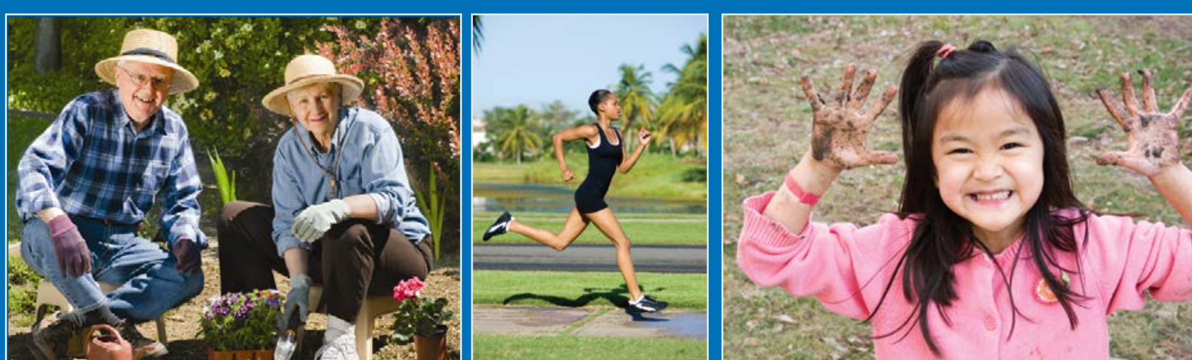
United States Environmental Protection Agency

Exposure Assessment (EXA)
Course Series

Assessing Uncertainty and Variability in the Context of Exposure Assessment

Reading Packet

EXA 407



EPA's Risk Assessment Training and Experience (RATE) Program

EXA 407: Assessing Uncertainty and Variability in the Context of Exposure Assessment

READING PACKET

Exposure Assessment (EXA) Course Series

EPA's Risk Assessment Training and Experience Program

EXA 407: Assessing Uncertainty and Variability in the Context of Exposure Assessment

The purpose of this module is to teach students how to assess uncertainty and variability in the context of exposure assessment. The differences in the concepts with regard to exposure will be stressed. For example, variability pertains to aspects of the assessment which are judged as being known with some "certainty," but which are also known to "vary," such as body weight. On the other hand, uncertainty pertains to aspects which may or may not "vary," but for which little (or no) information is available, such as contaminant soil half-lives for fate modeling. Participants will learn about the different types of variability and uncertainty and will explore methods for analyzing, coping with, and reducing uncertainty and variability. Suggestions will also be provided for presenting the results of uncertainty analyses and variation in human exposures.

Table of Contents

List of Figures

1. INTRODUCTION

In previous EXA courses, the concepts of variability and uncertainty were introduced. This module will further describe how variability and uncertainty are important in the context of exposure assessment. Variability and uncertainty are introduced at various stages of an exposure assessment—for example, when characterizing extent of contamination, defining exposure factors and other exposure assumptions, during monitoring/modeling. This course will address the following key questions:

- How are variability and uncertainty defined?
- What are the differences between the two terms?
- What are the different types of uncertainty and variability?
- How can these concepts be addressed within an exposure assessment?

Variability refers to heterogeneity or diversity within a data set. It is an inherent property of all data sets and it cannot be reduced or eliminated. Variability can, however, be characterized or described using more data (U.S. EPA, 2010).

Uncertainty occurs due to a lack of knowledge stemming either from incomplete data or an incomplete understanding of a process. Uncertainty can often be reduced by collecting more and better data (U.S. EPA, 2010). In exposure assessment, just as in other components of the risk assessment process, uncertainty is accounted for by using approximations and making assumptions.

One major difference between variability and uncertainty is that variability in the population can be known but uncertainty cannot. Although variability cannot be reduced or eliminated, it can be characterized. Uncertainty, on the other hand, exists because the information needed to completely characterize the situation is unknown. Properly addressing variability and uncertainty will increase the likelihood that results of an assessment will be realistic (and useful). The adjacent table summarizes key differences between variability and uncertainty.

Variability	Uncertainty
Inherent property of a population (heterogeneity or diversity)	Exists due to lack of knowledge and incomplete data
CANNOT be reduced or eliminated	**CAN** be reduced or eliminated with more or better data
Can be better characterized but not eliminated with more data	Unknown and cannot be completely characterized, but can be accounted for by using approximations and making assumptions

2. UNDERSTANDING VARIABILITY

2.1 Factors Contributing to Exposure Variability

Exposure variability can be dependent on the variability of source contaminant concentrations and environmental parameters as well as variability in human exposure factors (U.S. EPA, 2011). The following are some examples of exposure factors that might affect exposure variability.

Age

Differences in age affect certain aspects of exposure. For example, young children often exhibit increased hand-to-mouth contact rates, increased dermal contact with the floor and other surfaces through crawling, and higher ventilation rates compared with adults. EPA has developed the *Child-Specific Exposure Factors Handbook* (2008) to address the different factors attributed to children.

Gender

Males and females exhibit variability in their exposure related to their gender as a result of physiological differences, such as weight and body mass index, as well as activity patterns that are correlated with gender.

Behavioral Patterns

Variability in behaviors and activity levels can affect the type of exposures an individual might encounter. If a person spends more time outdoors, he or she will be exposed more frequently to outdoor air pollutants. Avid swimmers would exhibit increased exposures to chlorine and other chemical compounds in the pool water compared with those who do not swim. Daily commuters who take public transportation would be exposed to higher levels of vehicle exhaust while waiting at a train or bus stop versus drivers who are not at these locations. Individuals who frequently fly in airplanes are exposed to higher levels of radiation than the general population due to lack of the protective ozone layer to block out radiation at higher altitudes. These are just a few examples of how behaviors and activities might vary to affect exposure.

Location

Variability in a person's geographic location has an impact on the types of exposure they might encounter on a day-to-day basis. For example, natural deposits of radon and asbestos are scattered throughout the world, and residing in geographic locations containing high concentrations of radon or disturbed asbestos would increase an individual's exposure to these agents. EPA and others have conducted studies to investigate health effects of asbestos exposure to residents living near Libby, MT. As another example, residential areas close to highways are likely to experience higher exposures to particulate matter and vehicle exhaust compared with individuals who live in rural settings.

Socioeconomic Factors

Socioeconomic factors, such as job type, can affect exposure as well. For instance, common use of woks for cooking in Asian restaurants can lead to increased exposure to volatiles from the heating of unrefined cooking oils. Construction workers might be exposed to higher levels of particular matter during construction activities (e.g., earthmoving, demolition, building) conducted at their work site. Dry cleaners would have a higher exposure to certain chemical solvents used in their workplace.

2.2 Types of Variability

The Exposure Factors Handbook refers to four types of variability that can be present in an exposure assessment: spatial, temporal, inter-individual, or intra-individual. These types are not mutually exclusive, nor are they strict definitions, but they do provide a way to think about variability. Each of these factors is further described below.

Type of Variability	Description	Examples
Spatial variability	• Variability across locations • Can occur at a macroscale (regional) or microscale (local) level	• Geographic differences in environmental concentrations, including local and regional trends in pollutant levels • Outdoor versus indoor air concentrations
Temporal variability	• Variation over time • Can occur on a long-term or short-term time scale	• Seasonal fluctuations in weather and amount of time per week a person spends outdoors (long-term) • Differences in an individual's activities at different times of the day; differences in an industrial facility's operations during the week versus on weekends (short-term)
Inter-individual variability	• Variability among individuals • Human variability can be grouped into human characteristics and human behaviors • Can be related to spatial and temporal factors	• Human characteristics such as age, genetic predisposition, body weight • Human behaviors, such as activity patterns, ingestion and inhalation rates, and dietary preferences
Inter-individual variability	• Variation within an individual • Individual may demonstrate variability in physiologic or behavioral characteristics, usually over time	• Changes in body weight, ingestion rates, and daily food intake over time in a single individual • Changes in dietary intake of local food sources that change when a person changes residences

3. ADDRESSING VARIABILITY IN AN EXPOSURE ASSESSMENT

3.1 How Can Variability Be Addressed?

Variability in an exposure assessment can be presented in a number of ways, including through tabular outputs, probability distributions, or qualitative discussion. Tables might include percentiles, ranges of values, or mean values plus a variance measure (e.g., standard deviation, standard error). A probability distribution would be a graphical representation of a central tendency value plus a confidence interval or standard deviation. Variability can also be discussed qualitatively.

NRC's *Science and Judgment in Risk Assessment* (1994) outlines four other techniques for addressing variability in an exposure assessment. These include: ignoring the variability, disaggregating variability, using an average value, or using the maximum or minimum value. Bootstrapping and probabilistic techniques (e.g., Monte Carlo analysis) also can be used to address variability within an exposure assessment. Each of these techniques is described briefly below.

Ignore Variability

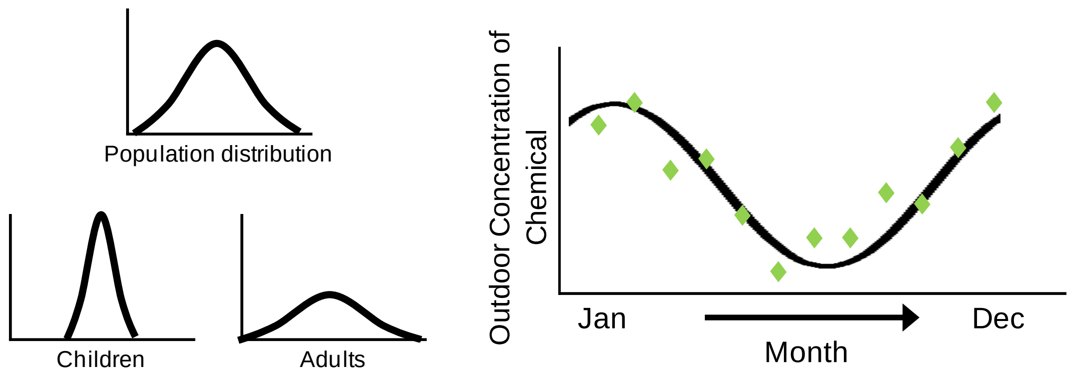
Employing this technique entails taking the simplest approach and not explicitly changing anything in the exposure calculations to account for variability. It is important to note that the concept of ignoring variability (by taking a single value, and ignoring any variability) actually requires the consideration of possible consequences of ignoring it. This approach will be effective only if the variability is small and all estimates are similar to the assumed value. One example would be using EPA's default assumption in calculating exposures that all adults weigh 80 kg. This estimate ignores the variability in adult body weights, but the estimate is correct within 25% for most adults (U.S. EPA, 2011). Therefore, in order to "ignore" variability in adult body weight, there must be some prior knowledge about the variability, followed by a decision not to explicitly incorporate this variability into exposure assessment calculations.

The NRC also notes that this approach is used in combination with other methods (which, it could be argued, is ***not*** ignoring variability).

Disaggregate Variability

Another way to address variability is to disaggregate the parts, or to break up the data in some way so that it can be more easily characterized and quantified. For example, to address differences in inter-individual variability, the general population distribution can be disaggregated into categories such as males and females or children and adults (see Figure 1). The variability within each cohort can be smaller than the variability of the population as a whole. Similar techniques could be used by considering shorter periods of time, smaller regions, and microenvironments. For temporal variability, discrete time points could be measured (e.g., air monitoring samples taken over 15-minute intervals), rather than presenting a continuous distribution. We can also use mathematical models or equations to disaggregate variability. For example, instead of using an annual average outdoor concentration of a chemical, we could fit a sine wave to the data to represent the seasonal variability, as shown in Figure 1.

Figure 1. Disaggregating Variability in a Population by Gender and Time



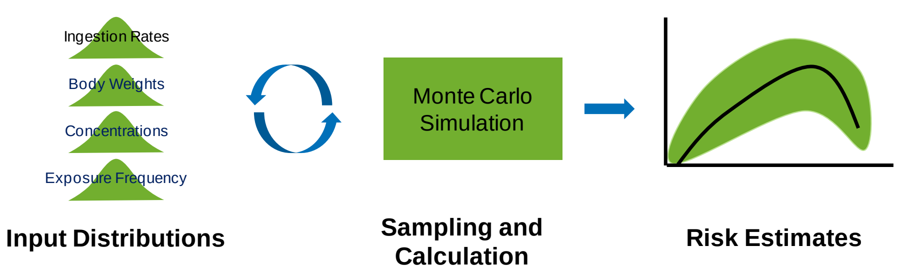
Use Minimum/Maximum or Average Values

The third approach recommended by NRC (1994) is to use the average value of the distribution and use the minimum or maximum (or values approaching the min or max). As noted above, the use of a single point value to characterize a parameter value effectively for a population requires confidence that the value was estimated reliably and that the assessor has adequately characterized the bounds of the distribution. Using a maximum or minimum value is most useful when the measures needed to account for an individual (or situation) using an extreme value will suffice for the remainder of the distribution (NRC, 1994). Using an upper- or lower-bound value can be used to determine the maximum or minimum exposure to the chemical of interest as a worst- or best-case scenario. However, this technique typically results in over- or under-estimation of risk.

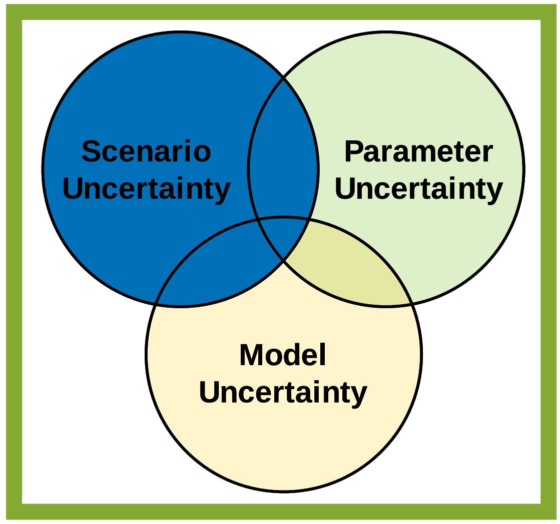
Using an average value is not the same as ignoring the variability, but rather involves the use of a reliably estimated value with well-characterized bounds of the distribution. Use of an average value can be beneficial by "evening out" the parameter's value over the long run (NRC, 1994). However, an average value would not be useful if the variability is dichotomous, where an average value is not representative or, in some cases, does not actually exist.

Probabilistic or Bootstrapping Techniques

A final approach for managing variability in an exposure assessment is to use probabilistic or bootstrapping techniques as illustrated in the graphic below. Probabilistic assessments characterize the variability in risk estimates by repeated sampling of the probability distributions of variables. Then, these results are used to calculate a distribution of risk. Bootstrapping can be used to estimate confidence intervals around specific exposure parameters by resampling from empirical distributions. This is useful when there is a lack of specific knowledge regarding the distribution for a parameter.



4. UNDERSTANDING UNCERTAINTY IN AN EXPOSURE ASSESSMENT



Uncertainty arises in an exposure assessment due to incomplete knowledge of the data within the assessment. The three main types of uncertainty described in EPA's *Exposure Factor Handbook* (2011) are:

- Scenario uncertainty
- Parameter uncertainty
- Model uncertainty

Each of these types of uncertainty is described below. It helps to understand the type of uncertainty in order to reduce or eliminate its effects. Specifically, identification of the sources of uncertainty in an exposure assessment is the first step toward determining the necessary steps to reduce or ideally eliminate uncertainty. It should be noted that classification of uncertainty into these three categories is not as strict as it may seem. In practice, these uncertainties may arise in overlapping areas.

Scenario Uncertainty

Scenario uncertainty is defined as the lack of data regarding exposures that affects the characterization of the exposure scenario. It is uncertainty that is present because an assessor is not able to fully characterize the exposure scenario being evaluated. Sources of scenario uncertainty can usually be attributed to incomplete descriptions of key information, such as the physical and chemical properties and sources of the chemical of concern; the population of concern, including activity pattern data; spatial and temporal information (IPCS, 2008; U.S. EPA, 1992).

Sources of scenario uncertainty can include the following (U.S. EPA, 1992):

- **Descriptive errors:** Errors in the basic information about the exposure pathway, scenario, or population. Examples include misidentifying chemical properties or population cohorts.
- **Aggregation errors:** Inaccurate grouping or lumping of information to the extent that the assessor overlooks important differences within an exposed population or contaminated area. Examples include grouping adolescents with infants on a study of exposures due to crawling behaviors or grouping air quality data from an urban area with a rural area.
- **Errors in professional judgment:** Incorrect selection of a variable that requires expert knowledge. For example, if the exposure scenario is not accurately defined, we might not be able to accurately identify the population of concern or the relevant exposure routes and pathways, or even the chemical of concern. This clearly overlaps with scenario uncertainty. An exposure assessor must also identify the appropriate models to conduct the exposure assessment. This could include environmental fate and transport models or human exposure models. In terms of fate and transport modeling, errors in professional judgment might be easier to identify. An assessor might have to select a value for a parameter based on little or no site-specific data.
- **Incomplete analysis:** Lack of complete consideration of all relevant variables that may affect an exposure assessment. An example is failure to identify an important lifestage in an exposure

assessment. Although this type of uncertainty is hard to quantify, an exposure assessor should always include a rationale for excluding known potential exposure scenarios and identify and discuss the estimated uncertainty associated with excluding them. In addition, the assessor should explain whether the decision to exclude exposure scenarios was based on data, analogs (e.g., using results from an animal study to predict human effects), or professional judgment. If the uncertainty is high, the assessor should consider performing a "what if" analysis.

Parameter Uncertainty

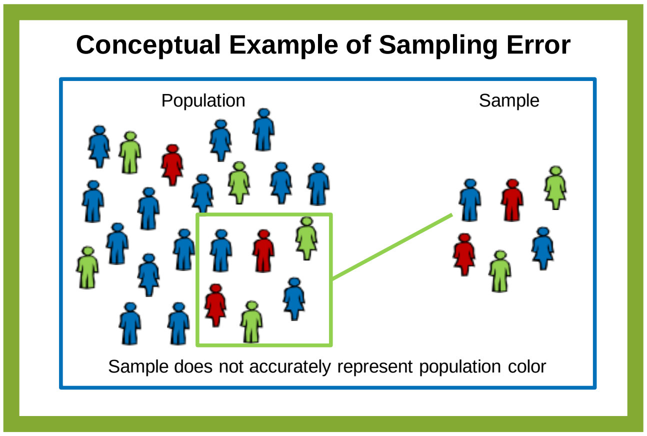
Parameter uncertainty refers to uncertainty in the parameter estimates used in the exposure assessment such as inhalation rates. Values for biological parameters in human exposure assessments are often derived from EPA's *Exposure Factors Handbook* (2011). Because the values used in our exposure scenario or model will directly affect the exposure estimate, it is important to try to identify the potential sources of parameter uncertainty. Uncertainty can result from small sample sizes, imprecise measurements, samples that are not representative, or data from a study that is poorly designed. In EPA's Exposure Assessment Guidelines, parameter uncertainty is attributed to four sources: measurement errors, sampling errors, variability, and uncertainty surrounding the type of data included in your assessment (U.S. EPA, 1992).

Measurement errors are mistakes associated with anything that is measured, including an exposure concentration itself. These errors can be random or systematic.

- **Random errors** result from imprecision in the measurement process. For example, there could be measurement error associated with a questionnaire on use of a specific consumer product. Measurement error would result if use was under- or over-reported in the questionnaire. Random measurement errors can be compounded by variability. Using the same example, the variability in the use of a consumer product can be compounded by random error introduced by use of the questionnaire.
- **Systematic error** is a bias or tendency away from the true value. The average of the measurements of an exposure parameter can differ from its true value. We call the difference between the average of the measurements and its true value bias. Bias may result from incorrect calibration of the measurement tool or from systematic over- or under-reporting in questionnaires. Failures in measurement techniques; examples include imprecise air monitoring samplers (resulting in random error) or failure to properly tare or deduct the weight of an object's receptacle prior to weighing the object (resulting in systematic error).

Sampling errors are errors in obtaining a representative sample of a population. The purpose of sampling is to make an inference about the whole; therefore, it is very important that the subset be representative of the whole. A small, random, and representative sample might be extrapolated to represent a large population, and in this case, the statistical methods used to make inferences about the mean might result in large confidence intervals on the results (IPCS, 2008; U.S. EPA, 1992).

In determining the representativeness of the subset, we have to consider the reason why the data on the subset were generated. If the purpose of the study is not consistent with the purpose of the assessment at hand, it is more likely that sampling errors might be introduced into our assessment. In the conceptual example shown



Conceptual Example of Sampling Error

in the adjacent box, a subset of the population has been sampled to determine the typical color. Unfortunately, blue, which is the most common color in the whole population, is underrepresented in the sample.

Variability errors result from an inability to characterize the true variability in a population. As discussed previously, there are four basic types of variability—temporal, spatial, intra-, and inter-individual variability—and errors can be associated with each of these.

Data type errors arise when surrogate or generic data are used in place of actual data of interest. Data type uncertainty is a lack of knowledge about whether the data used in an assessment are appropriate—that is, are they the correct "type." Evaluating representativeness is important.

As an example, we could use fish consumption data from the *Exposure Factors Handbook* for recreational fishers to characterize the fish consumption behavior in another population that is not included in the Handbook, if we think they are similar populations. In this example, the types and amounts of fish consumed by the recreational population might not be comparable to the types and amounts of fish consumed by the other population. This introduces data type uncertainty.

In some cases, an assessor might call on an expert to apply his professional judgment to select appropriate surrogate data. In this case, it is still possible to introduce uncertainty if the expert is biased, or if the expert is not as good as expected. One way to get around this is expert elicitation. This involves obtaining input and advice from multiple experts using methods designed to avoid bias and maximize accuracy. Defaults can also be used when scenario-specific data are absent. This approach is often used in screening assessments. The uncertainty surrounding these values depends on the quality of the data set used to derive the defaults and their applicability to the situation of interest.

Model Uncertainty

Model uncertainty results from gaps in scientific knowledge required to make predictions. As noted in EXA 405 on models and monitoring, exposure models and fate and transport models use mathematical relationships, ranging from simple static equations to complex, dynamic algorithms, to describe the relationship between input parameters and responses to changes in these inputs. The use of models in an exposure assessment introduces additional uncertainties. Primary sources of model uncertainty include relationship errors, modeling errors, and selection of an incorrect model (IPCS, 2008; U.S. EPA, 1992).

- **Relationship errors** occur when incorrect conclusions are drawn from correlations. For example, an assessor might incorrectly infer correlations between chemical structure and biological activity.
- **Modeling errors** are the failure to consider exposure parameters in an exposure scenario. For example, a failure to account for water consumed in food preparations and as drinking water in a dietary intake model would be a modeling error.
- **Selection of an incorrect model** can introduce uncertainty given a lack of consideration to boundary conditions, dependencies, assumptions, level of detail, extrapolation, implementation, or technical aspects.
- **Parameter uncertainty** is a lack of certainty in the input parameters included in the model, which increases overall uncertainty in the model. For example, uncertainty in partition coefficient parameters in a physiologically based pharmacokinetic (PBPK) model.

5. ADDRESSING UNCERTAINTY IN AN EXPOSURE ASSESSMENT

5.1 Why Address Uncertainty?

EPA policy requires clarity, transparency, reasonableness, and consistency in exposure assessment. Addressing uncertainty in our exposure assessment helps us to fulfill these requirements. EPA's *Exposure Assessment Guidelines* (1992) outlines seven benefits of uncertainty analysis in exposure assessment:

1.) Demonstrates understanding and confidence in the exposure estimate

2.) Allows for the combination of uncertainties from different sources and levels of data quality

3.) Provides context for evaluating the results of the assessment

4.) Improves quality of the best estimate by identifying and exploring areas of uncertainty

5.) Informs decision makers about the reliability of results and allows for the evaluation of resource allocation to acquire more data in an effort to reduce uncertainty

6.) Guides the process of refining the exposure estimate

7.) Increases transparency by showing some of the limitations of the analysis

5.2 How Can Uncertainty Be Addressed?

Uncertainties in exposure or modeling assumptions and parameters can be addressed in a qualitative discussion or by using quantitative methods (IPCS, 2008).

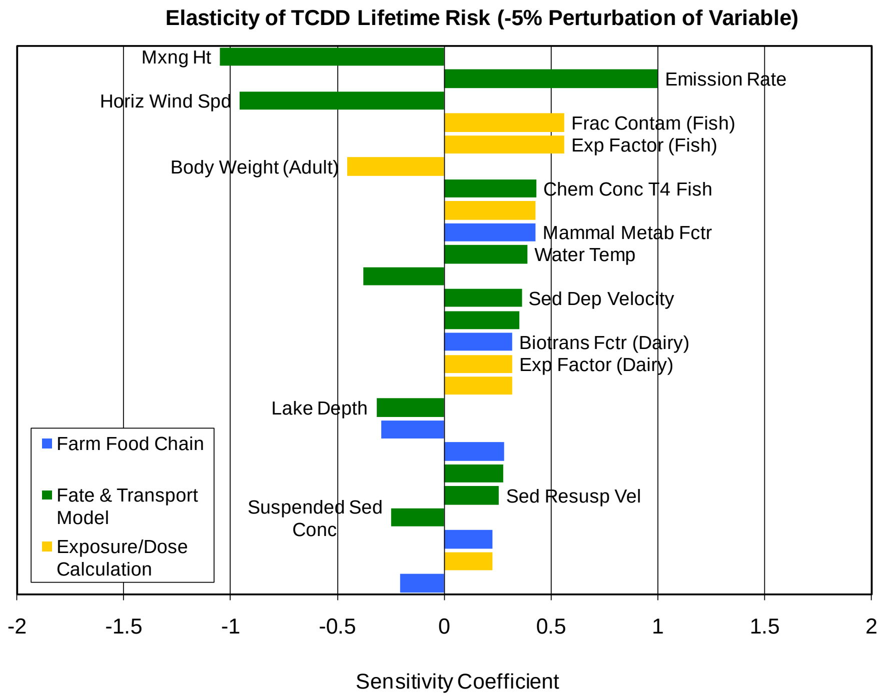
Qualitative discussion of uncertainties might address the following questions:

- What is the level of uncertainty in influential parameters?
- What data gaps exist?
- Were any subjective decisions made?
- Are there instances where professional judgment was used?
- What are the impacts of the choices made?

Quantitative uncertainty analyses can use both probabilistic and non-probabilistic methods. Our quantitative analysis can assess both uncertainty and the impact of variability in the data set. To do this we can use non-probabilistic approaches as well as probabilistic ones like those we have already discussed.

Sensitivity analysis allows the assessor to determine what variable may have the most impact on the exposure assessment while holding all other variables constant. An example of the kind of output one might obtain from a sensitivity analysis is presented in Figure 2.

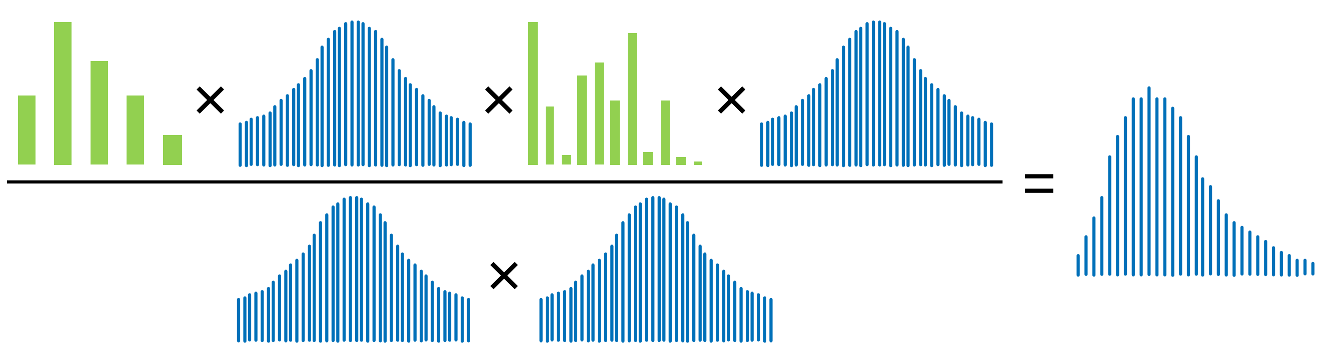
Figure 2. Example Output of a Sensitivity Analysis of a Risk Modeling Application



Source: Report to the EPA's Science Advisory Board on Risk and Technology Review (RTR) risk assessment methodology (U.S. EPA, 2009)

Probabilistic approaches such as Monte Carlo analysis allow for probability density functions to be assigned to each parameter, and values from the distribution are selected randomly and inserted into an exposure equation. This process is repeated many times and results in a distribution of values that reflects the overall uncertainty in the inputs. A conceptual illustration of this process is presented in Figure 3.

Figure 3. Graphical Representation of Monte Carlo Analysis



There are strengths and complications to the Monte Carlo technique. The major strength is that the approach is generally applicable. There are no restrictions on the form of the input distribution and the computations are relatively straightforward. However, there are some drawbacks and precautions related using Monte Carlo methods.

- First, it is critical that we have confidence in the distributions of values used for each parameter.
- We must know the relationships (i.e., the correlations) between parameters or know which parameters are independent.
- Changing the distribution for one parameter can require that the entire simulation be run again, so it is sometimes difficult to assess the sensitivity of the results to the input distributions.
- In addition, the results of a standard Monte Carlo analysis do not tell the assessor which variables are the most important contributors to uncertainty.

A Monte Carlo analysis provides a classic example of GIGO – garbage in, garbage out. The outputs look "valid," interesting, and powerful, but they will have no bearing on reality if parameter distributions are invalid, correlations between parameters are ignored, and if the model itself is flawed (U.S. EPA, 1997, 1992).

6. CONCLUSIONS

- Variability refers to true heterogeneity or diversity and is an inherent property of a population.
- Uncertainty refers to a lack of knowledge due to incomplete data.
- Variability cannot be reduced, only better characterized by collection of more or better data. Uncertainty can be reduced or even eliminated by collecting more or better data.
- Uncertainty and variability in exposure assessment can be addressed both qualitatively and quantitatively.

7. REFERENCES

IPCS. (International Programme on Chemical Safety). (2008). Uncertainty and data quality in exposure assessment. Geneva: World Health Organization. http://extranet.who.int/iris/handle/123456789/647.

NRC. (National Research Council). (1994). Science and judgment in risk assessment. Washington, DC: National Academy Press.

U.S. EPA. (U.S. Environmental Protection Agency). (1992). Guidelines for exposure assessment. (EPA/600/Z-92/001). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263.

U.S. EPA. (U.S. Environmental Protection Agency). (1997). Guiding principles for Monte Carlo analysis. (EPA/630/R-97/001). Washington, DC. http://www.epa.gov/raf/publications/guiding-monte-carlo-analysis.htm.

U.S. EPA. (U.S. Environmental Protection Agency). (2008). Child-specific exposure factors handbook. (EPA/600/R-06/096F). Washington, DC: U.S. Environmental Protection Agency, National Center for Environmental Assessment. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=199243.

U.S. EPA. (U.S. Environmental Protection Agency). (2009). Risk and technology review (RTR) risk assessment methodologies: For review by the EPA's Science Advisory Board, case studies, MACT I petroleum refining sources, Portland cement manufacturing. (EPA-452/R-09-006).

U.S. EPA. (U.S. Environmental Protection Agency). (2010). IRIS site help and tools: Glossary, acronyms and abbreviations Retrieved August 23, 2010, from http://www.epa.gov/ncea/iris/help_gloss.htm

U.S. EPA. (U.S. Environmental Protection Agency). (2011). Exposure factors handbook 2011 edition (final). (EPA/600/R-09/052F). http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=236252.