling platform to predict contaminant fate and transport of environmental pollutants and to perform exposure assessments in support of the Hazardous Waste Identification Rule in 1996 - 1997.

She developed and worked with a variety of computational models to describe the simultaneous mass transport and reaction of inhaled gases in the airway lining. This work was part of a larger project (from 1992-1996)designed to reduce uncertainty in risk assessment for inhaled toxicants, and included research in the area of industrial pollution prevention. She developed the framework to evaluate environmental impact of pollution prevention activities which directly relates energy requirements to process air, water and solid waste emissions. The framework can be used to facilitate lifecycle analysis.

CPDB - Carcinogenic Potency Database:
The Carcinogenic Potency Database (CPDB) is a widely used resource on the results of chronic, long-term animal cancer tests. It provides a single, standardized and easily accessible database that includes sufficient information on each experiment to permit investigations into many research areas of carcinogenesis. Both qualitative and quantitative information on positive and negative experiments are reported, including all bioassays from the National Cancer Institute/National Toxicology Program (NCI/NTP) and experimental results from the general literature that meet a set of inclusion criteria. Analyses of 5152 experiments on 1298

chemicals are presented. For each experiment, information is included on the species, strain, and sex of the test animal; features of experimental protocol such as route of administration, duration of dosing, dose level(s) in mg/kg body weight/day, and duration of experiment; histopathology and tumor incidence; carcinogenic potency (TD50) and its statistical significance; shape of the dose-response curve; author's opinion as to carcinogenicity; and literature citation.
http://potency.berkeley.edu/cpdb.html

CSFII - Continuing Survey of Food Intakes by Individuals:
Continuing Survey of Food Intakes by Individuals (CSFII) is conducted by US Department of Agriculture (USDA). The results of the survey can be found at
http://www.barc.usda.gov

EPA's Child-Specific Exposure Factors Handbook:
In April, 1997, President Clinton signed an Executive Order to Protect Children from Environmental Health Risks and Safety Risks. The Order requires all federal agencies to address health and safety risks to children, coordinate research priorities on children's health, and ensure that their standards take into account special risks to children. To implement the President's Executive Order, EPA established the Office of Children's Health Protection (OCHP), and offices within EPA increased their efforts to provide a safe and healthy environment for children by ensuring that all regulations, standards, policies, and risk assessments take into account risks to children.

In 1997, EPA/ORD/NCEA published the Exposure Factors Handbook (U.S. EPA, 1997b). The Handbook includes exposure factors and related data on both adults and children. OCHP's recently-issued child-related risk assessment policy and methodology guidance document survey (U.S. EPA, 1999b), highlighted the Exposure Factors Handbook (U.S. EPA, 1997b) as a source of information on exposure factors for children.
http://www.epa.gov

EPA Handbook - EPA Exposure Factors Handbook Database:
The Exposure Factors Handbook Database provides a summary of the available statistical data on various factors used in assessing human exposure. This Handbook is addressed to exposure assessors inside the U.S. Environmental Protection Agency as well as outside who need to obtain data on standard factors to calculate human exposure to toxic chemicals. Recommended values are for the general population and also for various segments of the population who may have characteristics different from the general population.
http://www.epa.gov/ncea/exposfac.htm

HazDat:
HazDat, the Agency for Toxic Substances and Disease Registry's Hazardous Substance Release/Health Effects Database, is the scientific and administrative database developed to provide access to information on the release of hazardous substances from Superfund sites or from emergency events and on the effects of hazardous substances on the health of human populations. The following information is included in HazDat: site characteristics, activities and site events, contaminants found, contaminant media and maximum concentration levels, impact on population, community health concerns, ATSDR public health threat categorization, ATSDR recommendations, environmental fate of hazardous substances, exposure routes, and physical hazards at the site/event. In addition, HazDat contains substance-specific information such as the ATSDR Priority List of Hazardous Substances, health effects by route and duration of exposure, metabolites, interactions of substances, susceptible populations, and biomarkers of exposure and effects. HazDat also contains data from the U.S. Environmental Protection Agency (EPA) Comprehensive Environmental Response, Compensation, and Liability Information System (CERCLIS) database, including site CERCLIS number, site description, latitude/longitude, operable units, and additional site information.
http://www.atsdr.cdc.gov/hazdat

IRIS - Integrated Risk Information System:
The Integrated Risk Information System (IRIS), prepared and maintained by the U.S. Environmental Protection Agency (U.S. EPA), is an electronic data base containing information on human health effects that may result from exposure to various chemicals in the environment. IRIS was initially developed for EPA staff in response to a growing demand for consistent information on chemical substances for use in risk assessments, decision-making and regulatory activities. The information in IRIS is intended for those without extensive training in toxicology, but with some knowledge of health sciences.

The heart of the IRIS system is its collection of computer files covering individual chemicals. These chemical files contain descriptive and quantitative information in the following categories:

- Oral reference doses and inhalation reference concentrations (RfDs and RfCs, respectively) for chronic noncarcinogenic health effects.
- Hazard identification, oral slope factors, and oral and inhalation unit risks for carcinogenic effects.

http://www.epa.gov/iris

ITER - International Toxicity Estimates for Risk:
ITER is a free Internet database of human health risk values for over 500 chemicals of environmental concern from several organizations worldwide. ITER is the only database that provides this data in a table format that allows side-by-side comparisons of risk values from different organizations. Below the table is a synopsis that includes an explanation for any differences among the organizations' values. ITER provides links to these organizations for more detailed information. ITER currently contains data from Agency for Toxic Substances and Disease Registry (ATSDR), Health Canada, National Institute of Public Health and Environment (RIVM), The Netherlands, US Environmental Protection Agency (EPA), and independent parties whose risk values have undergone peer review.
http://www.tera.gov/iter

NCHS:
NCHS is the Federal Government's principal vital and health statistics agency. Since 1960, when the National Office of Vital Statistics and the National Health Survey merged to form NCHS, the agency has provided a wide variety of data with which to monitor the Nation's health. Since then, NCHS has received several legislative mandates and authorities.

The National Center for Health Statistics (NCHS) is a part of the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. To meet priority data needs for public health, NCHS works closely with other Federal agencies as well as researchers and academic institutions.

NCHS data systems include data on vital events as well as information on health status, lifestyle, and exposure to unhealthy influences, the onset and diagnosis of illness and disability, and the use of health care. These data are used by policymakers in Congress and the Administration, by medical researchers, and by others in the health community.
http://www.cdc.gov/nchs

NHANES - National Health and Nutrition Examination Survey:
The National Health and Nutrition Examination Survey (NHANES) is a survey conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention. This survey has been designed to collect information about the health and diet of people in the United States. NHANES is unique in that it combines a home interview with health tests that are done in a Mobile Examination Center.

The National Health and Nutrition Examination Survey provides estimates of the health of Americans by examining a sample of people who represent the American population. To accomplish this, medical staff and other professionals travel across the U.S. in specially equipped mobile examination centers.

NHAPS - National Human Activity Pattern Survey:
The National Human Activity Pattern Survey (NHAPS) was initiated to fill a need for updated activity information on a nationwide scale. Several recent exposure field monitoring studies have shown that human activities play a critical role in explaining the variation in human exposure because they impact the frequency, duration, and intensity of exposure to pollutants. Currently, activity pattern data bases with adequate potential pollutant exposure information are available only for a few cities (Cincinnati, Denver, Washington, DC) or a state (California), and only for limited months of the year. The NHAPS, which began in September, 1992, was a two-year probability-based national telephone interview survey of approximately 10,000 persons that is being conducted by the University of Maryland Survey Research Center assisted by the U.S. EPA to ascertain the time, location, and other characteristics of those activities which are most relevant to estimating pollutant exposure. The survey design, location and activity codes, data examples, and appropriate analyses are described for NHAPS data base.

Time-diary data from this survey were designed to provide standardized activity reports which, when made available in early 1995, will be used to refine current human exposure models. Activity diary data have been effectively used in the following types of analyses: descriptive, relational, temporal, and exposure modeling.

NHEXAS - National Human Exposure Assessment Survey:
The National Human Exposure Assessment Survey (NHEXAS) was developed by the Office of Research and Development (ORD) of the U.S. Environmental Protection Agency (EPA) early in the 1990s to provide critical information about multipathway, multimedia population exposure distribution to chemical classes. The first phase consisted of three pilot studies with the objectives of:

1. Evaluating the feasibility of NHEXAS concepts, methods, and approaches for the conduct of future population-based exposure studies;
2. Evaluating the utility of NHEXAS data for improved risk assessment and management decisions;
3. Testing the hypothesis that the distributions of exposure given by modeling and extant data do not differ from the measurement-based distributions of exposure;
4. Defining the distribution of multipathway human exposures for a relatively large geographic area;
5. Stimulating exposure research and forging strong working relationships between government and non-government scientists.
6. NHEXAS began before the enactment of the Government Performance and Results Act (GPRA), which was written to ensure accountability in the use of resources. Thus, we add a "new" objective in the form of a hypothesis: NHEXAS approaches can be used to develop a "GPRA Report Card" on the efficiency of EPA's regulations to reduce exposure.

NHGPUS - National Home and Garden Pesticide Use Survey:
The National Home and Garden Pesticide Use Survey (NHGPUS) was conducted for EPA during August and September 1990. The purpose was to collect data on the use of pesticides in and around homes in the United States. The study was designed as a national probability-based sample of households, with personal interviews conducted at the participants' residence. The target population in the survey was housing units in the conterminous United States occupied as primary residences (home where a person lives for half the year or more), excluding institutions, group quarters, military reservations, and Native American reservations (Whitmore et al., 1992).
http://www.epa.gov

OEHHA - Office of Environmental Health Hazard Assessment:
The mission of the Office of Environmental Health Hazard Assessment (OEHHA) is to protect and enhance public health and the environment by objective scientific evaluation of risks posed by hazardous substances.
http://www.oehha.ca.gov

RAIS - Risk Assessment Information System:
Risk Assessment Information System (RAIS) website contains risk assessment tools and information. The Risk Assessment Tools include: Risk-Based Preliminary Remediation Goal (PRG) calculations, a Toxicity database, Risk Calculations, and Ecological Benchmarks. The Tools are designed for use at all DOE sites and can be customized for site-specific conditions. The RAIS also includes information, guidance, and risk results applicable to the Oak Ridge Reservation.
http://risk.lsd.ornl.gov/rap_hp.shtml

RTECS® - Registry of Toxic Effects of Chemical Substances:
Registry of Toxic Effects of Chemical Substances (RTECS) from the US National Institute for Occupational Safety and Health (NIOSH) provides toxicological information with citations on over 140,000 chemical substances. These detailed profiles include toxicological data and reviews; international workplace exposure limits; references to US standards and regulations; analytical methods; and exposure and hazard survey data. The data are compiled into substance records for ease-of-use, and updated data is fully integrated.

SRD - Standard Reference Data Group:
The NIST Standard Reference Data Group (SRDG) at NIST has been proving well-documented numeric data to scientists and engineers for use in technical problem-solving research and development. These recommended values are based on data which have been extracted from the world's literature, assessed for reliability, and then evaluated to select the preferred values. These data activities are conducted by scientists at NIST and in university data centers.

The formal existence of the National Standard Reference Data System dates from 1963, when the Federal Council for Science and Technology asked the then-National Bureau of Standards (now NIST) to assume primary responsibility in the Federal Government for promoting and coordinating the critical evaluation of numerical data in the physical sciences. The program was conceived as a decentralized national effort with financial support coming from a variety of government and private sources, but the NBS was responsible for the overall planning and coordination. In 1968 congress provided a specific legislative mandate for the program through passage of Public Law 90-396, the Standard Reference Data Act. This Act details the policy of Congress to make reliable, critically evaluated data compilations available to scientists, engineers, and the general public.
http://www.nist.gov/srd

Superfund Resource Center:
The EPA administers the Superfund program in cooperation with individual states and tribal governments. The office that oversees management of the program is the Office of Emergency and Remedial Response (OERR).

TOMES:
Handling hazardous chemicals is routine in many workplaces. Precautions must be in place to protect workers and to meet regulatory and safety guideline compliance. The TOMES Plus® System offers rapid, easy access to the critical medical and hazard data needed for immediate, effective response to any situation. Whether reducing the risk of injury or determining safe levels of exposure, TOMES Plus databases include treatment guidelines for acute chemical exposures, evacuation procedures, personal protection procedures, and chemical containment and disposal information. General areas unrelated to chemicals such as ergonomics and human health risk assessment are addressed. The System's proprietary and government databases are integrated to ensure quick access to the fully reviewed, referenced information.

The TOMES Plus System is ideal for:

- Industrial hygienists and hazardous waste chemists
- Safety & risk managers
- Fire department personnel
- Environmental engineers and toxicologists
- Occupational health physicians and chief medical officers

TOXNET - Toxicology and Environmental Health Information Program:
The Toxicology and Environmental Health Information Program (TEHIP) is responsible for the Toxicology Data Network (TOXNET®), an integrated system of toxicology and environmental health databases that are available free of charge on the web. The following databases are available for searching via TOXNET: HSDB®, TOXLINE®, ChemIDplus, IRIS , TRI (Toxic Chemical Release Inventory), CCRIS (Chemical Carcinogenesis Research Information System), GENE-TOX, and DART®/ETIC (Developmental and Reproductive Toxicology/Environmental Teratology Information Center). http://www.nlm.nih.gov

US Census:
http://www.census.gov

USEPA: USEPA Exposure Models Library - focused on standard models, mainly fate and transport (1996).
http://esm.versar.com/emlimes/emlintro.htm

Identified Processes Lacking a Specified Model

Dust Resuspension:
A *Dust Resuspension* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take surface concentrations from house objects estimated by the indoor air transport model (CONTAMW) and estimate the atmospheric emission rates of dust from resuspension. This information would feed back into the indoor air transport model (CONTAMW).

Fuel Spill Frequency & Volume:
A *Fuel Spill Frequency & Volume* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take in information related to the fueling of a gasoline-powered lawn mower, lawn trimmer, or automobile.

Mainstream Cigarette Smoke Emission
A variety of *Mainstream Cigarette Smoke Emissions* models were identified by the research study. However, it is not known if these models can take information related to contaminant inhalation and release by mainstream smoking and estimate the emission rates of contaminants in mainstream smoke indifferent rooms as input to the indoor air transport model (CONTAMW).

Micro-Environmental Air Transport Outdoors:
An *Micro-Environmental Air Transport Outdoors* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take emission information related to fueling and painting spills and estimate the outdoor air concentrations that could impact a human. This information could also be used as an outdoor source to the indoor air transport model (CONTAMW).

Paint Spill Frequency and Volume:
A *Paint Spill Frequency and Volume* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take information related to indoor painting of walls by a nonprofessional and potential for spills. Output would be number and volume of spills associated with indoor painting of walls.

Partitioning Between Vapor and Particle Phase:
A *Partitioning Between Vapor and Particle Phase* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take air concentrations estimated by the indoor air transport model (CONTAMW) and partitions the air concentrations into vapor (gaseous) and particle components. These partitioned air concentrations can then be used by the indoor air transport model (CONTAMW) to provide refined air concentrations for more realistic exposure modeling.

Source Emission from Fueling, Combustion, and Service:
Source Emission from Fueling, Combustion, and Service models were not identified by the research study. This means that such models do not exist or are not widely used or published for this process. If these models existed, they would take information related to the fueling, operation, and maintenance of a gasoline-powered lawn mower, lawn trimmer, or automobile for a typical household. Output would be emission rates of volatile compounds associated with fueling, operation, and maintenance of a gasoline-powered lawn mower, lawn trimmer, or automobile.

VOC Fugitive Emission from Mixing Vessel:
A *VOC Fugitive Emission from Mixing Vessel* model was not identified by the research study. This means that a model does not exist, or it is not widely used or published for this process. If this model existed, it would take information related to fugitive emission of volatile organic compounds (VOCs) from a mixing vessel and estimate the emission rates of these compounds as input to the indoor air transport model (CONTAMW).

2.2 Exposure and Impact Models, Databases, and Algorithms

This section provides a review of exposure and impact models, databases, and algorithms that are readily available via the Internet and other forms of open literature. The review included all types of models, databases, and algorithms necessary to conduct detailed exposure and exposure micro-environmental modeling. This review is only meant to be quick review of information readily available via the Internet or technical libraries and is not an in-depth literature review.

2.2.1 Reference List by Category

PubMed Search Date: November 7, 2000

Categories:

Table 2.2.1 Chemical-Specific PBPK Models for Dose to Embryo/Fetus
Table 2.2.2 Chemical-Specific Biologically Based Dose-Response Models for Pregnancy
Table 2.2.3 Chemical-Specific PBPK Models for Neonatal Exposure via Lactation
Table 2.2.4 Basic Biology Data Useful in PBPK Model Development
Table 2.2.5 General Models and Dosimetry Considerations Useful in PBPK Model Development
Table 2.2.6 Reviews of PK/PD in Developmental Toxicology
Table 2.2.7 Role for kinetics/dosimetry in Children's Health Issues
Table 2.2.8 PD Models of the Endocrine System
Table 2.2.9 Dose-Response Modeling for Endocrine Active Compounds
Table 2.2.10 Metabolizing Enzymes as a Function of Age or Gestational Development (Reviews)
Table 2.2.11 Standard Kinetics during Pregnancy or Lactation (only selected articles from a large database captured during PBPK searches)

Table 2.2.1 Chemical-Specific PBPK Models for Dose to Embryo/Fetus

1. Clarke, D. O., Elswick, B. A., Welsch, F., and Conolly, R. B. (1993). Pharmacokinetics of 2-methoxyethanol and 2-methoxyacetic acid in the pregnant mouse: a physiologically based mathematical model. *Toxicol. Appl. Pharmacol.* 121, 239-252.

2. Clewell, H. J., Gearhart, J. M., Gentry, P. R., Covington, T. R., VanLandingham, C. B., Crump, K. S., and Shipp, A. M. (1999). Evaluation of the uncertainty in an oral reference dose for methylmercury due to interindividual variability in pharmacokinetics. *Risk Anal*. 19, 547-558.

3. Clewell, H. J., III, Andersen, M. E., Wills, R. J., and Latriano, L. (1997). A physiologically based pharmacokinetic model for retinoic acid and its metabolites. *J. Am. Acad. Dermatol.* 36, S77-S85.

4. Faustman, E.M., Lewandowski, T.A., Ponce, R.A. and Bartell, S.M. (1999). Biologically based dose-response models for developmental toxicants: Lessons from methylmercury. *Inhal. Toxicol.* 11, 559-572.

5. Fisher, J. W., Whittaker, T. A., Taylor, D. H., Clewell, H. J., III, and Andersen, M. E. (1989). Physiologically based pharmacokinetic modeling of the pregnant rat: a multiroute exposure model for trichloroethylene and its metabolite, trichloroacetic acid. *Toxicol. Appl. Pharmacol.* 99, 395-414.

6. Gabrielsson, J. L. and Paalzow, L. K. (1983). A physiological pharmacokinetic model for morphine disposition in the pregnant rat. *J. Pharmacokinet. Biopharm.* 11, 147-163.

7. Gabrielsson, J. L., Paalzow, L. K., and Nordstrom, L. (1984). A physiologically based pharmacokinetic model for theophylline disposition in the pregnant and nonpregnant rat. *J. Pharmacokinet. Biopharm.* 12, 149-165.

8. Gabrielsson, J. L., Johansson, P., Bondesson, U., and Paalzow, L. K. (1985). Analysis of methadone disposition in the pregnant rat by means of a physiological flow model. *J. Pharmacokinet. Biopharm.* 13, 355-372.

9. Gabrielsson, J. L., Johansson, P., Bondesson, U., Karlsson, M., and Paalzow, L. K. (1986). Analysis of pethidine disposition in the pregnant rat by means of a physiological flow model. *J. Pharmacokinet. Biopharm.* 14, 381-395.

10. Gabrielsson, J. L. and Groth, T. (1988). An extended physiological pharmacokinetic model of methadone disposition in the rat: validation and sensitivity analysis. *J. Pharmacokinet. Biopharm.* 16, 183-201.

11. Gargas, M. L., Tyler, T. R., Sweeney, L. M., Corley, R. A., Weitz, K. K., Mast, T. J., Paustenbach, D. J., and Hays, S. M. (2000). A toxicokinetic study of inhaled ethylene glycol ethyl ether acetate and validation of a physiologically based pharmacokinetic model for rat and human. *Toxicol. Appl. Pharmacol.* 165, 63-73.

12. Gargas, M. L., Tyler, T. R., Sweeney, L. M., Corley, R. A., Weitz, K. K., Mast, T. J., Paustenbach, D. J., and Hays, S. M. (2000). A toxicokinetic study of inhaled ethylene glycol monomethyl ether (2- ME) and validation of a physiologically based pharmacokinetic model for the pregnant rat and human. *Toxicol. Appl. Pharmacol.* 165, 53-62.

13. Gray, D. G. (1995). A physiologically based pharmacokinetic model for methyl mercury in the pregnant rat and fetus. *Toxicol. Appl. Pharmacol.* 132, 91-102.

14. Hays, S. M., Elswick, B. A., Blumenthal, G. M., Welsch, F., Conolly, R. B., and Gargas, M. L. (2000). Development of a physiologically based pharmacokinetic model of 2-methoxyethanol and 2-methoxyacetic acid disposition in pregnant rats. *Toxicol. Appl. Pharmacol.* 163, 67-74.

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16. O'Flaherty, E. J., Scott, W., Schreiner, C., and Beliles, R. P. (1992). A physiologically based kinetic model of rat and mouse gestation: disposition of a weak acid. *Toxicol. Appl. Pharmacol.* 112, 245-256.

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species and potential use in prenatal toxicity risk assessments. *Toxicol. Lett.* 82-83, 539-547.

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Table 2.2.2 Chemical-Specific Biologically Based Dose-Response Models for Pregnancy

23. Lau, C., Andersen, M. E., Crawford-Brown, D. J., Kavlock, R. J., Kimmel, C. A., Knudsen, T. B., Muneoka, K., Rogers, J. M., Setzer, R. W., Smith, G., and Tyl, R. (2000). Evaluation of biologically based dose-response modeling for developmental toxicity: a workshop report. *Regul. Toxicol. Pharmacol.* 31, 190-199.

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25. Leroux, B. G., Leisenring, W. M., Moolgavkar, S. H., and Faustman, E. M. (1996). A biologically-based dose-response model for developmental toxicology. *Risk Anal.* 16, 449-458.

26. Setzer, R. W., Lau, C., Mole, M. L., Copeland, M. F., Rogers, J. M. and Kavlock, R. J. (2001). Toward a biologically based dose-response model for developmental toxicity of 5-Fluorouracil in the rat: A mathematical construct. *Toxicol. Sci.* 59, 49-58.

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Table 2.2.3 Chemical-Specific PBPK Models for Neonatal Exposure via Lactation

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2.2.2 Exposure Models and Methods

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2.2.3 Exposure Information Databases and Information Resources

AHS

- American Housing Survey

AIHC

- American Industrial Health Council Exposure Factors Sourcebook (AIHC 1994)

ATW

- (Air Toxics Website) Fact sheets from "EPA Health Effects Notebook for Hazardous Air Pollutants-Draft" describe the effects on human health of substances that are defined as hazardous by the 1990 amendments of the Clean Air Act.
- http://www.epa.gov/ttn/atw/hapindex.html

Basic Biology Data Useful in PBPK Model Development

CARB database

- California Air Resources Board; information on activity patterns associated with California populations with regards to air exposures (e.g., breathing rates associated with activities and driving patterns)

CHAD

- Consolidated Human Activities Database
- CHAD contains data from pre-existing human activity studies that can be used for exposure/intake dose modeling.
- http://www.epa.gov/chadnet1/

Child-Specific Exposure Factors Handbook (EPA, 2000)

Cohen Hubal, et al. (2000).

- Assessement of time spent by children, by age, in various microenvironments and the time spent by children, by age, in various macroactivities while indoors in the home microenvironment. Microenvironments include indoors at home, outdoors at home, indoors at school, outdoors at park, and in vehicle. Macroactivities at home include: eat, sleep or nap, shower or bathe, play, watch TV/listen to music, read/write/do homework, think/relax/passive.

CPDB

- Carcinogenic Potency Database
- A summary table of chemicals in the CPDB that contains results for positivity, potency (TD50), and target sites in rats and mice.
- http://potency.berkeley.edu/hybrid.html

CRAFT

- Chemical Reaction and Fate Transport Database
- CRAFT includes a lot of parameters of use in transport and exposure assessment modeling

CSFII

- Continuing Survey of Food Intake by Individuals (USDA)

Exposure Factors Handbook

- Exposure Factors Handbook (EPA) provides a summary of the available statistical data on various factors used in assessing human exposure. This Handbook includes standard factors to calculate human exposure to toxic chemicals. These factors include: drinking water consumption, soil ingestion, inhalation rates, dermal factors including skin area and soil adherence factors, consumption of fruits and vegetables, fish, meats, dairy products, homegrown foods, breast milk intake, human activity factors, consumer product use, and residential characteristics.
- http://www.epa.gov/ncea/exposfac.htm

GIS

- Graphical Information Systems

HazDat

- Hazardous Substance Release and Health Effects Database
- HazDat is from Agency for Toxic Substances and Disease Registry (ATSDR).
- http://www.atsdr.cdc.gov/gsql/toxprof.script

IARC

- International Agency for Research on Cancer
- List of IARC conclusions on carcinogenicity.
- http://193.51.164.11/monoeval/crthall.html

IRIS

- Integrated Risk Information System from EPA
- http://www.epa.gov/IRIS/

ITER

- International Toxicity Estimates for Risk
- Human health risk values for over 500 chemicals of environmental concern from several organizations worldwide.
- http://www.tera.org/iter/welcome.htm

NCHS

- Birth records and other National Center for Health Statistics [NCHS] data.

NHANES

- National Health and Nutrition Examination Survey (EPA & NCHS)

NHAPS

- National Human Activity Pattern Survey (EPA)

NHEXAS

- National Human Exposure Assessment Survey (EPA)

NHGPUS

- National Home and Garden Pesticide Use Survey

OEHHA Toxicity Criteria Database

- Office of Environmental Health Hazard Assessment
- OEHHA is from California EPA and includes risk assessment levels for hazardous substances.
- http://www.oehha.org/risk/chemicalDB/index.asp

RAIS

- Risk Assessment Information System
- The toxicity profiles in this database were developed using information taken from EPA's Integrated Risk Information System (IRIS) and Health Effects Assessment Summary Tables (HEAST) and other literature sources.
- http://risk.lsd.ornl.gov/tox/rap_toxp.shtml

RDBMS

- Relational Database Management Systems

RTECS

- The Registry of Toxic Effects of Chemical Substances
- RTECS® is a database of toxicological information compiled, maintained, and updated by the National Institute for Occupational Safety and Health. The program is mandated by the Occupational Safety and Health Act of 1970. The original edition, known as the "Toxic Substances List," was published on June 28, 1971, and included toxicological data for approximately 5,000 chemicals. Since that time, the list has continuously grown and been updated, and its name changed to the current title, "Registry of Toxic Effects of Chemical Substances." RTECS® now contains over 133,000 chemicals as NIOSH strive to fulfill the mandate to list "all known toxic substances...and the concentrations at which...toxicity is known to occur."

Superfund Resource Center

- http://www.epa.gov/superfund/resources/index.htm

TOMES

- TOMES (and associated databases linked and available for access) provides a source of physical property values, toxicological values (e.g. PELs), and industrial hygiene information.

TOXNET

- Toxicology Data Network
- TOXNET from National Library of Medicine includes the following group of databases:
- HSDB (Hazardous Substances Database) Broad scope in human and animal toxicity
- IRIS (Integrated Risk Information System) in support of human health risk assessment, focusing on hazard identification and dose-response assessment.
- CCRIS (Chemical Carcinogenesis Research Information System) carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition data provided by the National Cancer Institute (NCI).
- GENE-TOX - Peer-reviewed mutagenicity test data from the EPA
- http://toxnet.nlm.nih.gov/

US Census data

- http://www.census.gov/

3.0 Model Framework

This section provides information on the *objections, approach, requirements, design, and data exchange protocol* of the Comprehensive Chemical Exposure Framework (CCEF) and generic Model Flow Diagrams developed for the framework.

The *objectives* provides the aims and goals of the Framework, the *approach* provides a brief proposed work, the *requirements* provides "what" the framework should do, the *design* provides "how" the framework should do it, and the *data exchange protocol* provides the file types, structure, and format for models and databases to communicate.

3.1 CCEF OBJECTIVES

The purpose of this research is twofold: design an overarching framework that is comprehensive, logical, and useful for industrial needs; and within that framework identify research needs based on gap and sensitivity analyses. The overarching framework, called the Comprehensive Chemical Exposure Framework, will be used to house models, algorithms, and databases associated with micro-environmental exposure modeling. The research needs are defined for representative high volume compounds that could be involved in exposure scenarios.

The Attributes for the CCEF are listed here with a detailed description in the Requirements section.

· *Comprehensive*
· *Modular*
· *User-friendly*
· *Multi-route, Multi-pathway, & Multi-source for Varying durations*
· *Accurate*
· *Open code*

· *Probabilistic*
· *Dose-responsive*
· *Mass-conservative*

3.2 CCEF Approach

The American Chemistry Council's Human Health Exposure Assessment Technical Implementation Panel identified four example exposure scenarios associated with different high-volume compounds that the design of the Comprehensive Chemical Exposure Framework (CCEF) should address. Using the design of the CCEF and its applicability to the four example exposure scenarios, research gaps and needs were identified. The filling of these research gaps and needs would increase the confidence and reduce the uncertainty of the human health exposure assessment results.

The four example exposure scenarios were used to guide the types of models, algorithms, and databases required to evaluate each scenario. Model and Process Flow Diagrams were developed for each exposure scenario and research gaps were identified based on publicly available information. Once the gap analysis was completed for the source, transport, exposure, and health impact components of each scenario, a qualitative sensitivity of the entire system was conducted.

The Gap Analysis focused on reviewing the Process Flow Diagrams that had been developed to properly evaluate each of the four example exposure scenarios to identify models, algorithms, and databases that were missing or unknown. This was done for the Source, Transport, Exposure, and Impacts components of the exposure scenarios. In some cases, models existed but they were determined to be too simplistic or conservative and were considered a research gap. In these cases, alternative paths were explored to determine the type of model or algorithm required to fill the research gap.

A qualitative Sensitivity Analysis was also performed on the models and algorithms identified for the various compounds and exposure scenarios. This was conducted on the four modeling components using the following guidelines:

1. Models associated with the primary exposure pathway were believed to introduce more sensitivity than those on secondary exposure pathways
2. Missing models and databases were considered a high priority
3. Inaccurate models were ranked as a high priority
4. Models of lesser compatibility in temporal and spatial scales with the other models were considered a high priority

The Gap and Sensitivity Analyses provide guidance on what research should be conducted in the near future to improve the risk estimates from exposure to high volume compounds.

The design of the CCEF leverages the concepts associated with multiple existing framework system software and exposure modeling methods that are in the forefront of the scientific community as well as new innovative concepts. The key to the CCEF will be the flexibility of the CCEF in its usability and ability to integrate and accommodate different exposure models (existing and future) required for the American Chemistry Council and industry needs.

The CCEF design links models and databases together so they can transparently communicate between each other. The CCEF is the overarching framework that houses the models and databases as "separate" components and provides the data file protocols for communication between components. A model is represented by a specific set of algorithms that perform a specific function (e.g., drinking water ingestion model). A module represents a general set of model types, defined by their "real world" functions, and includes the model, its user interface, and any pre- and post-processors that facilitate linkages and communication with/to other components (e.g., models and databases). This effort focuses on the design of an overarching framework and not on the models that are housed within the framework.

3.3 Requirements for the CCEF

To adequately assess the risks associated with chemicals released into the environment, researchers require software tools for accurately estimating human exposure under a variety of exposure scenarios. The design of a software technology system begins with a set of requirements. Requirements are characteristics and behaviors that a piece of software must possess to function adequately for its intended purpose. A requirement is sometimes called an attribute, and a good requirement is testable.

The purpose of these requirements is to state those conditions that define the design associated with the CCEF. To help define and develop requirements that will provide some legacy as the state-of-the-art in software technology advances, the requirements for the design of the CCEF shall initially consider those that have been suggested by experts, including those recently documented and outlined by Whelan and Nicholson (2001). The following requirements are grouped by the categories outlined by the American Chemistry Council for the CCEF.

- *Comprehensive*
  - Design the input/output and spatial/temporal linkage data-file specifications in the system through an Application Programming Interface, which accounts for units and range checking, and parameter attributes.
  - Allow for models to run on different platforms (e.g., remote computing).
  - Be configured to handle multiple directories for scenario and module files.
  - Ability to link outside frameworks to the system by allowing for icons on the icon palette to describe those outside frameworks.
  - Provide for different database types (e.g., chemical, ecological benchmarks, and human-health benchmarks) by representing each type by separate icons on the icon palette.
  - Allow a set of databases to supply information to a receiving module, establishing data priority on the same information.
  - Account for Graphical Information System connectivity.
- *Modular*
  - Consist of modules (algorithms and databases), which can be easily updated and exchanged without affecting other parts of the framework.
  - Allow for the functionality of entering the system at specified locations (e.g., import a file, user-specified information).
  - Allow for tiered icons (i.e., primary and secondary icons).
  - Allow for an icon palette to expand including additional icons, when appropriate.
  - Allow for the functionality to add new module icons, if desired.
  - Allow for the linkage of disparate models (e.g., analytical and numerical) in space and time.
- *User-friendly*
  - Operate on an IBM or compatible personal computer with Microsoft WIN98, or Win2000 platforms with a minimum of 128 MB RAM Pentium or equivalent, and 1 GB free disk space.
  - Support multiple computer languages and compilers.
  - Provide standardized reports, tables, and plots.
  - Contain a print feature.
  - Include on-line help for system-only components.
  - Provide for units conversion.
  - Develop user-friendly, graphically based conceptual site model.

- Be capable of developing a conceptual site model with the Drag & Drop features.
- Allow viewing of data requirements for modules chosen to represent icons in the conceptual site model, prior to implementation of the conceptual site model.

- *Multi-route, Multi-pathway, & Multi-source for Varying durations*
  - Be applicable to exposures via different routes and through multiple pathways, i.e., inhalation, oral, and dermal contact with consumer products.
  - Allow for single or multiple compounds with the same or different target organ.
  - Provide data client editors for system chemical- and lifeform-specific databases, which allow for identifying surrogates for (i.e., aliasing of) chemicals and/or lifeforms associated with each database-type.
  - Be applicable to acute, intermediate, and long-term exposures.
- *Accurate*
  - Provide the ability to benchmark models and databases.
  - Integrates state-of-the-art estimation methods and databases to estimate or reasonably overestimate the "ground-truth" of the actual exposure.
  - Incorporate lock and key features that allow a user to lock a conceptual site model picture, available models, and/or both.
- *Open code*
  - Be accessible for inspection and review by users and stakeholders (no proprietary or "black box" code).
  - Allow for the inclusion of commercial off the shelf software.
  - Be capable of documenting assumptions, surrogate names (i.e., aliases), changes in imported data from database, and version-control changes in pop-up or sticky notes, summary file(s), and/or a report generator.
- *Probabilistic*
  - Provide realistic distribution of exposures within the exposed population based on probabilistic modeling of key exposure factors, and allow for multistage Sensitivity/Uncertainty.
- *Dose-response*
  - Convert exposure estimates to corresponding dose and risk values, whenever appropriate.
- *Mass-conservative*
  - Use a mass balance approach whenever feasible to account for fate and transport of pollutant mass, and include, as part of module specifications, mass entering/leaving a module, where appropriate.

Continue reading the detailed requirements in the **Design** section.

3.4 CCEF Design

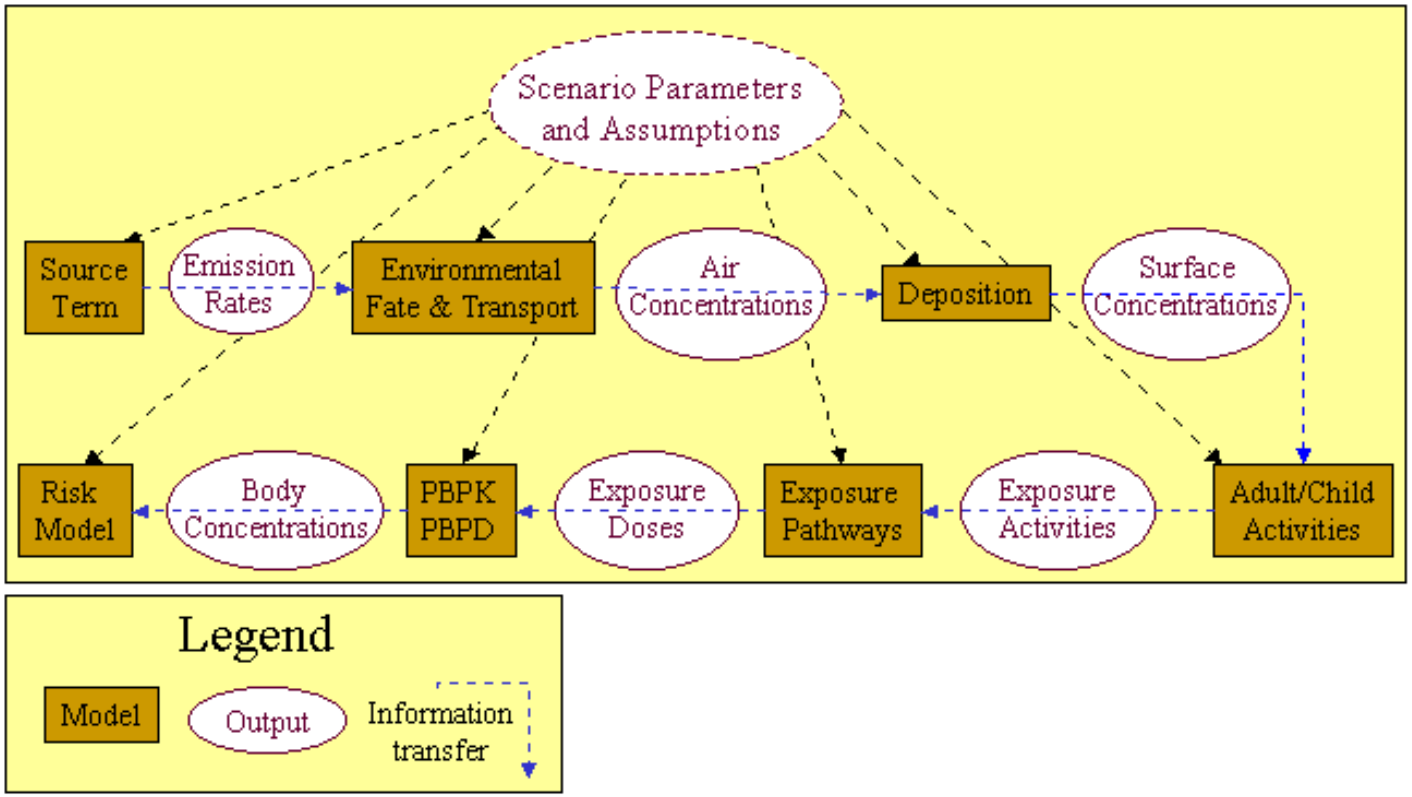
The design of a *Framework* is a strategy for meeting requirements and determines how a requirement is implemented. purpose of design is to state those conditions upon which software specifications can be developed to support development of Comprehensive Chemical Exposure Framework (CCEF).

3.4.1 Task and Sequence Manager

Figure 3.4.1 below depicts following aspects of Manager:

- Manages scenario being analyzed and sequence of modules being executed
- Provides information on a global basis which includes scenario-specific information
- Manages feedback between modules.

3.4.1 Task and Sequence Manager Diagram



A Module consists of following components:

- Computational code and algorithm
- User interface
- Pre- and post- processors (if needed)
- Module-specific databases (if needed).

Output consists of following:

- Boundary condition information for next module downstream
- Common format and data protocols so all other modules know how to read
- Minimal amount of information.

Note: Some data sources may feed more than one module. When multiple data sources fill same data need of a module but data sources differ on what value should be, some sort of hierarchy must be determined to select which data to use. assumptions of scenarios (chemicals, ages, exposure situations, etc.) will always be primary data source to use.

3.4.2 Client Side

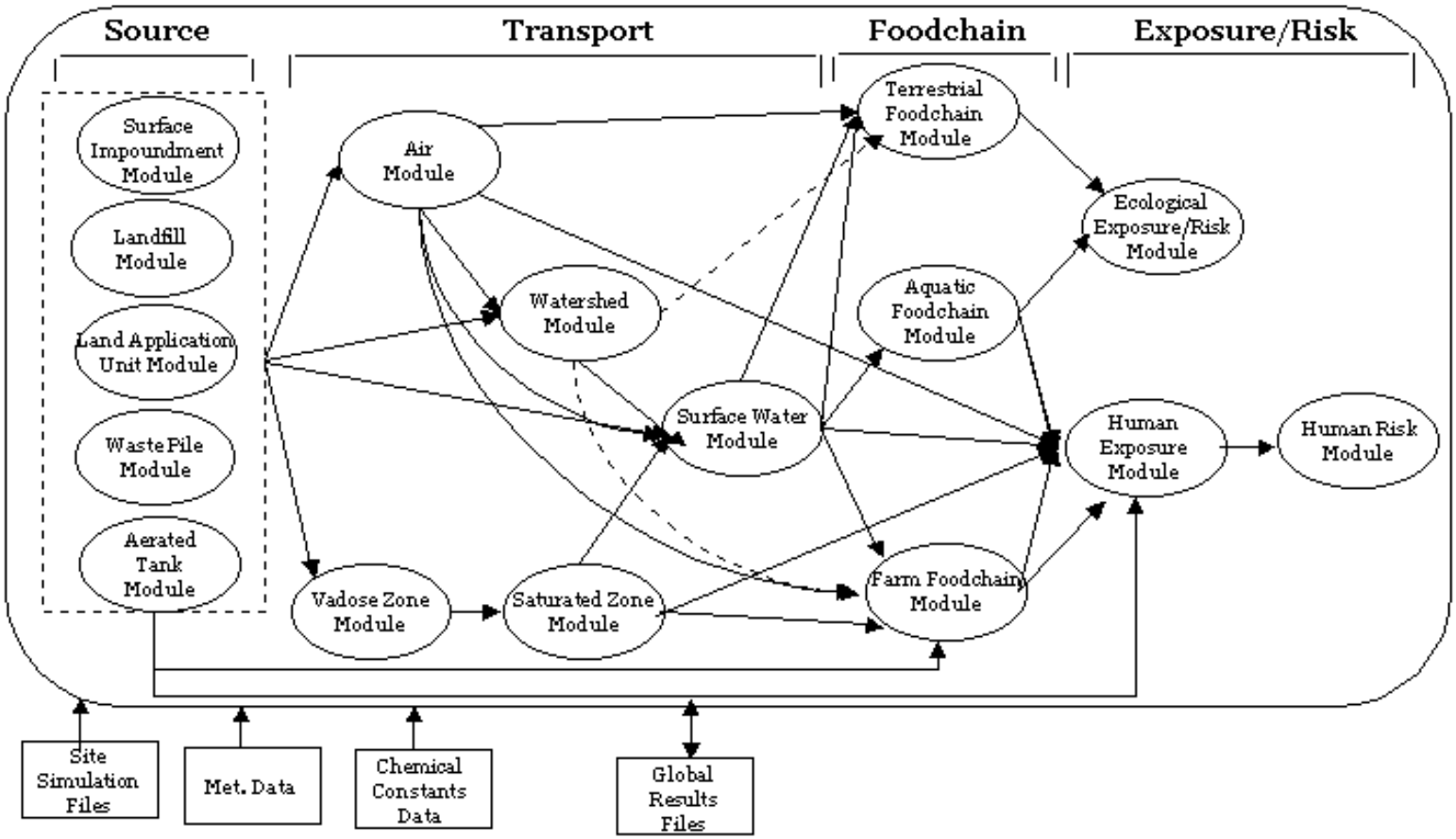
The client (local user) side of CCEF refers to host system. In this case, as noted by requirements, host system will be a personal computer, operating within Windows environment. Therefore, System User Interface will be personal computer compatible, but operation of models and databases is not limited to a personal computer and can exist on and operate from remote personal computer and non- personal computer locations. client side (local user) of design focuses on data transfer protocol, data structure, and system structure. server side (remote user) of design focuses on linkage protocol to remotely access and utilizes databases and models. design of CCEF is divided into following subject areas:

1. *Concepts of a Framework* - Architectural differences between a framework, model and module are discussed
2. *System User Interface* - system interface is proposed for CCEF, which represents forum for visually describing conceptual site model, is presented. conceptual site model is a mechanism to convey problem to user in graphical form. System User Interface directly interacts with user, so is very important to ensure is user-friendly and relatively intuitive
3. *Data Exchange Protocols* - data transfer protocols describe foundation upon which data is universally transferred throughout system. These protocols represent heart of CCEF
4. *Sensitivity/Uncertainty Considerations* - Utilizing data transfer protocols, section discusses how sensitivity/uncertainty models and parameter estimation models can be incorporated into system
5. *Model Space and Time Considerations* - Protocol for disparate models in both space and time are discussed
6. *System Integration Tools* - To help facilitate ability of linking disparate models, databases, and frameworks into Comprehensive Chemical Exposure Framework, a series of system software helpers (i.e., “editors”) are required to step model or database developer integration (and application) process
7. *Server Side of CCEF* - Software tools, which allow user to link to remote models and databases, are presented
8. *Lock and Key* - Software tools, which allow a user to fix conceptual site model by locking icon types and connections between icons, and lock models are available under each icon
9. *Summary of CCEF Design* - A summary of design, requirement-by-requirement, is presented.

The concept of developing a *Framework*, as opposed to a model, is critical in design philosophy of a technology software system, which meets needs outlined by requirements. Models are designed to perform a specific set of calculations. Although models exist describe a given real-world phenomenon (e.g., fate and transport in aquifer, exposure to contaminated sediments, etc.), a model can also be composed of many parts (e.g., LifeLine, CARES, TRIM, HWIR, etc.), which does not lend itself as a mechanism to link disparate components together to more accurately describe a solution to problem. *Framework* takes on responsibility for connectivity, while model takes on responsibility of consuming and producing information as part of assessment.

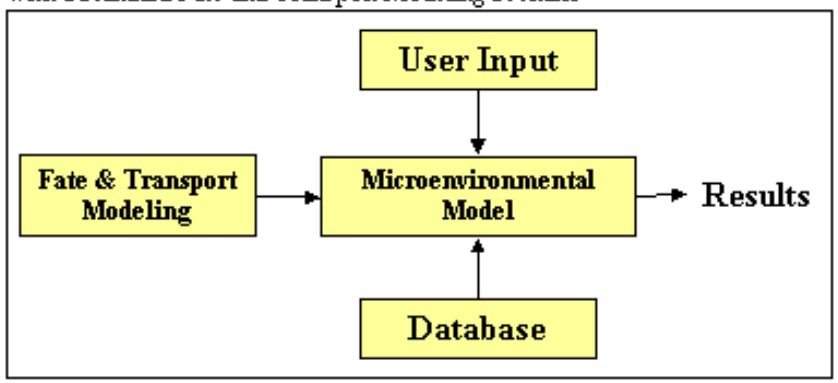
For example, **Figure 3.4.2.1** presents an example of a standard U.S. Environmental Protection Agency risk paradigm for performing a multiple media risk assessment, linking source, fate & transport, exposure, and risk/hazard (http://www.epa.gov/epaoswer/hazwaste/id/hwirwste/risk.htm). The ellipsoids provide examples of models (e.g., “modules” in figure). The essence of the *Framework* is represented by arrows connecting the models (i.e., modules). The protocol for transferring information from one model or database to the next is the responsibility of the *Framework*. The choice of the model, which represents the best solution to problem, is the responsibility of the analyst or the user. The *Framework* should take no responsibility for what happens inside of the model but takes full responsibility to ensure data consumed and produced are appropriately provided to the next model in line, and models fire in the correct sequence. The *Framework* controls the flow of information but not how the information is used.

Figure 3.4.2.1 Illustrative Example of Linking Models Together into a Standard Risk Paradigm, using the 3MRA-HWIR Assessment Methodology



By utilizing this approach in defining the difference between models and frameworks, solutions to problems can be designed to best meet the needs of the client.

Figure 3.4.2.2 Example Illustrating the Linkage of a Microenvironmental Model with a Standard Fate and Transport Modeling Scenario



For example, Figure 3.4.2.2 illustrates how best the features of micro-environmental exposure modeling can be combined with the U.S. Environmental Protection Agency's standard fate and transport, exposure modeling. In this example, the analyst is interested in using a micro-environmental

model to track ramifications of chemical exposures, including a discrete (i.e., short period of time) exposure from a nearby waste site. Because fate and transport models and their results are considerably more accurate, using standard risk assessment approaches, than those inherently included in micro-environmental model, they can be linked to the micro-environmental models. A similar design could be established when a more accurate lung model is needed to produce/consume information for/from the micro-environmental model. Not only that, the user could set up a comparison between two different micro-environmental models to determine differences between them using the same input data, and which ones would best meet the needs of problem.

Figure 3.4.2.2 also illustrates that databases can be viewed in a similar manner as models. Using this design, any database can be linked to any model, and the user is free to input user-specific information. As with linking models, any database can be linked to any other database. For example, if a site-specific database lacks necessary information to fulfill all of needs of a model, regional and national databases could be linked to site-specific database to fill gaps that might exist, prioritizing data, where appropriate.

As an illustrative example of design, four exposure scenarios have been identified for conceptual analysis; definitions of each are presented in **scenarios** section. Typical information flow diagrams, used to describe these four exposure scenarios, are presented in **Figure 3.4.1.** Figure 3.4.1 illustrates connectivity from source term through risk with boxes representing models and ellipsoids representing information flow between models. *Framework* concept can easily be expanded to four exposure scenarios, outlined in **scenarios** section, with each information flow diagram described therein.

Using **Scenario 3** as illustrative example, a process flow diagram as illustrated in **Scenario Model 3 Flow Diagram,** can be developed to describe the process of implementing occupational exposure of VOC compound Group D (benzene, toluene, and n-hexane) to adult male. In the process flow diagram, algorithms and models can be used to describe each of the boxes, and these process boxes can be matched to information flow diagram, to provide substance behind source, fate and transport, and effects/impacts modeling.

3.4.3 Design Associated with System Functionality

following design corresponds with **Requirements.**

Comprehensive

- *Application Programming Interface* represents protocol to communicate with Dynamic Link Libraries, which control flow of information between components within system. This requirement covers and is related to a unified data exchange protocol, which covers specific spatial and temporal data-file specifications at boundary conditions between modules and general design associated with input./output, system read only, system write, and system conversions.

  Application Programming Interface, using a series of Dynamic Link Libraries, will be utilized to transfer information between modules and between modules and databases. DICtionary files will describe characteristics of data to be transferred and boundary conditions link modules together. Data transfer will be through Dynamic Link Libraries, where quality of data can be inspected. Four universal data *Application Programming Interfaces* have been identified to support data exchange protocol:

  A. Input/Output - input/output *Application Programming Interface* shall consider
  • range checking of parameters with storage of information
  • data retrieval
  • data storage
  • units checking
  • open/close data sources
  • monotonic checks (e.g., time in a time series)

• meta data functions [cardinality, units, definitions, type (e.g., real, integer, etc.), number of elements, etc.]
• automatic call for conversions (e.g., units conversion)

B. System (Read Only) - System Read Only *Application Programming Interface* shall consider
• error handling functions (e.g., assertions, errors, and warnings)
• Command line functions (not standard in FORTRAN)
• producer/consumer relationships
• conceptual site meta data (e.g., type, qualifiers, counts, available models, description files, Domain, Class, Group, SubGroup)
• Read note

C. System (Write) - System Write *Application Programming Interface* shall consider
• setting arguments
• setting producer/consumer relationships
• creating a new module
• locking/unlocking conceptual site models
• model selection
• calling and running interfaces and models
• Run calls between models
• move icon placement routines
• Call-back when error occurs
• adding notes

D. Conversion - Conversion *Application Programming Interface* shall consider
• a list of available units

- The design of CCEF allows for multiple perspectives when solving exposure problem. By utilizing this approach in defining difference between models and frameworks, solutions to problems can be designed to best meet needs of client.

  For example, best features of micro-environmental exposure modeling can be combined with Environmental Protection Agency's standard fate and transport, exposure modeling. In this example, analyst is interested in using a micro-environmental model to track ramifications of chemical exposures, including a discrete (i.e., short period of time) exposure from a nearby waste site. Because fate and transport models and their results are considerably more accurate, using standard risk assessment approaches, than those inherently included in micro-environmental model, they can be linked to micro-environmental.

  A similar design could be established when a more accurate lung model is needed to produce/consume information for/from micro-environmental model. Not only , but user could set up a comparison between two different micro-environmental models to determine differences between them using same input data, and which ones would best meet needs of problem.
- Software linkage tools allow for communication between host (i.e., local) and remote systems (i.e., running models remotely or accessing data from remote databases). relationships between Linkage and Module Servers, Host Client, and Remote Databases and Models are presented in **Figure 3.4.3** (below).

  The explanation of Figure 3.4.3, as it relates to components comprising server side of CCEF design is presented in the Appendix. The various editors represent software for accessing remote databases. The Model Owner Tool, Module Execution Tool, and Remote Module Client represent software for accessing and running remote models (i.e., remote computing).
- The design of the CCEF would allow the user to store and access files, programs, databases, and models on different systems and in directories are different than those housing executables.
- With the advent of Dictionary files and a system-based Application Programming Interface, the fundamental responsibility of the framework shifts from

being model-oriented to being object-oriented, where the framework is charged with the transfer of information between components and not what calculations are being performed within each component. In other words, the framework is associated with arrows connect models and databases, and not what is inside of the models and databases. The models and databases are the responsibility of the technical users and researchers. Because of the object-oriented approach, the frameworks can be viewed as just another object with specific inputs and outputs. The

tiered icon system allows for the CCEF to link to outside frameworks, especially those at remote locations. The icon pallet includes a *Class* for *Frameworks*, both *Closed* and *Linkable*, and therefore, represents the icon choice under Class type. If these Frameworks have correct linkage specifications to communicate with other icons, then they could be pictorially connected directly to those icons. It is anticipated that Frameworks could be located in different directories, as a "remote" application. The server side of CCEF design accounts for linkages to remote locations, where models, databases, or other frameworks might be housed. Frameworks would be linked with the system in a manner in which all components are linked, using Application Programming Interface with the consuming and producing Dictionaries.

- Different databases will be represented by different icons. Datasets are slightly different from models. Under the *Class* of *Database*, there will be two Groups: *System* and *Module*. *System* refers to those databases that all modules have access to. The *Module* identifies those databases that can be specifically connected to certain icons. Under the Group or SubGroup, specific types of databases are identified (e.g., eco-benchmarks, physical properties of chemicals).

  If the system provides a database, it has responsibility to "support" the database. This means the system developers (i.e., system) are responsible for the content of the database and to ensure that the database is consistent and conforms to the description files, dictionary files, and Date Client Editor specifications and linkage protocols; therefore, the Date Client Editor, dictionary and description files are system's responsibility.

  A system database (i.e., original database) can be located on the local server or at a remote location. As with models, anyone can "access" a new database, not supported by system (i.e., system developers), but supported by someone else. They can "add" functionality to access the new database. Note this procedure is similar to someone adding a new model to system, a model is only applicable to their needs. To add a new model, the developer addresses protocols for a dictionary file and description file. The main difference between model-based icons and database icons is the linkage information between the model icons must be complete, but the linkage information between a database icon and other icons can be incomplete, because the database may not be able to service all of the data needs of the model.

  System databases are supported by the system (e.g., chemical or lifeform lists). To a certain extent, the system also services and supports the content of databases. For example, if the analyst is implementing a chemical assessment, all of the modules need to know what the chemical is; otherwise, all the modules will expect a different name and identifier, and none of the models will understand which chemical is being passed. This information is global and needs to reside in a system database. Currently envisioned system databases will be separated out from module databases. Because system databases are global, they do not need to be physically linked into the conceptual site model as they are already available to all modules in the system.

  Module databases are module specific and those databases are linked directly to models to which they will supply information. These databases are identified through traditional Drag & Drop features of conceptual site model work space. These *Module* databases (which constitute linkages to databases outside system) are not supported by the system but link into the system through editors, which are system-supported, universal software works for most well-structured and -designed databases. These "other" databases support specific models or model types. The Date Client Editor is database-specific and has a specific dictionary file associated with it. These databases are akin to models in thesystem. The system takes no responsibility for the models, only ensures that when specifications are met, the information is transferred properly. The same is true for the databases. In effect, the module-linkage philosophy is being reused for database linkage.
- transfer of information from a database to a downstream icon (module or another database) conceptually can be viewed the same as when two module icons are linked. When two modules are linked, the producing (i.e., upstream) module, provides information and stores it in a location the consuming (i.e., downstream) module can access. The downstream module reads the file and transfers data for its consumption. In effect, the downstream module "takes" the data needs from the intermediate file. Conceptually, it is important to note the upstream module DOES NOT populate downstream module. Similarly, when two database icons are linked, the upstream database does not populate downstream database. In reality, the upstream database populates intermediate

file, which the downstream database accesses and only utilizes those data which do not overlap with its own data. In effect, downstream database takes those data only fill data gaps in its database. This implies there is priority associated with the data. In other words, the data in downstream database has priority over the data in upstream database.

For example, when linking national and regional databases, the national database would be associated with upstream database icon, and the regional database would be associated with the downstream database icon. Under this situation, regional database would populate its data gaps with data from the national database. The conceptual site model icon linkage sequence would have a national database icon linked to a regional database icon linked to module icon. Because the regional database and module icons are directly linked, the user is being informed that the most detailed and appropriate data are being used in assessment, that is, the regional database is the primary database supplying information to module. The design for this requirement will be enforced for each system-supported Date Client Editor. This will also be strongly recommended for each Date Client Editor not supported by the system (i.e., developed by those not representing the system).

- The essential spatial information required to define conceptual site model is passed, via th edictionary data file specifications, containing all the spatial modeling data. The dictionary files have been structured to allow for the model developer to specify those parameters that are spatially aware. Data are spatially aware, when they have been designated as having a *Location* index, constituting coordinates of vertices associated with a polygon. Clear distinctions have to be made between spatial system data (i.e., spatial layout of components, such as sources and receptors) and non-spatial model data (i.e., porosity, temperature, Kds, toxicity, age, etc.). The spatial data entered through the conceptual site model Graphical User Interface is divided into three object categories: points, lines, and polygons, all requiring coordinates of their vertices.

Modular

- The fundamental responsibility of the framework is associated with the arrows connecting models and databases. Those arrows represent the transfer of information from one component to another. The system is charged with managing the model and database linkages, firing sequence of models, and data transfer between components. The system is not responsible for what happens within models. The key to a successful transfer is to ensure the producing component provides information and meets the needs of the consuming component and the information is in a form that is recognizable by both components. This shared responsibility for managing data transfer is based on datasets, whose meta data information is described by the Dictionary files. Data specifications, between communicating models, represent the "contract" between what the upstream model produces and what the downstream model consumes.

  The Application Programming Interface and Dictionary file design allows for the "Plug & Play" feature, which is the most important feature of design. By ensuring Plug & Play, CCEF inherently includes the ability to
  • link any type of model, database, or framework into the system to communicate with any other component.
  • allow model developers, government organization, private companies, etc. to incorporate their own models and databases into the system without the necessity of going through the system developer as a middle-man.
  • ensure backward compatibility between legacy models and databases, and new models and databases.
  • allow linkage specifications to change with time and company.
  • link to remote databases or models.
  • link to remote frameworks, without having to integrate remote frameworks into CCEF.
  • link to remote databases and only download information necessary for assessment.
  • integrate change into system without having to redesign components are already included in system.
- The basic design of the CCEF allows for data to be imported to or exported from system at specified locations correspond to the Dictionary files. A user can also enter the system at any specified location, and they do not have to begin with a source module. Importing a file is different from importing a file that meets the specifications of a Dictionary file. System will allow for access into system though boundary conditions between icons. The imported information may be provided by a module, file, spreadsheet, etc. Regardless of importation mechanism, information must match the Dictionary file information (e.g., boundary condition file specifications associated with the boundary condition or system specifications), where appropriate. For example,

chemical names must coincide with those recognized by system.

- The icon pallet in the System would be designed to expand into unlimited number of tiered levels. Because usability is severely compromised when too many tiered levels are at disposal of the user, only four main levels will be utilized in the first version of the system with first level or Domain being icon-less level identifies type of assessment being performed [e.g., Chemical Life Cycle, Travel Life Cycle, Human Life Cycle, Process Life Cycle, Activities Life Cycle, Idea Life Cycle, or some other unique Domain].
- The icon pallet in the System will allow for the unlimited number of icons from which to choose. The design is to have a vertical scroll bar from which the user can choose the most appropriate icon. Text will be permanently visible with all icons.
- With the Drag & Drop feature, the user will have the icon pallet from which to chose their modeling categories, which contains the choice of models. The icon pallet will be tiered, so intricate divisions in simulations can be captured. For example in transport and fate, surface water modeling can be divided into rivers, lakes, reservoirs, estuaries, bays, oceans, etc. Exposure route modeling can be divided into inhalation, oral, and dermal contact. The icons and icon categories can be changed to meet whatever need is identified. The standard Environmental Protection Agency risk assessment paradigm and micro-environmental modeling would have separate Domains associated with it, as such would have its own Classes, Groups, and SubGroups.
- The icon pallet is designed to allow new module icons, in addition to expanding icon list.
- Using Application Programming Interface, the linkage of disparate models in space and time will follow approach outlined elsewhere in document. The linkage will occur through boundary conditions. Supplemental linking software will be provided for those consuming models that do not have a protocol for converting information from a producing model.

User-Friendly

- The System will be designed to operate on a PC, with Microsoft NT or Win2000 platforms with a minimum of 128MB RAM Pentium or equivalent, and 1GB free disk space.
- The System should at least support latest versions of Borland C++ Builder, Microsoft Visual C++, Lahey FORTRAN-90, and Digital Visual FORTRAN-90 compilers. Supporting these compilers are not necessarily issue, unless the number of compilers propagate to unmanageable number, as Application Programing Interface calling conventions in Dynamic Link Library are a function of compiler. The users need to meet the standard calling convention to Application Programming Interface.
- The CCEF would provide a standardized set of reports and plots correspond to typical information currently requested from assessments (e.g., time-varying concentrations at a location, spatially varying concentrations for a given time, probability of excedence versus risk, etc.). The user would also have theability to link model-specific unique graphical and tabular interfaces (e.g., report generator and Environmental Protection Agency's RAGS Part D tables). These features would be associated with the *Viewers*.
- The first version of the System will print, as a minimum, tables and figures, designated as system *Viewers*. A print feature will be available to print on-screen information (e.g., conceptual site model), viewers, tables, figures, and files.
- The HTML procedure will be utilized to provide on-line help for system components. The models are the responsibility of the modelers. The linkage specifications are the responsibility of the system. On-line help for system components will be provided such that links back to a standard "document" containing necessary information, which lends itself to be updated and modified independent of software system. On-line help would include Date Client Editor associated with system-supported databases, interface requirements at boundary condition (i.e., system-supported, user-specified boundary conditions). System databases would also need a database editor for system-supported databases.
- A Units Conversion Dynamic Link Library will be provided to ensure models work with their specific units and all conversions between models will be handled by the system. The Data Owner Tool and database server will include units with database information.
- A conceptual site model work space, similar to that exhibited by FRAMES, GoldSim, or MMS will form the basis for representing user-friendly graphical interface. This interface would be developed using Visual Basic, possibly American National Standards Institute C, or Java.
- The Drag & Drop design will be incorporated into System. The System will allow a user to develop a conceptual site model with Drag & Drop features,

similar to existing state-of-the-art graphically based interfaces (e.g., Stella, FRAMES, ARAMS, GoldSim, MMS, etc.).

- Based on Input and Boundary Condition Dictionary files, a summary of data requirements will be made available for models chosen under conceptual site model.

Multi-route

- The design of the CCEF promotes the ability of the system to respond to the user-specified conceptual site model are applicable to exposures via inhalation, oral, and dermal contact with consumer products. If models, databases, or frameworks exist, which provide adequate description of these exposures, then the framework allows for the user to address these conceptual site models. The user could use the Environmental Protection Agency standard risk models, which typically integrates exposure routes and pathways, not modularizing them by inhalation, dermal contact, or inhalation.

Multi-pathway

- As with exposure routes, the CCEF design promotes the ability of the system to specify, not only exposure route but, specific exposure pathways associated with the route, for example when a more accurate lung model is needed to produce/consume information for/from micro-environmental model for air-to-lung exposures. The CCEF design allows the user to design the conceptual site models within conceptual site models to telescope into the problem and allow for most applicable tools to be used to solve the problem.

Multi-source

- The design of the CCEF anticipates the transfer of data associated with multiple constituents from one component to another within the system. The design promotes not only the ability to transfer the degradation/decay products but allows the user to chemicals and lifeforms when data associated with those classifications do not exist. The framework provides the model developer with the ability to transfer computer synergistic or other forms of impacts from exposures to multiple constituents.
- The Data Client Editor will allow for the aliasing of chemicals and/or life forms, where appropriate. If the database is supported by System, then the Data Client Editor is supported by the system. If a new database is added to the system and is not supported by the system but is unique to support a given module, then the Data Client Editor is the responsibility of the database and module owners. A Data Client Editor would need to be written for each of modules. The Data Client Editor will allow for surrogates on chemicals and lifeforms. Data Client Editor will allow the user to change any value at any point in time. If the user changes a value, a reference note will be invoked, tracking and noting the value was "Entered by User." The Data Owner has the responsibility to provide a reference for every value in the database. When extracting data, data editors will have the functionality to extract references.

Varying Duration

- Time can be handled in several manners within the design of the CCEF. The information is provided to the models has aspect of time associated with it, and the models themselves are designed with respect to a particular reference time:

  A. The CCEF design allows for time-varying concentrations or doses to be expressed in fractions of seconds, minutes, hours, days, years, or millennia. Each model, especially numerical models, calculate time stepping and have a nodal-spacing mesh are consistent with their own model, while ensuring numerical convergence and stability. Temporal considerations for linking models with disparate time-stepping requirements are independent of any model. To remove model-specific time stepping from dictating manner in which models communicate, each of model's time-stepping requirements are accounted for when passing information between models. Each producing model will provide time-varying output corresponding with each producing model's area-based polygons, if polygons describe boundary interface between models. The time-varying output from producing model is a function of time steps used in generating time-varying curve. system does not know if time information between data-points on time-varying curve is linear, constant, nonlinear, etc., as such, each producing model's time-varying curves will have their own time-stepping protocol for each parameter for each polygon. When

consuming model maps producing model's polygon outputs and transfers information from producing model's gridding system its own, the consuming model is responsible to account for time-stepping system producing models provides.

B. The models are inherently designed with respect to a particular reference time. For example, the standard Environmental Protection Agency's risk paradigm assumes long-term, chronic exposures in their assessments. Acute exposures traditionally are not part of SUPERFUND calculations and Risk Assessment Guidelines for SUPERFUND (RAGS). Models that are designed for acute exposures would typically expect time-varying data from producing models or databases, which are consistent with design of model. For example, the upstream model produces the time-varying output in thousand-year increments that would not be a good candidate to link to acute exposure model expects variations in data in terms of hours. The CCEF design allows for the Dictionary files to be designed to specifically filter acute versus chronic forms of information. As an example, the air pathway traditionally has Dictionary files that are specific to Gaussian, sector-averaged models and a different set associated with puff models. A similar solution to the problem can be implemented for other components in CCEF.

Accurate

- Each model or database inherently contains implied assumptions that are not always known as a priority by the user. Similar models do not necessarily produce similar results, as developers tend to factor unintended differences into their models. By coupling the Plug & Play features with Drag & Drop approach, the CCEF design provides the user with the ability to directly compare ramifications of different models or databases are intended to have the same functionality. The user would have the ability to benchmark these models or databases to support more accurate assessments by allowing the analyst to the determine most appropriate components for addressing the problem.
- The CCEF design allows the user to select the most appropriate state-of-the-art estimation methods and databases to estimate or reasonably overestimate the "ground-truth" of the actual exposure. The framework is flexible enough to allow the user to also select the most appropriate time and spatial requirements. The modularity of CCEF design supports the notion that the best science-support tools can be utilized to more accurately address the problem at hand.
- A Password-protection system will form the basis for allowing the user to lock the conceptual site model (i.e., icon picture screen) and/or the model selections associated with each icon. To provide the ability to easily reproduce the standard assessments, the CCEF design will incorporate lock and key features that allow a user to: a) fix the conceptual site model by locking icon types and connections between icons, and b) lock the models that are available under each icon.

  The user should be allowed to choose either option or both options together. The first option implies the conceptual site model picture (i.e., user-defined icons and connections) is locked and the user cannot make new connections between icons. The second option restricts models that are available to user, greying out those models that are not allowed as a choice. Lock and Key software shall
  a. allow for a user option to have the conceptual site model locked.
  b. allow for a user option to have the models beneath icons locked.
  c. allow for a user option to have the conceptual site model and models beneath icons locked.
  d. allow for a user-defined password
  e. allow for use of no password.
  f. include algorithms that will alert users when source codes have been modified when system is locked.
  g. include algorithms that will prevent users from using modified source codes when system is locked.
  h. design the CCEF so the framework works the same, regardless of whether the lock-and-key option is implemented.

Open Code

- The design of the CCEF is based on the premise all software associated with framework is nonproprietary. This does not, though, preclude the user from linking the proprietary software into the system.
- The design of the CCEF allows for the inclusion of commercial-off-the-shelf software (e.g., Risk*Assistant, Risk*Works, LifeLine, LCAdvantage, etc.).
- A file will be available for documenting scenarios. The "Pop-Up Notes" will be used to document module assumptions by using the "Right Click" feature. Summary files and tables will be generated summarize assumptions used in problem. The user will be allowed to modify data retrieved from a database using Date Client Editor at time data are retrieved. The user will also be allowed to view, but not change, data in module user interface of modules database icons are connected to. A file will be developed to document assessment name and associated files, assumptions of assessment; conceptual site model; databases and models chosen for assessment; descriptions of databases and models; input requirements, descriptions, and references for data; dates and versions of databases and models, etc. This may be HTML file. Some of this information may be captured in a report generator, which summarizes the assessment.

Probabilistic

- Using Application Programming Interface design and the Dictionary files, the System design allows for multistage sensitivity uncertainty analyses by allowing sensitivity uncertainty modules to be connected to the framework at multiple specified locations. For example, the sensitivity uncertainty module could be connected to outside of module, representing a framework, which contains sensitivity uncertainty module. In other words, one could literally link the sensitivity uncertainty to frameworks, treating them as objects, or one could place them inside the Framework conceptual site model, treating sensitivity uncertainty as the object. Sensitivity uncertainty models could also be nested with sensitivity uncertainty modules, as long as appropriate Dictionary files are compatible.

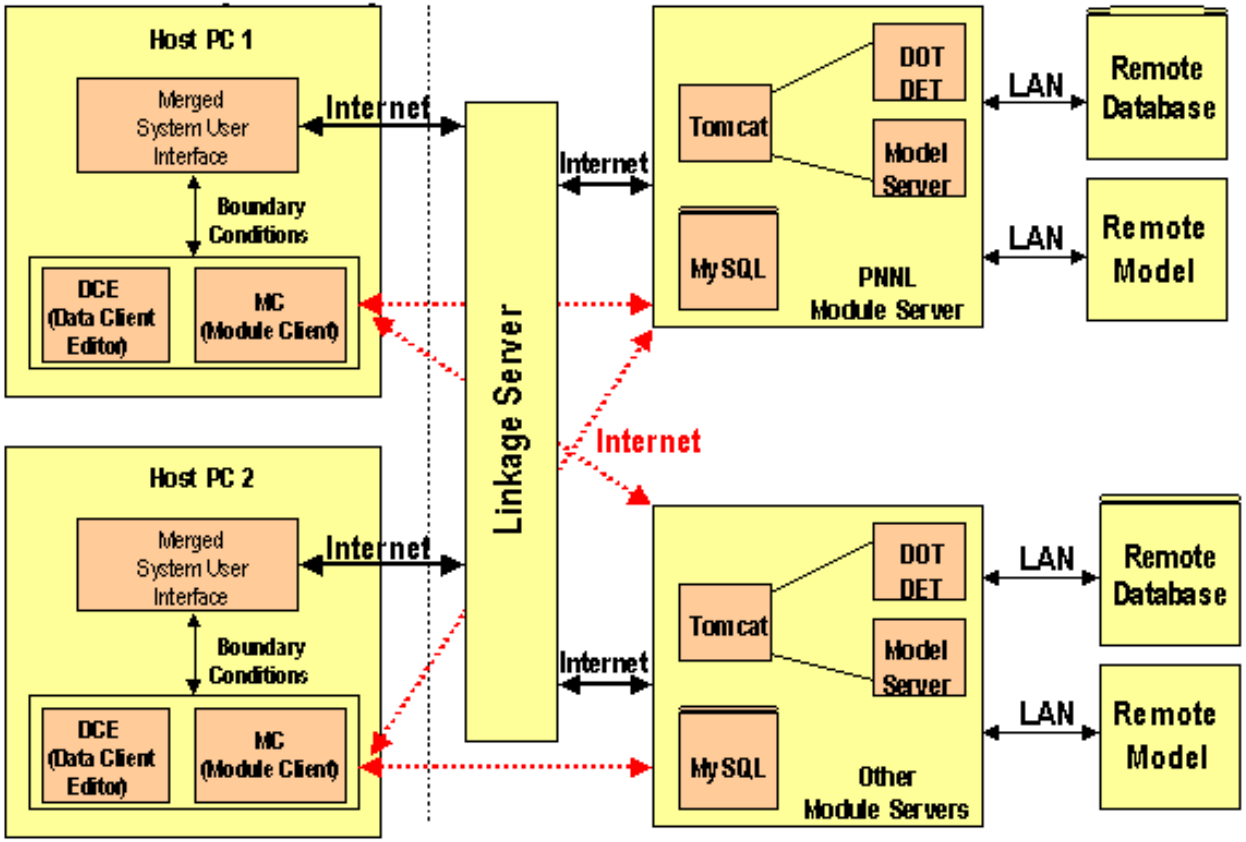
Dose-response

- The design of the CCEF allows the user the ability to link in the most appropriate models and databases to convert exposure estimates to corresponding dose and risk values, whenever appropriate. The system also allows the user to view these estimates with either system or unique graphical or tabular viewers.

Mass-conservative

- One of the linkage requirements of each model, where appropriate (e.g., transport models) will be to report total mass leaving module. This information will be the responsibility of the module not the system. The system will only pass this information along to downstream modules and user. This is a requirement of every model in the system to conserve mass and account for mass balance in their model. Each model is responsible to ensure mass is conserved within its system. As a minimum, the system will provide to the user, if produced by the module:
  a. total mass exiting, associated with each of its boundary conditions [i.e., leaving system through a particular mechanism (e.g., leaching, volatilization, suspension, runoff, etc.].
  b. mass flux rate versus time for boundary conditions requiring mass flux rate.
  c. mass versus time remaining in module.

Figure 3.4.3 CCEF Design Relationships between Linkage and Model Servers, Host Client, and Remote Databases and Models

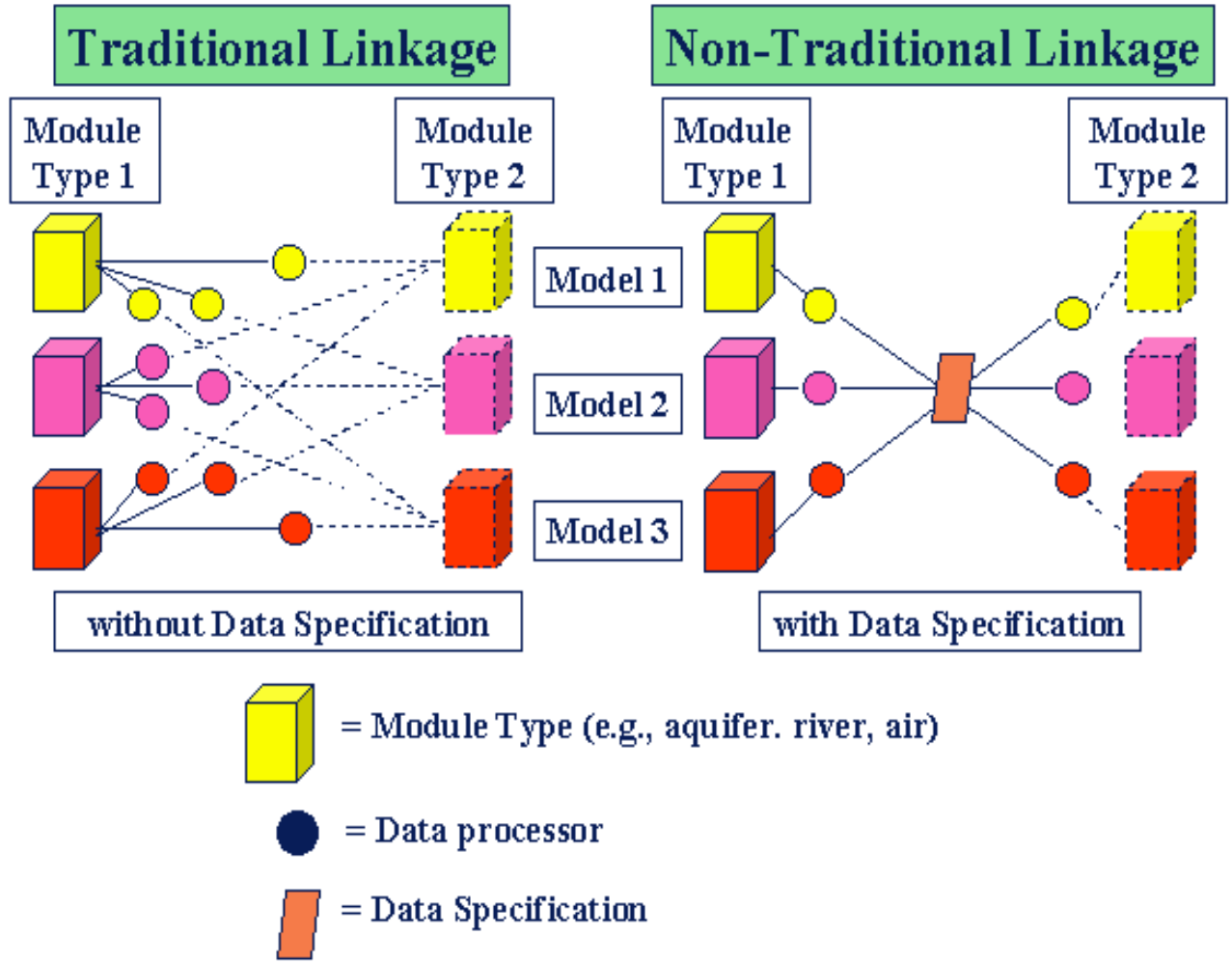


Return to text.

3.5 Data Exchange Protocol

In the past, the traditional approach for linking models was to directly connect (i.e., “hard-wire”) module types (e.g., aquifer models to river models). Each connection specifically reflected the data needs of the consuming model, resulting in an efficient transfer of data but also resulting in a confusing model structure, difficult to manage and update. Under the traditional approach, if a user wanted the ability to link several models of a certain type (e.g., 1-dimensional, 2-dimensional, and 3- dimensional aquifer models) to several models of a different type (i.e., 1- dimensional, 2- dimensional, and 3- dimensional river models), each model was directly linked (i.e., hard-wired”) to each other through a processor. With this approach, a user could choose to link any one of the aquifer models to any one of the river models. The following figure illustrates the traditional approach for linking models (i.e., module types in the figure) and data transfer. This linkage scheme is very efficient and exact, allowing for direct communication between models and providing an environment for dynamic feedback between models. Unfortunately, as illustrated by the figure, this scheme can become extremely complicated and unmanageable and does not allow the user to add new models, parameters, data requirements, databases, etc. to the system without having to modify the entire system and revamp legacy models.

Figure 3.5.1 Traditional and Nontraditional approach for Linking Models and Transferring Data



With the advent of "object-oriented" modeling concepts, each of the models, which enters into the system, agrees on a data exchange protocol. The non-traditional approach identifies system data specifications to which models adhere when passing information between model types and databases, as illustrated in the above figure. Pre- and post-data processors allow legacy models to remain unaffected and facilitate the ability to "plug" legacy models directly into the system, enhance quality control, and simplify management of and modifications to multiple models. This Plug & Play attribute is an extremely powerful and desirable feature, as it allows users and model developers to insert the most appropriate models to meet specific needs.

Data specifications between communicating models represent the contract between what the upstream model produces (e.g., aquifer model) and what the downstream model consumes (e.g., river model). The data specification is similar to the telephone numbers in a telephone book. Both parties agree to the telephone numbers, and, when each wants to communicate, they do so using the appropriate telephone number (see the following figure). Each year the telephone books are updated (see the following figure); as such, the design of the CCEF must accommodate new models, data requirements, parameters, and linkages but still maintain backward compatibility with existing models in the system.

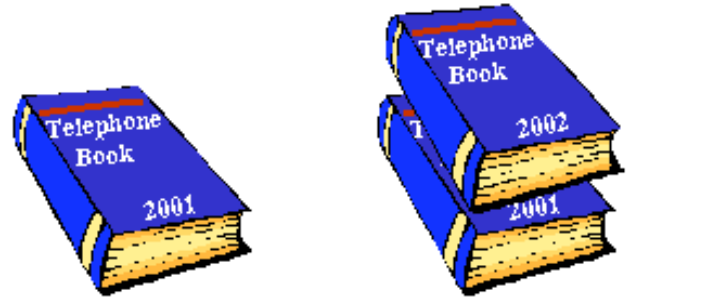


Figure 3.5.2 Using Annual Telephone Books to Illustrate the Concept of Backward Compatibility

As noted earlier, the fundamental responsibility of the *Framework* is associated with the arrows that connect the models and databases, as illustrated in the figures below and in the model flow diagrams for **scenario 1**, **scenario 2**, **scenario 3** and **scenario 4**. Those arrows represent the transfer of information from one component to another. The system is charged with managing model and database linkages, the firing sequence of the models, and data transfer between components. The system is not responsible for what happens within the models. The key to a successful transfer is to ensure that the producing component provides information that meets the needs of the consuming component and that the information is in a form that is recognizable by both components. This shared responsibility for managing data transfer is based on datasets, whose metadata information is described by Data Dictionary File.

Figure 3.4.2.1 Illustrative Example of Linking Models Together into a Standard Risk Paradigm, using the 3MRA-HWIR Assessment Methodology

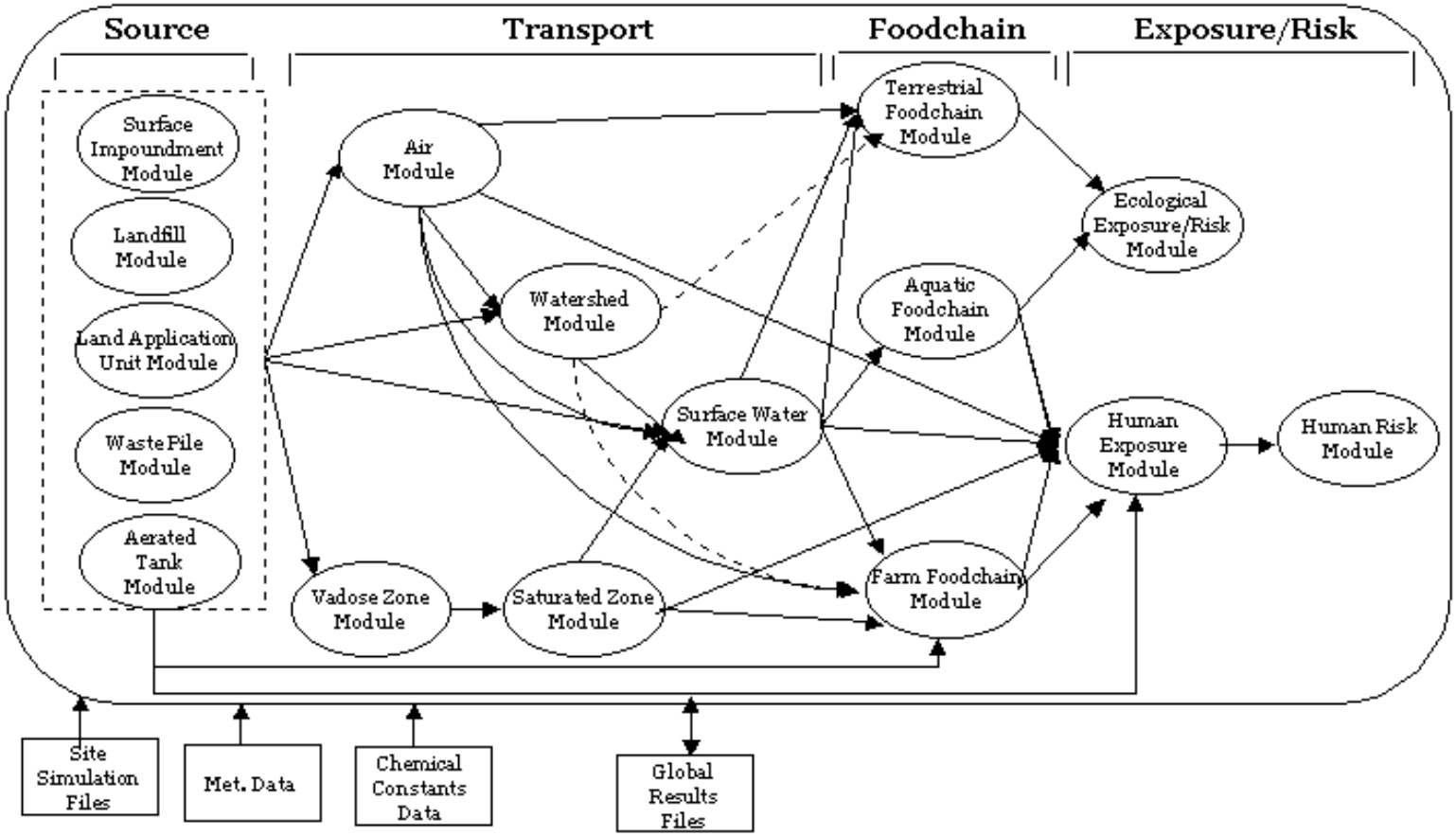
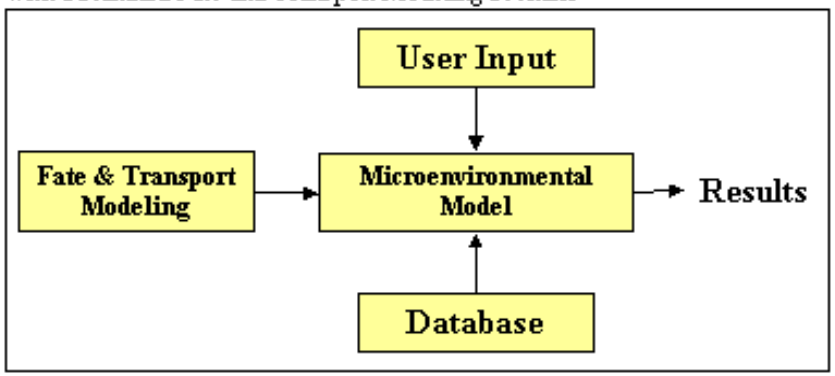


Figure 3.4.2.2 Example Illustrating the Linkage of a Microenvironmental Model with a Standard Fate and Transport Modeling Scenario



4.0 CCEF Scenarios and Gap Analysis

This section provides the scenario-specific Model and Process Flow Diagrams based on the CCEF design, as well as the research gaps identified in the process of developing the flow diagrams.

These diagrams were developed for this study based on the compounds and exposure scenarios that the American Chemistry Council Human Health Exposure Assessment Technical Implementation Panel identified.

The gap analysis was conducted based on the four example exposure scenarios associated with the CCEF. A gap analysis provides a list of research needs associated with the specific topic of interest.

In this case, the gap analysis will provide the research needs for the framework, models, algorithms, and databases associated with the four exposure scenarios developed to define the design of the CCEF. The gap analysis consists of a three-step process in evaluating the Modeling and Process Flow Diagrams developed for the design of the CCEF. The three steps of the gap analysis are: 1) define what exists, 2) define what is needed, and 3) define the process to achieve the identified needs.

4.1 CCEF Life Stages

It is critical that the CCEF be able to accommodate the various life stages of a human to develop the aggregate and cumulative health effects. To effectively model the aggregate and cumulative health effects of high volume compounds, a number of different life stages must be taken into account for each scenario. The age definitions of each life stage and terminology may vary but the presented information is a good guideline to follow.

This section introduces these life stages. Move your mouse over the timeline for a description of the life stages. For information on the specific life stages involved in each Exposure Scenario, click on the individual scenario of interest.

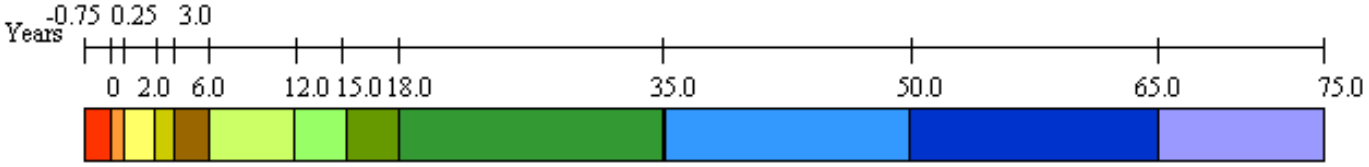


Figure 4.1.1 Life Stages For Exposure Scenarios

Scenario 1
Scenario 2
Scenario 3
Scenario 4

4.2 Scenario 1

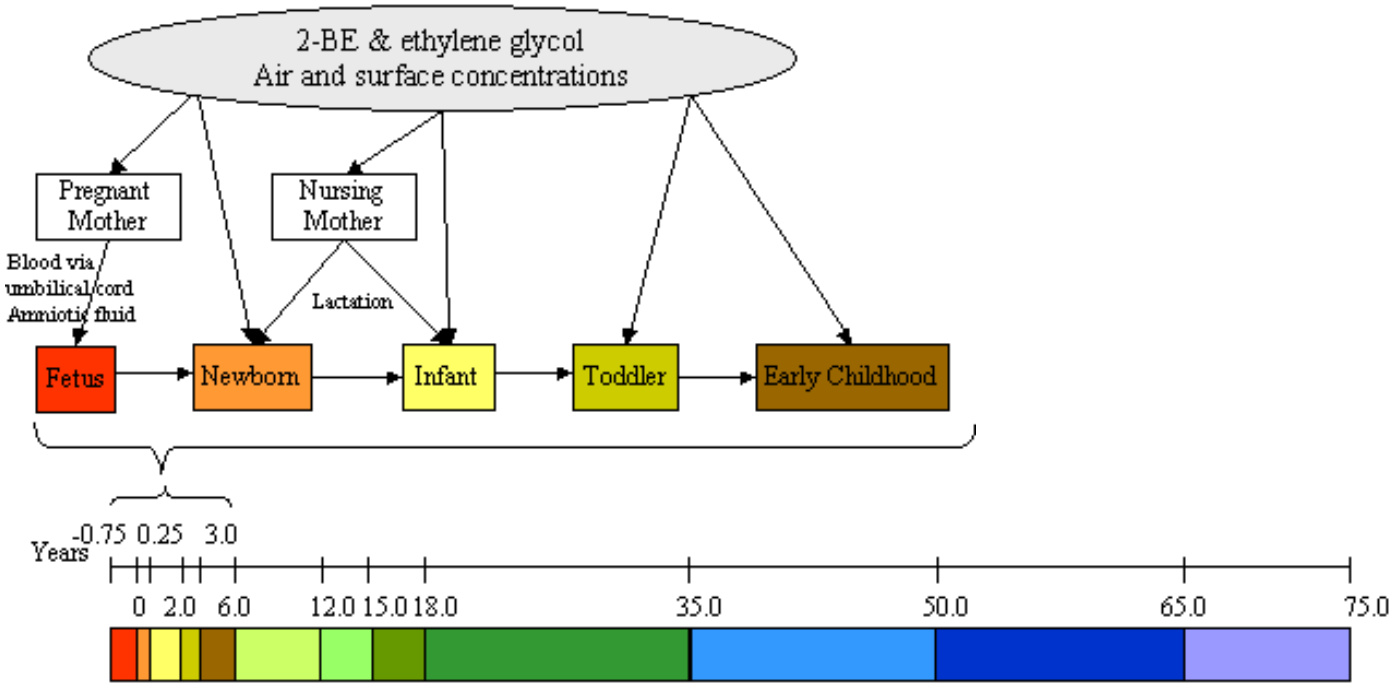


Figure 4.2.1 Life Stages For Exposure Scenario 1

Scenario 1
Scenario 2
Scenario 3
Scenario 4

Scenario 1

This section provides the conceptual model for the exposure pathways associated with Exposure Scenario 1. The conceptual model and associated assumptions are critical in determining the type of the models, algorithms, and databases required to satisfy the needs of the modeling scenario. Figure 4.2.2 provides an illustration of the conceptual model for Exposure Scenario 1.

Residential Indoor Description

- 1-story Townhouse with 1700 ft2 in MA
- Electric heat pump, forced air and AC
- 3 bedrooms, 1.5 baths, kitchen, living & dining rooms

Exposure in Home to SVOC Compounds A & B

- Compound A: **2-butoxyethanol** applied in mineral spirits solution by immersion of wooden strip ceiling at factory
- Infant born 12 months after moving into home
- Mother stays at home and nurses baby

- Compound B: **ethylene glycol** contained in latex wall paint
- Entire living space painted when moved into home (-1 year) and repainted 1 wk after baby arrives

Figure 4.2.2 Illustration Depicting The Setting For Exposure Scenario 1 In Study

Assumptions about Exposure and Activities

- Embryo embedded at day 11 after fertilization
- Normal length of pregnancy (9 months)
- Nursing from birth until 0.5 yrs (6 months)
- Repaint home when child is age 4

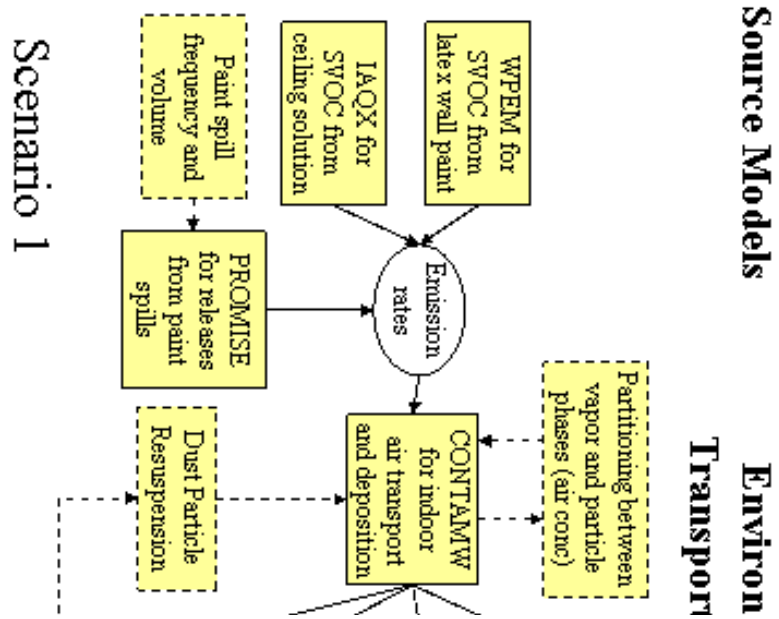
Child Age Timeline

- Fetus (-0.75 years until birth)
- Newborn (birth to 0.25 yrs) (3 months)
- Infant (0.25-2 years)
- Toddler (2-3 years)
- Early Childhood (3-6 years)

Notes

- Health effects will be calculated for the fetus through child. Depending on model outputs, this can be a cumulative time distribution or a time-weighted value.
- The infant is born 12 months after moving into home.
- The mother works at home and nurses baby.
- There will be a spiked increase in **ethylene glycol** at week 1 when fresh paint is applied over the entire living space.

Figure 4.2.3 CCEF Model Flow Diagram Scenario 1



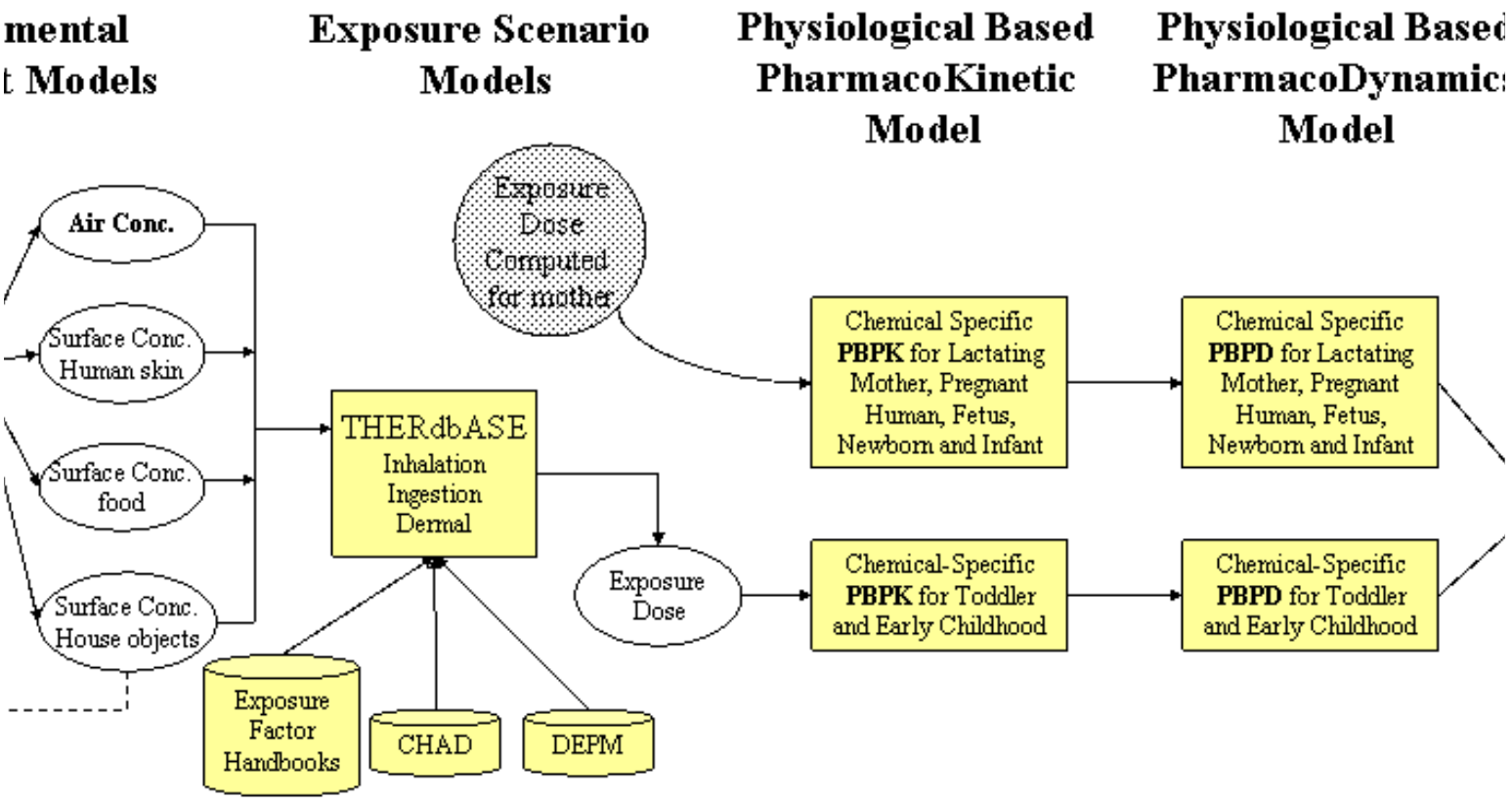


Figure 4.2.3 CCEF Model Flow Diagram Scenario 1

Diagram Legend	
Solid boxes	Models with known codes available
Dashed boxes	Models with codes not available
Ovals	Input/output files with specific data specifications
Checkered Ovals	Output from separate scenario/input to this scenario
Cylinders	Model-Specific databases
Arrows	Indicates the flow of the data
PBPK	Physiologically-based Pharmacokinetics
PBPD	Physiologically-based Pharmacodynamics

Notes

- Health effects will be calculated for the child from birth through year 18. Depending on model outputs, this can be a cumulative time distribution or a time-weighted value.
- WPEM was developed for latex or alkyd paint
- IAQX can be used for the solution on wood ceiling strips, since it is for emissions from building materials, including dry sources
- Indoor air transport modeling (SVOC emission) can be handled by many models, we selected CONTAM for this case, because it can handle aerosols and predicts airflows based on room sizes, but at least 4 other models identified in the literature review could be used. Some of the transport models are planning to add aerosol, and particle deposition components and in some cases separate models could handle deposition to product surface concentrations.
- THERdbASE is used to estimate human activity patterns and exposure doses. We would prefer to use LifeLine, Cares and other multi-route, multi-source models but it is difficult to integrate them because they are proprietary and much of the needed information is not readily available.
- DEPM includes information on food intake for estimating dietary exposure.
- CHAD is a master database that provides information on human activity.
- EPA's Exposure Factors Handbook for adults (http://www.epa.gov/ncea/exposfac.htm) and the Child-Specific Exposure Factors Handbook will be used as appropriate.
- Note that the exposure dose to the mother is assumed to have been computed by a different scenario and those results are incorporated into this scenario and feed to the PBPK/PBPD model for pregnant and nursing mothers.
- There are PBPK or PBPD model for each of the two chemicals of concern but only the ethylene glycol model was developed using a pregnant animal

model (Sprague-Dawley rat). The 2-BE model was developed in an adult male.

- A PBPK model for a newborn or child could not be found and is necessary because of their unique characteristics.
- It should also be noted that interactions and competing causes of action could also be incorporated in the PBPK and PBPD models if the information were available
- LifeLine, CARES, and other lifestyle aggregate codes will overlay onto the PBPK, PBPD and Mode of Action models.

4.3 Scenario 2

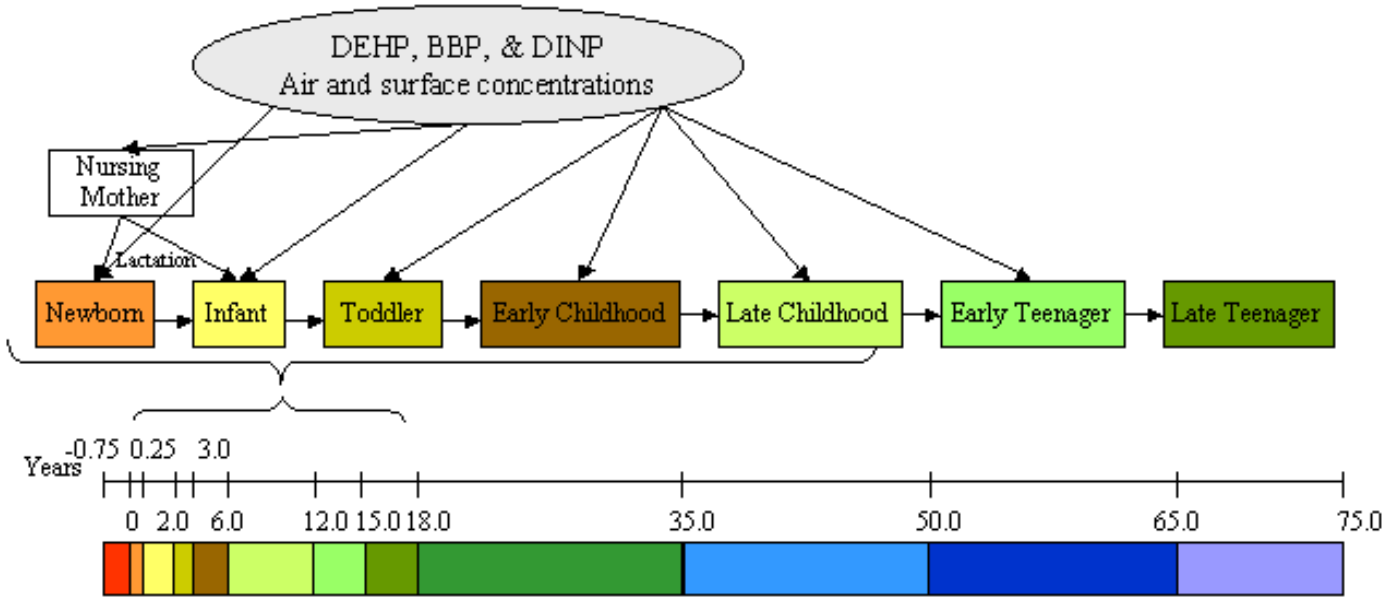


Figure 4.3.1 Life Stages For Exposure Scenario 2

[Scenario 1]
Scenario 2
[Scenario 3]
[Scenario 4]

Scenario 2

This section provides the conceptual model for the exposure pathways associated with Exposure Scenario 2. The conceptual model and associated assumptions are critical in determining the type of the models, algorithms, and databases required to satisfy the needs of the modeling scenario. Figure 4.3.2 provides an illustration of the conceptual model for Exposure Scenario 2.

Residential Indoor Description

- 1-story Townhouse with 1700 ft2 in MA
- Electric heat pump, forced air and AC
- 3 bedrooms, 1.5 baths, kitchen, living & dining rooms

Exposure in Home to SVOC Compound Group C

- Compound Group C: phthalate esters (DEHP, BBP, & DINP) in plastic

    DEHP: diethyl hexyl phthalate
    BBP: butyl benzyl phthalate
    DINP: diisononyl phthalate

- Exposure to phthalates in plastic furniture covers, carpet backing, and shower curtains
- Exposure to phthalates in plastic food wrap and containers
- Exposure to phthalates in plastic toys

Figure 4.3.2 Illustration Depicting The Setting For Exposure Scenario 2 In Study

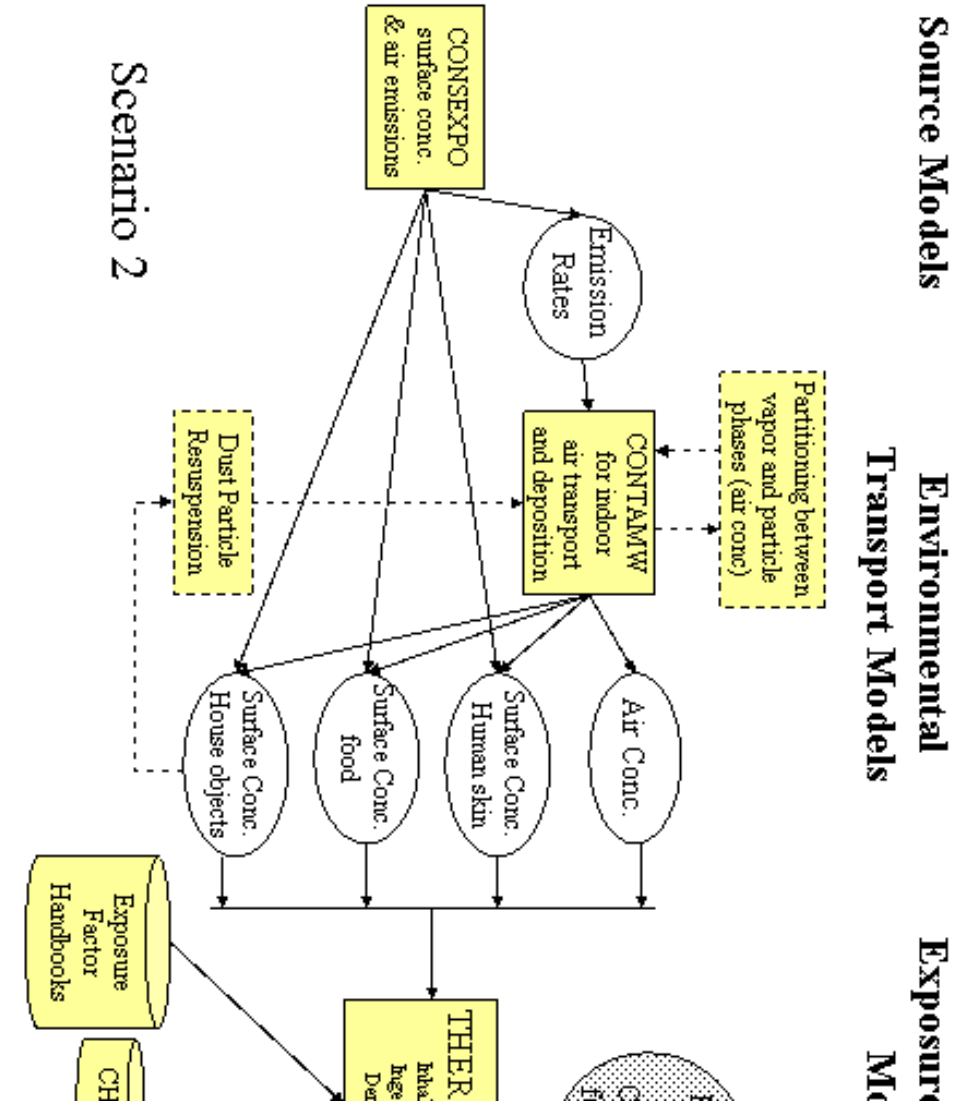
Assumptions about Exposures and Activities

- Nursing from birth until 0.5 yrs (6 months)
- Standard growth patterns
- Standard lactation and nursing patterns

Child Age Timeline

- Newborn (birth- 0.25 yrs) (3 months)
- Infant (0.25-2 years)
- Toddler (2-3 years)
- Early Childhood (3-6 years)
- Late Childhood (6-12 years)
- Early Teenager (12-15 years)
- Late Teenager (15-18 years)

Figure 4.3.3 CCEF Model Flow Diagram Scenario 2



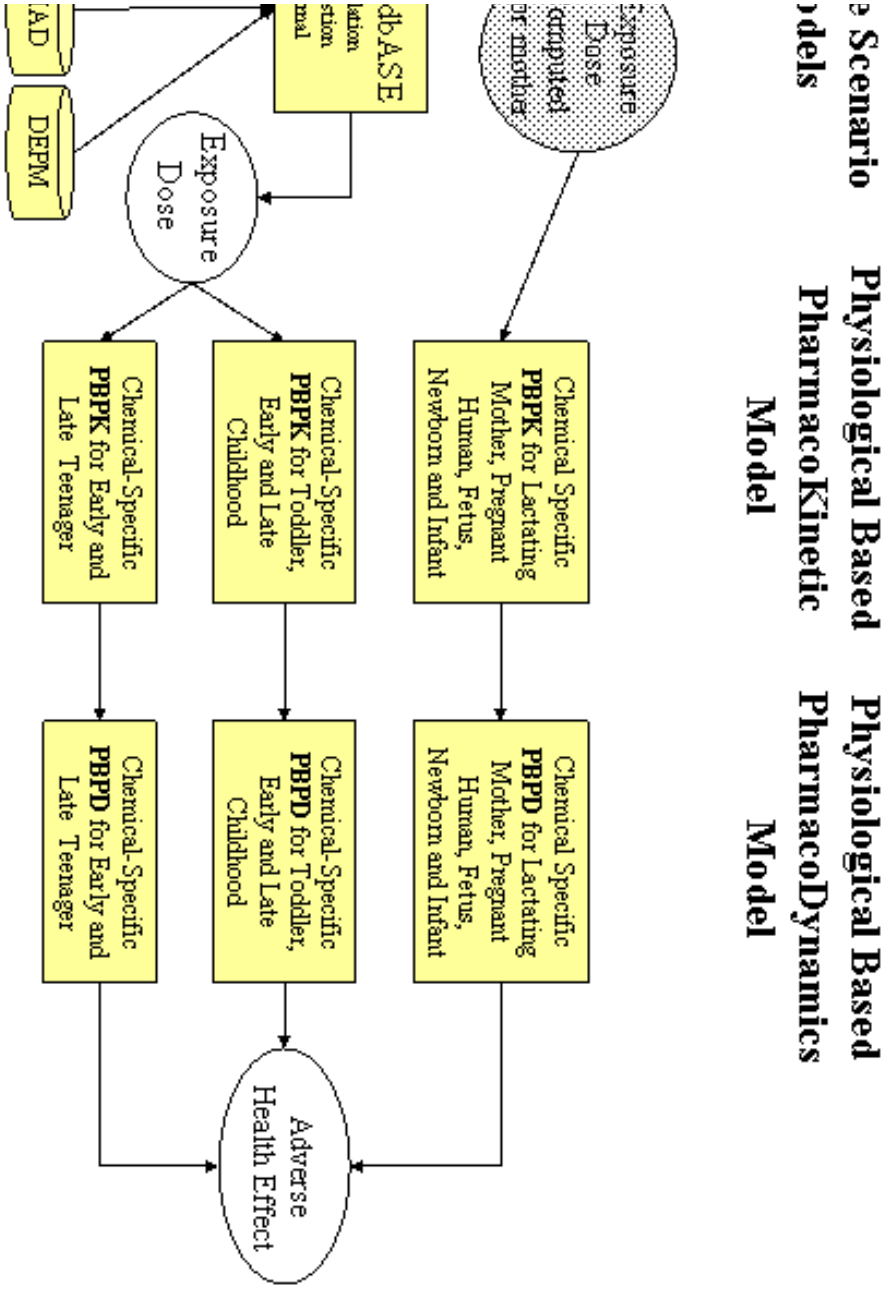


Figure 4.3.3 CCEF Model Flow Diagram Scenario 2

Diagram Legend	
Solid boxes	Models with known codes available
Dashed boxes	Models with codes not available
Ovals	Input/output files with specific data specifications

Checkered Ovals	Output from separate scenario/input to this scenario
Cylinders	Model-Specific databases
Arrows	Indicates the flow of the data
PBPK	Physiologically-based Pharmacokinetics
PBPD	Physiologically-based Pharmacodynamics

Notes

- Note that there is a PBPK or PBPD model for each of the three chemicals of concern, but these were developed specifically for an adult male. It may be possible to adapt for a child using different physiological parameters.
- It should also be noted that possible interactions and competing modes of action, could be incorporated into a PBPD model depending on available information
- LifeLine, CARES, and other lifestyle aggregate codes will overlay onto the PBPK and PBPD models.
- Indoor air transport modeling (SVOC emission) can be handled by many models, we selected CONTAM for this case because it can handle aerosols. However, there are at least 4 other models identified in the literature review that could be used. Some of the transport models are planning to add aerosol and particle deposition components, and in some cases, separate models could handle deposition to product surface concentrations.
- THERdbASE is used to estimate human activity patterns and exposure doses. We would prefer to use LifeLine, Cares and other multi-route, multi-source models but it is difficult to integrate them because they are proprietary and much of the needed information is not readily available.
- DEPM includes information on food intake for estimating dietary exposure.
- CHAD is a master database that provides information on human activity.
- EPA's Exposure Factors Handbook for adults (http://www.epa.gov/ncea/exposfac.htm) and the Child-Specific Exposure Factors Handbook will be usedas appropriate.
- CONSEXPO includes hand-to-mouth, leaching from objects in mouth, and leaching of contaminants into food items.

4.4 Scenario 3

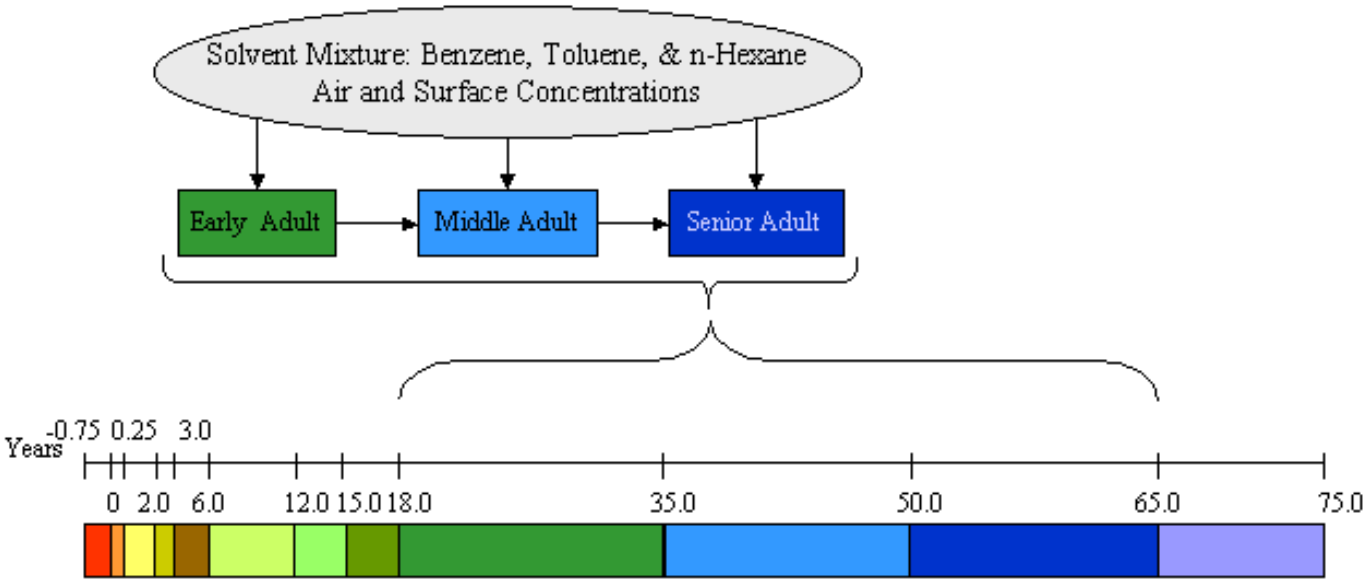


Figure 4.4.1 Life Stages For Exposure Scenario 3

Scenario 1
Scenario 2
Scenario 3
Scenario 4

Scenario 3

This section provides the conceptual model for the exposure pathways associated with Exposure Scenario 3. The conceptual model and associated assumptions are critical in determining the type of the models, algorithms, and databases required to satisfy the needs of the modeling scenario. Figure 4.4 provides an illustration of the conceptual model for Exposure Scenario 3.

Occupational Indoor Smoking Description

- Smokes 15-20 cigarettes per day since age 18, including 60% indoors and 10% outdoors at home and 30% indoors at work

Adhesive Compounding Facility Description

- Blending of solvent-based adhesive in 700,000 ft3 room

Occupational Exposure to VOC Compound Group D

- Compound Group D solvent mixture: benzene, toluene, n-hexane
- Exposure from routine compounding and hourly product sampling
- Exposure from cleaning agitator blades 2-3 times/week with one of solvents

- Exposure during cleaning of spill 2-3 times/year of cleaning solvent (1 gal), compounding solvent (30 gal), or product (50 gal)

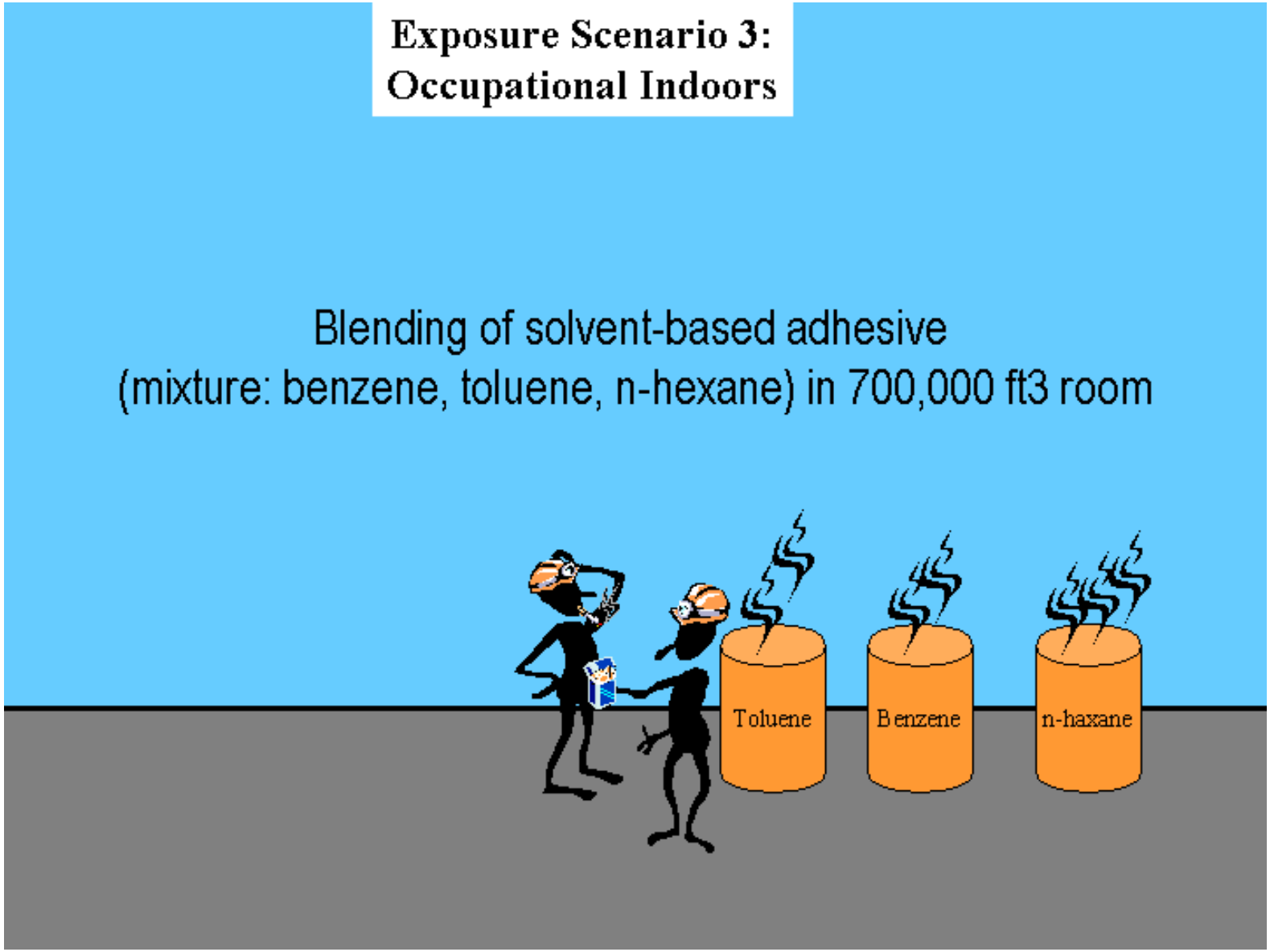


Figure 4.4.2 Illustration Depicting The Setting For Exposure Scenario 3 In Study

Assumptions about Working Conditions

- Work facility has separate smoking room
- Separate lunch room and no food or tobacco allowed in work area
- Attached shower/locker room with same heating/ventilation system as manufacturing room, where worker stores lunch and cigarettes
- Worker wears protective coveralls, neoprene gloves & apron, goggles, and full-face respirator with organic vapor cartridge to fill drums

- Worker adds protective full-face, positive-pressure SCBA and Tyvek coveralls for blade cleaning & spills
- Works typical schedule and hours

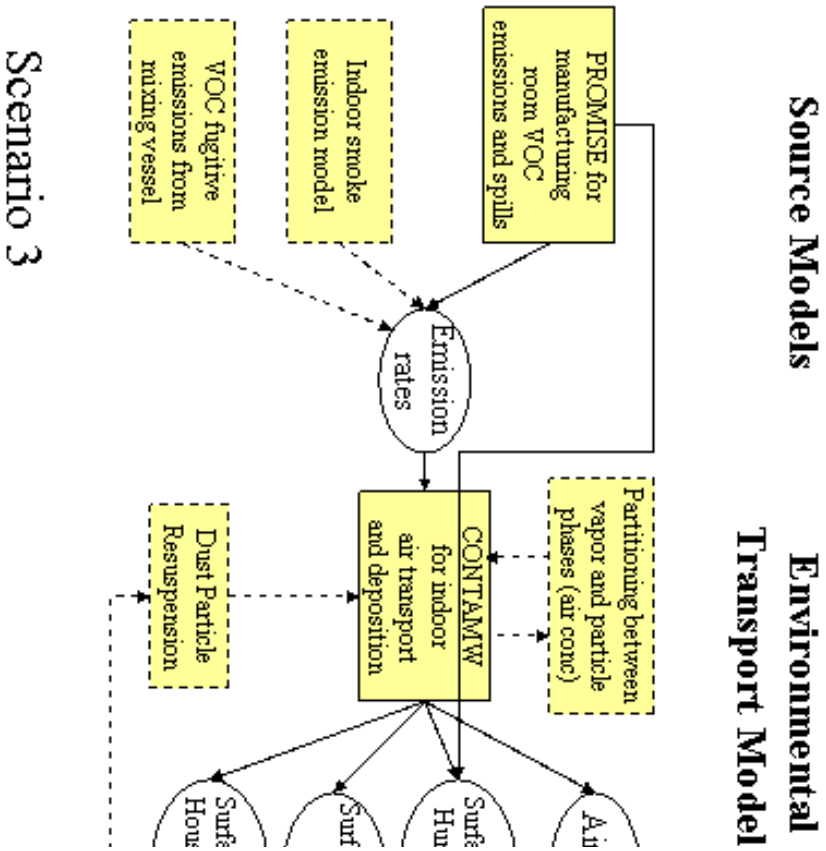
Adult Age Timeline

- Early Adult (18-35 years)
- Middle Adult (35-50 years)
- Senior Adult (50-65 years)

Notes

-Question: Exposure to solvent mixture at different intervals of time can/cannot cause harmful health effects. The longer the exposure the greater the potential for toxicity.
- Health effects will be calculated for the adult age 18 through 65. Depending on model outputs, this can be a cumulative time distribution or a time-weighted value.
---- Exposure from routine compounding and hourly product sampling.
---- Exposure from cleaning agitator blades 2-3 times/week with one of solvents.
---- Exposure during cleaning of spill 2-3 times/year of cleaning solvent (1 gal), compounding solvent (30 gal), or product (50 gal).

Figure 4.4.3 CCEF Model Flow Diagram Scenario 3



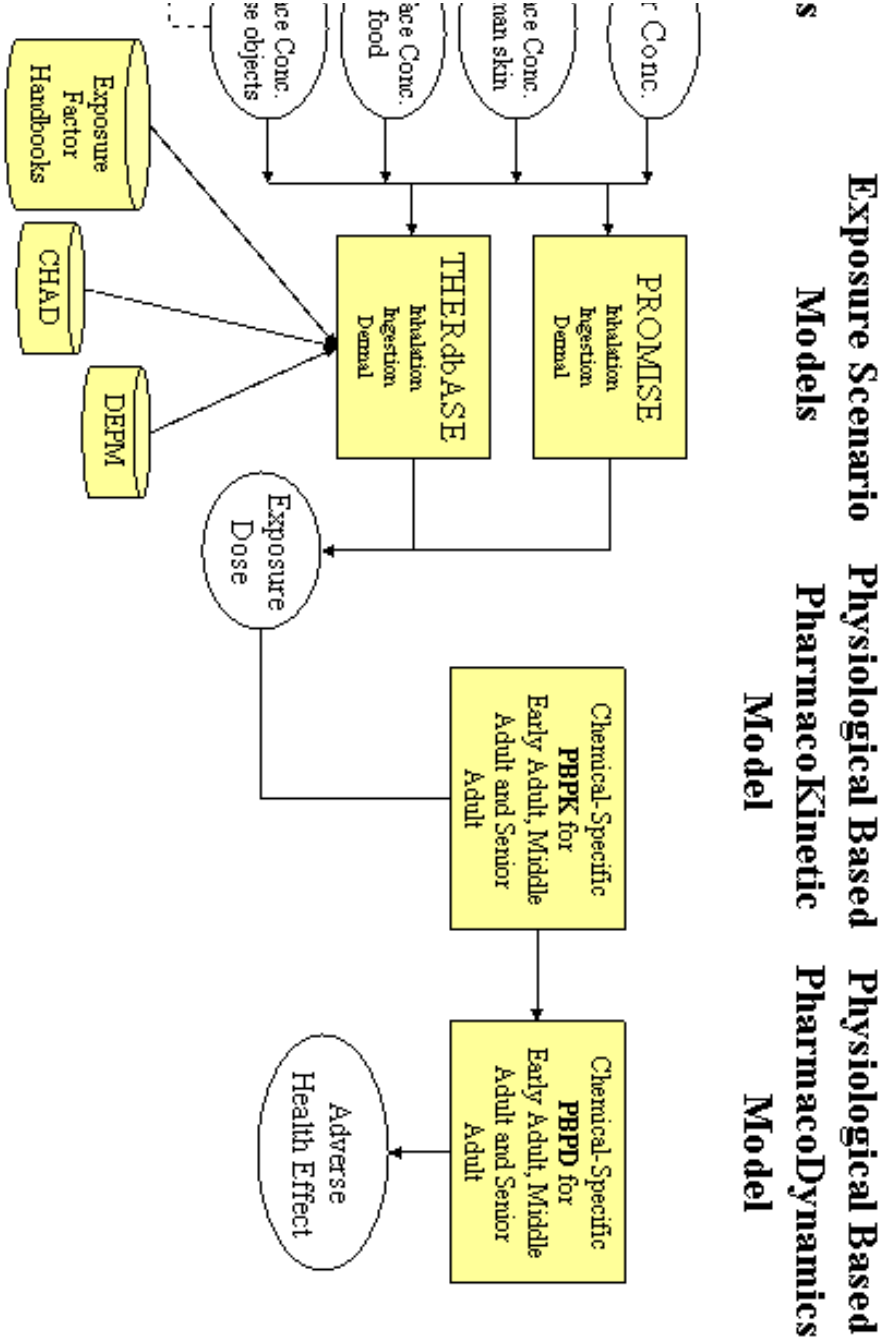


Figure 4.4.3 CCEF Model Flow Diagram Scenario 3

Diagram Legend	
Solid boxes	Models with known codes available

Dashed boxes	Models with codes not available
Ovals	Input/output files with specific data specifications
Cylinders	Model-Specific databases
Arrows	Indicates the flow of the data
PBPK	Physiologically-based Pharmacokinectics
PBPD	Physiologically-based Pharmacodynamics

Notes

- One possible source of models to use for mainstream smoking is from the external review article http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html for smoking release.
- Indoor air transport modeling (VOC emission) can be handled by many models, we selected CONTAM for this case, because it can handle aerosols, but at least 4 other models identified in the literature review could be used. Some of the transport models are planning to add VOC, aerosol, and particle deposition components and in some cases separate models could handle deposition to product surface concentrations.
- PROMISE and THERdbASE are used to estimate human activity patterns and exposure doses. We would prefer to use LifeLine, Cares and other multi-route, multi-source models but it is difficult to integrate them because they proprietary and much of the needed information is not readily available.
- DEPM includes information on food intake for estimating dietary exposure
- CHAD is a master database that provides information on human activity
- EPA's Exposure Factors Handbook for adults will be used accordingly.
- Note that there are PBPK or PBPD model for each of the three chemicals of concern but were developed specifically for an adult male.
- It should also be noted that interactions and competing causes of action can also be incorporated in the PBPK and Mode of Action models depending on available information
- LifeLine, CARES, and other lifestyle aggregate codes will overlay onto the PBPK and Mode of Action models.

4.5 Scenario 4

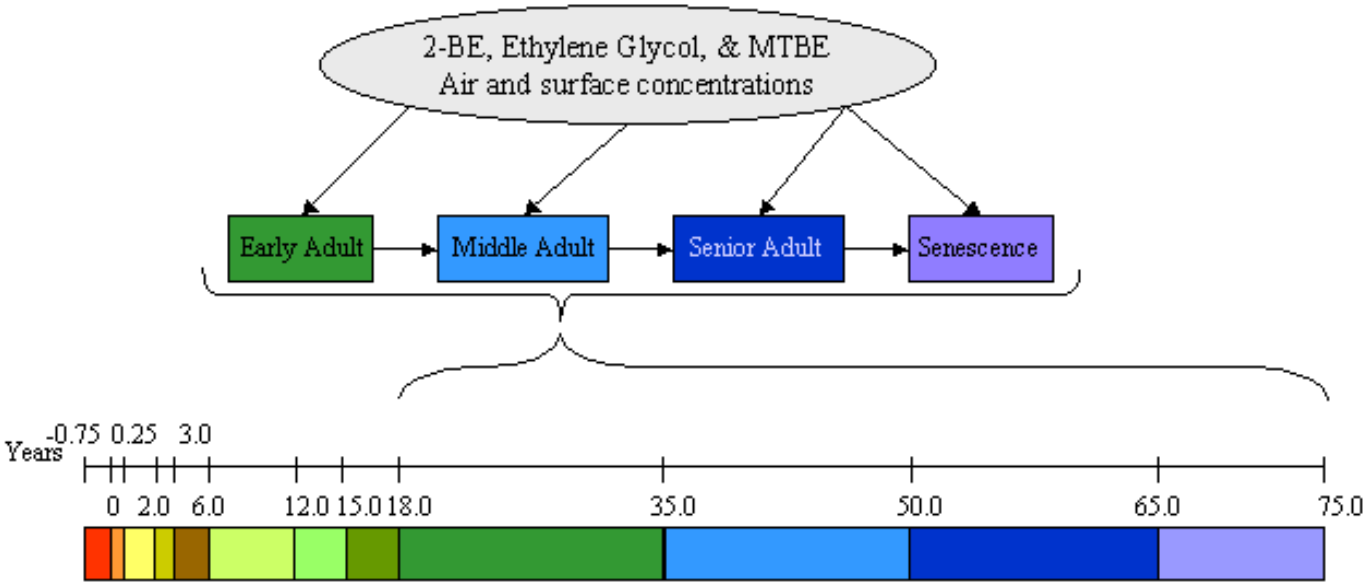


Figure 4.5.1 Life Stages For Exposure Scenario 4

Scenario 1
Scenario 2
Scenario 3
Scenario 4

Scenario 4

This section provides the conceptual model for the exposure pathways associated with Exposure Scenario 4. The conceptual model and associated assumptions are critical in determining the type of the models, algorithms, and databases required to satisfy the needs of the modeling scenario. Figure 4.5.2 provides an illustration of the conceptual model for Exposure Scenario 4.

Residential Outdoor Description

- 1-story Townhouse in MA with small grass lawn and shrubbery

Smoking Description

- Smokes 15-20 cigarettes per day since age 18
- Assume man smokes indoors and outdoors at home

Exposure at Home to SVOC Compound Groups A & B (Scenario 1)

Exposure at Home and in Car to VOC Compound Group E

- Compound Group E: MTBE in gasoline
- Exposure during car repair (4 times/year)
- Exposure during lawn mowing (20 times/year), lawn trimming (20 times/year), and shrubbery trimming (4 times/year)
- Exposure during auto fueling (52 times/year) & driving (1 hour/day)
- Background exposure indoors

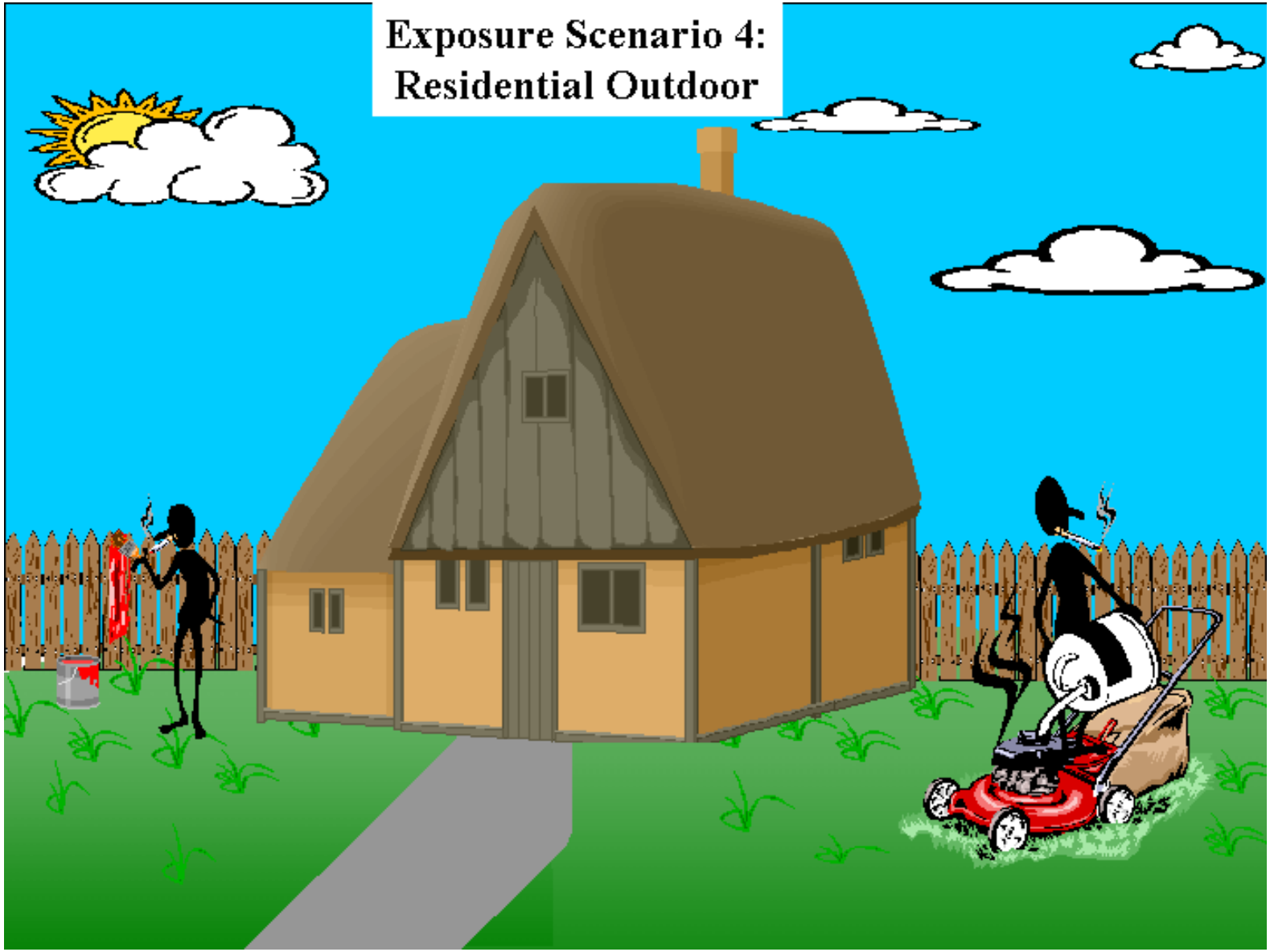


Figure 4.5.2 Illustration Depicting The Setting For Exposure Scenario 4 In Study

Assumptions about Working Conditions, Home Conditions, Exposures & Activities

- Workplace exposures unknown so considered negligible and part of background
- No protective gear when working on car, lawnmower, and other at-home jobs
- Paints the home interior every 5 years
- Exterior is brick so no painting needed

Adult Age Timeline

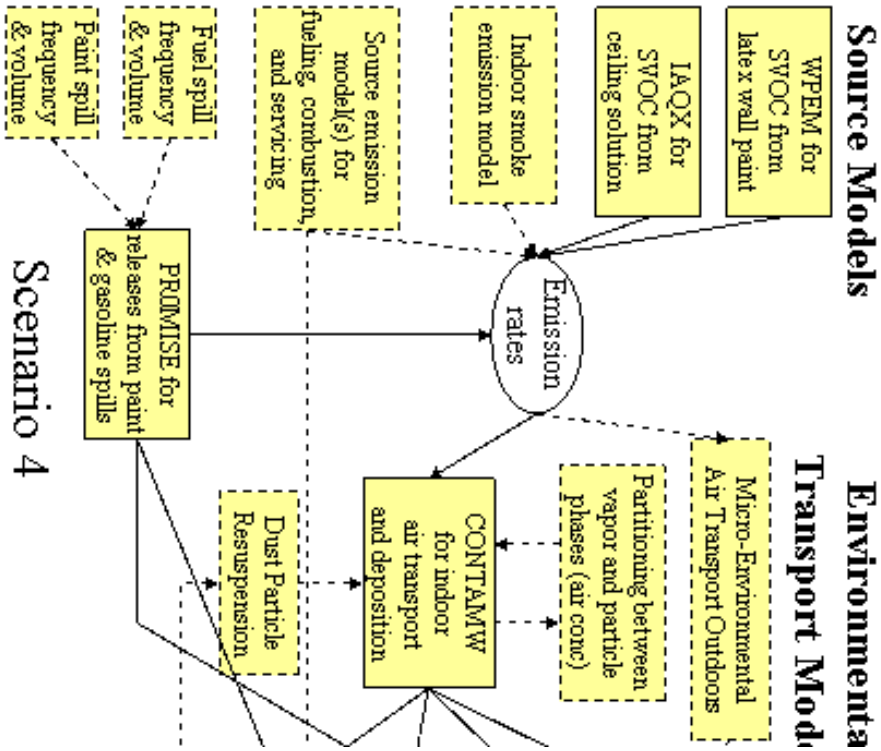
- Working
- - Adult (25-35 years)
- - Middle Adult (35-50 years)
- - Senior Adult (50-65 years)
- Senescence (65-75 years)

Adult Age Timeline

- Health effects will be calculated for the adult from 25 years of age through retirement. Depending on model outputs, this can be a cumulative time distribution or a time-weighted value.

---- Exposure during car repair (4 times/year); assume no protective gear
---- Exposure during lawn mowing (20 times/year), lawn trimming (20 times/year), and shrubbery trimming (4 times/year)
---- Exposure during auto fueling (52 times/year) & driving (1 hour/day)

Figure 4.5.3 CCEF Model Flow Diagram Scenario 4



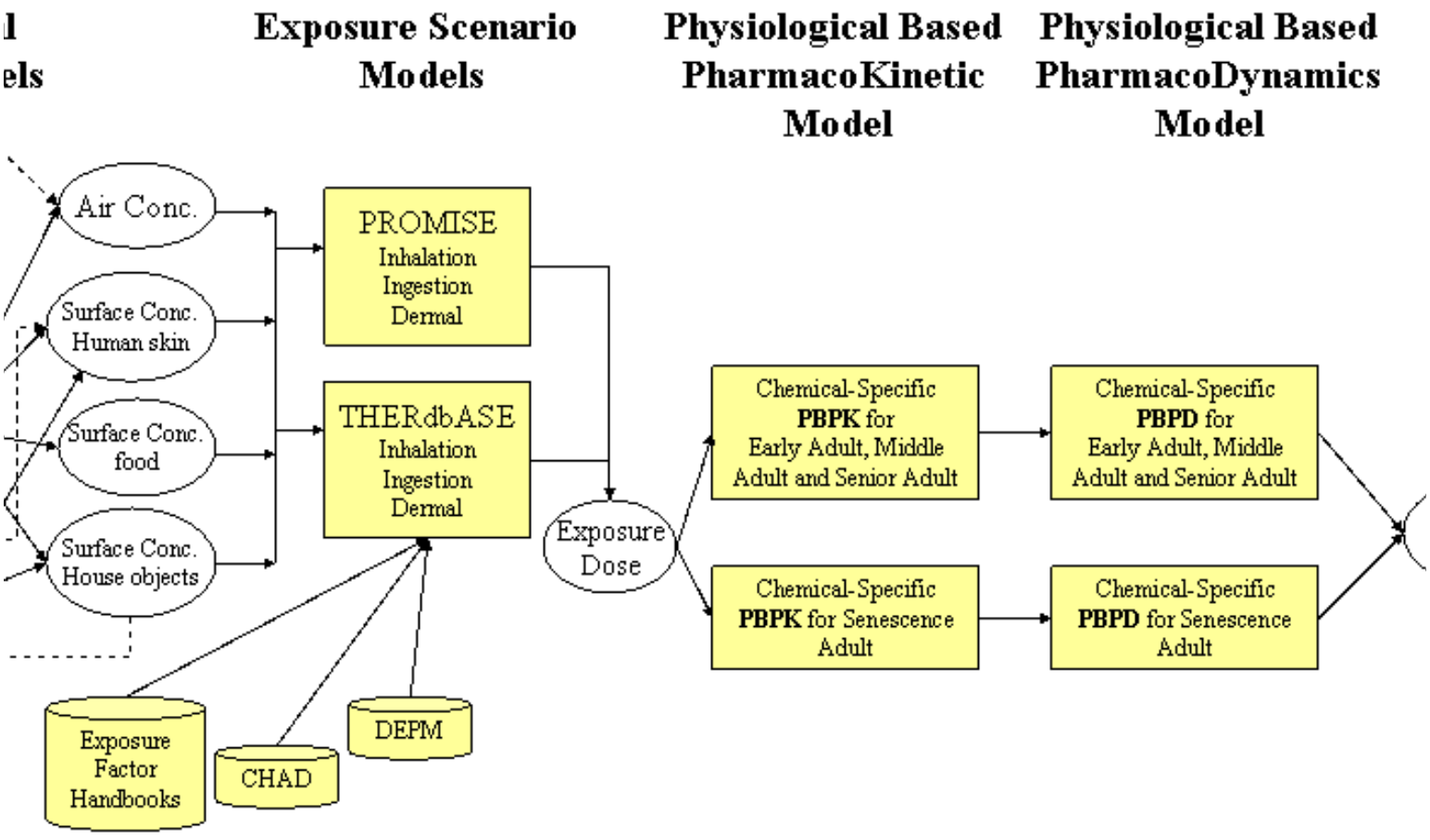


Figure 4.5.3 CCEF Model Flow Diagram Scenario 4

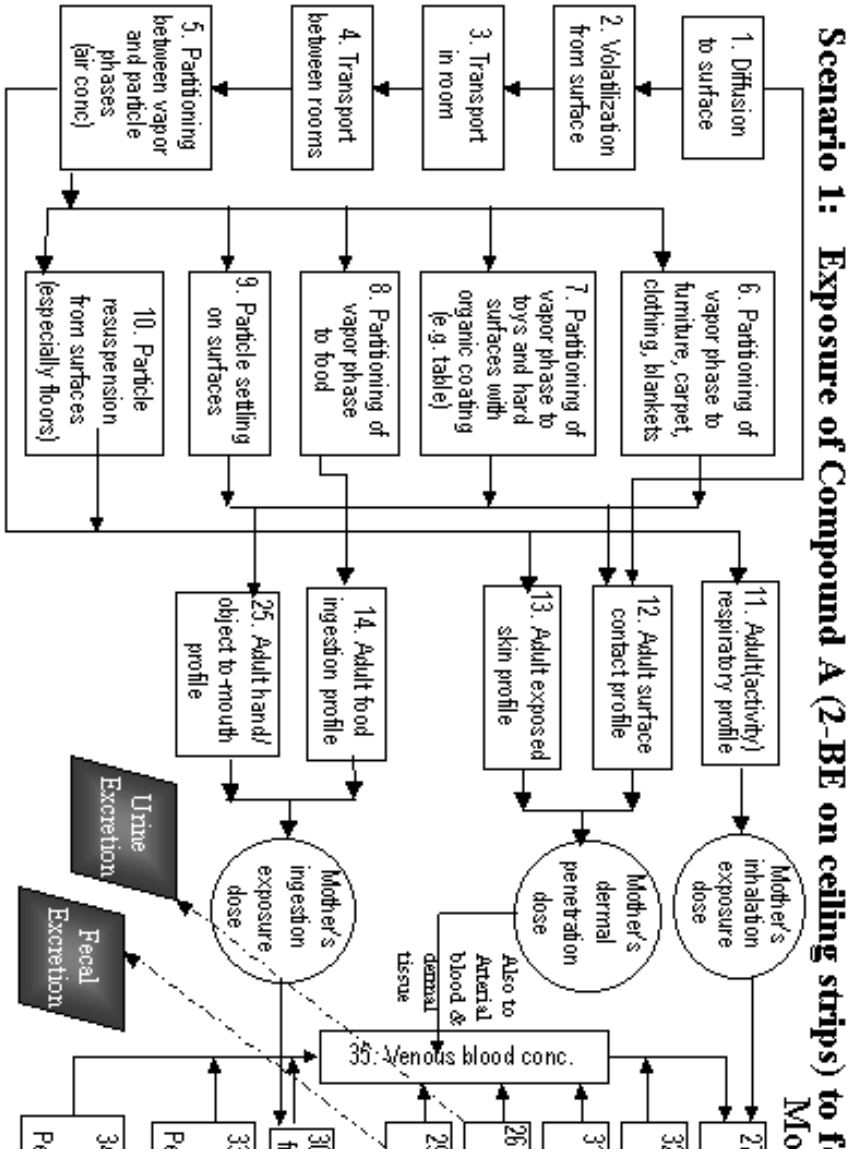
Diagram Legend	
Solid boxes	Models with known codes available
Dashed boxes	Models with codes not available
Ovals	Input/output files with specific data specifications
Cylinders	Model-Specific databases
Arrows	Indicates the flow of the data
PBPK	Physiologically-based Pharmacokinetics
PBPD	Physiologically-based Pharmacodynamics

- WPEM was developed for latex or alkyd paint.
- IAQX can be used for the solution on wood ceiling strips, since it is for emissions from building materials, including dry sources.
- One possible source of models to use for mainstream smoking is from the external review article http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html for smoking release.
- Indoor air transport modeling (VOC emission) can be handled by many models, we selected CONTAM for this case, because it can handle aerosols, but at least 4 other models identified in the literature review could be used. Some of the transport models are planning to add VOC, aerosol, and particle deposition components and in some cases separate models could handle deposition to product surface concentrations.
- PROMISE and THERdbASE are used to estimate human activity patterns and exposure doses. We would prefer to use LifeLine, Cares and other multi-route, multi-source models but it is difficult to integrate them because they proprietary and much of the needed information is not readily available.
- DEPM includes information on food intake for estimating dietary exposure
- CHAD is a master database that provides information on human activity
- EPA's Exposure Factors Handbook for adults will be used accordingly.
- Note that there is a PBPK or PBPD model for each of the three chemicals of concern developed specifically for an adult male.
- Data gap: There are no current models incorporating the effects of cigarette smoking on PBPK model parameters.
- It should also be noted that interactions and competing causes of action can also be incorporated in the PBPK and Mode of Action models depending on available information
- LifeLine, CARES, and other lifestyle aggregate codes will overlay onto the PBPK and Mode of Action models.

4.6 CCEF Process Flow Diagrams

The purpose of the Process flow diagrams is to show the flow of information for key information and data processing steps, describe the four scenarios as a framework of connected processes, and identify gaps in knowledge.

The Process Flow Diagrams illustrate the mapping between the models and the process numbers. Select a model or model description from the corresponding interactive hyperlinked pages (table ordered alphabetically), and the corresponding processes on the diagram will be highlighted.



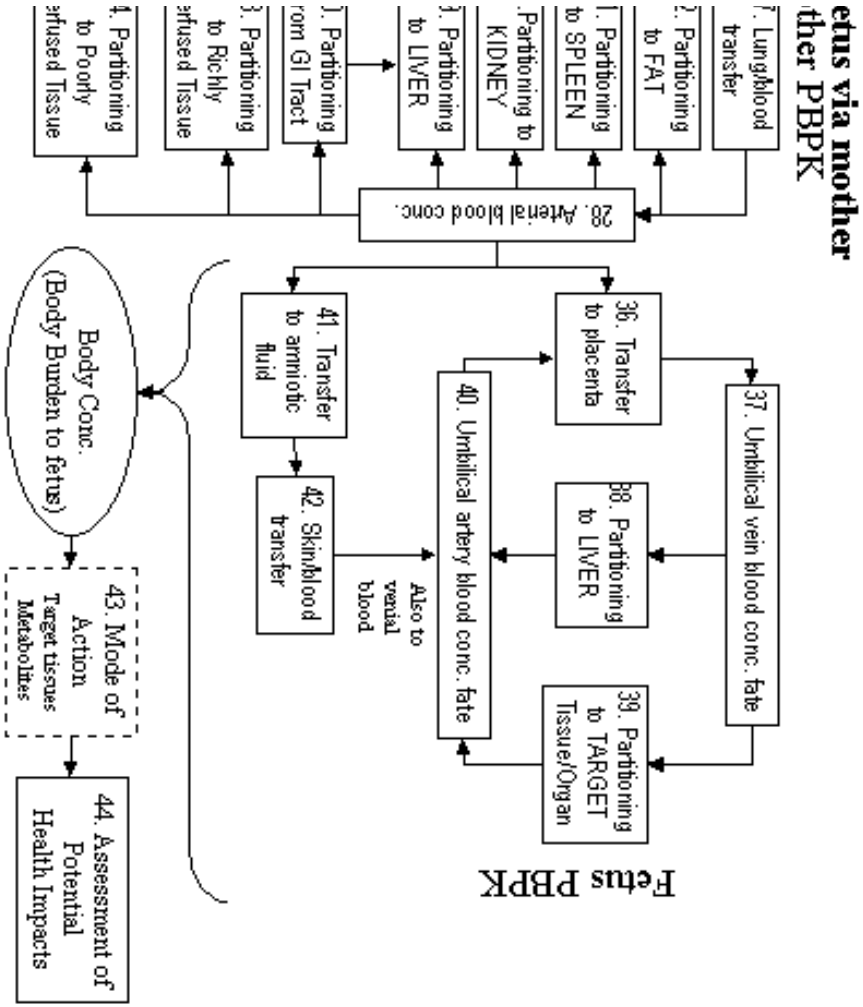
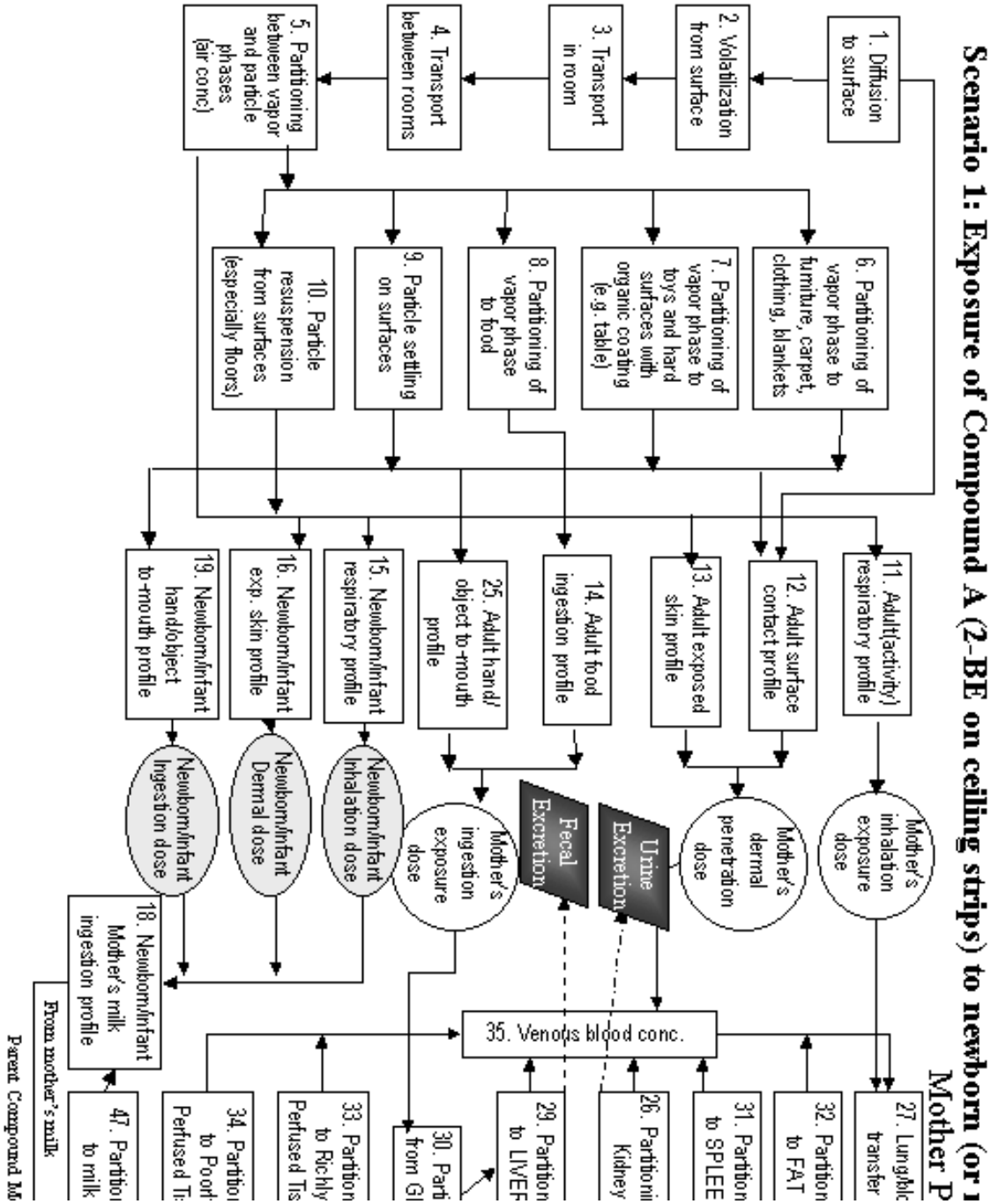


Figure 4.6.1 Scenario 1 Process Framework: Exposure of Compound A (2-BE on ceiling strips) to fetus via mother

Notes

- Compound A: 2-BE
- Metabolite: Butoxyacetic acid (primary), butoxyethanol glucuronide, butoxyethanol sulfate
- Mode of Action: fetal effects, maternal liver and spleen
- Pregnant/Nursing Mother: 2-methoxyethanol models based on mouse/rat studies
- Adult male PBPK available – need to scale & adapt for child
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)

- Data gaps: no maternal/fetal PBPK for 2-BE
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



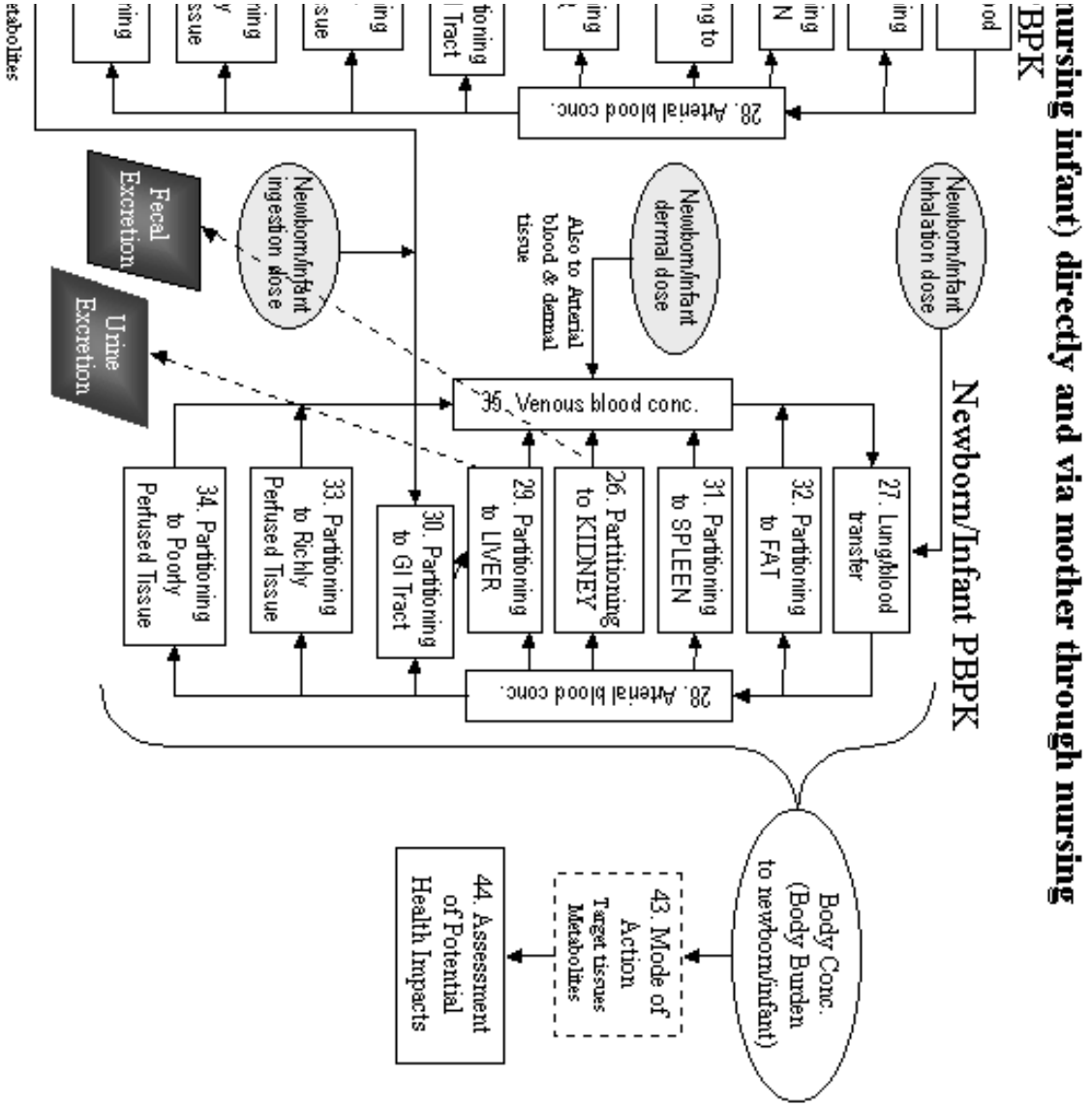


Figure 4.6.2 Scenario 1 Process Framework: Exposure of Compound A (2-BE on ceiling strips) to newborn (or nursing infant) directly and via mother through nursing

Notes

- Compound A: 2-BE
- Metabolite: Butoxyacetic acid (primary), butoxyethanol glucuronide, butoxyethanol sulfate

- Mode of Action: Effects on fetus, maternal liver and spleen
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle
- resuspension from surfaces (especially floors)
- Data gap: newborn and nursing infant PBPK for 2-BE
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu

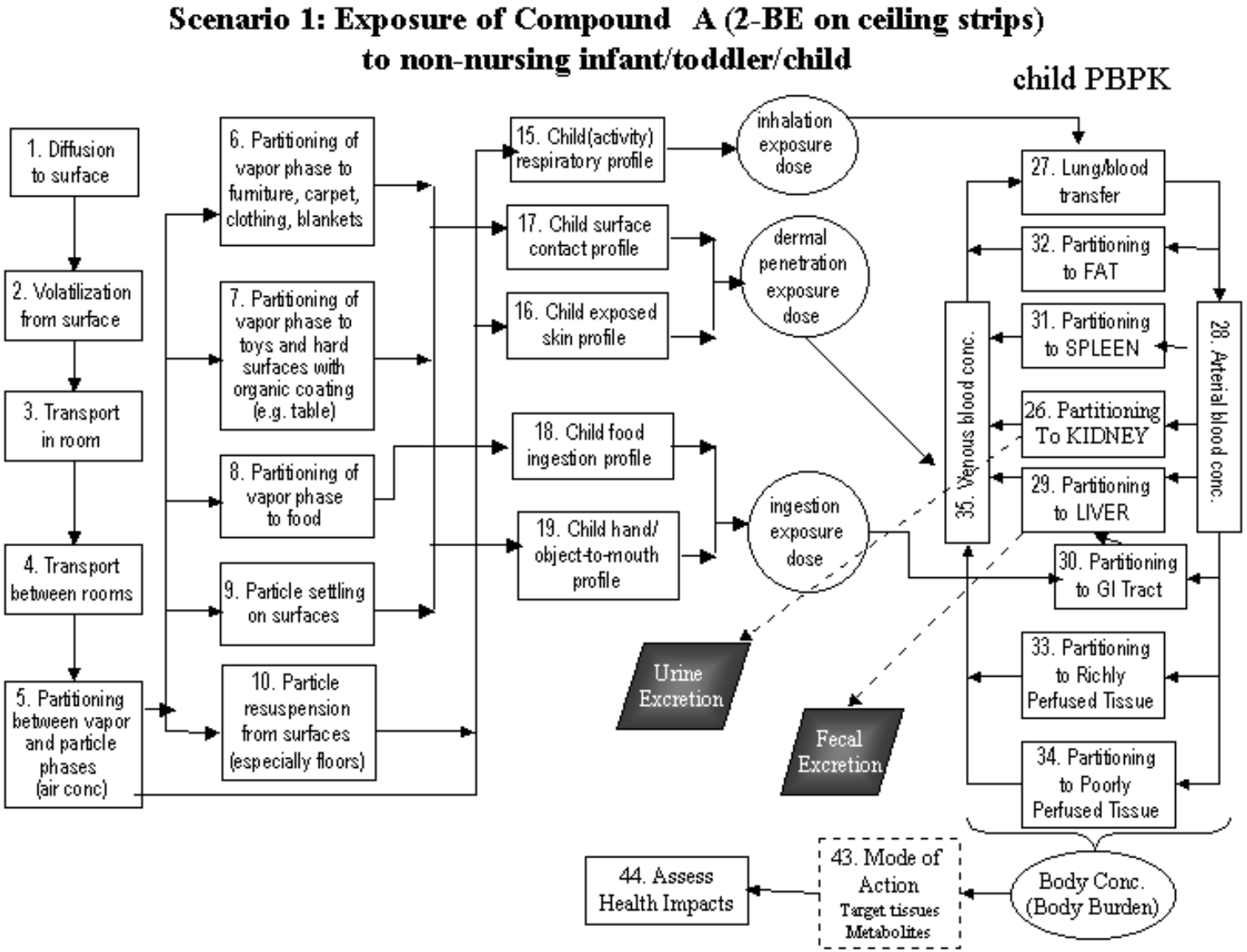
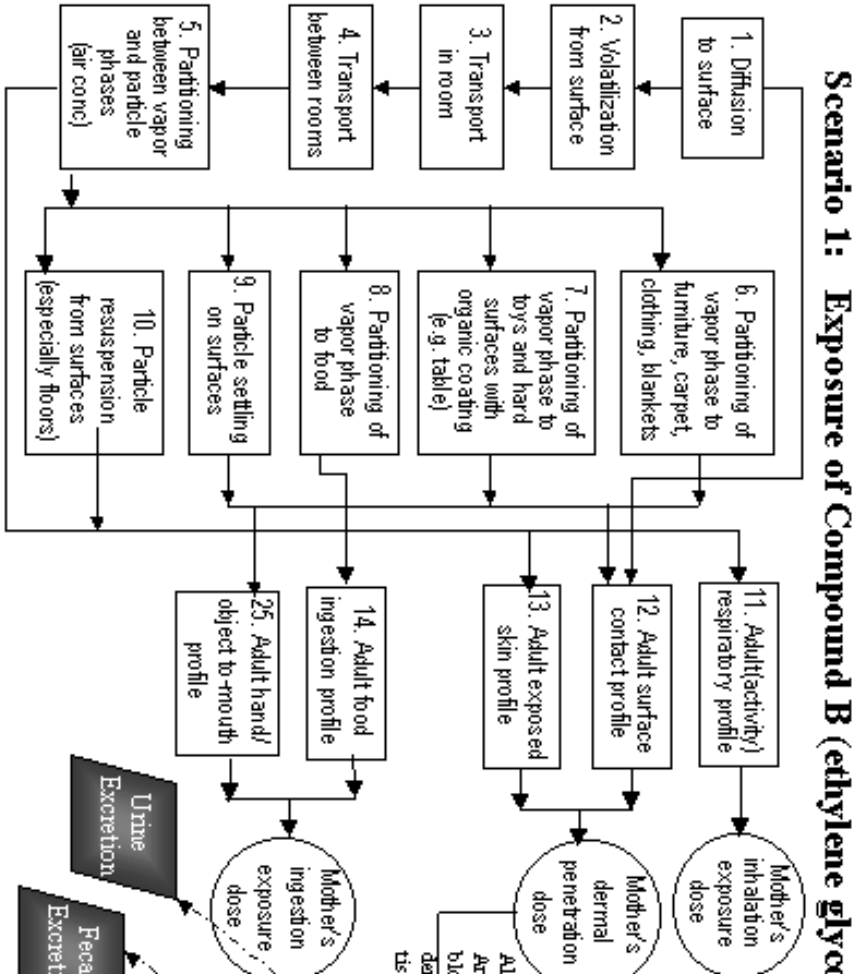


Figure 4.6.3 Scenario 1 Process Framework: Exposure of Compound A (2-BE on ceiling strips) to non-nursing infant/toddler/child

Notes

- Compound A: 2-BE
- Metabolite: Butoxyacetic acid (primary), butoxyethanol glucuronide, butoxyethanol sulfate
- Mode of Action: liver and spleen
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: No PBPK or PBPD models available for newborns or children, current information available on metabolism, distribution, etc insufficient for model development
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



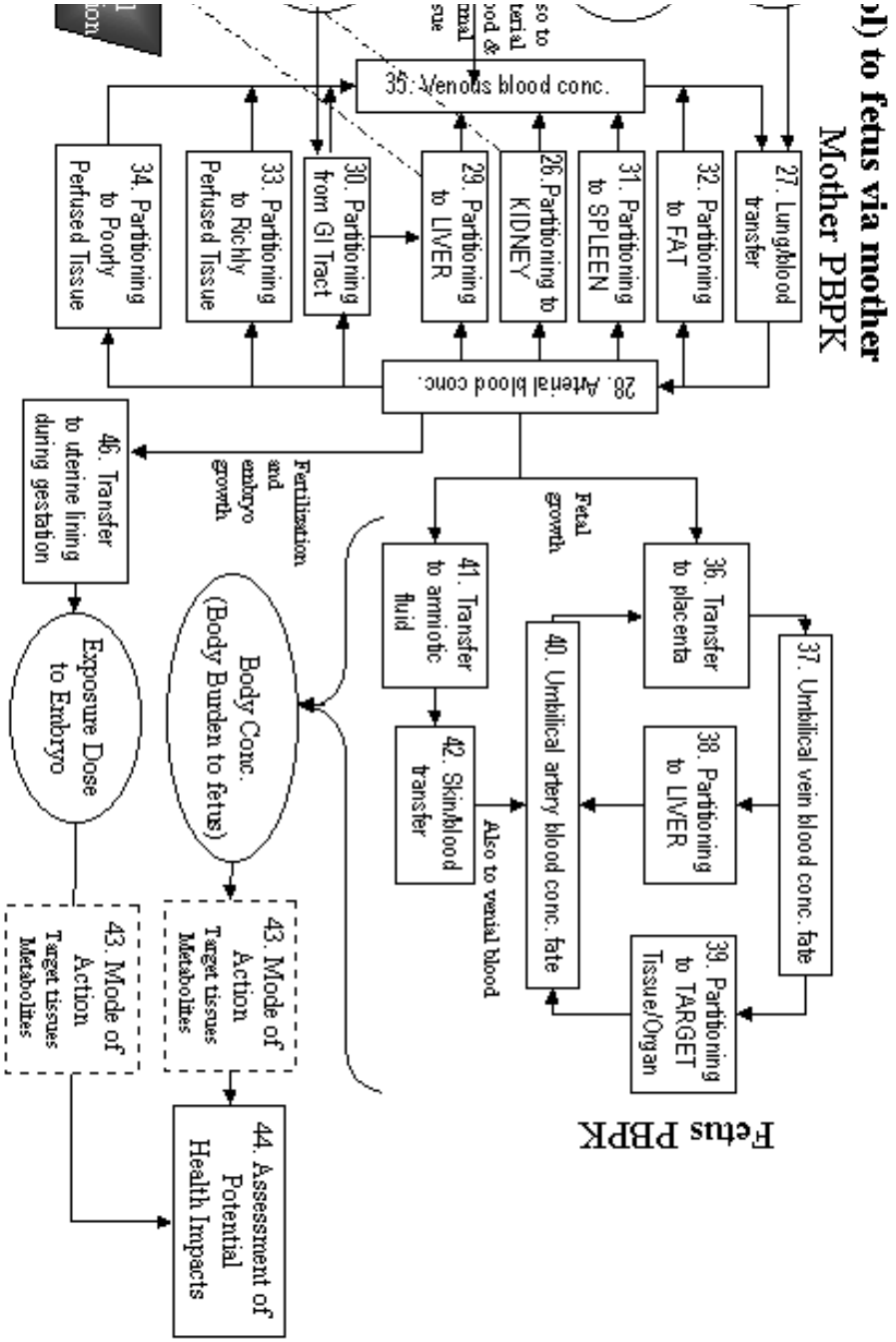
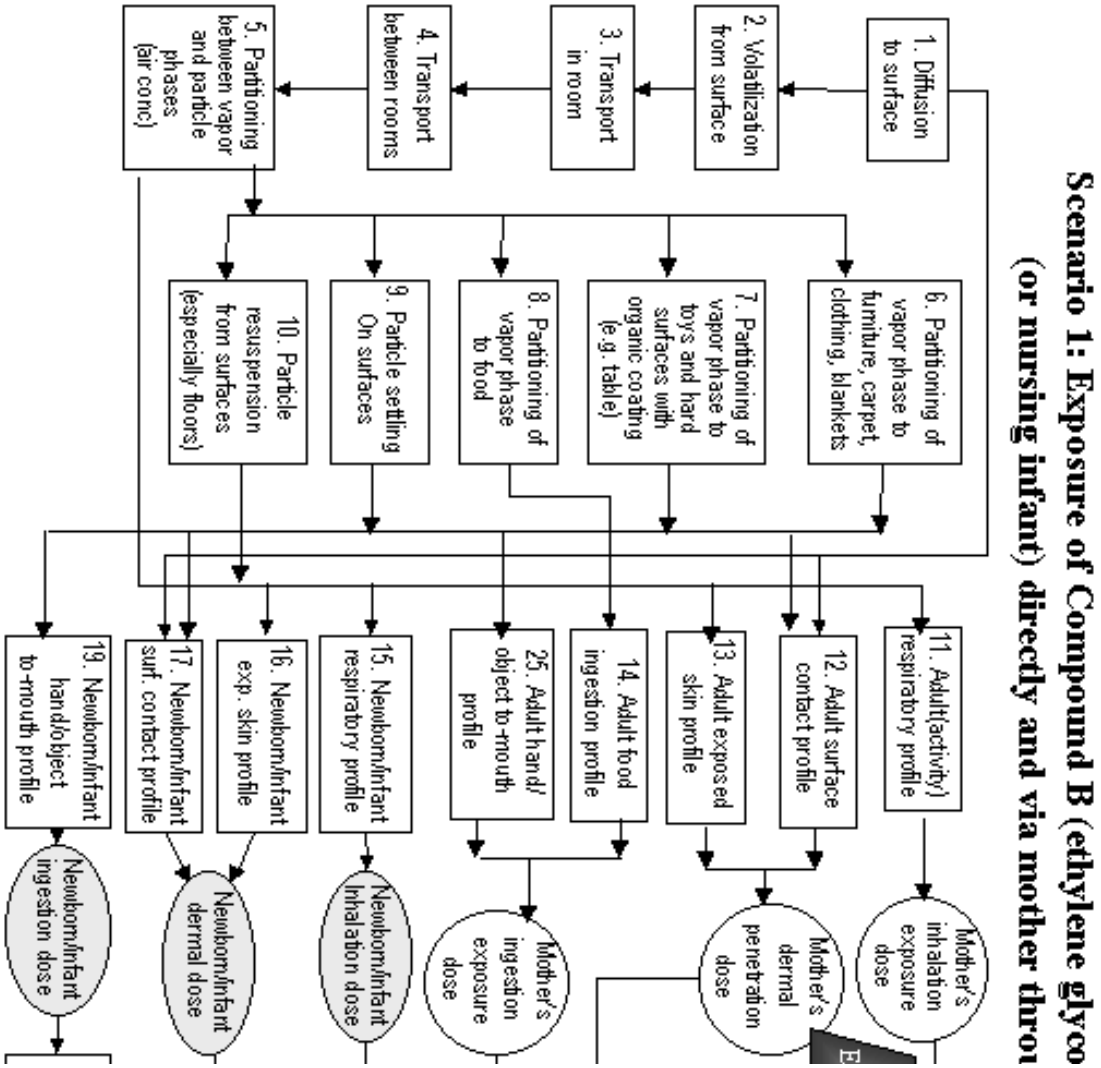


Figure 4.6.4 Scenario 1 Process Framework: Exposure of Compound B (ethylene glycol) to fetus via mother

Notes

- Compound B: Ethylene Glycol
- Metabolite: methoxyacetic acid
- Mode of Action: effects on the developing embryo, adult kidney
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Validation of ethylene glycol PBPK models in the human pregnant females, currently has only been partially validated in males (Gargas, et al. 2000)
- PBPK model not validated in the child
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



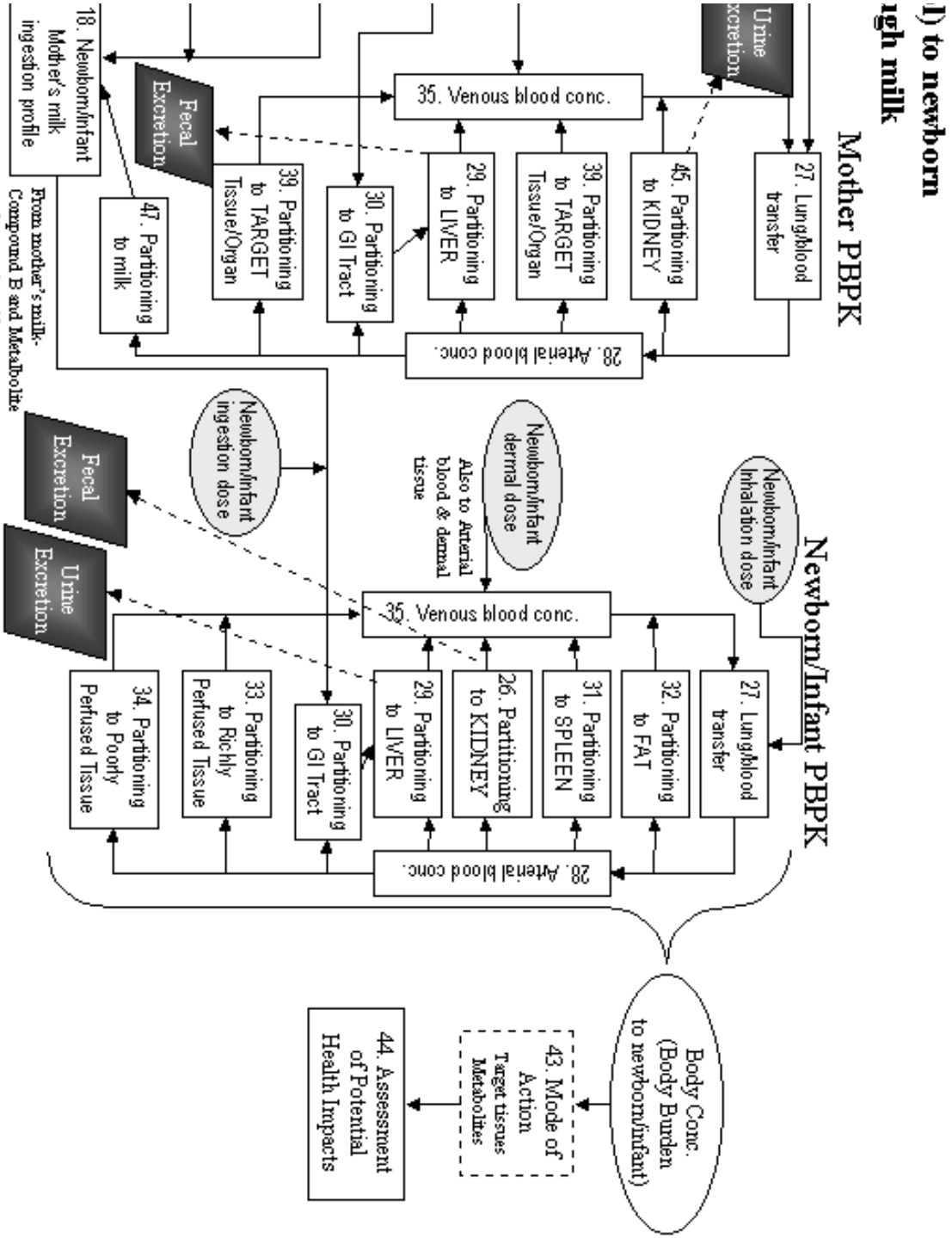

l) to newborn
igh milk
Mother PBPK
Urine excretion
27. Lung/blood transfer
45. Partitioning to KIDNEY
39. Partitioning to TARGET Tissue/Organ
29. Partitioning to LIVER
30. Partitioning to GI Tract
35. Venous blood conc.
Fecal Excretion
39. Partitioning to TARGET Tissue/Organ
47. Partitioning to milk
18. Newborn/Infant Mother's milk ingestion profile
From mother's milk-Compound B and Metabolite methoxyacetic acid
28. Arterial blood conc.
Newborn/Infant PBPK
Newborn/Infant Inhalation dose
Newborn/Infant dermal dose
Also to Arterial blood & dermal tissue
Newborn/Infant ingestion dose
Fecal Excretion
Urine Excretion
35. Venous blood conc.
27. Lung/blood transfer
32. Partitioning to FAT
31. Partitioning to SPLEEN
26. Partitioning to KIDNEY
29. Partitioning to LIVER
30. Partitioning to GI Tract
33. Partitioning to Richly Perfused Tissue
34. Partitioning to Poorly Perfused Tissue
28. Arterial blood conc.
Body Conc. (Body Burden to newborn/infant)
43. Mode of Action
Target tissues
Metabolites
44. Assessment of Potential Health Impacts

Figure 4.6.5 Scenario 1 Process Framework: Exposure of Compound B (ethylene glycol) to newborn (or nursing infant) directly and via mother through milk

Notes

- Compound B: Ethylene Glycol
- Metabolite: methoxyacetic acid
- Mode of Action: Developing embryo, kidney
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: newborn and nursing infant PBPK for ethylene glycol and methoxyacetic acid
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.

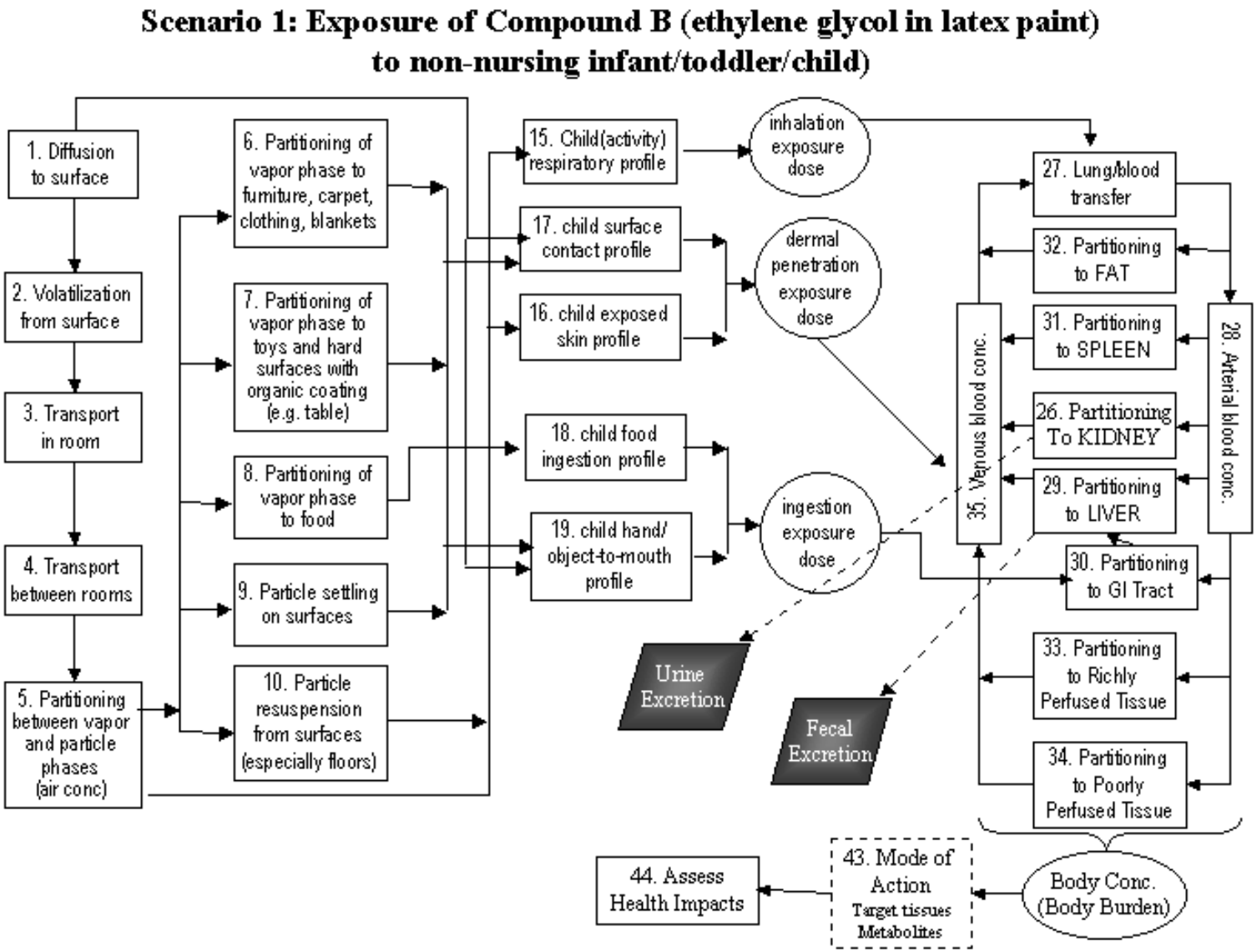
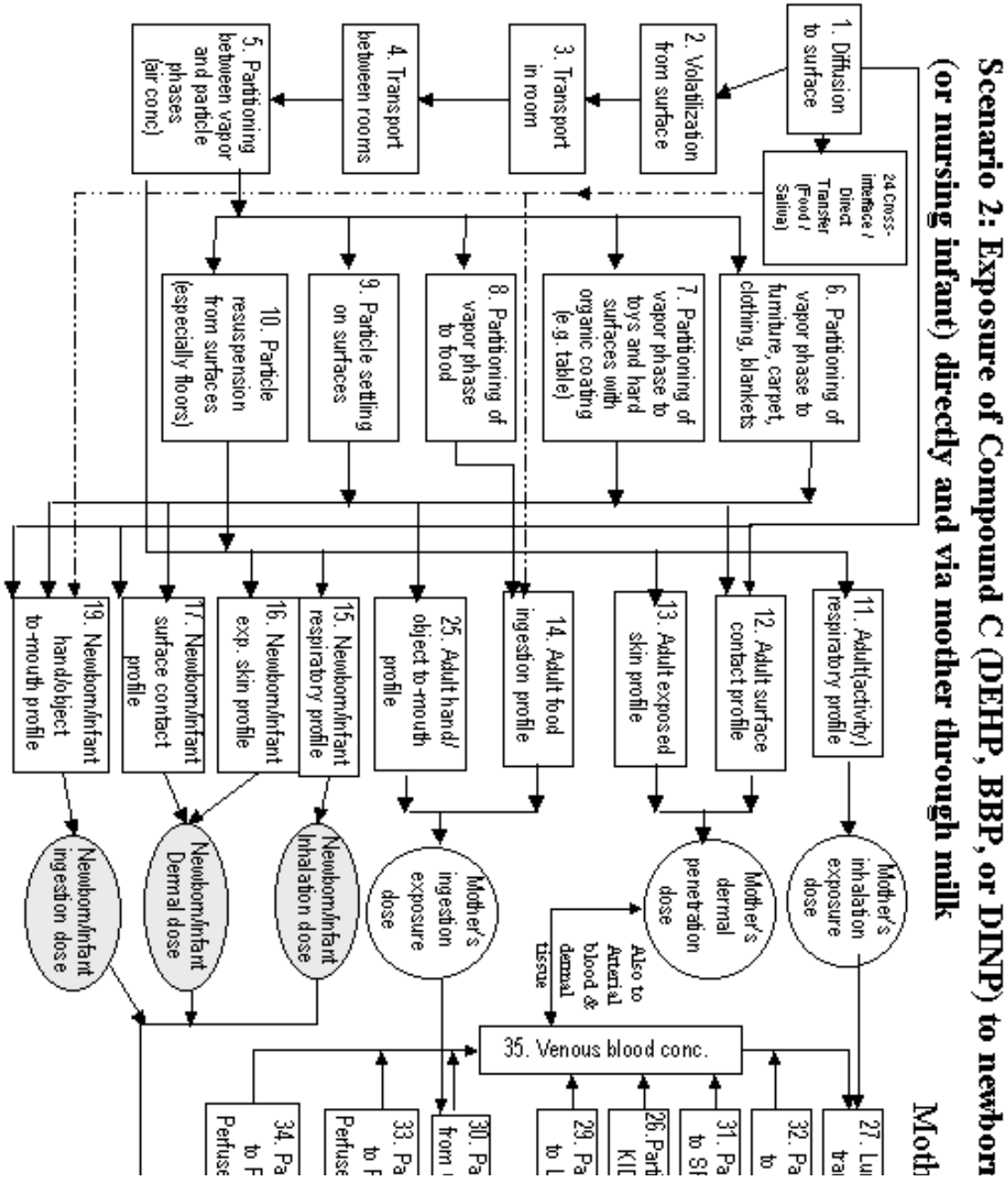


Figure 4.6.6 Scenario 1 Process Framework: Exposure of Compound B (ethylene glycol in latex paint)

Notes

- Compound B: Ethylene Glycol
- Metabolite: methoxyacetic acid
- Mode of Action: Kidney

- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: No PBPK or PBPD model for ethylene glycol in the newborn or child, current available information is insufficient to develop a PBPK or PBPD model for this age group
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



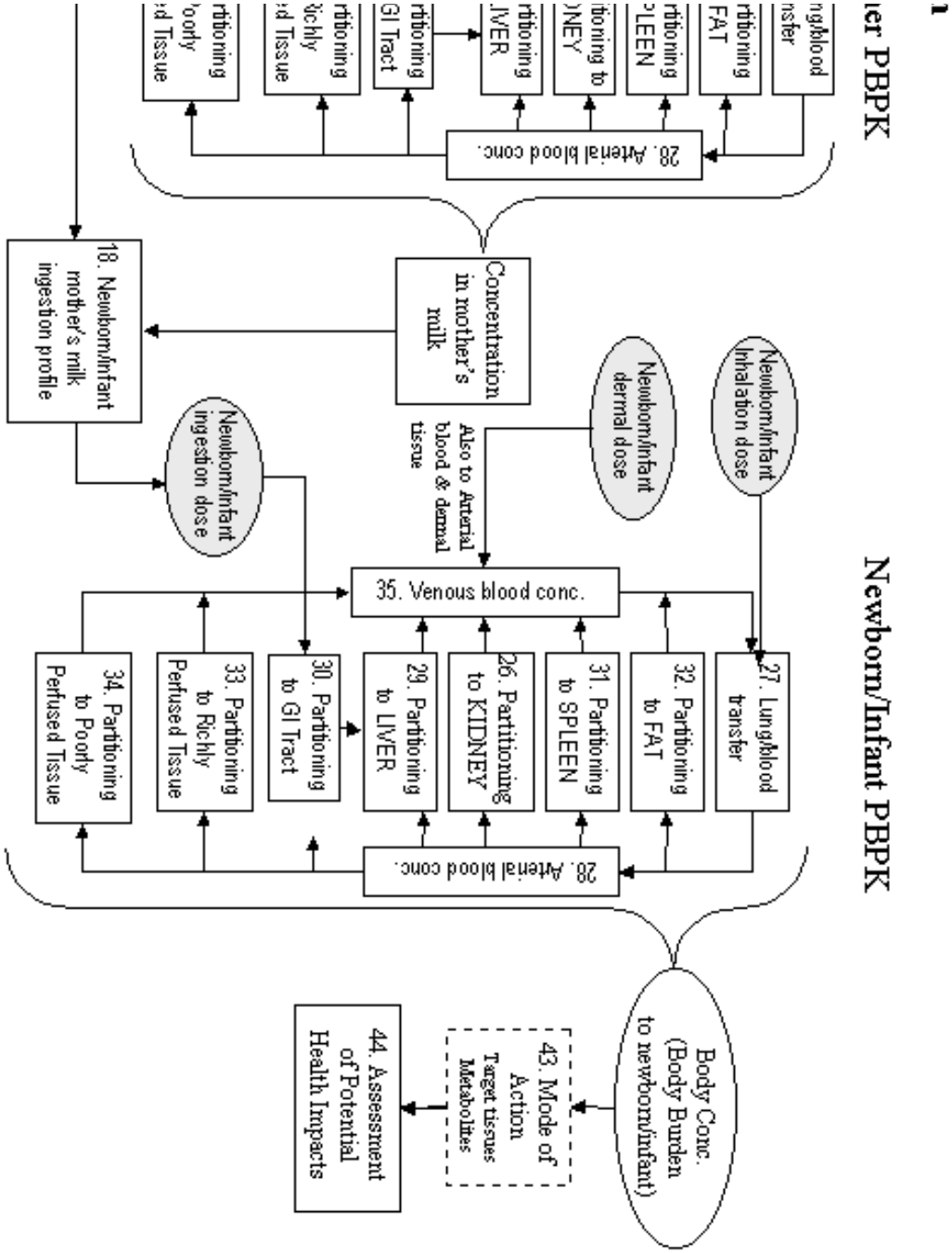


Figure 4.6.7 Scenario 2 Process Framework: Exposure of Compound C (DEHP or BBP or DINP) to newborn (or nursing infant) directly and via mother through milk

Notes

- Compound C: DEHP: diethyl hexyl phthalate
- Metabolite: Not Known
- Mode of Action: Not Known
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: newborn and nursing infant PBPK or PBPD for DEHP

- Compound C: BBP: butyl benzyl phthalate
- Metabolite: Not found during literature search
- Mode of Action: Not found during literature search
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: nursing infant PBPK for BBP

- Compound C: DINP: diisononyl phthalate
- Metabolite: Not Known
- Mode of Action: Not Known
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Data gap: newborn and nursing infant PBPK for DINP

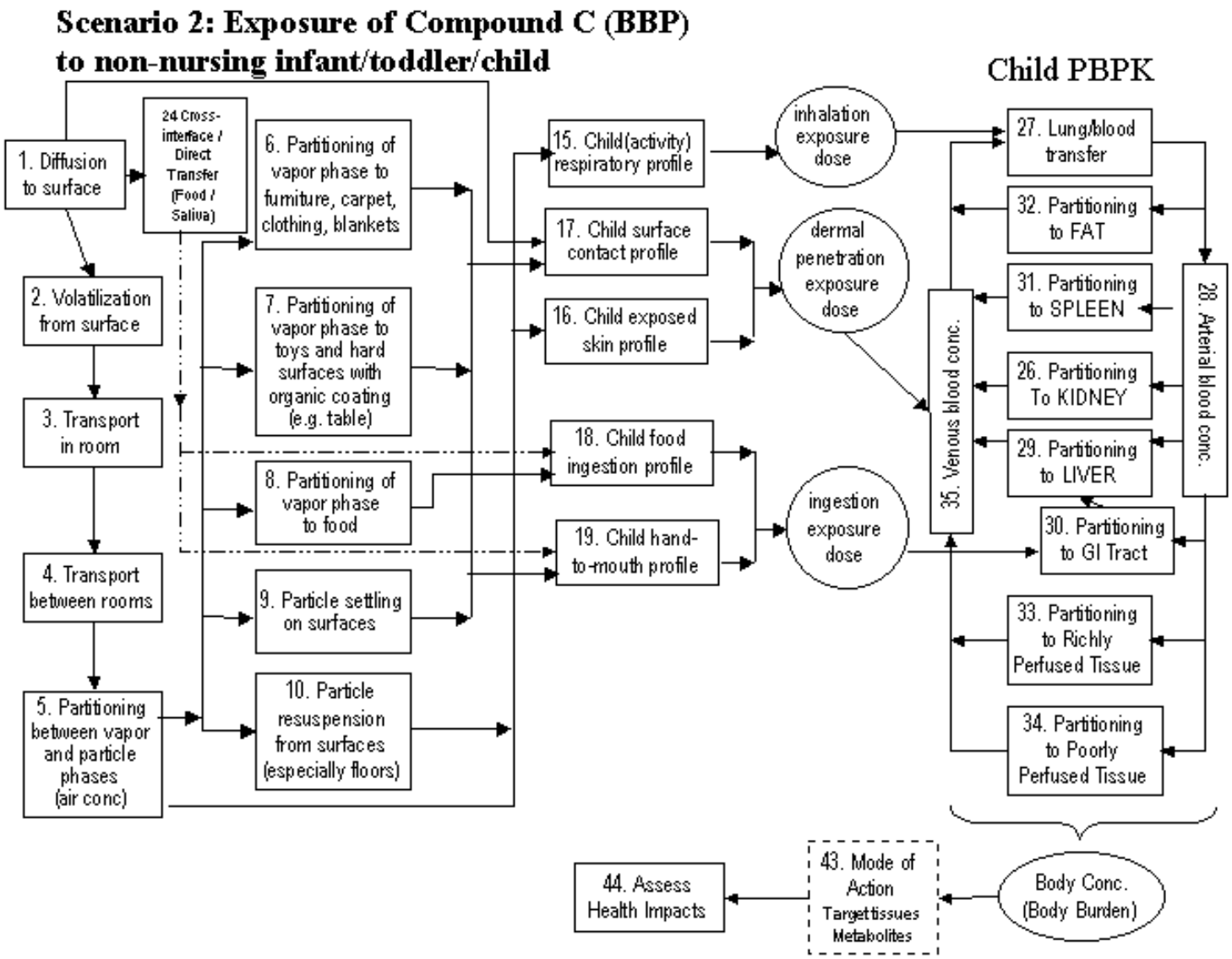


Figure 4.6.8 Scenario 2 Process Framework: Exposure of Compound C (BBP) to non-nursing infant/toddler/child

Notes

- Compound C: BBP: butyl benzyl phthalate
- Metabolite: Not Known
- Mode of Action: Not Known

- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.

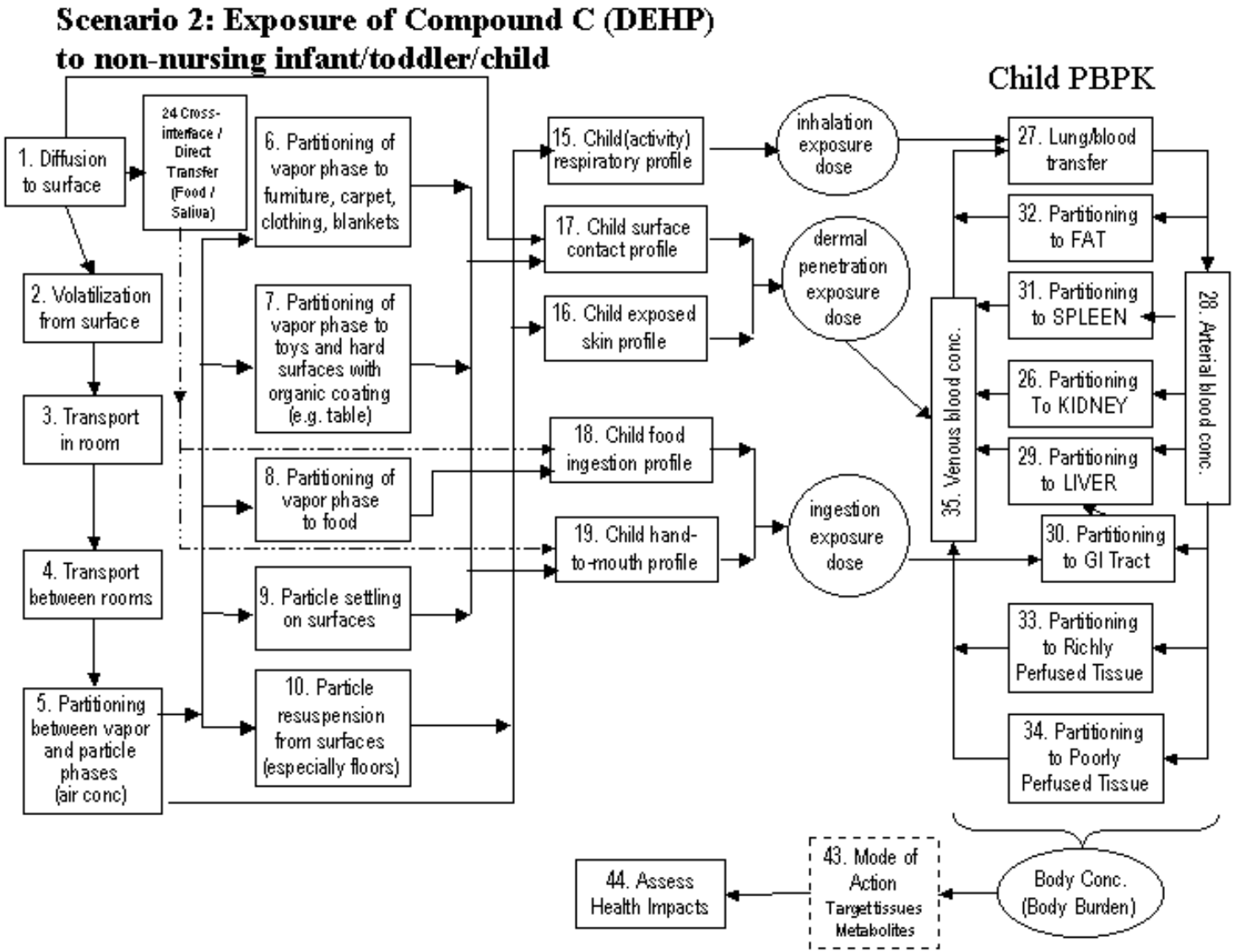


Figure 4.6.9 Scenario 2 Process Framework: Exposure of Compound C (DEHP) to non-nursing infant/toddler/child

Notes

- Compound C: DEHP: diethyl hexyl phthalate
- Metabolite: Not Known
- Mode of Action: Not Known
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)

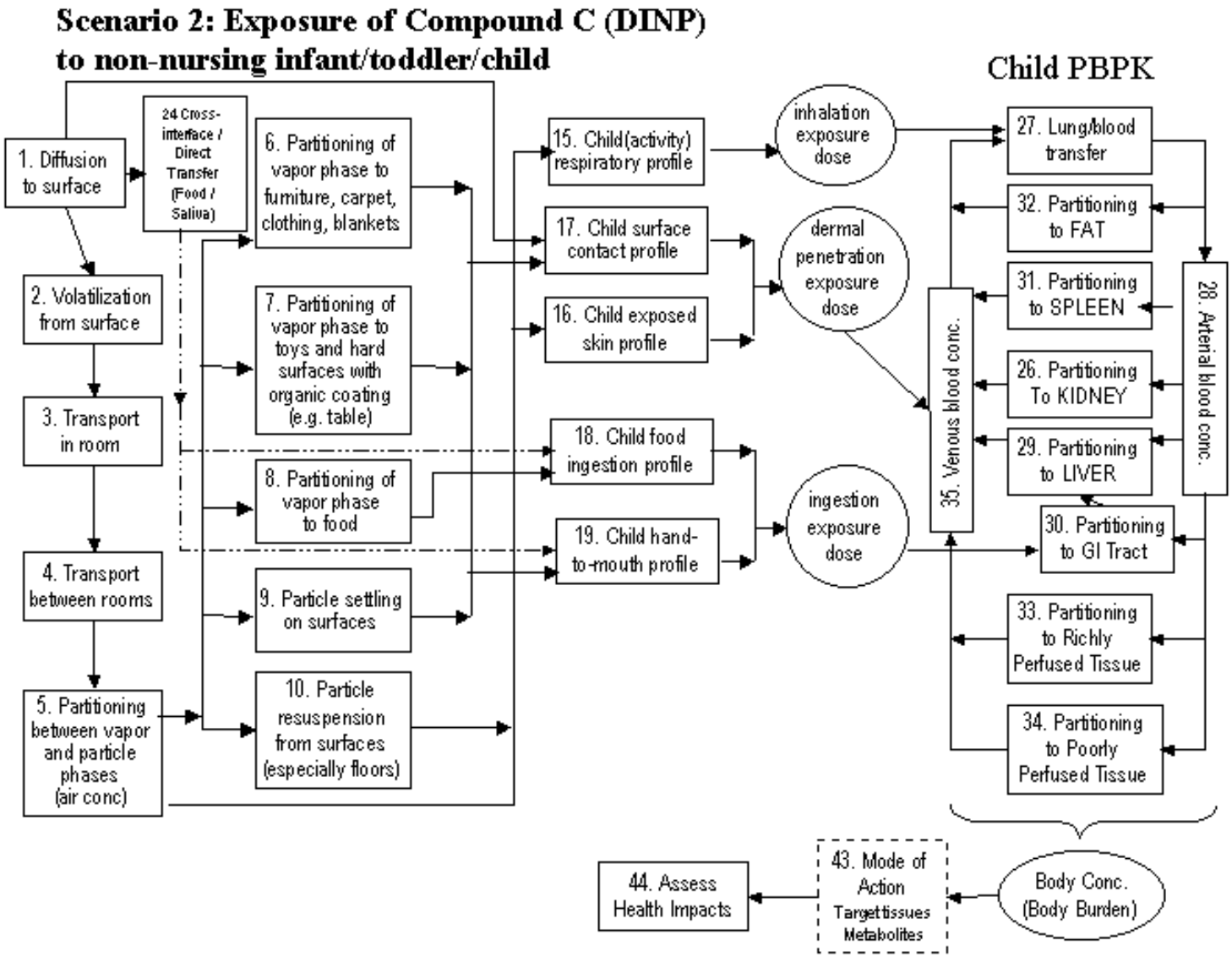


Figure 4.6.10 Scenario 2 Process Framework: Exposure of Compound C (DINP) to non-nursing infant/toddler/child

Notes

- Compound C: DINP: diisononyl phthalate
- Metabolite: Not Known
- Mode of Action: Not Known
- Data gap: No models for #5 partitioning between vapor and particle phase or #10 particle resuspension from surfaces (especially floors)

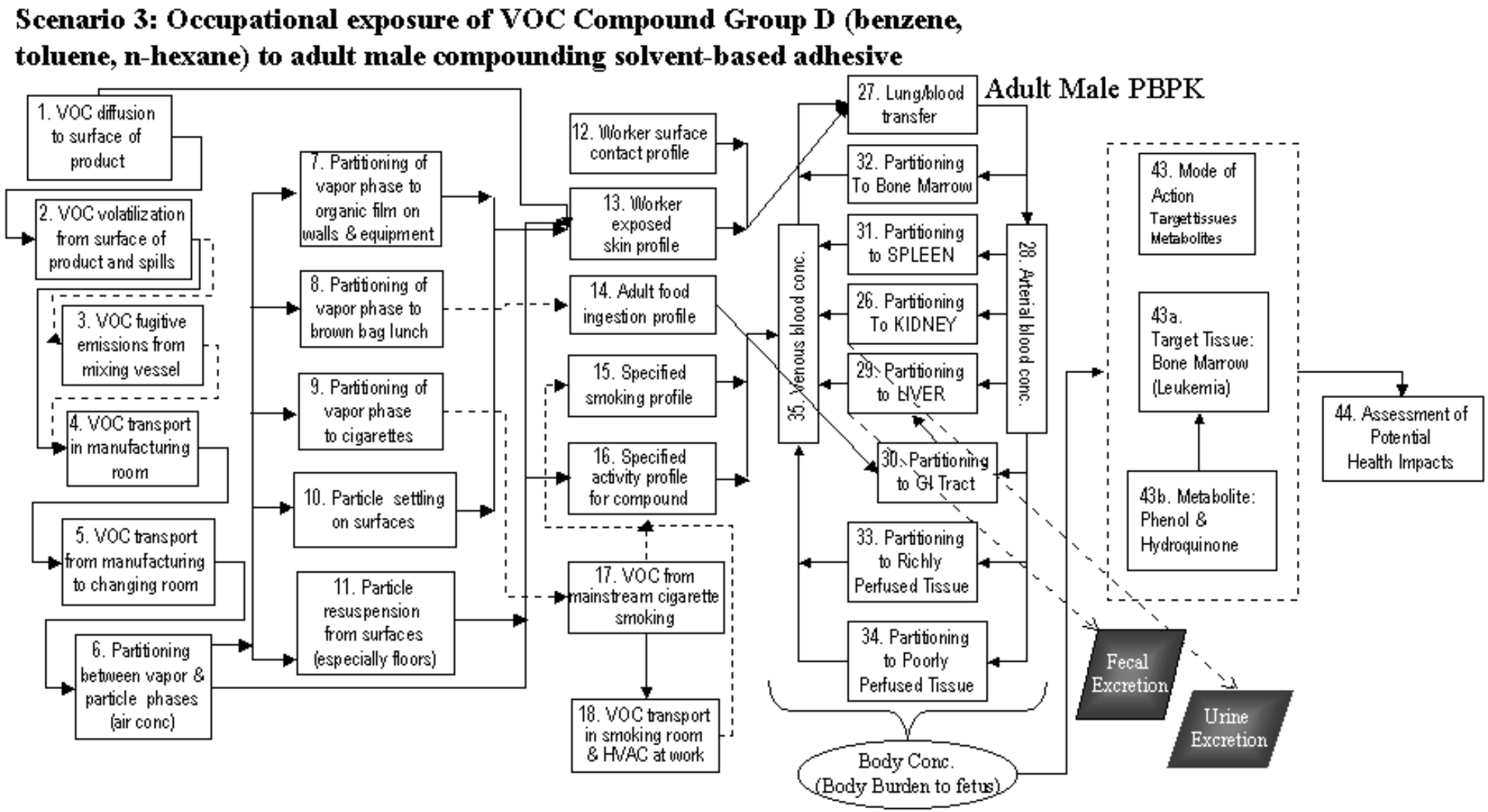
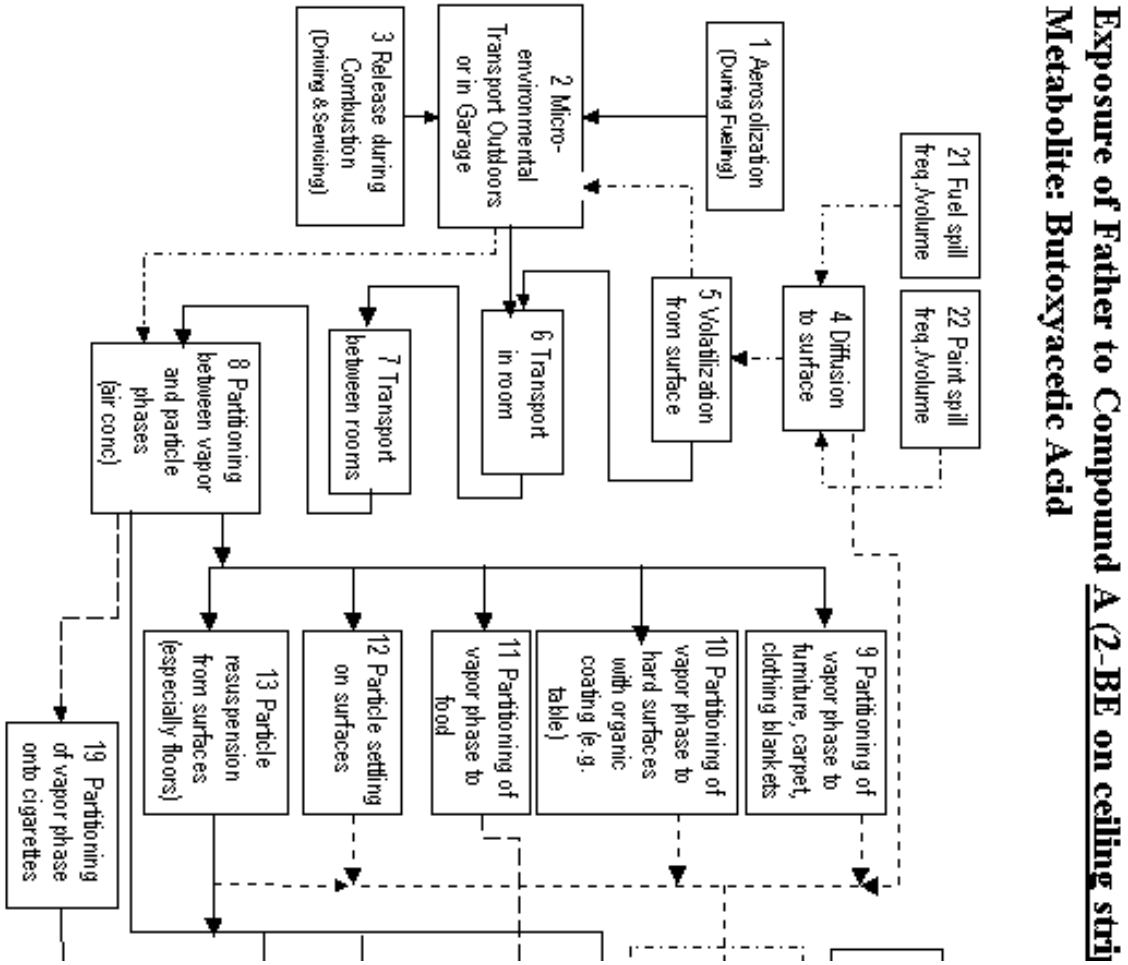


Figure 4.6.11 Scenario 3 Process Framework: Occupational exposure of VOC Compound Group D (benzene, toluene, n-hexane) to adult male compounding solvent-based adhesive

Notes

- Compound D: Benzene, Toluene, n-Hexane
- Metabolite: Combination of Phenol & Hydroquinone
- Mode of Action: Bone Marrow
- The combination of the three VOC's produce the health effects of concern.
- Data gaps: No models for #3 VOC fugitive emissions from mixing vessel, #6 partitioning between vapor and particle phases (air conc.), #11 particle resuspension from surfaces (especially floors), #17 VOC from mainstream smoking (may be able to use something from review article on smoking release from website [http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)](http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



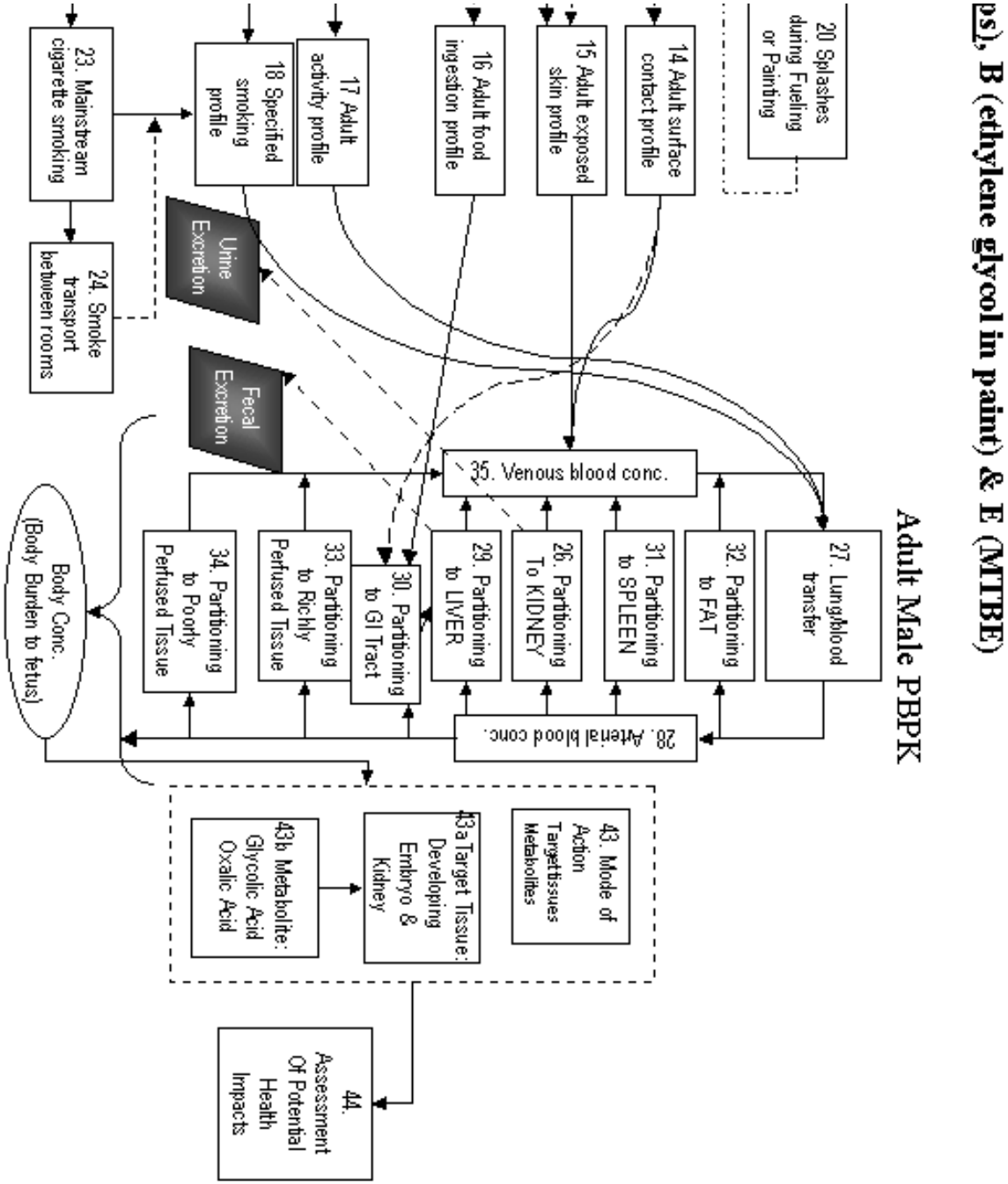
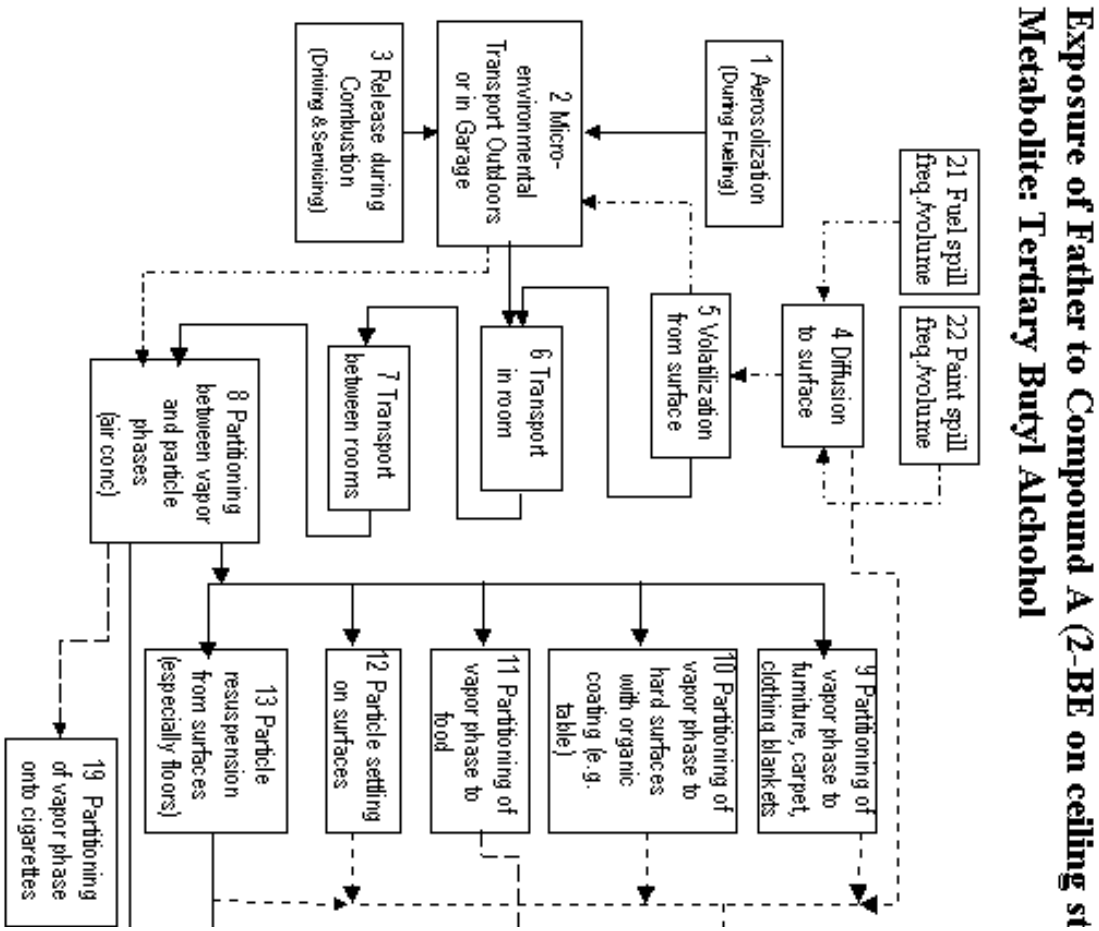


Figure 4.6.12 Scenario 4 Process Framework: Exposure of Father to Compound A (2-BE on ceiling strips), B (ethylene glycol in paint) & E (MTBE) Metabolite: Butoxyacetic Acid

Notes

- Compound A: 2-BE
- Metabolite: Butoxyacetic acid (primary), butoxyethanol glucuronide, butoxyethanol sulfate
- Mode of Action: liver and spleen
- Mode of Action: Bone Marrow
- Data gaps: No models for #1 aerosolization of contaminant during fueling, #3 release of contaminant from internal combustion engine, #8 partitioning between vapor and particle phase, #13 particle resuspension from surfaces (especially floors), #20 splashes during fueling or painting, #21 Fuel spill frequency/volume, #22 Paint spill frequency/volume, or #23 Mainstream smoking (may be able to use something from review article on smoking release from website [http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)](http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



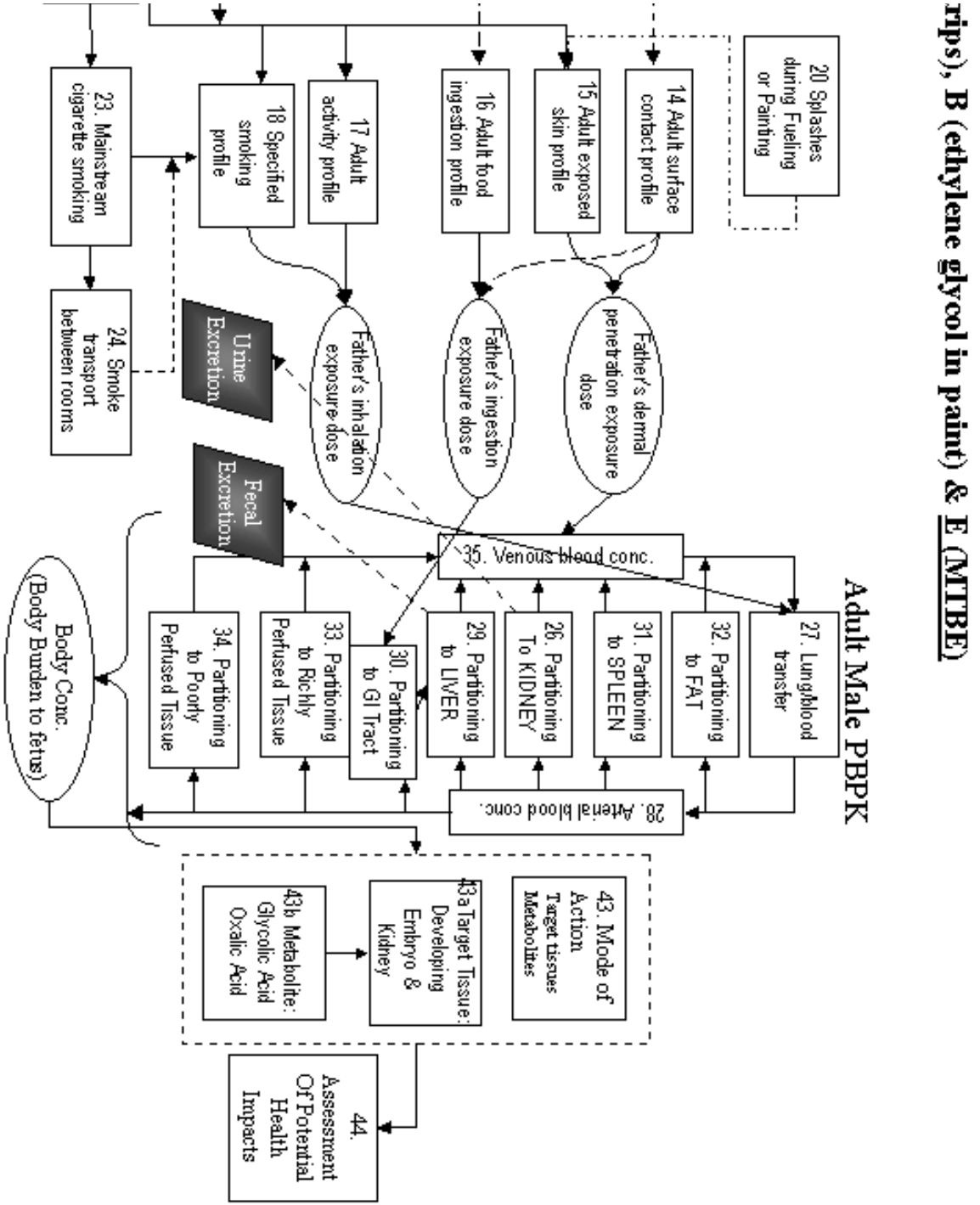
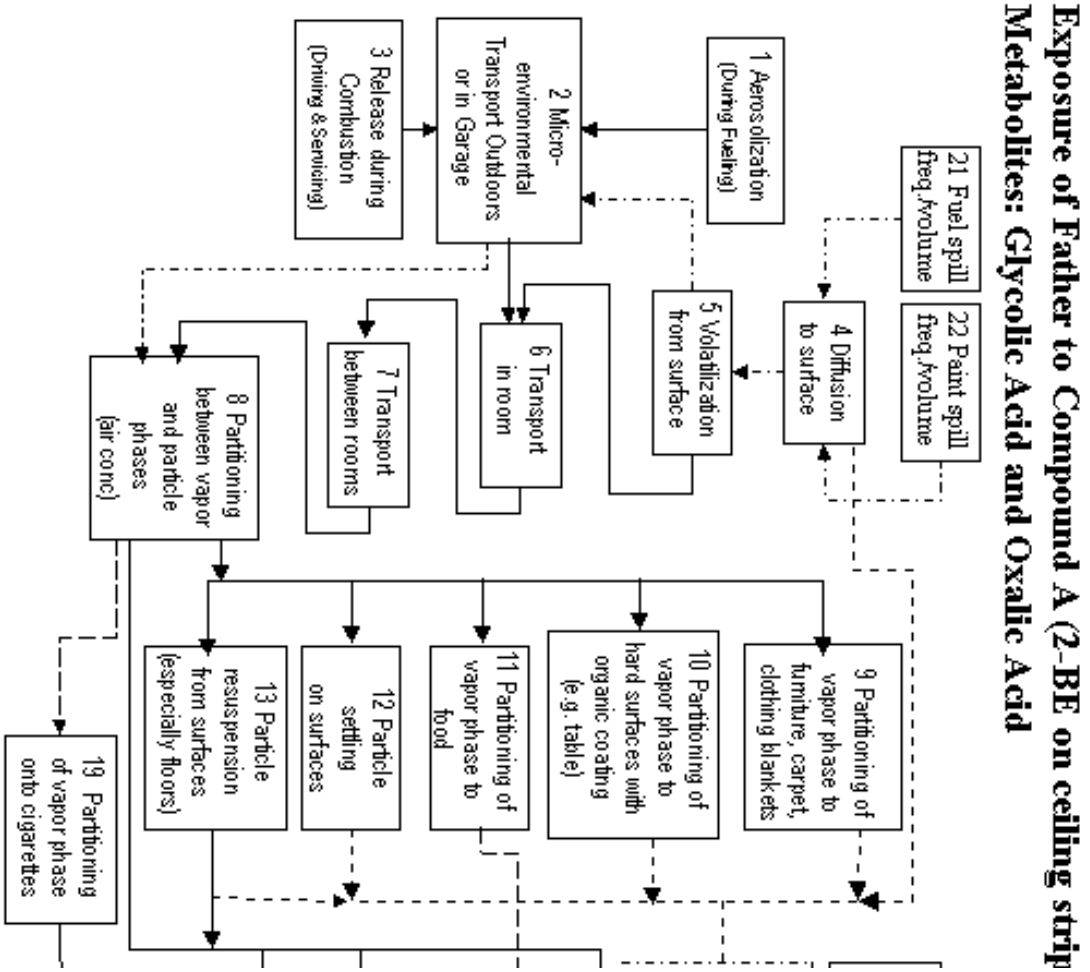


Figure 4.6.14 Scenario 4 Process Framework:Exposure of Father to Compound A (2-BE on ceiling strips), B (ethylene glycol in paint) & E (MTBE) Metabolite: Tertiary Butyl Alchohol

Notes

- Compound B: Ethylene Glycol
- Metabolite: Tertiary Butyl Alcohol
- Mode of Action: Uterus, Testes, Liver (some of these are animal specific…don't know which ones yet)
- Data gaps: No models for #1 aerosolization of contaminant during fueling, #3 release of contaminant from internal combustion engine, #8 partitioning between vapor and particle phase, #13 particle resuspension from surfaces (especially floors), #20 splashes during fueling or painting, #21 Fuel spill frequency/volume, #22 Paint spill frequency/volume, or #23 Mainstream smoking (may be able to use something from review article on smoking release from website http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.



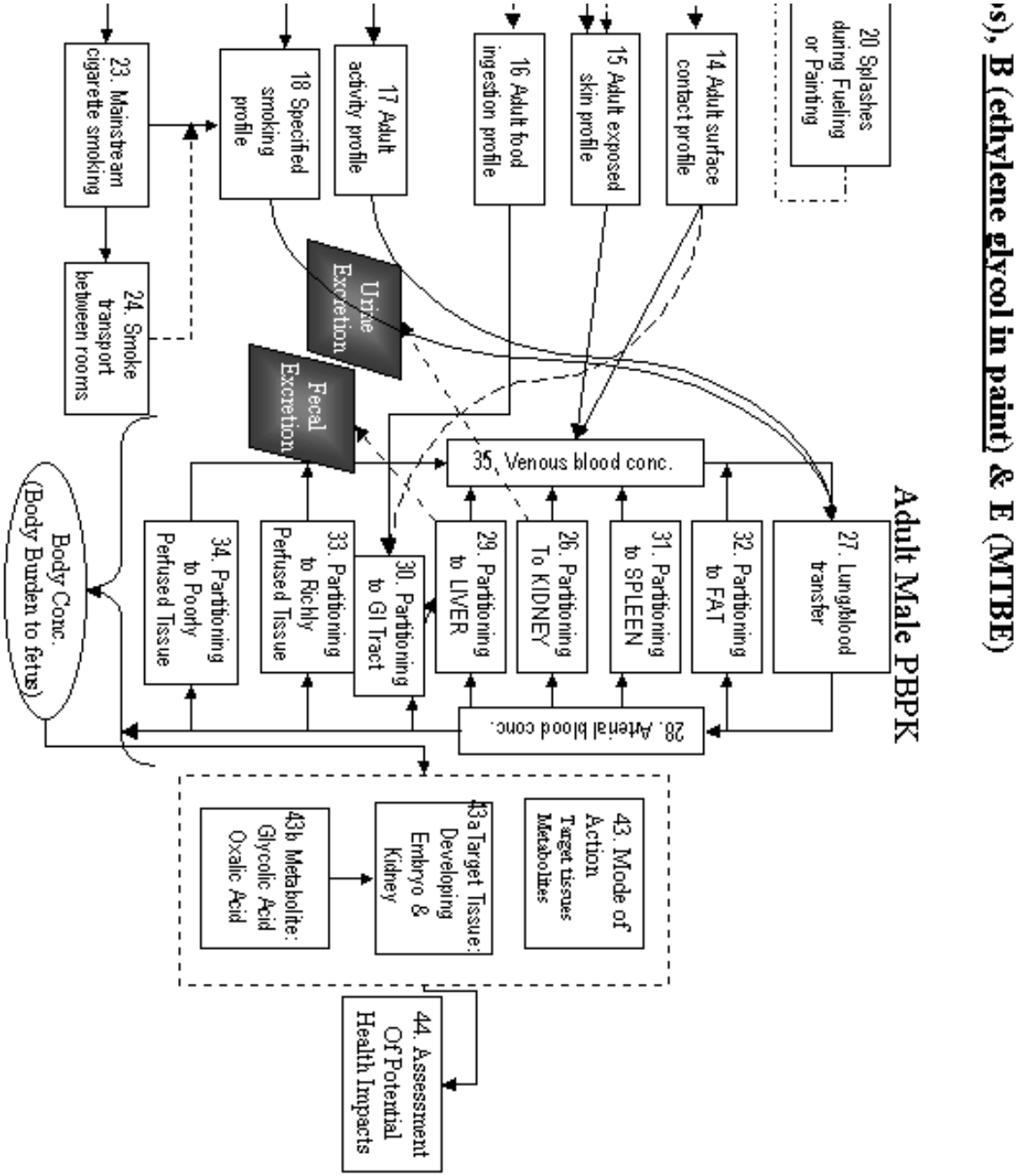


Figure 4.6.13 Scenario 4 Process Framework: Exposure of Father to Compound A (2-BE on ceiling strips),B (ethylene glycol in paint) & E (MTBE) Metabolites: Glycolic Acid and Oxalic Acid

Notes

- Compound B: Ethylene Glycol
- Metabolite: Glycolic Acid, Oxalic Acid
- Mode of Action: developing embryo, Kidney
- Data gaps: No models for #1 aerosolization of contaminant during fueling, #3 release of contaminant from internal combustion engine, #8 partitioning between vapor and particle phase, #13 particle resuspension from surfaces (especially floors), #20 splashes during fueling or painting, #21 Fuel spill frequency/volume, #22 Paint spill frequency/volume, or #23 Mainstream smoking (may be able to use something from review article on smoking release from website http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html)
- Dr. John Little and others at Virginia Tech in Blacksburg, VA have developed diffusion algorithms for VOCs that may be an improvement over existing models for diffusion-controlled release in process #1 and the reversible, diffusive sink effect for processes #6, #7, & #8. Papers describing these algorithms have recently been accepted in the journals "Indoor Air" and " Environmental Science & Technology". Dr. Little's e-mail address is jcl@vt.edu.

4.7 Exposure-Specific Model and Process Flow Diagrams and Associated Gap Analysis

This section of the report describes the gap analysis that was conducted based on the four example exposure scenarios associated with the CCEF. A gap analysis provides a list of research needs associated with the specific topic of interest. In this case, the gap analysis will provide the research needs for the framework, models, algorithms, and databases associated with the four exposure scenarios developed to define the design of the CCEF. The gap analysis consists of a three-step process in evaluating the Modeling and Process Flow Diagrams developed for the design of the CCEF. The three steps of the gap analysis are to define: 1) what exists, 2) what is needed, and 3) what process is required to achieved the needs.

The gap analysis is focused on the main components of the CCEF and will be discussed based on these components. These four components are: Source, Transport, Exposure, and Impacts. The Exposure and Impacts components were combined in this analysis because they are so closely linked. The gap analysis will be provided for each component based on each compound and scenario of interest. The results of this analysis will be input to the Qualitative Sensitivity analysis and prioritization of research needs that will be discussed in the following sections.

4.7.1 Gap Analysis of Source Component

The source component of the CCEF involves the release of a contaminant from its initial matrix. The primary mechanisms for release to the air are diffusion/volatilization or combustion. We have listed the gaps in models for relevant scenarios and indicated potential sources or research studies needed to fill these gaps for the source component of the CCEF.

1. Fugitive VOC Emissions from Mixing Vessel: Scenario 3 (Sources or Research Needs: We expect that algorithms already exist and may be available from sources such as handbooks by the American Petroleum Institute or EPA.)
2. Aerosolization of Contaminant During Auto Fueling: Scenario 4 (Sources or Research Needs: We expect that algorithms, or data to develop algorithms, for personal exposure may be available from the South Coast Air Quality Management District, California Air Resources Board, or EPA.)
3. Release of Contaminant (in breathing zone from Internal Combustion Engine (auto, lawn mower, and trimmer): Scenario 4 (Sources or Research Needs: We expect that algorithms, or data to develop algorithms, for personal exposure may be available from the South Coast Air Quality Management District,

California Air Resources Board, EPA, lawn mower manufacturers, or auto manufacturers.)
4. Source Emissions During Auto Servicing: Scenario 4 (Sources or Research Needs: Filling this gap requires data on frequency of servicing personal automobiles at home and observation or personal logs of typical activities and use of protective gear during auto servicing by individuals.)
5. Splash Frequency and Volume to Skin During Fueling: Scenario 4 (Sources or Research Needs: Filling this gap requires laboratory studies of splash characteristics and frequency logs for fueling automobiles, lawn mowers, and trimmers.)
6. Splash Frequency and Volume to Skin During Painting: Scenario 1 & 4 (Sources or Research Needs: Filling this gap requires laboratory studies of splash characteristics and frequency logs for number of splashes during painting of a typical room by a nonprofessional.)
7. Spill Frequency and Volume During Fueling: Scenario 4 (Sources or Research Needs: Filling this gap requires spill frequency and volume logs for fueling automobiles, lawn mowers, and trimmers.)
8. Spill Frequency and Volume During Painting: Scenario 1 & 4 (Sources or Research Needs: Filling this gap requires spill frequency and volume logs for painting of a typical room by a nonprofessional.)

4.7.2 Gap Analysis of Transport Component

For the CCEF, we focused on micro-environmental models for transport indoors or near source outdoors. Indoor models evaluated transport within and between rooms or other small spaces and fate and partitioning of vapor on to aerosols or particles (dust), walls, floors, and sinks (e.g., furniture, carpet, clothing, blankets). Transport for this component of the CCEF ends when it reaches the human body and does not include movement within the body. Ingestion and hand-to-mouth transfer were considered part of the exposure component of the CCEF. We have listed the gaps in models for relevant scenarios and indicated potential sources or research studies needed to fill these gaps for the transport component of the CCEF.

1. Partitioning Between Vapor and Particle (Aerosol) Phases in Air: Scenarios 1-4 (Sources or Research Needs: We expect there may be some algorithms for partitioning of vapor to particulates. Controlled laboratory partitioning studies are needed for a wide variety of combinations of contaminants and types of particles.)
2. Particle Resuspension from Floors: Scenarios 1, 3, & 4 (Sources or Research Needs: There is a major gap in models or algorithms for particle resuspension from floors. Controlled laboratory studies are needed to determine resuspension of different types of particulates with different indoor air currents and simulated human activity.)
3. Contaminant Inhalation and Release by Mainstream Cigarette Smoking: Scenarios 3 & 4 (Sources or Research Needs: Models or algorithms already exist for mainstream cigarette smoking, which can be located by a literature search or from review articles on smoking release, such as the article at http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/375-381ott/abstract.html. The reference for this review article is Ott, W.R. 1999. Mathematical Models for Predicting Indoor Air Quality from Smoking Activity. Environmental Health Perspectives Volume 107, Supplement 2, May 1999)

4.7.3 Gap Analysis of Exposure and Impact Components

There are several approaches that can be taken when choosing exposure models, algorithms, and databases for estimating human health exposure and impacts using microenvironmental modeling scenarios; however, the choice is most frequently made based on the available data and/or models. A gap analysis of the approaches to modeling exposures and health impacts from chemical concentrations in the environment in humans follows:

4.7.3.1. Physiologically Based Pharmacokinetic and Pharmacodynamic Models: The best approach to predicting blood and tissue concentrations as a function of time following an administered dose (exposure) as well as interaction of the bioactive form of the compound with the target tissue(s) is to use a combination of a Physiologically Based Pharmacokinetic (PBPK) model and a Physiologically Based Pharmacodynamic (PBPD) model. PBPK modeling refers to the development of mathematical descriptions of the uptake and disposition (absorption, distribution, metabolism and excretion) of chemicals based on quantitative interrelationships among the critical biological determinants of these processes (Krishnan and Andersen, 1994). PBPD modeling refers to developing mathematical descriptions of interactions of the actual toxicant with its receptor to produce the observed toxic effect. These models are specific to species, compound, exposure route, and life stage. Because their bases lie in the use of physiological parameters such as blood flow, respiration rate, kidney filtration

rates, etc., in addition to chemical-specific parameters, i.e. binding constants, solubilities, etc., they aid in extrapolation of data from a laboratory animal model such as a rat to the human.

Unfortunately, a full suite of these types of models applicable to the conditions described in the four exposure scenarios implemented in this study does not exist. In lieu of a well-defined PBPK and PBPD model for each scenario, a hierarchy of alternatives may be employed.

4.7.3.2. PBPK model, no PBPD model: If PBPD models are not available, compound- and exposure-specific bioavailability data obtained from toxicokinetic studies can be used to estimate body, organ, and tissue concentrations. For instance, a PBPK model may be used to provide target tissue concentrations of a toxicant for a given dose, which can then be plotted against experimental data to extrapolate dose to effect relationships without specific knowledge of how the toxicant interacts with the receptor (i.e. PBPK model without a PBPD model). There is research being conducted to generate compound-specific bioavailability data for specific exposure pathways and routes, but there are many gaps that need to be filled to complete the suite of exposure scenarios being evaluated for this study.

4.7.3.3. Neither PBPK or PBPD models available: If compound- and exposure-specific bioavailability data are not available, bioavailability models for surrogate compounds and/or alternate exposure routes can be used to estimate body, organ, or tissue concentrations. Reference doses (Rfd) or cancer slope factors may also be used to predict health effects.

4.7.3.4. Generic bioavailability models: If no appropriate surrogate compounds or exposure-specific bioavailability models are available, default generic bioavailability models can be used to provide a very rough estimate of body, organ, or tissue concentrations. These are very generic and conservative models but can be used if no other models or chemical-specific data exist.

The tiered approach for addressing the exposure component of the framework ensures that the best available information and models are used while filling as many data gaps as possible when completing the exposure scenarios. Below is the list of 18 specific research gaps identified in the exposure scenarios.

Scenario 1

1. PBPK/PBPD Model for 2-Butoxyethanol for Residential Exposure of Pregnant Mother. Source or Research Needs: PBPK/PBPD model for pregnant mother needs to be developed and validated. See American Chemistry Council Exposure Technical Implementation Panel Developmental Dosimetry/Lactation Model Review for existing models. Adopt initial parameter from related chemical (2-methoxyethanol). Refine and include information from 2-butoxyethanol specific studies on developmental dosimetry that already exists for male adult and rats/mice as a starting point.

2. PBPK/PBPD Model for 2-Butoxyethanol for Residential Exposure of Fetus (-0.75 to 0.0 years old). Source or Research Needs: See above for exposure of pregnant mother. PBPK/PBPD model for fetus also needs to be developed and validated. Existing PBPK/PBPD model for male adult rats/mice may be used as a starting point to develop fetus model with subsequent extrapolation to the human.

3. PBPK/PBPD Model for 2-Butoxyethanol for Residential Exposure of Child (2 to 6 years old). Source or Research Needs: PBPK/PBPD model for child needs to be developed and validated. Existing PBPK/PBPD model for male adult rats/mice may be used as a starting point to develop model for the child with subsequent extrapolation to the human.

4. PBPK/PBPD Model for 2-Butoxyethanol for Residential Exposure of Lactation Child (0.0 to 2 years old). Source or Research Needs: PBPK/PBPD model for nursing child needs to be developed and validated. Existing PBPK/PBPD model for male adult rats/mice may be used as a starting point to develop model for the nursing offspring with subsequent extrapolation to the human.

5. PBPK/PBPD Model for Ethylene Glycol for Residential Exposure of Fetus (-0.75 to 0.0 years old). (Source or Research Needs: PBPK/PBPD model for fetus based on rat embryo data has been developed but has not yet been published. Existing information for male adult (human) and rats/mice may be compared with new model. Also compare to adult human male controlled inhalation and dermal study conducted in Germany (Dr. Filser). Some of these key studies are being conducted under the guidance of the American Chemistry Council Ethylene Glycol Panel.

6. PBPK/PBPD Model for Ethylene Glycol for Residential Exposure of Lactation Child (0.0 to 2 years old). Source or Research Needs: PBPK/PBPD model for nursing child needs to be developed and validated. Information from the already existing PBPK/PBPD model for male adult (human) and rats/mice may be used as a starting point to develop the nursing child model.

7. PBPK/PBPD Model for Ethylene Glycol for Residential Exposure of Child (2 to 6 years old). Source or Research Needs: PBPK/PBPD model for child

needs to be developed and validated. Scaling from existing male adult (human) and rats/mice may be used but must be validated.

8. PBPK/PBPD Model for Ethylene Glycol for Residential Exposure of Pregnant Mother. Source or Research Needs: PBPK/PBPD model for pregnant mother needs to be developed and validated. See American Chemistry Council Exposure Technical Implementation Panel Developmental Dosimetry/Lactation Model Review for existing structures. Initial parameters could be adopted from model for related chemical (2-methoxyethanol), then refine and include data from 2-butoxyethanol specific studies on developmental dosimetry. Existing information for male adult (human) and rats/mice may be used as a starting point.

Scenario 2

9. PBPK/PBPD Model for Three Phthalates: DEHP, BBP, DINP for Residential Exposure of Lactation Child (0.0 to 2 years old). Source or Research Needs: PBPK/PBPD model for nursing child needs to be developed and validated. Existing information for male adult (human) and rats/mice may be used as a starting point to develop model for nursing child.

10. PBPK/PBPD Model for Three Phthalates: DEHP, BBP, DINP for Residential Exposure of Child (2 to 6 years old). Source or Research Needs: PBPK/PBPD model for child needs to be developed and validated. Scaling with existing male adult (human) and rats/mice data may be used but must be validated.

11. PBPK/PBPD Model for Three Phthalates: DEHP, BBP, DINP for Residential Exposure of Adolescent (6 to 16 years old). Source or Research Needs: PBPK/PBPD model for adolescent needs to be developed and validated. Scaling with existing male adult (human) and rats/mice may be used but must be validated. Some phthalates have been shown to be endocrine disruptors; however, no models exist specifically for laboratory animals or humans as they go through puberty.

Scenario 3

12. PBPK/PBPD Model for Benzene, Toluene, or n-Hexane for Occupational Exposure of Adult Male (18 to 65 years old). Source or Research Needs: PBPK/PBPD models exist for male adult (human) and rats/mice, but need to be extended to PBPD model. Ideally a model should incorporate interactions between the three solvents, as well as with cigarette smoke. No models at this level of sophistication were identified in the literature. No accommodation is made for advancing age in this scenario or in published models. Such an accommodation is important as metabolic capacity and other physiological functions may change with advancing age.

13. Influence of Smoking on PBPK/PBPD Model for Mixtures of Benzene, Toluene, N-Hexane for Occupational Exposure of Adult Male (18 to 65 years old). Research is needed to understand the impacts of smoking on this exposure scenario based on 1) addition to the source, 2) alternate behavior, and 3) change in behavior.

Scenario 4

14. PBPK/PBPD Model for 2-Butoxyethanol for Backyard Exposure of Adult Male (25 to 50 years old): Source or Research Needs: Need to understand potential interactions between smoking and 2-butoxyethanol and effect these may have on PBPK/PBPD model that already exists for male adult (human) and rats/mice.

15. PBPK/PBPD Model for 2-Butoxyethanol for Backyard Exposure of Adult Male (50 to 75 years old). Source or Research Needs: Need research on PBPK/PBPD model for aging male. Possibly the existing human male adult model can be scaled appropriately.

16. PBPK/PBPD Model for Ethylene Glycol for Backyard Exposure of Adult Male (25 to 50 years old). Source or Research Needs: Need to understand potential interactions between smoking and ethylene glycol and effect these may have on PBPK/PBPD model that already exists for male adult (human) and rats/mice.

17. PBPK/PBPD Model for Ethylene Glycol for Backyard Exposure of Adult Male (50 to 75 years old). Source or Research Needs: Need research on PBPK/PBPD model for aging male. Possibly the existing human male adult model can be scaled appropriately.

18. PBPK/PBPD Model for MTBE for Backyard Exposure of Adult Male (25 to 50 years old). Source or Research Needs: Need to understand potential interactions between smoking and 2-butoxyethanol and effect these may have on PBPK model that already exists for male adult (human) and rats/mice.

19. PBPK/PBPD Model for MTBE for Backyard Exposure of Adult Male (50 to 75 years old). Source or Research Needs: Need research on PBPK/PBPD model for aging male. Possibly the existing human male adult model can be scaled appropriately.

20. PBPK/PBPD Model for 2-butoxyethanol for Backyard Exposure of Adult Male (50 to 75 years old): Scenario 4 (Source or Research Needs: Need research on PBPK/PBPD model for geriatric male human. The existing human male adult model can be used to scale to the geriatric model)

21. PBPK/PBPD Model for Ethylene Glycol for Backyard Exposure of Adult Male (25 to 50 years old): Scenario 4 (Source or Research Needs: Need to understand how mixtures of compound and smoking has on PBPK/PBPD model that already exists for male adult and rats/mice)
22. PBPK/PBPD Model for Ethylene Glycol for Backyard Exposure of Adult Male (50 to 75 years old): Scenario 4 (Source or Research Needs: PBPK/PBPD model already exists for male adult and rats/mice)
23. PBPK/PBPD Model for MTBE for Backyard Exposure of Adult Male (25 to 50 years old): Scenario 4 (Source or Research Needs: Need to understand how smoking affects parameters of the PBPK/PBPD model that already exists for male adult and rats/mice)
24. PBPK/PBPD Model for MTBE for Backyard Exposure of Adult Male (50 to 75 years old): Scenario 4 (Source or Research Needs: Need research on PBPK/PBPD model for the aging male human. The existing human male adult model could be used to scale to the geriatric model)

4.7.4 Summary of Gap Analysis for Source, Transport, Exposure and Impacts Components

A number of research gaps were identified in the models or frequency/usage logs needed for the source and transport components of the four exposure scenarios used as examples in the CCEF. Three of the research gaps in models for the source component (i.e., fugitive VOC emissions from mixing vessel, aerosolization during auto fueling, and release of contaminant in combustion zone from internal combustion engine) may already exist as algorithms, but they were not identified as part of this study because they are not widely published. Five research gaps in frequency/usage logs needed for the source component were also not readily available (i.e., frequency of auto servicing and associated protective gear used at home, splash frequency/volume during fueling, splash frequency/volume during painting, spill frequency/volume during fueling, and spill frequency/volume during painting). Two major research gaps in models needed for the transport component of most of the example scenarios include: (1) partitioning between vapor and particle (aerosol) phases in air (Scenarios 1-4) and (2) particle resuspension from floors (Scenarios 1, 3, & 4).

Currently, considerable research is underway, funded by other parts of the American Chemistry Council (i.e., Endocrine Disruptor Technical Implementation Panel and CHEMSTAR Program), as well as government agencies and universities, with the goal of generating data necessary to construct PBPK and PBPD models for many chemicals to which humans of all life stages are exposed. Due to the complexity and expense of this research, it will be several years before enough new information is available to fill in the data gaps that have been identified when designing the preceding CCEF components. Further difficulties exist in that the quality of the physiological data available for many of the parameters needed to develop the models is inadequate. This is especially true when attempting to model maternal-placental-fetal transfer and metabolism of chemical substances as well as lactational transfer. The lack of accurate physiological parameters during pregnancy and lactation not only prevents construction of a substantive model in laboratory animals, it also precludes useful extrapolation to the human. Another data gap lies in the lack of knowledge regarding the effects of exogenous compounds on physiological parameters during the onset of puberty in both laboratory animal models and humans.

5.0 Qualitative Sensitivity Analysis of CCEF Modeling Components

purpose of this analysis was to identify model elements (estimation algorithms and parameter databases) likely to produce greatest uncertainty in exposure estimates obtained from model. Given list of existing computer models and gaps in models needed, next step was to rank model elements according to their relative contribution to resulting output.

5.0.1 Qualitative Sensitivity Analysis of Source and Transport Modeling Components

primary computer models selected for source or transport in one or more of four scenarios evaluated for CCEF were: CONTAM, PROMISE, IAQX, WPEM, and CONSEXPO. was also assumed a good model or algorithm already exists for mainstream and sidestream cigarette smoke. Data gaps have already been discussed in gap analysis for source and transport models.

5.0.2 Source and Transport Process of Ranking Needs

1. Models & Databases on primary exposure pathway were believed to introduce more sensitivity, and therefore be of higher priority, than those on secondary exposure pathways;
2. Missing models and databases were considered a higher priority research need than known models;
3. Models earlier in chain were believed to have potential to introduce more uncertainty than models later in chain;
4. Inaccurate models were ranked as a higher priority research need than accurate models; and
5. Models were of lesser compatibility (e.g., differing time and spatial scale) with upstream and downstream models were considered a higher priority.

5.1 Qualitative Analysis of CCEF Source and Transport

Ranking of models considered a number of factors, which are listed here roughly in decreasing level of importance: (1) whether model evaluated is on primary exposure pathway (e.g., inhalation, ingestion, dermal) for scenario of interest, (2) whether model recommended for a particular scenario needs to be developed or already exists, (3) how close model is to beginning of chain of analyses from source through effects (i.e., "garbage in, garbage out") (4) accuracy of model, (5) whether model provides output and time units needed for downstream components of CCEF.

Determination of primary exposure pathway depends on physical/chemical characteristics (e.g., volatility) of contaminant and nature of matrix containing contaminant (e.g., paint or plastic). Exposure pathway determination also depends on specifics of scenario, such as age, sex, and habits of exposed individual; physical characteristics of exposure location; or frequency and length of exposure. For some scenarios, primary exposure pathway is fairly obvious, i.e. inhalation for **Scenario 1** and ingestion for **Scenario 2**. For **Scenario 3**, primary exposure pathway is inhalation, but is not clear whether more benzene and toluene are inhaled from fugitive emissions or as natural constituents of cigarette smoke. For **Scenario 4**, primary exposure pathway is not obvious without evaluating actual modeling results, since there are multiple chemicals with different exposure routes.

Table 5.1 Qualitative Ranking of Model Elements for Source and Transport Based on their Relative Contribution to Total Uncertainty (highest uncertainty listed first) and Research Need

Scenario	Source*	Transport*
1	1. WPEM (walls largest area painted)	1. Partitioning between vapor and particle phases (gap)
	2. IAQX (smaller area wood ceiling)	2. Dust particle resuspension (gap)
		3. CONTAMW
2	1. CONSEXPO	1. CONSEXPO (primary exposure pathway)
		2. Partitioning between vapor and particle phases (gap)
		3. CONTAMW
3	1. Fugitive Emissions (gap)	1. Partitioning between vapor and particle phases (gap)
	2. PROMISE (less accurate)	Dust particle resuspension (gap)
	3. Cigarette model** (most accurate)	3. CONTAMW
4	1. Combustion model (gap)	1. Partitioning between vapor and particle phases (gap)
	2. Fueling model (gap)	2. Dust particle resuspension (gap)
	3. Fuel spill (gap; higher frequency)	3. CONTAMW
	4. Paint spill (gap; higher frequency)	

5. PROMISE (input less well known)
6. WPEM (input more well known)
7. IAQX (less accurate)
8. Cigarette model (most accurate)

* - Primary basis for ranking indicated in parentheses. Gap = no model or algorithm currently identified.
** - Two of contaminants of interest for **Scenario 3** are benzene and toluene, which are natural constituents of cigarette smoke. is not obvious whether primary exposure pathway to worker compounding adhesives is inhalation of fugitive emissions or cigarette smoke.

Table 5.1 ranks models or algorithms identified for each scenario. Models are listed in order of those expected to contribute from most to least toward results in exposure estimates. Model gaps were included in prioritization and given especially high priority as a research need when they were believed to be a component of primary exposure pathway. explicit rules of prioritization used for ranking each of five factors were listed above.

5.2 Qualitative Sensitivity Analysis of Exposure and Impact Components

Conduct of detailed qualitative sensitivity analyses of existing models for exposure and impact components of four scenarios is not possible at this time due to significant lack of models available for use in these processes. This lack of adequate and/or appropriate models for use in estimating exposure and impact processes clearly points out need for a broad range of research in this area.

However, a few generalizations can be made would apply to any physiologically-based pharmacokinetic or pharmacodynamic model. Any model using physiological parameters as its foundation will be sensitive to changes in values of those parameters; thus, is essential values for parameters used in model be as accurate as possible. accuracy of physiological parameters will also aid in extrapolating from one species to another, or from one physiological state to another, i.e. non-pregnant to pregnant female. At this time is not possible to develop defendable values for many physiological parameters. For instance, is known blood flow into and through liver increases during pregnancy in mammalian species; however, accurate data for liver blood flow during pregnancy is not available for most species. Exposure and impact models are also sensitive to chemical specific parameters such as absorption coefficients and partition coefficients. imprecise absorption coefficient for a compound to bloodstream will generate inaccurate values for all calculations downstream in model, inaccuracies which may be further amplified when extrapolating from one species to next.

6.0 Recommendations for Future Research in Micro-Environmental Modeling

This section of the report provides recommendations for future research priorities based on the design of the CCEF and the current state of the models, databases, and algorithms associated with micro-environmental modeling. These recommendations are specifically based in the design developed in this report for the CCEF and the exposure scenarios and representative compounds defined by the American Chemistry Council for this research. The design of the CCEF allows for detailed computational toxicology, linkages to appropriate databases, and access to sensitivity/uncertainty analyses. The CCEF also facilitates the transformation of the basic science into information that is understandable and directly useable by the decision-maker to scientifically support policy issues.

There is a growing awareness in recent years that a person's exposure to particular chemicals may occur via multiple routes from multiple sources. To adequately evaluate such exposures, the scientific community requires models that can predict the occurrence of exposures for each potential combination of pathway and source and then accumulate these exposures over time. Ideally, the models will account for variations in people's activity patterns that are influenced by age, gender, occupation, and other demographic factors. These activity patterns should realistically simulate the movements of representative people through zones defined by geographic location and microenvironment.

The recommendations for the development of the CCEF are based on the micro-environmental modeling needs of the American Chemistry Council and companies associated with high volume chemicals. They are also based on Battelle's experience in designing, developing, and applying modeling Frameworks for the U.S. Environmental Protection Agency, the U.S. Department of Energy, the U.S. Department of Defense, and the U.S. Nuclear Regulatory Commission. In many cases, Battelle has coordinated development of Frameworks among these different governmental agencies to create a "merged system" that meets the needs of each individual agency but also supports the needs of various modeling types, scopes, scales (both time and space), and resources.

The priority of research conducted by this project is based on the Gap and Qualitative Sensitivity Analyses for each of the four components of the CCEF, which are: Source, Transport, Exposure, and Impacts. A Gap Analysis was conducted for each of these components to identify areas where more than one piece of the modeling puzzle might be missing. This could be a process that requires a model, database, or algorithm that currently does not exist or is in development. A Qualitative Sensitivity Analysis was also conducted on the four components of the CCEF to identify inadequacies in existing models, databases, or algorithms and determine their impact on the overall Framework.

6.1 Specific Research Recommendations for Development of the CCEF

This study developed the requirements and design of the CCEF for the American Chemistry Council. In addition, the Lifeline Team has independently developed requirements and design for the CCEF. An obvious next step would be to merge the two sets of requirements and design to include the best from both studies. This should be a combined effort of the American Chemistry Council, the Lifeline Team, and Battelle.

As for the CCEF development in general, this Framework should satisfy the current and future needs of the American Chemistry Council and chemical companies. It is a difficult task to satisfy future needs, but if the CCEF is developed to be a flexible system that can accept new models, databases, and algorithms of various scales and purposes, then the CCEF can be a tool that can accommodate future research needs and changes in policies and regulations. The CCEF that is presented in this report is designed to be flexible and to support the micro-environmental modeling scale as well as to span various scales of modeling (i.e. meso- and macro-environmental modeling).

There is an interrelationship between basic science, information, and decisions. The basic science provides the foundation upon which decisions are made, but direct use of these results are generally cumbersome, confusing, highly technical, and not in a format that is readily comprehensible. Linkages between meso-scale (i.e., first-order) modeling and visualization, which provide information for decision-makers, and the science-support basic research and modeling, which provide the foundation for expressing information upon which decisions are made, are sorely needed. By formalizing the interrelationships between basic science, information, and decisions, one integrates modern computing and information technology with the technology of molecular biology and chemistry to improve the prioritization of data requirements and risk assessments for toxic chemicals. The overarching goal is for science-based quantitative risk assessments to manage chemicals in the environment without overly burdening the chemistry industry.

The design of a CCEF provides an overarching software framework that links basic science, information, and decisions by informing and advising the American Chemistry Council. CCEF supports the American Chemistry Council in its effort to identify, facilitate, and communicate generic research that will characterize people's exposure to chemicals, especially nonagricultural chemicals, and raise the confidence and lower the uncertainty for quantitative estimates of exposure associated with potential human health effects to chemicals. The CCEF facilitates key elements of science-based decisions including risk analysis (human, ecological, financial, and programmatic), hazard assessment, exposure characterization, micro-environmental modeling, computational toxicology, cost analysis, and decision analysis. The CCEF provides scientific information needed to establish and defend science-informed policy and assistance in setting programmatic direction and research agendas.

If the American Chemistry Council decides to develop the CCEF into a full system, a critical piece of the development is documentation and testing. If full sets of documents are developed that include the unit and system testing, any modification and upgrades can be made easily and efficiently. Well-documented test plans that are based on the system requirements and design ensure proper operation, but this also ensures easier modifications and upgrades to the components and the overall framework. A fine balance between the development and the documentation of the framework is critical. Unfortunately, many well-designed and currently developed frameworks and models are never used because of lack of testing and adequate documentation. Battelle has learned this lesson and has found that

testing and documentation require a significant investment of the budget to create a defensible and useful framework, set of models and databases.

Following the design of the CCEF, the following recommendations are made:

- Formulate software specifications for the CCEF, which implement the CCEF design, as the initial step for the development of the software package that will facilitate the implementation of science-based modeling and linkage to regulatory and compliance standards, which are directly influenced by the science-based modeling.
- Coordinate the development effort with the Multimedia Development and Modeling Committee, organized under a Federal Memorandum of Understanding (MOU) between the U.S. Environmental Protection Agency (Office of Research and Development), U.S. Department of Energy (Office of Environmental Management), U.S. Nuclear Regulatory Commission (Office of Research), U.S. Department of Interior (U.S. Geological Survey), U.S. Department of Agriculture (Agricultural Research Service), and the U.S. Department of Defense (Engineer Research and Development Center).
- Identify databases and science-support models for inclusion into the framework.
- Identify regulatory and compliance databases and software for inclusion into the framework.
- Link appropriate databases and software to the CCEF to evaluate the risk paradigm from multiple perspectives (science-support and meso-level).
- Develop the support tools (e.g., visualization and tabularization) to allow the decision-makers to readily establish science-based policy or challenge ill-conceived regulatory mandates.
- Test and apply the framework to a policy issue of concern to the ACC.

6.2.1 Summary of Recommendation for Gap and Sensitivity Analyses

This table summarizes the priority analysis for the four components of each scenario (Source, Transport, and Exposure & Impact). Select a hyperlinked priority (high, medium, or low) for additional information based on each scenario. The reader can click on the different boxes of the table to see the details of the priority or scroll down and read the details manually in sections 6.2.2, 6.2.3, and 6.3.4.

Table 6.2.1 Table of priority analysis conducted to produce a high, medium, and low scale for each model, database, and algorithm identified in the Gap and Sensitivity Analyses.

	Source	Transport	Exposure/Impact
Scenario 1	**Low (6.2.2.1)**	**Medium (6.2.3.1)**	**High (6.2.4.1)**
Scenario 2	**Low (6.2.2.2)**	**Low (6.2.3.2)**	**High (6.2.4.2)**
Scenario 3	**High (6.2.2.3)**	**High (6.2.3.3)**	**Medium (6.2.4.3)**
Scenario 4	**High (6.2.2.4)**	**High (6.2.3.4)**	**Medium (6.2.4.4)**

High-missing data critical to model
Medium-could be missing data or poor algorithms
Low-improve algorithms or data

6.2.2 Recommendations for Source Component

The research recommendations for the Source Component of the analysis will be defined by scenario because these components are very sensitive to the type of activities associated with each scenario. These recommendations for the Source Component are associated with the Gap and Sensitivity Analyses conducted in this study.

Ranking of the models considered a number of factors, which are listed here roughly in decreasing level of importance: (1) whether the model evaluated is on the primary exposure pathway (e.g., inhalation, ingestion, dermal) for the scenario of interest, (2) whether the model recommended for a particular scenario needs to be developed or already exists, (3) how close the model is to the beginning of the chain of analyses from source through effects (i.e., “garbage in, garbage out”), (4) the accuracy of the model, and (5) whether the model provides the output and time units needed for downstream components of the CCEF.

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6.2.2.1 Recommendations for Source Component for Scenario 1

It is critical to have the important processes associated with the source of high volume chemicals to estimate the environmental concentration that may be available for exposure to humans of different sex and age. Fortunately, there are many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *low* priority for Source components in Scenario 1:

- There is a low priority to improve the algorithms associated with the source releases from painted walls. It was determined that the WPEM model did an adequate job of estimating the emissions of chemicals from painted walls. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother and fetus.
- There is a low priority to improve the algorithms associated with the source release from the stained wood ceilings. It was determined that the IAQX model did an adequate job of estimating the emissions of chemicals from wood stains. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother and fetus.

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6.2.2.2 Recommendations for Source Component for Scenario 2

It is critical to have the important processes associated with the source of high volume chemicals to estimate the environmental concentration that may be available for exposure to humans of different sex and age. Fortunately, there are a several models and algorithms that have been developed to support the micro-environmental modeling area for Scenario 2. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *low* priority for Source component in Scenario 2:

- There is a low priority to improve the algorithms associated with the source-term and transport modeling of the CONSEXPO model, which can be used to evaluate the primary exposure pathway for phthalate esters. It was determined that the CONSEXPO model did an adequate job of estimating indoor

chemical concentrations of phthalate esters. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother, fetus, and pubescent offspring.

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6.2.2.3 Recommendations for Source Component for Scenario 3

It is critical to have the important processes associated with the source of high volume chemicals to estimate the environmental concentration that may be available for exposure to adult male throughout his life. Fortunately, there are a good many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *high* priority for Source component in Scenario 3:

- There is a high priority for filling a research gap for a Fugitive Emissions source-term model. Currently, there are no readily available models to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from fugitive emissions. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a low priority for improvement of the PROMISE source-term model. It was determined that the PROMISE model did an adequate job of estimating the emissions of chemicals from spills. Thus, these research needs are low priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a low priority for improvement of a cigarette source-term model. Although a specific cigarette source term model was not identified, it was determined that cigarette models exist that can do an adequate job of estimating the emissions of chemicals from mainstream smoking. Thus, these research needs are low priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.

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6.2.2.4 Recommendations for Source Component for Scenario 4

It is critical to have the important processes associated with the source of high volume chemicals to estimate the environmental concentration that may be available for exposure to adult male throughout his life. Fortunately, there are a good many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *high* priority for Source component in Scenario 4:

- There is a high priority for filling a research gap for to model internal combustion engine source-term model. No widely published models were found to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations in the breathing zone resulting from the combustion process. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a high priority for filling a research gap for a Fueling source-term model. No widely published models were found to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from the fueling process. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a high priority for filling a research gap for Fueling Spills . No widely published frequency/volume data were found to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from fueling spills. Thus, these

research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.

- There is a medium priority for filling a research gap for Paint Spills. No widely published frequency/volume data were found to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from fueling spills. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a low priority for improvement of the PROMISE, WPEM, IAQX, and Cigarette source-term model. It was determined that all these model did an adequate job of estimating the emissions of this scenario and chemicals. Thus, these research needs are low priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.

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6.2.3 Recommendations for Transport Component

The research recommendations for the Transport Component of the analysis will be defined by scenario because these components are very sensitive to the type of activities associated with each scenario. These recommendations for the Transport Component are associated with the Gap and Sensitivity Analyses conducted in this study.

Ranking of the models considered a number of factors, which are listed here roughly in decreasing level of importance: (1) whether the model evaluated is on the primary exposure pathway (e.g., inhalation, ingestion, dermal) for the scenario of interest, (2) whether the model recommended for a particular scenario needs to be developed or already exists, (3) how close the model is to the beginning of the chain of analyses from source through effects (i.e., "garbage in, garbage out"), (4) the accuracy of the model, and (5) whether the model provides the output and time units needed for downstream components of the CCEF.

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6.2.3.1 Recommendations for Transport Component for Scenario 1

It is critical to have the important processes associated with transport of high volume chemicals to estimate the environmental concentration that may be available for exposure to humans of different sex and age. Fortunately, there are a good many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a medium priority for transport component in Scenario 1:

- There is a medium priority to fill a gap in the transport modeling of partitioning between vapor and particle phases. Currently, there are no models to estimate this important partitioning process and the lack of this information can potentially result in erroneous estimates of chemical concentrations in the vapor and particle phases. However, these research needs are medium priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother and fetus.
- There is a medium priority to fill a gap in the transport modeling of dust particles via the resuspension process. Currently, there are no models to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from the resuspension process. However, these research needs are medium priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother and fetus.
- There is a low priority to improve the algorithms associated with the transport modeling of chemicals inside the room. It was determined that the CONTAMW model did an adequate job of estimating indoor chemical concentrations. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of lack of physiologic and chemical-specific data for the mother and fetus.

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6.2.3.2 Recommendations for Transport Component for Scenario 2

It is critical to have the important processes associated with transport of high volume chemicals to estimate the environmental concentration that may be available for exposure to humans of different sex and age. Fortunately, there are a several models and algorithms that have been developed to support the micro-environmental modeling area for Scenario 2. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *low* priority for the transport component in Scenario 2:

- There is a low priority to improve the algorithms associated with the source-term and transport modeling of the CONSEXPO model, which can be used to evaluate the primary exposure pathway for phthalate esters. It was determined that the CONSEXPO model did an adequate job of estimating indoor chemical concentrations of phthalate esters. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother, fetus, and pubescent offspring.
- There is a low priority to fill a gap in the transport modeling of partitioning between vapor and particle phases. Currently, there are no models to estimate this important partitioning process and the lack of this information can potentially result in erroneous estimates of chemical concentrations in the vapor and particle phases. However, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother, fetus, and pubescent offspring, and because partitioning between vapor and particle phases is not part of the primary exposure pathway of phthalate esters.
- There is a low priority to improve the algorithms associated with the transport modeling of chemicals inside the room. It was determined that the CONTAMW model did an adequate job of estimating indoor chemical. Thus, these research needs are low priority compared to the high priority research needs of the Exposure and Impacts Components for this scenario where models do not exist because of the lack of physiologic and chemical-specific data for the mother, fetus, and pubescent offspring.

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6.2.3.3 Recommendations for Transport Component for Scenario 3

It is critical to have the important processes associated with transport of high volume chemicals to estimate the environmental concentration that may be available for exposure to adult male throughout his life. Fortunately, there are a good many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *high* priority for transport component in Scenario 3:

- There is a high priority to fill a gap in the transport modeling of partitioning between vapor and particle phases. Currently, there are no models to estimate this important partitioning process and the lack of this information can potentially result in erroneous estimates of chemical concentrations in the vapor and particle phases. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a high priority to fill a gap in the transport modeling of dust particles via the resuspension process. Currently, there are no models to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from the resuspension process. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a low priority to improve the algorithms associated with the transport modeling of chemicals inside the room. It was determined that the CONTAMW model did an adequate job of estimating indoor chemical concentrations. Thus, these research needs are low priority compared to the research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and

chemical-specific data.

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6.2.3.4 Recommendations for Transport Component for Scenario 4

It is critical to have the important processes associated with transport of high volume chemicals to estimate the environmental concentration that may be available for exposure to adult male throughout his life. Fortunately, there are a good many models and algorithms that have been developed to support the micro-environmental modeling area. Based on Gap and Sensitivity Analyses, the following research recommendations are given a *high* priority for transport component in Scenario 4:

- There is a high priority to fill a gap in the transport modeling of partitioning between vapor and particle phases. Currently, there are no models to estimate this important partitioning process and the lack of this information can potentially result in erroneous estimates of chemical concentrations in the vapor and particle phases. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a high priority to fill a gap in the transport modeling of dust particles via the resuspension process. Currently, there are no models to estimate this important process, and the lack of this information can potentially result in erroneous estimates of chemical concentrations resulting from the resuspension Process. Thus, these research needs are high priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.
- There is a low priority to improve the algorithms associated with the transport modeling of chemicals inside the room. It was determined that the CONTAMW model did an adequate job of estimating indoor chemical concentrations. Thus, these research needs are low priority compared to the medium priority research needs of the Exposure and Impacts Components for this scenario where adult male PBPK and PBPD models exist and have adequate physiologic and chemical-specific data.

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6.2.4 Recommendations for Exposure and Impact Components

The research recommendations for the Exposure and Impact Components of the analysis will be defined by scenario because these components are very sensitive to the type and age of the human involved. All of the recommendations for the Exposure and Impact Components are associated with the Gap Analysis because there were so little data to conduct a qualitative sensitivity analysis on these components.

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6.2.4.1 Recommendations for Exposure and Impact Components for Scenario 1

Physiologic and chemical-specific data are needed for both humans and appropriate laboratory animal species in order to construct useful PBPK and PBPD models. Based on gap analysis and the inadequate data for the models associated with pregnant mother and fetuses compared to the Source and Transport Components, the following research recommendations are given a *high* priority for Scenario 1:

- Obtain key physiological data for pregnant female and the fetus (including maternal fetal transfer).
- Obtain key physiological data for lactating female and nursing and non-nursing offspring.
- Identify target tissues and the specific nature of the interactions of parent compound and/or metabolites with those tissues that result in toxicity to the organism.
- Correlate alterations in physiologic status (i.e. due to pregnancy, parturition, lactation, etc) with changes in interactions with target tissues.

Specific processes are identified in the Process Flow Diagram for Scenario 1, Compounds A & B in Section 4 of this document.

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6.2.4.2 Recommendations for Exposure and Impact Components for Scenario 2

Physiologic and chemical-specific data are needed for both humans and appropriate laboratory animal species in order to construct useful PBPK and PBPD models. Based on gap analysis and the inadequate data for the models associated with pregnant mother and fetuses compared to the Source and Transport Components, the following research recommendations are given a *high* priority for Scenario 2:

- Obtain key physiological data for pregnant female and the fetus (including maternal fetal transfer).
- Obtain key physiological data for lactating female and nursing and non-nursing offspring.
- Obtain key physiological data for developing and pubescent offspring. Knowledge of key hormonal changes and status during development and puberty are especially important when modeling the effects of exposure to phthalates as they are known or suspected to cause endocrine disruption.
- Identify target tissues and the specific nature of the interactions of parent compound and/or metabolites with those tissues that result in toxicity to the organism.
- Correlate alterations in physiologic status (i.e. due to pregnancy, parturition, lactation, puberty, etc) with changes in interactions with target tissues.

Specific processes are identified in the Process Flow Diagram for Scenario 2, Compound C in Section 4 of this document.

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6.2.4.3 Recommendations for Exposure and Impact Components for Scenario 3

Based on gap analysis and the adequate data for the models associated with adult males compared to the Source and Transport Components, the following research recommendations are given a *medium* priority for Scenario 3:

- Available physiological data for the adult male, both human and rat, are more detailed than for pregnant females, fetuses, and offspring although more accurate values would increase the usefulness of the models.
- Research into the nature of the interactions between cigarette smoke and the Compounds in Group D would help in formulating appropriate models for this scenario.

Specific processes are identified in the Process Flow Diagram for Scenario 3, Compound D in Section 4 of this document.

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6.2.4.4 Recommendations for Exposure and Impact Components for Scenario 4

Based on gap analysis and the adequate data for the models associated with adult males compared to the Source and Transport Components, the following research recommendations are given a *medium* priority for Scenario 4:

- Obtain key physiological data pertinent to senescent males (>65 year for the human), human and rat, to allow formulation of models that are capable of accounting for age-related changes in physiological parameters.
- As identified in Scenario 1, in order to accurately model toxicant and/or metabolite interactions with target tissues the specific nature of the interactions needs to be more specifically identified for Compounds A and B and E, 2-butoxyethanol, ethylene glycol and methyl *t*-butyl ether, respectively. Further, these interactions need to be correlated with age-related changes in physiologic status.

Specific processes are identified in the Process Flow Diagram for Scenario 4, Compounds A, B, & E in Section 4 of this document.

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7.0 CCEF Scenarios and Gap Analysis References

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Appendix A

Attributes of the Comprehensive Chemical Exposure Framework

To adequately assess the risks associated with chemicals released into the environment, researchers require tools for accurately estimating human exposure under a variety of exposure scenarios. Battelle will design a single overarching exposure modeling framework with the following features:

- **Comprehensive:** applicable to exposure scenarios of interest to the chemical industry
- **Modular:** consisting of modules (algorithms and databases), which can be easily updated and exchanged without affecting other parts of the framework

- **User-friendly:** IBM or compatible personal computer application with a menu-driven interface
- **Multi-route:** applicable to exposures via inhalation, oral, and dermal contact with consumer products
- **Multi-pathway:** inhalation (air-to-lungs); dermal (liquid-to-skin, solid-to-skin, air-to-skin); oral (ingestion in food, hand-to-mouth, inhalation-to-ingestion, air-to-food-to-ingestion)
- **Multi-source:** single or multiple compounds with the same target organ
- **Varying duration:** applicable to acute, intermediate, and long-term exposures
- **Accurate:** integrates state-of-the-art estimation methods and databases to estimate or reasonably overestimate the "ground-truth" of the actual exposure
- **Open code:** accessible for inspection and review by users and stakeholders (no proprietary or "black box" code)
- **Probabilistic:** provides realistic distribution of exposures within the exposed population based on probabilistic modeling of key exposure factors
- **Dose-response:** converts exposure estimates to corresponding dose and risk values whenever appropriate
- **Mass-conservative:** uses a mass balance approach whenever feasible to account for fate and transport of pollutant mass.

The design of the CCEF leverages the concepts associated with multiple existing framework system software and exposure modeling methods that are in the forefront of the scientific community, as well as new innovative concepts. The key to the Comprehensive Chemical Exposure Framework will be its flexibility of use and ability to integrate and accommodate different exposure models (existing and future) required for the American Chemistry Council and industry needs.

The CCEF design links models and databases together so they can transparently communicate with each other. The CCEF is the overarching framework that houses the models and databases as "separate" objects and provides the data file protocols for communication between objects. A model is represented by a specific set of algorithms that perform a specific function (e.g., drinking water ingestion model). A module represents a general set of model types, defined by their "real world" functions, and includes the model, its user interface, and any pre- and post-processors that facilitate linkages and communication with/to other components (e.g., models and databases). This effort focuses on the design of an overarching framework and not on the models that are housed within the framework.

The name, Comprehensive Chemical Exposure Framework, evokes the nature of the software system, whose design is described herein.

- **Comprehensive** refers to the ability to capture a wide scope of problems, issues, perspectives, and exposure scenarios of interest to the chemical industry.
- **Chemical** refers most importantly to non-agricultural compounds, but when combined with **Comprehensive,** the design should allow for all types of chemicals (e.g., organic, inorganic, radioactive) to be addressed if a future requirement is needed. In other words, non-agricultural chemicals will be addressed, but the system should not necessarily be structured to exclude other chemicals.
- **Exposure** refers to the manner in which people come in contact with chemicals, which could include exposure routes (e.g., inhalation, oral, and dermal contact) and exposure pathways [ingestion to food, hand-to-mouth, etc. (i.e., oral), liquid-/solid-/air-to-skin (i.e, dermal contact), and air-to-lungs (i.e., oral)].
- **Framework** refers to the software structure of the CCEF, which allows for the incorporation and linkages of a confederation of models and databases. Note that the **Framework** houses models and databases, but the **Framework** itself does not represent a model in the system, although, technically speaking, it can and probably will be called a model. Within this document, the term “model” will refer to the software codes *inside* the **Framework,** and the **Framework** will represent the overall structure linking the models and databases to allow for a seamless transfer of data between components.

A.1 Data Dictionary File

The Data Dictionary File consists of three types of information: 1) parameter declarations, 2) table declarations, and 3) parameter relationships. A Data Dictionary File is a comma delimited text file that contains the metadata about the data that are contained in a particular dataset. The first line of the Data Dictionary File contains the number of parameters listed within the Data Dictionary File, the name of the dataset, and a universal reference location. The second line of the file contains the parameter field header of the file, which is outlined in **Table A1.1**.

Data Dictionary Files provide the metadata describing attributes of the actual data in datasets. The datasets contain the actual numbers that are consumed and

produced by each model and database using the Data Dictionary File metadata formats, as illustrated by Table A1.1 through A1.3. **Table A1.1** presents a definition of the data fields associated with a typical Data Dictionary File. Tables **A1.2** and **A1.3** illustrate the application of **Table A1.1** as they relate to the parameters describing the chemical list, including degradation/decay products, and chemical toxicity information. If a parameter is indexed to a parameter in another Data Dictionary File, then the index contains the name of the other Data Dictionary File and an extension containing the other parameter. For example, the *Inhalation Cancer Potency Factor* in **Table A1.3** is a function of chemical; therefore, it is indexed to the chemical CAS ID in the ChemList Data Dictionary File (i.e., *ChemList.CAS*). By providing indices and referenced parameters, the information only has to be stored once and an understandable mapping is provided for the user. Also identified in the Data Dictionary File tables are those parameters that exhibit statistical variation and can be represented by a distribution in a sensitivity/uncertainty analysis (e.g., Monte Carlo simulation) (see stochastic column in Tables **A1.2** and **A1.3**).

The Data Dictionary Files are an effective mechanism for transferring information between components. The Data Dictionary Files can be cataloged into five categories, although the design allows for expansion:

1. **System Delineation Data Dictionary Files** - Metadata that is developed and maintained by the system.
    - a. **Start-Up Data Dictionary File** - Metadata that describes the information necessary for the User Interface set-up, such as system path and run names, formatting information (e.g., font, color, size, etc.), screen and line colors (i.e., both background and foreground), interface flags indicating items such as visible logo image, visible identifier (e.g., American Chemistry Council, etc.), and window size and location. The dataset for this Data Dictionary File is initially populated with default settings, many of which can be modified by the user through the customize option in the user interface. The Star-Up Data Dictionary File contains all the necessary information for the user interface initialization settings and domain. **Table A1.4** illustrates a Start-Up Data Dictionary File.
    - b. **Simulation Data Dictionary File** - Metadata that contains the necessary information to reproduce any particular conceptual site model within the CCEF. This dataset contains module names, identifiers, dataset names and locations, module status, linkages, module locking information, and simulation comments. **Table A1.5** illustrates a Simulation Data Dictionary File.
2. **Module Description Data Dictionary File** - Metadata associated with the information describing the model and supporting information about the model (e.g., who to contact for more information, Input and boundary condition Data Dictionary Files consumed and boundary condition Data Dictionary Files produced by the model, and how the model fits into the system). This is a system maintained Data Dictionary File whose corresponding dataset is populated by the model developer. **Table A1.6** illustrates a Module Description Data Dictionary File.
3. **Input Data Dictionary File** - Metadata associated with the information required as user-supplied input to a model. Module developer Input Data Dictionary Files are specific to each model. **Table A1.7** illustrates an Input Data Dictionary File, which is unique to the Surface Impoundment Module in Hazardous Waste Identification Rule Project. Note that the Input Data Dictionary File, as with all Data Dictionary Files, can be accepted and understood system-wide, or they can be unique to a particular model and only understood by that model, as illustrated in **Table A1.7**. A system-supported Input Data Dictionary File is maintained by the system, while Unique Input Data Dictionary Files are developed and maintained by the model developer.
4. **Boundary Condition Data Dictionary Files** - Metadata defining data consumed by a model originating from an upstream model or database.
    - a. **Model Dictionary File** - Metadata associated with the information that is passed from a producing model to a consuming model. Model Dictionary Files represent the output results from the model. **Table A1.8** illustrates and Output Model Dictionary File Unique to the Surface Impoundment Module in Hazardous Waste Identification Rule Project
    - b. **Database Data Dictionary File** - Metadata associated with the mapping of information between the database and the system.
5. **Sensitivity/Uncertainty Data Dictionary Files** - Metadata defining the statistical information associated with the stochastic data.
    - a. **Seed Data Dictionary File** - Metadata defining the starting seed number associated with the random number generator for a Monte-Carlo simulation. **Table A1.9** illustrates a Seed Data Dictionary File
    - b. **Iteration Data Dictionary File** - Metadata defining the current iteration of the simulation. **Table A1.10** illustrates an Iteration Data Dictionary File

- c. **Sampled Values Data Dictionary File** - Metadata defining the model inputs that are sampled as being stochastic and available for sampling. **Table A1.11** illustrates a Sampled Values Data Dictionary File
- d. **SummaryValues Data Dictionary File** - Metadata defining the model outputs that are summarized as part of the statistical results. **Table A1.12** illustrates a Summary Values Data Dictionary File
- e. **Stochastic Data Dictionary File** - Metadata defining the distribution and attributes associated with the stochastic parameters. **Table A1.13** illustrates a Distribution Data Dictionary File for a Normal Distribution.

The major requirement of Data Dictionary Files, associated with model output, is that the associated datasets must be complete. Because many databases are incomplete to begin with, datasets associated with the Data Dictionary File associated with databases do not have to be complete. It is the model developer's responsibility to deal with incomplete datasets from databases (i.e., shared-responsibility).

With the advent of standardized Data Dictionary Files, an Application Programming Interface can be developed for the CCEF to coordinate and manage the input and outputs between components [e.g., range checking of parameters, data retrieval, data storage, units checking, open/close data sources, metadata functions (cardinality, units, definitions, etc.), etc.], Read and Write functionality (e.g., error handling, command line functions, producer-consumer relationships, conceptual site model security, model selection, run calls between models, documenting user comments, etc.), units conversion so each model can work with its own unique units without concern for unit conversion errors, and the conceptual site model graphical user interface (e.g., drag & drop functionality, tiered-icon pallet, etc.).

As noted earlier, if the producing component's output Data Dictionary Files match the consuming component's input Data Dictionary File requirements, then the two components can communicate. Figure A1.1 illustrates the linkage of two models with each model receiving input from a database (i.e., Database Data Dictionary File) and user (i.e., Input Data Dictionary File), and Model 2 receiving upstream boundary conditions from the upstream model (i.e., Model Data Dictionary File). In this case the models can communicate because all upstream model boundary condition requirements of Model 2 are met by the information produced by Model 1.

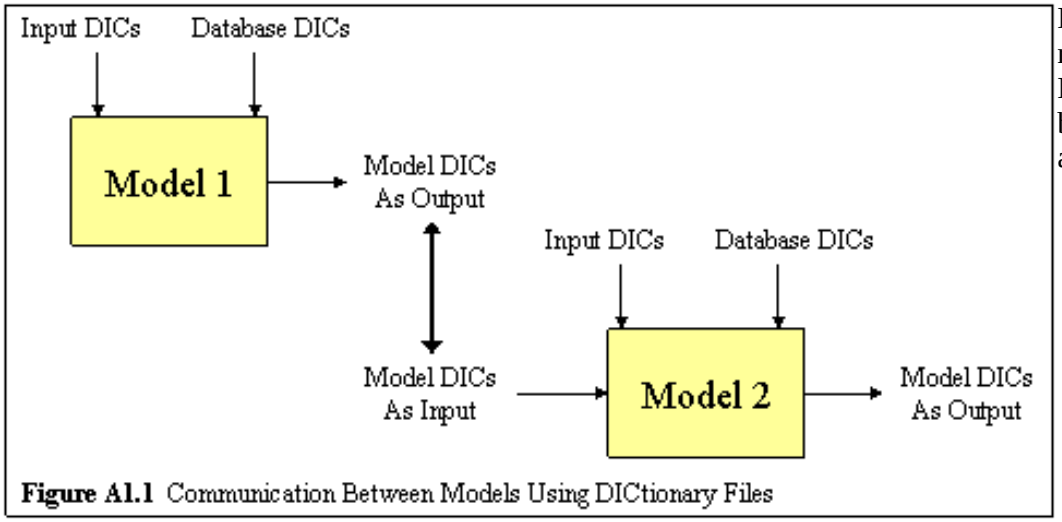


Figure A1.1 Communication Between Models Using DICtionary Files

The Application Programming Interface and Data Dictionary File design allows for the **Plug & Play** feature, which is the most important feature of the design. By ensuring Plug & Play, the CCEF inherently includes the ability to

- Link any type of model, database, or framework into the system to communicate with any other component
- Allow model developers, government organization, private companies, etc. to incorporate their own models and databases into the system with the necessity of going through the system developer as a middle-man
- Ensure backward compatibility between legacy models and databases, and new models and databases
- Allow linkage specifications to change with time and company

- Link to remote databases or models
- Link to remote frameworks, without having to integrate the remote frameworks into the CCEF
- Link to remote databases and only download the information necessary for the assessment
- Integrate change into the system without having to redesign the components that are already included in the system.

A.2 SENSITIVITY/UNCERTAINTY CONSIDERATIONS

It is envisioned that the system will include a Sensitivity/Uncertainty icon, containing at least one Monte Carlo driver (i.e., model) choice. The Monte Carlo will allow the user to;

- Select the models, which will implement the Sensitivity/Uncertainty analysis
- Select the input parameters, which will be varied automatically by the system
- Select the output parameters, which will be monitored for change
- Select the seed number for the random generating program
- Select the distributions associated with the input parameters
- Identify any cross-correlations between parameters
- Define analytical expressions relating one parameter to another parameter
- Populate the Sensitivity/Uncertainty model with statistical information contained in a database. In other words, if a database contains the stochastic information for the independent variables, the user should not have to manually enter this information into the Sensitivity/Uncertainty module.

The Sensitivity/Uncertainty component in the system will be divided into three parts:

- **Iterator** - defines the number of iterations (e.g., realizations) that are to be implemented. The Iterator passes the current and final iteration numbers to the Sampler and Summarizer, which allows the Sampler to execute the sub-set of modules that are designated by the set of icons connected to the Sampler for the defined number of iterations.
- **Sampler** - reads the distributions form one simulation or database, samples those distributions, and populates the input files in the copied simulations
- **Summarizer** - reads input and output files of the modules and generates and output datasets that conform to Sensitivity/Uncertainty Data Dictionary File.

Figures A2.1 through A2.3 illustrate how these three components fit into the overall design of the system. Figure A2.1 presents a schematic illustrating the

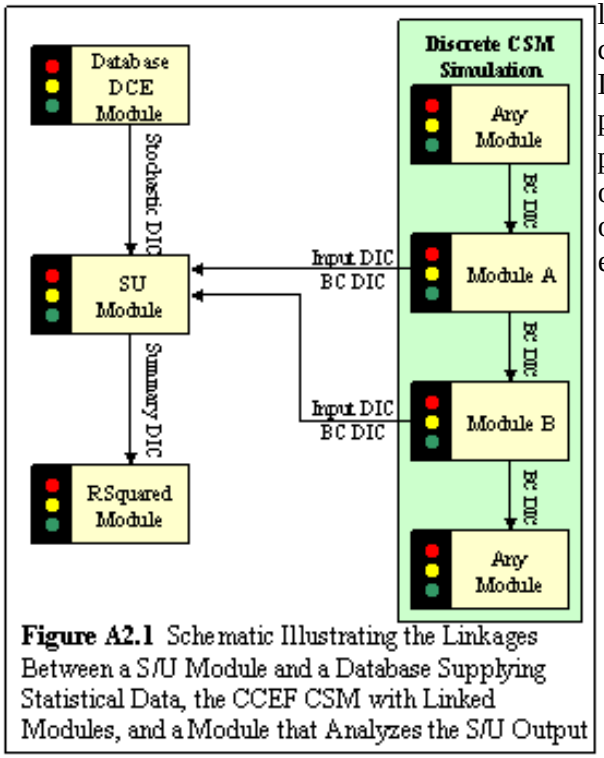


Figure A2.1 Schematic Illustrating the Linkages Between a S/U Module and a Database Supplying Statistical Data, the CCEF CSM with Linked Modules, and a Module that Analyzes the S/U Output

linkages between a Sensitivity/Uncertainty Module and a database supplying statistical data, the CCEF conceptual site model, with linked modules, and a module that analyzes the Sensitivity/Uncertainty output. The Database Data Client Editor Module represents a database supplying statistical information on the model input parameters. The R-Squared module represents an illustrative example of a model that statistical analyzes the probabilistic output results (i.e., generating r^2 values, which identify the parameters having the greatest influence on variations in the output results). The Discrete conceptual site model Simulation represents the linkage picture of the conceptual site model, developed by the user. The Sensitivity/Uncertainty module and its components are examined in more detail on Figure A2.3 (below).

Figure A2.2 presents a schematic highlighting the components of a "hard-wired" Sensitivity/Uncertainty module and its relationships to the system. Also highlighted in this figure is the sampling method, as different sampling techniques exist (e.g., straight Monte Carlo, Latin Hypercube Sampling Technique, etc.). In most situations, the Integrator, Sampler, and Summarizer modules will be bundled for the user and will operate as a single module. For those more advanced modelers with an affinity for more sophisticated statistical techniques, there is the ability to separate the Integrator, Sampler, and Summarizer into separate modules, and each can be assigned a specific model. Figure A2.3 presents a schematic highlighting the components of a user-defined Sensitivity/Uncertainty Module and its relationships to the system.

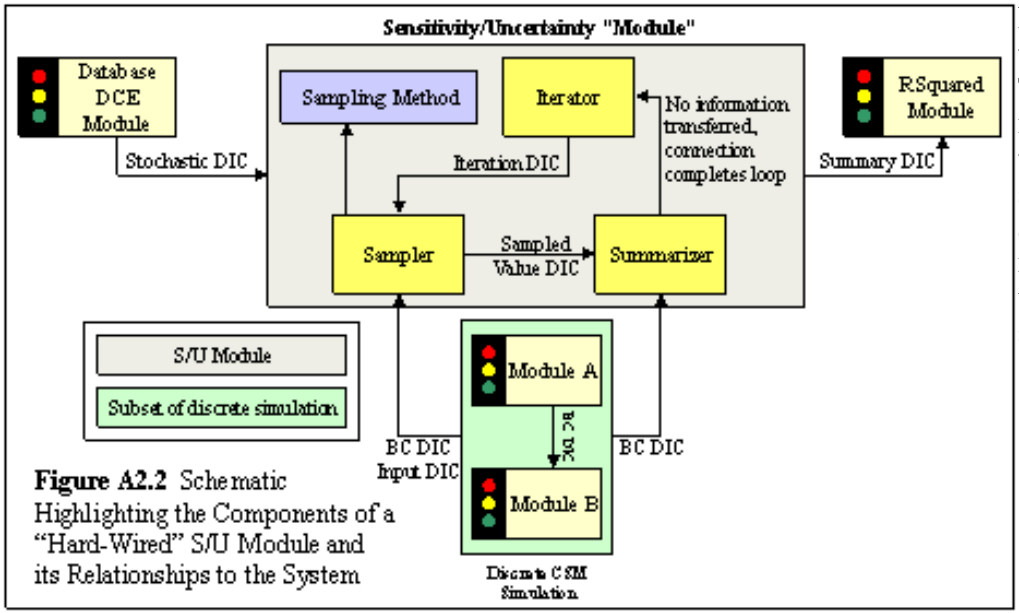


Figure A2.2 Schematic Highlighting the Components of a "Hard-Wired" S/U Module and its Relationships to the System

In addition to a Monte Carlo module, other types of modules that function in a similar manner to the Sensitivity/Uncertainty module (i.e., selection and modifying input parameters) would also fit under this category. For example, a number of parameter-estimation programs exist, which would lend themselves for direct

inclusion into the system, including UCODE and PEST.

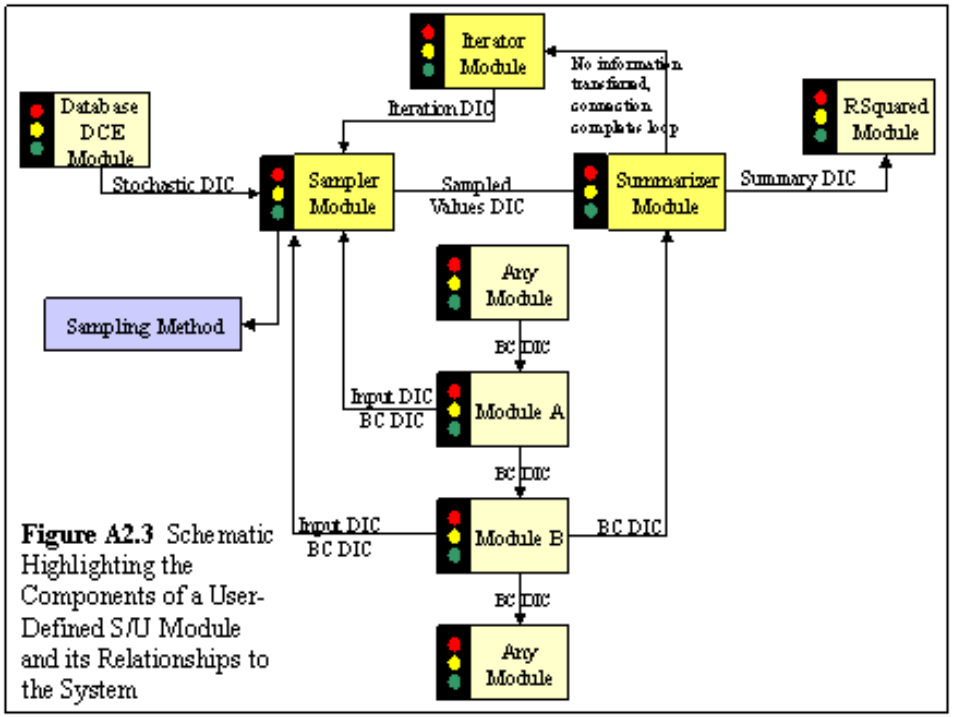


Figure A2.3 Schematic Highlighting the Components of a User-Defined S/U Module and its Relationships to the System

A.3 MODEL SPACE AND TIME CONSIDERATIONS

The ultimate intent is to propose a universal design for meeting protocols for linking disparate models and ensuring communication between environmental software products. The design is not intended to be parochial or inflexible but is intended to set the standard for allowing a number of different approaches to communicate within a framework. For example, if the requirement is to allow two models to seamlessly communicate, then the interface design between these two models should be such that data should seamlessly pass from one model to the next, irrespective of scale or resolution (within reason), and should not be model-dependent. These protocols are applicable, regardless of whether the models are on local or remote systems.

A.3.1 Model Connectivity

Model connectivity addresses the issues associated with ensuring the transparent linkage (i.e., how models communicate with each other) between models with different scale and resolution. Scale refers to the physical size and requirements of the problem (e.g., medium-specific, watershed, regional, and global). Resolution refers to the temporal- and spatial-mesh resolution associated with the assessment [i.e., requirements associated with the transfer of data at medium interfaces (i.e., boundary conditions)], designated as low (e.g., structured-value), medium (e.g., analytical), and high (e.g., numerical). For example, an analytical model, using mass flux across an infinite plane, should structure its output to be handled by another analytical model or numerical model containing a grid system. Any design should be general enough and structured to ensure that mass is conserved and that the linkage handles most types of traditional models.

The responsibilities of the consuming module would include processing, mapping, and transforming the producing model's output, as correlated to the Geo-Referencing system, to a standard format described by a Model Dictionary File. The consuming model would be charged with:

- recognizing and understanding the dataset corresponding to the Model Dictionary File

- mapping all spatially indexed parameters to the consuming model's input requirements
- ensuring that the Geo-Reference system associated with the producing model and the assessment scenario is consistent with the consuming model's Geo-Reference system.

The responsibilities of the producing module would include processing, mapping, and transforming the output to a standard format described by a Model Dictionary File. The producing model would be charged with:

- populating the Dataset corresponding to the Model Dictionary File
- mapping all spatially indexed parameters to meet system requirements
- mapping all temporally indexed parameters to meet system requirements
- ensuring that the Geo-Reference system associated with the producing model is consistent with the assessment scenario.

The boundary-condition data passing from one module to another will be handled through the Application Programming Interface Input/Output Dynamic Link Library. The linkage protocols and design will address the mapping of information between modules, specifically passing or calculating geo-spatial data, Geo-Reference coordinates, area-based polygons, and fractions of areas that overlap between producing and consuming model coordinate systems.

At the linkage or communication boundary, boundary information provided by the producing module would include the following:

- Spatially dependent, Geo-Referenced coordinates (i.e., vertices), describing points, lines, or polygons
- Associated with each set of vertices (e.g., polygon), will be spatially dependent, and constant or time-varying data.

The responsibilities of the consuming module would include processing, mapping, and transforming the producing models output, as described by the producing module's coordinate system, to the consuming model's coordinate system, which would involve mapping the producing model's spatially dependent, Geo-Referenced coordinates onto the consuming model's spatially dependent, Geo-Referenced coordinates and determining the fractions of areas that overlap. The mapping process will use the producing model's areas at the boundary that are projected onto the consuming model's boundary surface.

It is recognized that the consuming model may not have programs developed to perform the processing and mapping of and transformation associated with the producing model's output. Although not a responsibility of the system, the Application Programming Interface Input/Output Dynamically Link Library will provide a routine that:

1. Calculates area-based polygons associated with producing and consuming model boundary surfaces, as defined by its spatially dependent, Geo-Referenced coordinates
2. Maps the producing model polygons onto the consuming model polygons
3. Calculates the fractions of the producing model polygon areas that overlap with each consuming model polygons
4. Transforms the boundary conditions from the producing model's output to the consuming model's input by combining the producing model's output in an appropriate manner, so as to define the boundary conditions associated with each consuming model's boundary condition polygon.

In other words, if a consuming model needs assistance in transforming a producing model's output for consumption, a system program will be made available, which maps and assigns a producing model's output to all consuming models boundary-condition polygons. Based on this mapping, the consuming model would be charged with completing the mapping of the information associated with their polygons to their nodes, if required.

A.3.2 Geo-Referencing Considerations

The Model Dictionary Files contain information that allow for all spatially dependent boundary condition data to be referenced to a Geo-Reference system (i.e., x, y, z coordinates). The location aspect of the data is associated Geo-Referenced points, lines or polygons, as defined by their vertices. Tables **A3.2.1** and **A3.2.2** illustrate the Geo-Referencing scheme using Model Dictionary Files. **Table A3.2.1** presents an example set of Model Dictionary Files for boundary condition

polygon locations, and **Table A3.2.2** presents an example set of Model Dictionary Files for time-varying chemical groundwater concentrations by boundary-condition polygons. These Geo-Referenced vertices allow for the mapping of the spatially distributed and dependent boundary condition data from the producing model boundary condition polygons to consuming model boundary condition polygons. This conversion is facilitated by an Application Programming Interface through a Dynamically Linked Library.

A.3.3 Models with Spatial Boundary Conditions

Many models with spatial boundary conditions perform their boundary condition calculations at nodes, as opposed to the areas surrounding the nodes. Each node , though, represents a polygon that surrounds it. It is the polygon, and specifically the vertices of each polygon, which represents the basis for passing information between producing and consuming models. The nodes are represented by polygons, which, in turn, are described by their vertices portrayed within the model- and scenario-Geo-Referencing system (x, y, z coordinates). Tables **A3.2.1** and **A3.2.2** illustrate the metadata associated with the manner in which a model will describe and document the vertices of an area polygon. Figure A3.3.1 presents an illustrative example of producing and consuming model boundary condition nodes and associated polygon areas, whose corners represent polygon vertices.

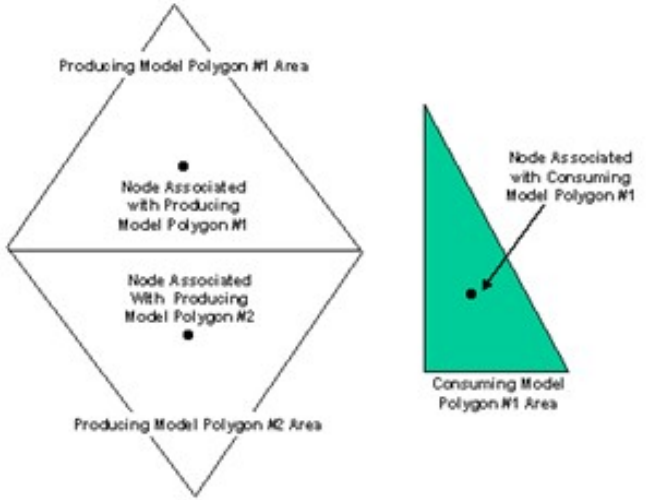


Figure A3.3.1 Illustrative Example of Producing and Consuming Model Boundary Condition Nodes and Associated Polygon Areas

For an analytical model, a rectangular plane traditionally defines the interface area with the vertices being defined at the four corners of the rectangle. For a numerical model containing a gridding system, multiple nodes and/or areas will be defined at the boundary interface. The producing model will be responsible for transforming its output to meet the boundary condition metadata requirements of the Model Dictionary Files, as illustrated in Tables **A3.2.1** and **A3.2.2**. If the producing model provides its output by node, it will have to convert its node-based output to correspond to an area (i.e., polygon) representing each node. Either the model can do the conversion or the model can request help from the system, and the system will provide software to help in this conversion.

The CCEF will assume that the boundary condition information is 1) associated with each polygon area, representing each boundary condition node, and 2) uniformly distributed across each polygon. Figure A3.3.2 illustrates two areas associated with the boundary of a producing model (i.e., polygons #1 and #2),

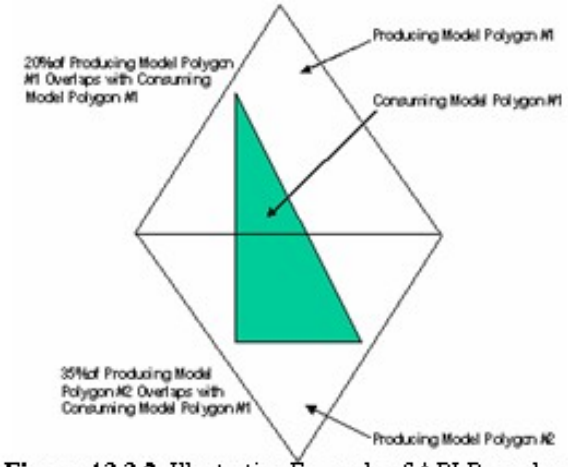


Figure A3.3.2 Illustrative Example of API Procedure for Overlapping Producing and Consuming Model Grid System Boundary Interface Polygons

overlapping with one area associated with the boundary of a consuming model (i.e., polygon #1). When the producing model defines the output at a node, the producing model is responsible for transforming that nodal output into a form representing the area-based polygon. The consuming model has the responsibility to map the output results of each producing model's polygons to the area-based polygons and corresponding nodal locations associated with the consuming model's grid system. All interface mapping will be assumed to occur across a flat plane. If the gridding system boundary for one of the models is curvilinear, the producing model's area, projected onto the consuming model's surface, will be used in the mapping exercise.

If a consuming model does not have a mapping routine that transfers the producing model's polygon-based output (e.g., time-varying mass flux and polygon vertices, which describe the area) to the appropriate and corresponding consuming model's polygons, then the system will provide software to assist the consuming model in the mapping exercise. The consuming model can use this mapping software through the Application Programming Interface, or it can utilize its own mapping software. If system software is used, the Application Programming Interface will compute polygons around each node, defining the polygons by their Geo-Referenced vertices. The system assumes that the output at each node is associated with the area surrounding the node and that the output is uniformly distributed across the node's assigned area. This assumption would be applicable for both producing and consuming models.

By utilizing the CCEF Application Programming Interface, a consistent procedure exists to develop the areas (i.e., polygons) associated with each producing or consuming model's nodes. There are a number of methods for generating polygons (i.e., multiple-connected planar domains) to describe irregular computational grids (e.g., Thiessen Polygon Method, Voronoi Diagrams); the CCEF will use Voronoi Diagrams (Icking, 2001). Either module can invoke the Application Programming Interface to help it with the development of polygons. The extent of the areal planes associated with the producing and consuming models do not have to be identical. In other words, the sizes of the overlapping consuming and producing model planes could be different, as illustrated in Figures A3.3.1 and A3.3.2(above). The CCEF would then calculate the fraction of each producing polygon that overlaps with a consuming polygon.

When the producing and consuming model areas do not exactly overlap, the output, being transferred from the producing module to the consuming module, will be defined by the weighted-average associated with the overlapping areas (i.e., fraction of the producing model polygon overlapping with the consuming model polygon). In other words, the output assigned to the consuming module's nodal area will be defined by the output of the producing module's nodal areas, whose nodal areas overlap, weighted by aerial extent. The polygons for both the producing and consuming models are assumed to be convex, that is, the angles between vertices will not contain any interior angles that are greater than 180 degrees.

The transformation (i.e., mapping) of a producing model's grid system onto a consuming model's grid system area is illustrated in Figure A3.3.2 (above). In this illustrative example, the producing model has two polygons associated with it, while the consuming model (shaded area) has one. Approximately 20% of the producing model polygon #1 overlaps with the consuming model polygon #1, and the 35% of the producing model polygon #1 overlaps with the consuming model polygon #2. In effect, the information passing from the producing model's to the consuming model's nodal area will be represented 20% and 35% of the output supplied by producing model polygons #1 and #2, respectively.

A.3.4 Models with Temporal Boundary Conditions

Each model, especially numerical models, calculate time stepping and have a nodal-spacing mesh that are consistent with their own model while ensuring numerical convergence and stability. Temporal considerations for linking models with disparate time-stepping requirements need to be independent of any model. To remove model-specific time stepping from dictating the manner in which models communicate, each of the model's time-stepping requirements need to be accounted for when passing information between models.

Each producing model will provide time-varying output corresponding with each producing model's area-based polygons, which describe the boundary interface between models. The time-varying output from the producing model is a function of the time steps used in generating the time-varying curve. The system does not know if the time information between data-points on the mass flux rate curve is linear, constant, nonlinear, etc.; as such, each producing model's time-varying curves will have their own time-stepping protocol for each parameter for each polygon. When the consuming model maps the producing model's polygon output and transfers the information from the producing model's gridding system to its own, the consuming model is responsible to account for the time-stepping system that the producing models provides. For example, if the producing model provides uneven time intervals with its output, but the consuming model requires even-incremented time steps, then the consuming model is responsible for ensuring the proper conversion.

For those consuming models that do not have a protocol for mapping producing model results into a form that they can recognize, the system Application Programming Interface provides software that can help in this mapping process. If the consuming model utilizes the system mapping protocol, then it is assumed that the consuming model's time-varying input, which corresponds to a nodal polygon, is defined by the producing model's area-weighted output, whose producing model's polygons overlap with the consuming model's polygon. By passing area-weighted information, the system can transform the data from the producing model's gridding system into a format that is consistent with the consuming model's gridding system. The mapping procedure, using the system Application Programming Interface, is as follows:

1. The system Application Programming Interface determines the fraction of the projection of the producing model's polygon areas onto each consuming model's polygons. For example, Figure A3.3.2 (above) illustrates the spatial mapping of two producing model polygons onto a consuming model polygon.
2. The system Application Programming Interface multiplies each time-varying curve by their respective fractions. Figure A3.4.1, correlated with Figure A3.3.2, provides an example, which maps time-varying output from the two producing model's polygons onto a corresponding consuming model's polygon.

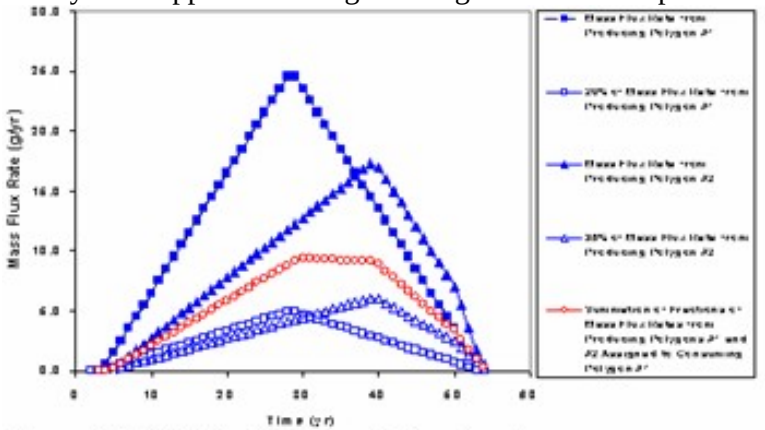


Figure A3.4.1 Illustrative Example Procedure for Calculating the Mass Flux Rate Curve for a Consuming Polygon from two Overlapping Producing Polygons

3. The system Application Programming Interface ensures that the time-stepping protocol associated with each producing model's time-varying curves are consistently mapped, ensuring that each time step is accounted for, assuming linear interpolation, when necessary. If the system Application Programming Interface needs to combine the output from two producing model polygons, and the time-step intervals associated with each output is different, then the Application Programming Interface will linearly interpolate to ensure that the time steps for both time-varying curves have values corresponding to not only their own polygon time-steps, but also to the other polygon time steps. For example, if polygon #1 provides output every 10 years, and polygon #2

provides output every 5 years, then values will be assigned to polygon #2 corresponding to every five years, using linearly interpolation.

4. The system Application Programming Interface summarizes the producing model's area-weighed output to produce time-varying input for manipulation and consumption by the consuming model. For each point in time,

(1)

where

(2)

where f_i represents the fraction of the producing model's area that overlaps with the consuming model's area, A_i represents the i-th producing model's area that overlaps with the consuming model's area, A_{Ti} represents the area in the i-th producing model's polygon, "i" is the index on the i-th polygon in the producing model's gridding system that overlaps with the area associated with the consuming model's polygon, n is the total number of producing model polygons whose areas overlap the area associated with each corresponding consuming-model polygon, and j is the index on the j-th polygon in the consuming model's gridding system.

Figures A3.3.2 and A3.4.1 (above) illustrate how a producing model's output for two polygons can be transformed to produce input to the consuming model's polygon. Figure A3.4.1 illustrates the mechanics of implementing Equations (1) and (2), as they relate to Figure A3.3.2. Five curves are presented in Figure A3.4.1: 1) two time-varying mass flux rate curves for the producing model's polygons #1 and #2 (represented by solid squares and triangles, respectively), 2) two time-varying producing model curves, adjusted for the fraction of overlap between the producing and consuming model polygons (e.g., 20% and 35%) (represented by open squares and triangles, respectively), and 3) consuming model's curve associated with its polygon (represented by open circles). Multiplying the aerial fractions times the corresponding polygon output and summing the results produces the input curve (i.e., open-circle curve in Figure A3.4.1 for the consuming model. The consuming model can then manipulate and transform this input curve to meet its model-specific input requirements.

A.3.5 Dynamic Simulation

Dynamic simulation refers to the ability of the system to allow for temporal dynamic feedback between models. Currently, the user has a choice between Plug & Play with no dynamic feedback or dynamic feedback where all of the models are "hard-wired" together with Plug & Play features. Under the design of the CCEF, the Plug & Play feature would be combined with the temporal feedback feature. This could be done by allowing the upstream model to proceed with calculations until the temporal results are available and encompass a time step associated with the downstream model. The downstream model would then begin calculations until its temporal results are available and encompass the next time step of the downstream model. The procedure is repeated until all time steps for both models have been addressed. This approach is consistent with the design structure of the Application Programming Interface and Data Dictionary Files.

A.4 SYSTEM INTEGRATION TOOLS: EDITORS

The following editors will provide the users with a mechanism to construct, update, or modify information associated with the system:

1. **Data Dictionary File Editor** - Allows the user to add or delete metadata information in all Data Dictionary Files, except the Description Data Dictionary File, which is fixed by the system. The editor will allow the user to add or delete parameters (e.g., rows of information) but will not allow the user to change attributes (e.g., column headings) associated with that parameter. The parameter attributes represent metadata about the metadata, which is fixed by the system.
2. **Units Conversion Editor** - Allows the user to add additional unit conversions not currently supported by the system.
3. **Module Description Editor** - Allows the user to input and edit the Description Data Dictionary File, which contains information about the model (e.g.,

icon Class, which Boundary Condition and Input Data Dictionary Files are consumed and which Boundary Condition Data Dictionary Files are produced, who to contact for more information, etc.).

4. **Domain Editor** - Allows the user to define where the model fits in the system (e.g., icon type, Domain, Group, and Subgroup, etc., but not Class).
5. **Dataset Editor** - Allows the user to build the input corresponding to a model's Input Data Dictionary File (i.e., Generic Module User Interface), and allows the user to build the input corresponding to the boundary conditions associated with the Model Dictionary File. Using this editor, the user actually defines values to the input parameters. This assumes that the model needs a mechanism to allow the user to populate the models's input file with data.
6. **Conceptual site model Editor** - Allows the user to edit the conceptual site model workspace containing the Drag & Drop functionality of constructing a conceptual site model and linking modules together. This editor is the FRAMES conceptual site model interface.

A.5 SERVER SIDE OF THE CCEF

Previous design considerations have dealt with the client (i.e., host) side of the CCEF design. The server side of the design addresses models, databases, and frameworks that may be located at remote locations. This section will briefly discuss how databases are dealt with within the CCEF, and it will also present the interrelationships between the host computer and the server side of the design, and interactions with Geographical Information Systems.

A.5.1 Databases

Databases represent repositories of information that provide data to populate models within the system. Databases can:

- Vary in size. Some databases are very large, but the user may only require access to a small portion of the information
- Be developed for specific models (e.g., aquifer) or applications (micro-environmental)
- Contain special information (e.g., statistical data)
- Be incomplete
- Be located on the host computer or at a remote location.

Based on the CCEF design describing data transfer protocol (i.e., use of Data Dictionary Files), the linkage of databases to other components in the system can be addressed in a similar manner to the linkage protocol associated with models. The model owner defines input requirements for the model through a series of Data Dictionary Files: Input and boundary condition Data Dictionary Files, of which the boundary condition Data Dictionary Files could be defined by upstream models and/or upstream databases. The boundary condition Data Dictionary Files provide the database owner with a template of the data needs of the models in the system and can map the data to the needs of the models.

Because the database owner understands the database structure better than anyone else, it is most appropriate for the database owner to perform the mapping. To avoid a "data dump," the initial mapping would be based on "Primary Keys" that only provide the most appropriate information for selection by the model. Examples of Primary Keys include chemical and organism. The CCEF system would provide the database owner with the necessary tools to map the database contents to the input requirements of the CCEF models, as identified by Database Data Dictionary Files. Therefore, by knowing the BC requirements of the models, Database Data Dictionary Files can be developed and the models would then have the option to consume only that information from the database that met the model's needs. A database would populate a dataset meeting the format specifications of a Database Data Dictionary File. To consume that information, the model would reference the same datasets (based on the Database Data Dictionary Files). Data would then be directly transferred from the database to the model.

In the instance where the boundary condition Data Dictionary File is describing a calculated result being transferred from one model to the next model (i.e., Model Dictionary File), there is an expectation that the dataset for that Data Dictionary File or set of Data Dictionary Files will be complete. In the instance where the boundary condition Data Dictionary File is describing information coming from a database, the expectation of completeness is not imposed. It is unrealistic to

require a database to understand and meet the input requirements of every possible model that might want to access its data repository. The module receiving information from a database must have provisions to accept incomplete datasets. This means that a default procedure for completing an incomplete dataset must be performed by the receiving model, or a user-interface option (i.e., user intervention) to fully populate the dataset must be provided.

Like models, databases could be linked to databases, thereby providing a simple mechanism to prioritize the same type of data (e.g., bulk density) from multiple databases. Figure A5.1 illustrates the linkage of three databases to a model: National, Regional, and Site-Specific. In this example, the databases closest to the model take precedence over those databases farther from the model. If a Site-Specific database did not fulfill the boundary condition requirements of the model, then data gaps would be filled by the Regional database, then the National database. For conflicting information (e.g., different cancer potency factors provided by each database), the closest database could take precedence.

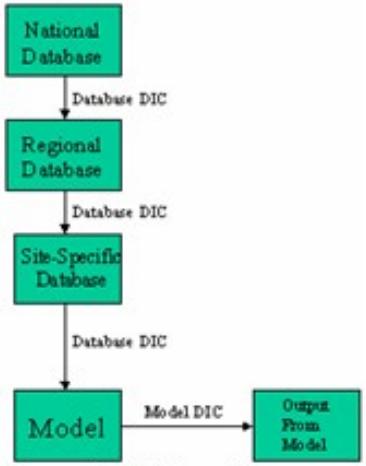
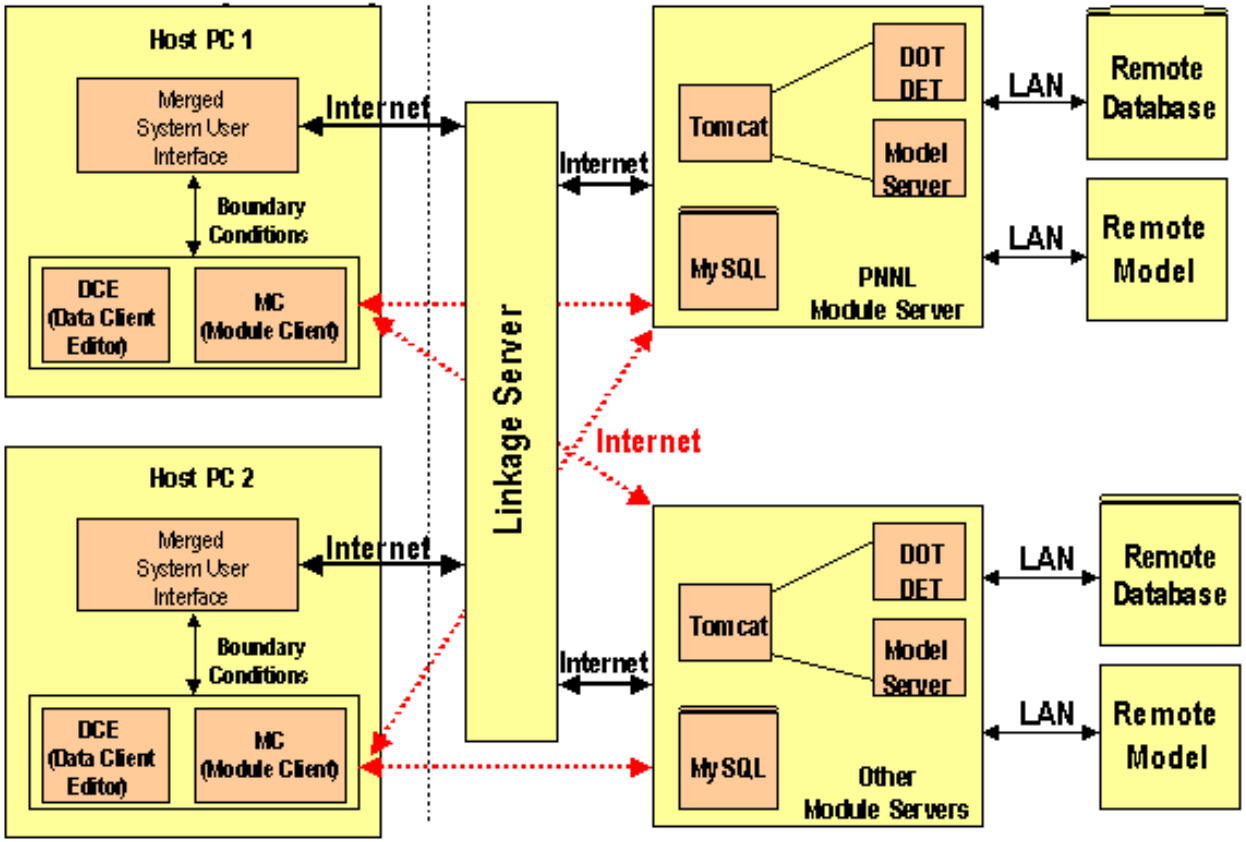


Figure A5.1 Schematic Illustrating the Linkage of Three Databases to a Model: National, Regional, and Site-Specific

A.5.2 Software Linkage Tools

Software linkage tools allow for communication between host (i.e., local) and remote systems (i.e., running models remotely or accessing data from remote databases). The relationships between Linkage and Module Servers, Host Client, and Remote Databases and Models are presented in Figure A5.2.1.

Figure A5.2.1 CCEF Design Relationships between Linkage and Model Servers, Host Client, and Remote Databases and Models



An explanation of Figure A5.2.1 as it relates to the components comprising the server side of the CCEF design is as follows.

1. **Data Owner Tool** - The Data Owner Tool is support software that allows the Data Owner to map the database structure to a file on the Module Server, which holds the developed extraction plans (mappings), database schema, and the schema of the Database Data Dictionary File. In effect, the Data Owner Tool documents the meta-information associated with the database and data to be extracted, when the extraction is invoked. The Data Owner Tool has already been developed and represents system (i.e., universal) software that needs to be installed and used by the Data Owner. Figure A5.2.2 presents a

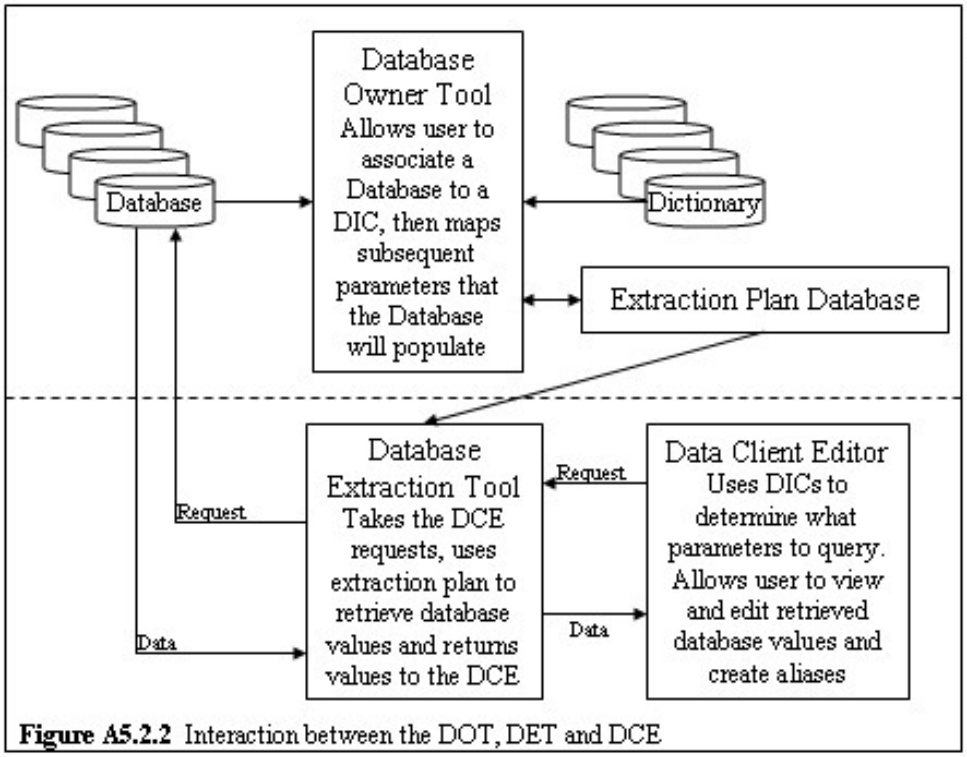


Figure A5.2.2 Interaction between the DOT, DET and DCE

graphical explanation of the relationship between the Data Owner Tool, Data Extraction Tool, and Data Client Editor.

2. **Data Extraction Tool** - Data Extraction Tool extracts the data from the designated database and returns it to the Data Client Editor through the Hypertext Transfer Protocol (http). When invoked by the Data Client Editor, the Data Extraction Tool goes out to the Data Owner Tool database, retrieves the desired extraction plan from the Data Owner Tool database, extracts the appropriate data through a Structured Query Language server, and returns it to the Data Client Editor. The Data Client Editor then stores these data on the local drive in a designated file for eventual consumption by module icons (and their underlying models) connected to the data-set icon. The Data Extraction Tool has already been developed and represents system (i.e., universal) software. Figure A5.2.2 presents a graphically explanation of the relationship between the Data Owner Tool, Data Extraction Tool, and Data Client Editor.
3. **Data Client Editor** - The Data Client Editor invokes the Data Extraction Tool, which extracts the data from the designated database and returns it to the Data Client Editor through the Hypertext Transfer Protocol (http), meeting the metadata requirements outlined by the Database Data Dictionary File, containing the appropriate Variable Referencing Keys. Only those data associated with the Variable Referencing Keys are extracted from the database. When invoked by the Data Client Editor, the Data Extraction Tool goes out to the Data Owner Tool database, retrieves the desired extraction plan, extracts the appropriate data from the database through a Structured Query Language server, and returns it to the Data Client Editor. The Data Client Editor then stores these data, meeting the specifications of the Database Data Dictionary File, on the local drive for eventual consumption by module icons (and their underlying models) connected to the data-set icon. A Data Client Editor is associated with one data-set icon. Aside from system Data Client Editors, each Database Data Dictionary File is associated with one Data Client Editor, although a Data Client Editor may have multiple Database Data Dictionary Files associated with it. Likewise, multiple Datasets may be associated with a Database Data Dictionary File. For example, for two distinct vadose zones, there will exist two distinct Datasets following the same metadata specifications outlined by a vadose zone Database Data Dictionary File. Likewise, a database (i.e., Data Client Editor) may contain information to populate files corresponding to vadose zone and aquifer Database Data Dictionary Files. Also, multiple databases may populate a Dataset, meeting the format specifications of multiple Database Data Dictionary Files. For example, the Data Client Editor is a user interface that can view and edit the data. The Model Owner is responsible for developing their own Data Client Editor, although the Model Owner can use existing Data Client Editors as a template for their model-specific Data Client Editor. Figure A5.2.2 presents a graphically explanation of the relationship between the Data Owner Tool, Data Extraction Tool, and Data Client Editor.

4. **Model Owner Tool** - The Model Owner Tool is used to define the connections between a Module Server and Remote Model over its Local Area Network, and between the Module Sever and Linkage Server. The Model Owner Tool will pass information, meeting the metadata formats of the Remote Model-specific Input Data Dictionary File and Description Data Dictionary File, from the Remote Model through the Module Server to the Linkage Server. For each new Remote Model being added to the system, the Model Owner Tool will be run, and new files created using the Module Description and Data Dictionary File editors corresponding to the Description and Input Data Dictionary File metadata formats, respectively, will be transferred to the Linkage Server. The Model Owner Tool will most likely be executed by a system analyst, who understands system and Internet protocols. The Model Owner Tool approaches the linkage from the Remote Model and Module Server side, while the Model Execution Tool approaches the linkage from the Client side. For each new Remote Model seeking consideration for inclusion to the system, a new Model Owner Tool needs to be invoked. The Model Owner Tool has already been developed and represents system (i.e., universal) software that needs to be executed by the Remote Model Owner.
5. **Model Execution Tool** - The Model Execution Tool represents a bridge between the Host computer containing the system (i.e., Client) and the Module Server. When coupled with the Model Owner Tool, which has defined the necessary connections to gain access to where the Remote Model is located, the Model Execution Tool can execute request commands from the system, allowing for the direct communication between the System and the Remote Model, so the Remote Model can be run at its remote location. The Model Execution Tool is invoked when linking the Client to the Remote Model with the ability to convert a web-based request to a socket-based request. A portion of the Model Execution Tool software resides on the Host computer, central Module Server (outside the fire wall), and computer where the Remote Model will be executed. The central Module Server coordinates communication with multiple Remote Model locations for that organization. The Module Client (a.k.a., Module Execution Client) resides on the Host computer and includes software that communicates with the Module Server to move files between the Remote Model and Client. The Model Owner Tool approaches the linkage from the Remote Model and Module Server side, while the Model Execution Tool approaches the linkage from the Client side. The Model Execution Tool represents system software, which is automatically executed by the system, when invoked.
6. **Client to Linkage Server Software** - Software is currently under development that will allow for communication between the Client and the Linkage Server. The Linkage Server will contain a listing of all remote models currently available to the Client. The Client has a master list of all currently installed models in the System. The software will be able to identify when models have been removed from service or been updated. This new software will link the Client to the Linkage Server, so the master list on the Client can be compared to the Linkage Server list; at which time, a web page with links to the Remote Model installs associated with the new models can be invoked, if the Client chooses to update the master list of available models. The software will automatically update the master list, if a Remote Model owner removes their model from consideration (e.g., major error in the model, obsolete model, a significantly new version of the software, etc.). Under other circumstances, the user will be asked if an update is required, if a new version of a model or even a new model becomes available for inclusion into the system. Client to Linkage Server Software represents system software, which is automatically executed by the system, when invoked.
7. **Remote Module Client** - The Remote Module Client is a piece of software that allows the Model Owner Tool / Model Execution Tool to setup and execute model runs on remote systems. This software should be written in Java and should be able to run on any platform that supports Java2. It must be installed and executed on all systems on which remote models will be run. All systems running the Remote Module Client will be registered and managed through the Model Owner Tool.

The Data Owner Tool, Data Client Editor, and Data Extraction Tool represent software for accessing remote databases. The Model Owner Tool, Model Execution Tool, and Remote Module Client represent software for accessing and running remote models.

A.5.3 Geographical Information System

Many modeling systems are beginning to take advantage of Geographical Information Systems as a powerful support tool to cross-correlate and relate spatial

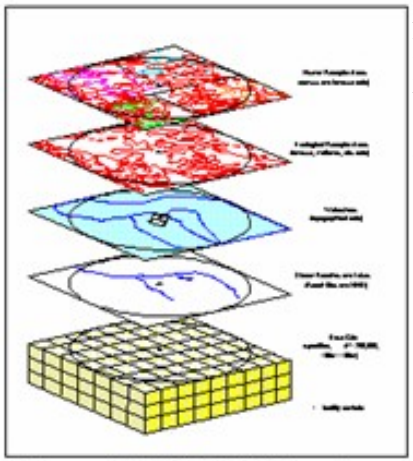


Figure A5.3.1 GIS Site-Specific Overlays used for HWIR (After Whelan and Laniak 1998; RTI 1998)

information between models. For example, the 200 sites, which form the underlying foundation of U.S. Environmental Protection Agency's Hazardous Waste identification Rule, are based on data collected with GIS site-specific overlays, as illustrated in Figure A5.3.1. As illustrated in the Hazardous Waste identification Rule example, many programs are moving to Geographical Information System formats to store, access, and correlate spatial data so multiple models are working from consistent data.

Under the design of the CCEF, a graphical user interface will allow the user to:

- Import Geographical Information System data files and incorporate Geographical Information System information into the CCEF, so that all modules can access this information through a single consistent interface.
- Graphically place spatial modeling attributes (e.g., contaminant sources and receptors) on a site base map as part of the conceptual site model development for a modeling scenario

The complete tool will allow decision makers and modelers to easily modify the conceptual site model for a modeling scenario. When the modeling has been completed, the environmental and risk results can then be analyzed to assess the risk implications of changing conceptual site models. The result will be to make this capability more directly accessible to client users and more useful for problems where decision makers disagree or are uncertain about important site parameters. The essential spatial information required to define the conceptual site model is passed, via the Data Dictionary File specifications, containing all spatial modeling data. The Data Dictionary Files have been structured to allow for the model developer to specify those parameters that are spatially aware.

Data are spatially aware when they have been designated as having a Location index, constituting the coordinates of the vertices associated with a polygon (see **Table A3.2.1**). Clear distinctions have to be made between spatial system data (i.e., spatial layout of components, such as sources and receptors) and non-spatial model data (i.e., porosity, temperature, Kds, toxicity, age, etc.). The spatial data entered through the conceptual site model graphical user interface is divided into three object categories: points, lines, and polygons, all requiring coordinates of their vertices.

Figure A5.3.2 presents an example illustrating the linkage of an existing Geographical Information System to the CCEF. Data are traditionally collected, and the

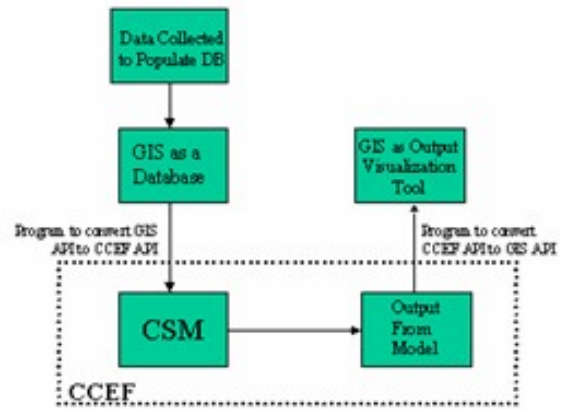


Figure A5.3.2 Example Illustrating the Linkage of an Existing GIS to the CCEF Needing Spacial Information

Geographical Information System database is populated with these data. This may be done outside of the assessment process (Figure A5.3.2), as was done with the Hazardous Waste identification Rule assessment, or the user may choose to have the spatial data requirements of the models designated by the user using a conceptual site model Geographical Information System graphical user interface, delivered as part of the conceptual site model (Figures A5.3.3 through A5.3.6, below). Each GIS has its own special file formats [e.g., ESRI Shape files (*.shp), AutoCAD (*.dwg), Drawing Interchange Files (*.dxf), Windows Bitmap (*.bmp), and Tag Image Files (*.tif and *.tff)]; as such a program will link the Application Programming Interface of the Geographical Information System system to that of the CCEF, thereby allowing for the conversion and transfer of data from the Geographical Information System to the CCEF. The CCEF uses the data and may produce spatially aware output results, which could be converted back to the Geographical Information System file formats for visualization as a Geographical Information System viewer (see Figure A5.3.2).

The user does not see the mechanics behind the linkage of the Geographical Information System to the CCEF conceptual site model, as illustrated in Figure A5.3.2 (above). In the user's work space (see Figure A5.3.7 below) and from a set of system icons, the user would choose the Geographical Information System icon and connect it to all of those models that require spatial information and expect to receive the spatial data from the Geographical Information System. The user would then link the Geographical Information System icon to those models requiring spatial data, as illustrated by Figure A5.3.7 (below). If the data comes from a standard database, then a Data Client Editor (coupled with a Data Owner Tool and Data Extraction Tool) is used to transfer the data to each model. If the user wants to develop a real-time spatial picture of the conceptual site model, then software would be available to identify the polygons, lines, and points associated with the conceptual site model, as illustrated in Figures A5.3.3 and A5.3.4 (below). Figure A5.3.3 pictorially illustrates a user-defined Geographical Information System -based conceptual site model, identifying well and air population-usage locations, sources, water bodies, farms, aquifers, watersheds, and ecological habitats. Figure A5.3.4 illustrates the use of a background map to facilitate the identification of polygons, lines, and points. Figures A5.3.5 and A5.3.6 illustrate how the Geographical Information System could be used as a visualization tool to inspect time varying at specific locations or spatially varying data at a point in time, respectively.

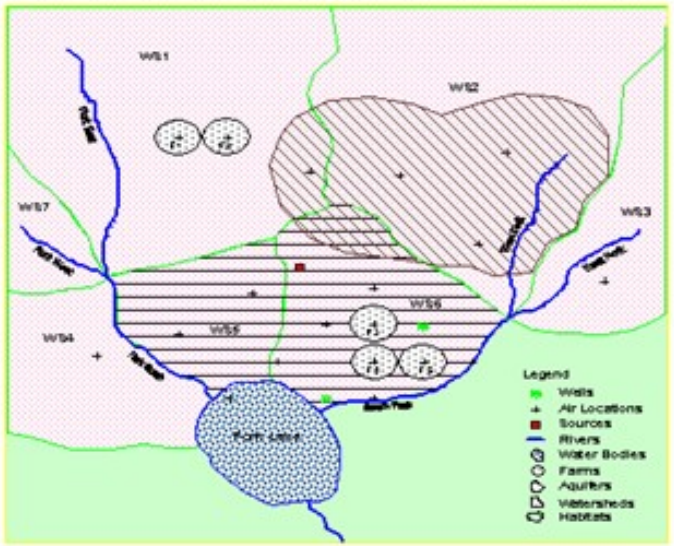


Figure A5.3.3 User-Defined Pictorial Illustration of a GIS-based CSM identifying Well and Air Population-Usage Locations, Sources, Water Bodies, Farms, Aquifers, Watersheds, and Ecological Habitats

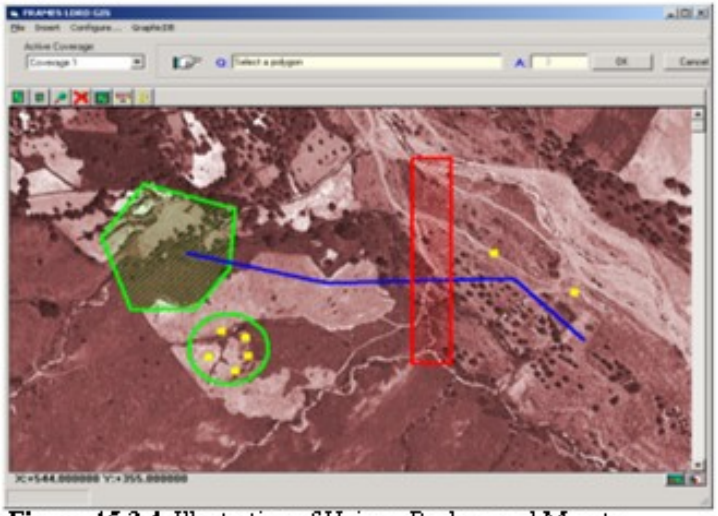


Figure A5.3.4 Illustration of Using a Background Map to Facilitate the Identification of Polygons, Lines and Points

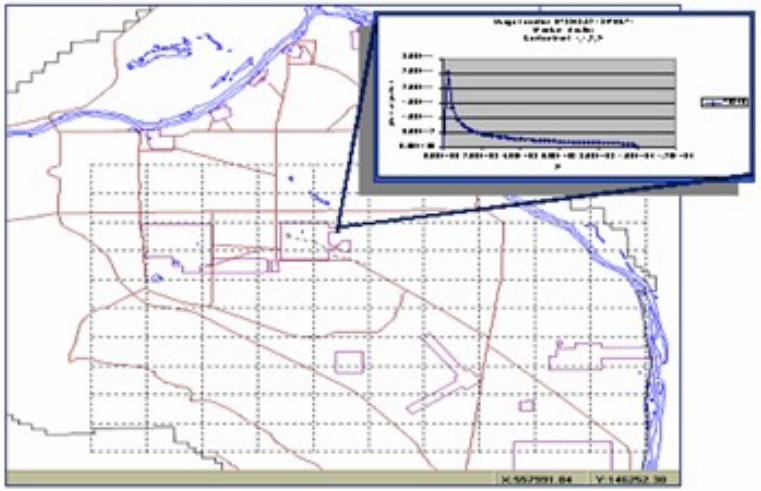


Figure A5.3.5 Use of the GIS as a Visualization Tool to Summarize Time Varying Results at Specific Locations

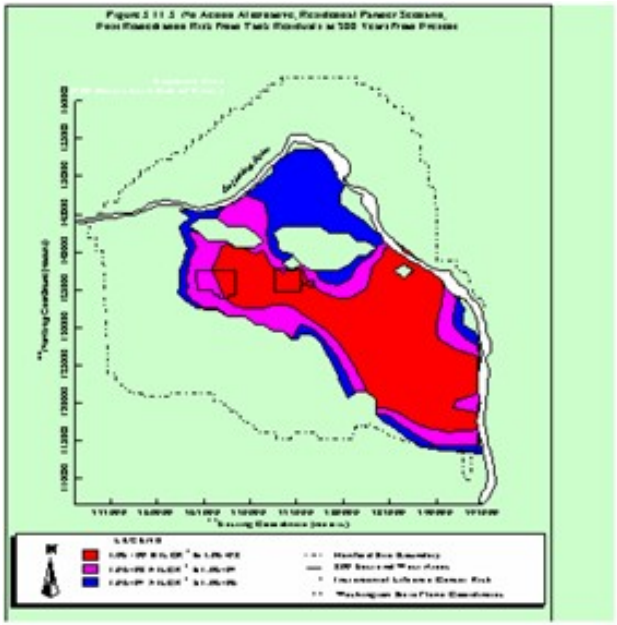


Figure A5.3.6 Use of the GIS as a Visualization Tool to Summarize Spacially Varying Results at a Point in Time

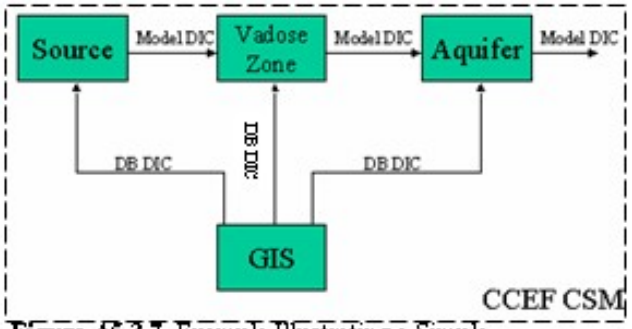


Figure A5.3.7 Example Illustrating a Simple Drag & Drop Pictorial of the GIS Module Linked to Other Models Needing Spacial Information, Including Inter-Model DIC Requirements

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Table A1.7 Illustrative Input DIC Unique to the Surface Impoundment Module in 3MRA-HWIR

Variable Count	Dictionary Description	Dictionary Name		Privilege								
26	SI	SI		3								
Parameter	Description	Dimension	Primary Key	DataType	Scalar	Min	Max	Measure	Units	Stochastic*	Preposition	Indexing Parameter(s)
bio_yield	biomass yield	0	FALSE	FLOAT		0	1		g/g	TRUE		
C_in	chemical concentration (influent)	0	FALSE	FLOAT		0	1000000		mg/L	TRUE		
CBOD	BOD (influent)	0	FALSE	FLOAT		0	1		g/cm3	TRUE		
d_imp	impeller diameter	0	FALSE	FLOAT		0	200		cm	TRUE		
d_setpt	fraction of SI occupied by sediments (max.)	0	FALSE	FLOAT		0.1	0.99		fraction	TRUE		
d_wmu	depth of wmu	0	FALSE	FLOAT		0.3	46		m	TRUE		
dmeanTSS	particle diameter (mean, waste suspended solids)	0	FALSE	FLOAT		0	0.01		cm	TRUE		
EconLife	economic life of a tank/SI	0	FALSE	INTEGER		0	100		year	TRUE		
F_aer	fraction surface area-turbulent	0	FALSE	FLOAT		0	1		fraction	TRUE		
focW	fraction organic carbon (waste solids)	0	FALSE	float		0	1		mass fraction	TRUE		
fwmu	fraction hazardous waste in WMU	0	FALSE	float		0	1		mass fraction	TRUE		
hydc_sed	saturated hydraulic conductivity (sediment layer)	0	FALSE	FLOAT		0	0.001		m/s	TRUE		
J	oxygen transfer factor	0	FALSE	FLOAT		2.9	3		lb O2/h-hp	TRUE		
k_dec	digestion (sediments)	0	FALSE	FLOAT		0	0.001		1/s	TRUE		
kba1	biologically active solids/total solids (ratio)	0	FALSE	FLOAT		0	1		unitless	TRUE		
MWt_H2O	molecular weight (liquid [water])	0	FALSE	FLOAT		18	18		g/mol	TRUE		
n_imp	impellers/aerators (number)	0	FALSE	INTEGER		0	66		unitless	TRUE		
NumEcon	number of economic lifetimes	0	FALSE	INTEGER		1	5			TRUE		
O2eff	oxygen transfer correction factor	0	FALSE	FLOAT		0.8	0.85		unitless	TRUE		
Powr	impellers/aerators (total power)	0	FALSE	FLOAT		0	5000		hp	TRUE		
Q_wmu	volumetric flow rate (tank)	0	FALSE	FLOAT		1.00E-20	10		m3/s	TRUE		
rho_l	density (liquid [water])	0	FALSE	FLOAT		0.96	1.5		g/cm3	TRUE		
rho_part	solids density	0	FALSE	FLOAT		1	5		g/cm3	TRUE		
TSS_in	total suspended solids (influent)	0	FALSE	FLOAT		0	1		g/cm3	TRUE		
w_imp	impeller speed	0	FALSE	FLOAT		0	260		rad/s	TRUE		
* Assumed for illustrative purposes. These parameters were not all necessarily randomly modified as part of the 3MRA-HWIR assessment.												

Table A1.8 Illustrative Output Model DIC Unique to the Surface Impoundment Module in 3MRA-HWIR

Variable Count	Dictionary Description	Dictionary Name	Privilege									
5	sl	sl	3									
Parameter	Description	Dimension	Primary Key	DataType	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Indexing Parameter(s)
MMSPTime		0	FALSE	Float		0	0		s	FALSE		
Models		1	FALSE	String		0	0			FALSE		
NumModels		0	FALSE	Integer		0	0			FALSE		
Times		1	FALSE	Float		0	0		s	FALSE		

Table A1.9 Example Seed DIC

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated							
1	Seed	Seed	3	0	1							
Name	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Unit	Stochastic	Preposition	Indexing Parameter(s)
Seed	Seed for random number generator	0	INTEGER	FALSE	FALSE	0	32767			TRUE		

Table A1.10 Example of an Iteration DIC

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated							
2	Iteration	Iteration	3	0	1							
Name	Description	Dimension	DataType	PrimaryKey	Scalar	Min	Max	Measure	Unit	Stochastic	Preposition	Indexing Parameter(s)
CurIter	Current Iteration	0	INTEGER	FALSE	FALSE	0	32767			FALSE		
LastIter	Last Iteration	0	INTEGER	FALSE	FALSE	0	32767			TRUE		

Table A1.11 Example of an SampledValues DIC

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated								
7	Sampled values from distributions	SampledValues	3	0	1								
Name	Description	Dimension	DataType	PrimaryKey	Scalar	Min	Max	Measure	Unit	Stochastic	Preposition	Index 1	Index 2
Set	Data set for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
Indices	Dimension indices for sampled variables	2	INTEGER	FALSE	FALSE	0	32767			FALSE		Variables	
Iterations	Set of iterations that have been sampled	1	INTEGER	FALSE	FALSE	0	0			FALSE	for		
Variables	variable names that have been sampled	1	STRING	FALSE	FALSE	0	0			FALSE	for		
VarUnits	Units for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
ShortName	Alias name for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
Value	Sampled value of variable	2	FLOAT	FALSE	TRUE	0	0			FALSE		Variables	Iterations

Table A1.12 Example SummaryValues DIC

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated								
7	Summary values from simulation	SummaryValues	3	0	1								
Name	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Unit	Stochastic	Preposition	Index 1	Index 2
Set	Data set name for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
Indices	Dimension indices for sampled variables	2	INTEGER	FALSE	FALSE	0	32767			FALSE		Variables	
Iterations	Set of iterations that have been sampled	1	INTEGER	FALSE	FALSE	0	0			FALSE	for		
Variables	variable names that have been sampled	1	STRING	FALSE	FALSE	0	0			FALSE	for		
VarUnits	Units for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
ShortName	Alias name for sampled variables	1	STRING	FALSE	TRUE	0	0			FALSE		Variables	
Value	Sampled value of variable	2	FLOAT	FALSE	TRUE	0	0			FALSE		Variables	Iterations

Table A1.13 Example of a Stochastic DIC for the Normal Distribution

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated								
7	Normal Distribution Parameters	NormalDist	3	0	1								
Name	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Unit	Stochastic	Preposition	Index 1	Index 2
AppDICs	Applicable DICtionaries	2	STRING	FALSE	FALSE	0	0			FALSE	in	Descriptions	
AppDICVars	Applicable DICtionary Variables	3	STRING	FALSE	FALSE	0	0			FALSE		Descriptions	AppDICs
Average	Average value for distribution	1	FLOAT	FALSE	TRUE	0	0			TRUE		Descriptions	
Descriptions	Descriptions of the set of distributions	1	STRING	FALSE	FALSE	0	0			FALSE	for	Descriptions	
Maximum	Maximum value for distribution	1	FLOAT	FALSE	TRUE	0	0			TRUE		Descriptions	
Minimum	Minimum value for distribution	1	FLOAT	FALSE	TRUE	0	0			TRUE		Descriptions	
StDev	Standard deviation value for distribution	1	FLOAT	FALSE	TRUE	0	0			TRUE		Descriptions	

Table A3.2.1 Example Module DICtionary for Boundary Condition Polygon Locations

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated								
3	Location	Location	3	0	1								
Parameter	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Indexing Parameter(s)	
RunInfo	The set of strings that describe the run	1	String	FALSE	TRUE	0	80			FALSE			
Vertice	The set of vertices in (x,y,z), where z is vertical	2	Float	FALSE	FALSE	0		Distance	m	FALSE	for	Poly	Vertice
Poly	The set of polygons and their associated vertex indices that make up the polygonal mesh	0	Integer	TRUE	FALSE	0				FALSE			

Table A3.2.2 Example Module DICtionary for Time-Varying Chemical Groundwater Concentrations by Boundary Condition Polygon

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated										
3	ChemGWConc	ChemGWConc	3	0	1										
Parameter	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Indexing Parameter(s)			
RunInfo	The set of strings that describe the run	1	String	FALSE	TRUE	0	80			FALSE					
TimePts	The set of time points for each location and chemical	4	Integer	FALSE	FALSE	0		Time	yr	FALSE		Location.Poly	ChemList.ChemCAS	ChemList.ChemCASDK	TimePts
ChemGWConc	The dissolved chemical Concentration in the aquifer at a location, chemical and time point	4	Float	FALSE	TRUE	0		Concentration	mg/L	TRUE	for	Location.Poly	ChemList.ChemCAS	ChemList.ChemCASDK	TimePts

Table 1.3.1 Standard EPA Risk Assessment Chemical Life Cycle Paradigm

DOMAIN: Chemical Life Cycle		
CLASS	**GROUP**	**SUBGROUP[(a)]**
Framework	Closed (no linkages)	
	Linkable	
System	Sensitivity/Uncertainty	
	Parameter Estimation	
	Unique	
Simulation Modules	Source	Surface Impoundment, Aerated Tank, Land Application Unit, Landfill, Waste Pile, Soil
	Vadose Zone	Porous Media, Fractured Media
	Aquifer	Porous Media, Fractured Media
	Air	
	Watershed	Local Watershed, Regional Watershed
	Surface Water	River, Wetland, Reservoir, Open Ocean, Lake/Impoundment, Coastal, Estuary
	Human Exposure	
	Human Intake	
	Human Risk/Hazard	
	Eco-Biotic Exposure	
	Ecological Intake	
	Ecological Hazard	
	Cultural	
	Economic/Cost	
Data Set	System	Chemical, Life-form, Spacial (GIS)
	Module	Human Exposure, Human Toxicity Benchmark, Ecological Toxicity Benchmark, Meteorologic, Chemical Properties, Physical Properties of Chemicals
Viewers	Text	
	Graphical[(b)]	

(a) Icons will only be provided if at least one model is available for choice. For example, even though Fractured Media is envisioned as a SubGroup category, the Merged System currently does not have fractured subsurface models in the system; therefore, this icon category will only be added when a fractured-medium model is incorporated into the system.

(b) *Viewers* will not be on the icon pallet, but will be accessed for each individual icon through a Mouse *Right Click* on the icon itself; only those applicable viewers will be available.

Table A1.1 Definition of the Data Fields Associated with DICtionary

Field Name	Data Type / [Value]	Definition
Parameter	PString	The name of this parameter
Dimensionality	[1 | 2 | 3 | 4 | 5 | 6]	The number of dimensions for this parameter
Data Type	[“String” | ”Integer”|	The data type of this parameter
Primary Key	[T | F]	Flag specifying if this parameter is a primary key for the retrieval of data from databases
Scalar	[T | F]	Flag specifying if only one value us associated with each set of indices. See Appendix B for a complete explanation.
Minimum	Integer	If ‘Data Type’ equal "String" the minimum inclusive length of the string
	Integer	If ‘Data Type’ equal "Integer" the lowest inclusive integer value
	Float	If ‘Data Type’ equal "Float" the lowest inclusive float value
	String	If ‘Data Type’ equal "Logical" the string to represent false
Maximum	Integer	If ‘Data Type’ equal "String" the maximum inclusive length of the string
	Integer	If ‘Data Type’ equal "Integer" the highest inclusive integer value
	Float	If ‘Data Type’ equal "Float" the highest inclusive float value
	String	If ‘Data Type’ equal "Logical" the string to represent true
Fill Value	Same as Maximum	Value to use when no value is given
Unit of measure	String[32]	The unit of measure for this parameter
Description	String	A short description of the parameter
Stochastic flag	[T | F]	Flag specifying if this parameter can be varied in a stochastic analysis
Preposition	[at | for | from | ...]	Used to precede this parameter’s values when generating a description
Key1 or Label1	PString | String	A parameter name or label that describes the corresponding indice
Key2 or Label2	PString | String	A parameter name or label that describes the corresponding indice
Key3 or Label3	PString | String	A parameter name or label that describes the corresponding indice
Key4 or Label4	PString | String	A parameter name or label that describes the corresponding indice
Key5 or Label5	PString | String	A parameter name or label that describes the corresponding indice
Key6 or Label6	PString | String	A parameter name or label that describes the corresponding indice

Table A1.2 Illustrative Chemical List DICtionary

Variable Count	Dictionary Description	Dictionary Name	Privilege	Version	Updated								
4	ChemList	ChemList	3										
Parameter	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Indexing Parameter(s)	
CAS	Chemical CASIDs	1	string	TRUE	FALSE	1	32			FALSE	for		
Name	Chemical common names	1	string	FALSE	TRUE	1	128			FALSE	for	CAS	
CASDK	Chemical degradation product CASIDs	2	string	TRUE	FALSE	1	32			FALSE	for	CAS	
NameDK	Chemical degradation product common names	2	string	FALSE	TRUE	1	128			FALSE	for	CAS	CASDK

Table A1.3 Illustrative Chemical Toxicity DICtionary

Variable Count	Dictionary Description	Dictionary Name	Privilege										
18	ChemToxicity	ChemToxicity	3										
Parameter	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Index 1	Index 2
InhCPF	Inhalation cancer potency factor	1	Float	FALSE	TRUE			health impact	1/(mg/kg/day)	TRUE		ChemList.CAS	
InhRefDose	Inhalation reference dose	1	Float	FALSE	TRUE			health impact	mg/kg/day	TRUE		ChemList.CAS	
IngCPF	Ingestion cancer potency factor	1	Float	FALSE	TRUE			health impact	1/(mg/kg/day)	TRUE		ChemList.CAS	
IngRefDose	Ingestion reference dose	1	Float	FALSE	TRUE			health impact	mg/kg/day	TRUE		ChemList.CAS	
InhURF	Inhalation unit risk factor	1	Float	FALSE	TRUE			health impact	risk/(mg/m^3)	TRUE		ChemList.CAS	
InhRefConc	Inhalation reference concentration	1	Float	FALSE	TRUE			health impact	mg/m^3	TRUE		ChemList.CAS	
IngURF	Ingestion unit risk factor	1	Float	FALSE	TRUE			health impact	risk/(mg/kg)	TRUE		ChemList.CAS	
IngRefConc	Ingestion reference concentration	1	Float	FALSE	TRUE			health impact	mg/kg	TRUE		ChemList.CAS	
WghtCarc	Weight of evidence for human carcinogenicity	1	Float	FALSE	TRUE			health impact		FALSE		ChemList.CAS	
DKInhCPF	Inhalation cancer potency factor decay products	2	Float	FALSE	TRUE			health impact	1/(mg/kg/day)	TRUE		ChemList.CAS	ChemList.CASDK
DKInhRefDose	Inhalation reference dose decay products	2	Float	FALSE	TRUE			health impact	mg/kg/day	TRUE		ChemList.CAS	ChemList.CASDK
DKIngCPF	Ingestion cancer potency factor decay products	2	Float	FALSE	TRUE			health impact	1/(mg/kg/day)	TRUE		ChemList.CAS	ChemList.CASDK
DKIngRefDose	Ingestion reference dose decay products	2	Float	FALSE	TRUE			health impact	mg/kg/day	TRUE		ChemList.CAS	ChemList.CASDK
DKInhURF	Inhalation unit risk factor decay products	2	Float	FALSE	TRUE			health impact	risk/(mg/m^3)	TRUE		ChemList.CAS	ChemList.CASDK
DKInhRefConc	Inhalation reference concentration decay products	2	Float	FALSE	TRUE			health impact	mg/m^3	TRUE		ChemList.CAS	ChemList.CASDK
DKIngURF	Ingestion unit risk factor decay products	2	Float	FALSE	TRUE			health impact	risk/(mg/kg)	TRUE		ChemList.CAS	ChemList.CASDK
DKIngRefConc	Ingestion reference concentration decay products	2	Float	FALSE	TRUE			health impact	mg/kg	TRUE		ChemList.CAS	ChemList.CASDK
DKWghtCarc	Weight of evidence for human carcinogenicity decay products	2	Float	FALSE	TRUE			health impact		FALSE		ChemList.CAS	ChemList.CASDK

Table A1.4 Illustrative Start-Up DIC

Variable Count	Dictionary Description	Dictionary Name		Privilege											
38	Start Up Settings	StartUp		0											
Parameter	Description	Dimension	Primary Key	DataType	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Index 1	Index 2	Index 3	Index 4
AppPath	Path to frames application	0	FALSE	STRING	TRUE	0	512			FALSE					
ClassIcons	Names of module class icons	2	FALSE	STRING	TRUE	0	512			FALSE		DomainNames	ClassNames		
ClassNames	Names of module classes	2	FALSE	STRING	FALSE	0	32			FALSE		DomainNames			
DataBackColor	Background color of database connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
DataForeColor	Foreground color of database connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
DataVisible	Database connection visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
Dictionaries	Path\filename of included dictionaries	1	FALSE	STRING	FALSE	0	512			FALSE					
DomainIcons	Names of the domain icons	1	FALSE	STRING	TRUE	0	512			FALSE		DomainNames			
DomainNames	Names of the domains	1	FALSE	STRING	FALSE	0	32			FALSE					
FontBold	Font Bold	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
FontColor	Font Color	0	FALSE	INTEGER	TRUE	0	0			FALSE					
FontItalic	Font Italic	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
FontName	Font Name	0	FALSE	STRING	TRUE	0	512			FALSE					
FontSize	Font Size	0	FALSE	FLOAT	TRUE	8	24			FALSE					
GroupIcons	Names of module group icons	3	FALSE	STRING	TRUE	0	512			FALSE		DomainNames	ClassNames	GroupNames	
GroupModules	Module name	4	FALSE	STRING	FALSE	0	512			FALSE		DomainNames	ClassNames	GroupNames	GroupModules
GroupNames	Names of module groups	3	FALSE	STRING	FALSE	0	32			FALSE		DomainNames	ClassNames		
LogoFile	Path and file name to logo image	0	FALSE	STRING	TRUE	0	512			FALSE					
LogoVisible	Logo image visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
ModBackColor	Background color of model connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
ModForeColor	Foreground color of model connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
ModIdVisible	Module Id visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
Modules	Path\filename of included modules	1	FALSE	STRING	FALSE	0	512			FALSE					
ModVisible	Model connection visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
NoticeVisible	Notice visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
RecentFiles	List of recent simulations	1	FALSE	STRING	FALSE	0	512			FALSE					
SubGrpIcons	Names of module sub-group icon	4	FALSE	STRING	TRUE	0	512			FALSE		DomainNames	ClassNames	GroupNames	SubGrpNames
SubGrpModules	Module description file path	5	FALSE	STRING	FALSE	0	512			FALSE		DomainNames	ClassNames	GroupNames	SubGrpNames
SubGrpNames	Names of module sub-groups	4	FALSE	STRING	FALSE	0	32			FALSE		DomainNames	ClassNames	GroupNames	
SysBackColor	Background color of system connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
SysForeColor	Foreground color of system connection	0	FALSE	INTEGER	TRUE	0	0			FALSE					
SysVisible	System connection visible flag	0	FALSE	LOGICAL	TRUE	0	0			FALSE					
WindowHeight	Height of the window	0	FALSE	INTEGER	TRUE	0	0			FALSE					
WindowPosX	X Screen position of window	0	FALSE	INTEGER	TRUE	0	0			FALSE					
WindowPosY	Y Screen position of window	0	FALSE	INTEGER	TRUE	0	0			FALSE					
WindowWidth	Width of the window	0	FALSE	INTEGER	TRUE	0	0			FALSE					
WorkBackColor	Background color of workspace	0	FALSE	INTEGER	TRUE	0	0			FALSE					
WorkForeColor	Foreground color of workspace	0	FALSE	INTEGER	TRUE	0	0			FALSE					

Table A1.5 Illustrative Simulation DIC

Variable Count	Dictionary Description	Dictionary Name	Privilege											
21	Simulation Script Definition	Simulation	1											
Parameter	Description	Dimension	DataType	Primary Key	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Index 1	Index 2	Index 3
ConDicName	Consumer dictionary name	3	STRING	FALSE	FALSE	1	32			FALSE		ModID	ConModID	
ConModID	Module's consumer module ID list	2	STRING	FALSE	FALSE	1	32			FALSE		ModID		
ConSetName	Consumer data set name	3	STRING	FALSE	TRUE	1	32			FALSE		ModID	ConModID	ConDicName
LockConnections	Lock Connections	0	LOGICAL	FALSE	TRUE	0	0			FALSE				
LockModules	Lock Modules	0	LOGICAL	FALSE	TRUE	0	0			FALSE				
LockPassword	Lock Password	0	STRING	FALSE	TRUE	0	32			FALSE				
ModClass	Module class name	1	STRING	FALSE	TRUE	1	32			FALSE		ModID		
ModGroup	Module group name	1	STRING	FALSE	TRUE	0	32			FALSE		ModID		
ModIcon	Module Icon	1	STRING	FALSE	TRUE	0	512			FALSE		ModID		
ModID	Module ID	1	STRING	FALSE	FALSE	0	32			FALSE				
ModLabel	Module user label	1	STRING	FALSE	TRUE	1	32			FALSE		ModID		
ModName	Module name	1	STRING	FALSE	TRUE	0	32			FALSE		ModID		
ModNote	Module user note	1	STRING	FALSE	TRUE	1	1024			FALSE		ModID		
ModPosX	X screen coordinate for module	1	INTEGER	FALSE	TRUE	0	0			FALSE		ModID		
ModPosY	Y screen coordinate for module	1	INTEGER	FALSE	TRUE	0	0			FALSE		ModID		
ModState	Module state	1	INTEGER	FALSE	TRUE	0	3			FALSE		ModID		
ModSubGroup	Module subgroup name	1	STRING	FALSE	TRUE	0	32			FALSE		ModID		
ProDicName	Producer dictionary name	3	STRING	FALSE	FALSE	1	32			FALSE		ModID	ProModID	
ProModID	Module's producer module ID list	2	STRING	FALSE	FALSE	1	32			FALSE		ModID		
ProSetName	Producer data set name	3	STRING	FALSE	TRUE	1	32			FALSE		ModID	ProModID	ProDicName
SDENote	Simulation comment	0	STRING	FALSE	TRUE	0	1024			FALSE				

Table A1.6 Illustrative Module DEScription DIC

Variable Count	Dictionary Description	Dictionary Name		Privilege								
29	Module Properties	Module		0								
Parameter	Description	Dimension	Primary Key	DataType	Scalar	Min	Max	Measure	Units	Stochastic	Preposition	Index 1
Class	Module class type	0	FALSE	STRING	TRUE	0	8			FALSE		
ConSchemeDic	Consumed dictionary names	2	FALSE	STRING	FALSE	1	4			FALSE		Scheme
Description	Module description lines	1	FALSE	STRING	FALSE	0	1024			FALSE		
Dictionary	Id(name) and path of input dictionary	0	FALSE	STRING	TRUE	0	512			FALSE		
Icon	Name and path of display icon	0	FALSE	STRING	TRUE	0	512			FALSE		
Login	Login for model server	0	FALSE	STRING	TRUE	0	32			FALSE		
ModelCmdLine	Model command line switches	0	FALSE	STRING	TRUE	0	64			FALSE		
ModelExe	Name and path of Model executable	0	FALSE	STRING	TRUE	0	512			FALSE		
ModelURL	Remote model server URL	0	FALSE	STRING	TRUE	0	512			FALSE		
Name	Module name	0	FALSE	STRING	TRUE	0	512			FALSE		
Password	Password for model server	0	FALSE	STRING	TRUE	0	32			FALSE		
POCAddress1	Point of contact first address	0	FALSE	STRING	TRUE	0	64			FALSE		
POCAddress2	Point of contact second address	0	FALSE	STRING	TRUE	0	64			FALSE		
POCCity	Point of contact city	0	FALSE	STRING	TRUE	0	32			FALSE		
POCCompany	Point of contact company name	0	FALSE	STRING	TRUE	0	64			FALSE		
POCCountry	Point of contact country	0	FALSE	STRING	TRUE	0	32			FALSE		
POCEmail	Point of contact email address	0	FALSE	STRING	TRUE	0	64			FALSE		
POCFax	Point of contact fax telephone number	0	FALSE	STRING	TRUE	0	16			FALSE		
POCPerson	Point of contact person	0	FALSE	STRING	TRUE	0	64			FALSE		
POCPhone	Point of contact telephone number	0	FALSE	STRING	TRUE	0	16			FALSE		
POCState	Point of contact state	0	FALSE	STRING	TRUE	0	16			FALSE		
POCUrl	Point of contact web address	0	FALSE	STRING	TRUE	0	512			FALSE		
POCZip	Point of contact zip code	0	FALSE	STRING	TRUE	0	16			FALSE		
ProSchemeDic	Produced dictionary names	2	FALSE	STRING	FALSE	1	4			FALSE		Scheme
Reference	Module reference lines	1	FALSE	STRING	FALSE	1	1024			FALSE		
Scheme	The name of a connection scheme	1	FALSE	STRING	FALSE	1	32			FALSE		
UICmdLine	UI command line switches	0	FALSE	STRING	TRUE	0	64			FALSE		
UIExe	Name and path of UI executable	0	FALSE	STRING	TRUE	0	512			FALSE		
Version	Module version description	0	FALSE	STRING	TRUE	0	32			FALSE		