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An Introductory Guide to Uncertainty Analysis in Environmental and Health Risk Assessment

J. S. Hammonds
F. O. Hoffman
S .M. Bartell

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Prepared by
SENES Oak Ridge, Inc.
Oak Ridge, Tennessee
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ACRONYMS AND ABBREVIATIONS

DOE	United States Department of Energy
EPA	United States Environmental Protection Agency
HQ	Hazard Quotient
LHS	Latin Hypercube Sampling
MMES	Martin Marietta Energy Systems, Inc.
RfD	Reference Dose
SRS	Simple Random Sampling

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EXECUTIVE SUMMARY

This report presents guidelines for evaluating uncertainty in mathematical equations and computer models applied to assess human health and environmental risk. Uncertainty analyses involve the propagation of uncertainty in model parameters and model structure to obtain confidence statements for the estimate of risk and identify the model components of dominant importance. Uncertainty analyses are required when there is no *a priori* knowledge about uncertainty in the risk estimate and when there is a chance that the failure to assess uncertainty may affect the selection of wrong options for risk reduction. Uncertainty analyses are effective when they are conducted in an iterative mode. When the uncertainty in the risk estimate is intolerable for decision-making, additional data are acquired for the dominant model components that contribute most to uncertainty. This process is repeated until the level of residual uncertainty can be tolerated.

In this report, analytical and numerical methods for error propagation are presented along with methods for identifying the most important contributors to uncertainty. Monte Carlo simulation with either Simple Random Sampling (SRS) or Latin Hypercube Sampling (LHS) is proposed as the most robust method for propagating uncertainty through either simple or complex models. A distinction is made between simulating a stochastically varying assessment endpoint (i.e., the distribution of individual risks in an exposed population) and quantifying uncertainty due to lack of knowledge about a fixed but unknown quantity (e.g., a specific individual, the maximally exposed individual, or the mean, median, or 95%-tile of the distribution of exposed individuals).

Emphasis is placed on the need for subjective judgment to quantify uncertainty when relevant data are absent or incomplete. Therefore, the results of an uncertainty analysis will differ among risk assessors because of differences in the interpretation of the current state of knowledge. Despite these differences, the subjective confidence intervals from an uncertainty analysis should produce a reasonably "high" probability of bounding the true risk provided that risk assessors avoid overconfidence in quantifying the level of certainty associated with important model components.

1. INTRODUCTION

When hazardous substances are released into the environment, an evaluation is necessary to determine the possible impact these substances may have on human health and other biota. To address this question, a risk assessment is performed to quantify the potential detriment and evaluate the effectiveness of proposed remediation measures. A baseline risk assessment performed according to currently recommended United States Environmental Protection Agency (EPA) methods (EPA, 1989) produces a single point estimate of risk. Such point estimates fail to address the inherent uncertainty in the estimates of risk. At best, the single values obtained from this method may be considered as upperbound (conservative) estimates of risk to a maximally exposed individual. The chance of underestimating the true risk to an exposed individual is minimized. However, the chance of overstating the risk may be large.

A less biased approach to risk assessment uses uncertainty analysis to estimate the degree of confidence that can be placed in the risk estimate. A discussion of uncertainty is critical to the full characterization of risk to more fully evaluate the implications and limitations of the risk assessment (EPA, 1992). To date, an uncertainty analysis, if performed at all, is usually restricted to a qualitative statement of confidence in the result; for instance, uncertainty in the point estimate that is less than one order of magnitude (a factor of 10) is considered "low," uncertainty in the point estimate greater than one order of magnitude but less than two orders of magnitude (a factor of 100) is considered "moderate," and uncertainty that exceeds two orders of magnitude is considered "high" (EPA, 1989). Unfortunately, these qualitative statements of uncertainty are difficult to assess, let alone defend, particularly when the assessment involves potential exposure to several contaminants transferred over a number of different pathways (Hoffman and Hammonds, 1994).

A more defensible approach is to perform a quantitative analysis of uncertainty using either analytical or numerical techniques to propagate uncertainty in the components of the risk assessment equations into an assessment of uncertainty in the overall result. If the risk assessment process can be modified to permit several iterations, then uncertainty analysis can be a valuable tool for identifying and ranking the contaminants and exposure pathways of concern. Such rankings can be used to guide the acquisition of additional data to reduce uncertainty in risk estimates. An uncertainty analysis is additionally useful to weigh the benefits against the costs of alternative remedial actions.

The primary objective of this report is to address the issue of uncertainty in quantitative risk assessments and present methods that can be used to perform a quantitative uncertainty analysis on risk estimates. This report is intended as a supplement to EPA's Exposure Assessment Guidance (1992) and provides the reader with an introduction to the concepts and approaches of quantitative uncertainty analysis. In addition, the manuscript suggests criteria for deciding when a quantitative analysis of uncertainty is necessary and when such analyses may not be necessary.

2. CRITERIA FOR PERFORMING A QUANTITATIVE UNCERTAINTY ANALYSIS

For most risk assessment analysts, a primary question is: Is it necessary to perform an uncertainty analysis? This section provides guidelines to identify 1) situations that might not warrant a formal quantitative

uncertainty analysis and 2) those situations that most likely would require such an analysis to evaluate the amount of confidence to be placed in the risk estimate.

Some circumstances exist in which it may not be necessary to undertake a formal quantitative assessment of uncertainty; the criteria delineating the need for a formal assessment should be identified at the outset of planning the risk assessment. A suggested set of criteria is given in the following list.

1. If screening calculations indicate that the risk is clearly below regulatory or risk levels of concern, a quantitative uncertainty analysis may not be necessary. Detailed analyses will likely demonstrate that the true risk is even less than initially estimated because screening calculations are designed to provide a risk estimate that is highly unlikely to underestimate the true risk.

2. If the cost of remediation required to reduce exposure or risk is low, a quantitative uncertainty analysis might not be warranted. For small contaminated sites with inexpensive remediation possibilities, it is more sensible to clean up the property than to undertake a detailed analysis of risk and its attendant uncertainty. Quantitative uncertainty analyses, however, might still be useful in evaluating the amount of contamination that will remain after remediation.

3. If the characterization of the nature and extent of the amount of contamination in a given environmental media at a site is inadequate to permit even a bounding estimate (an upper and lower estimate of risk), a quantitative uncertainty analysis cannot be performed. Under these conditions it is not even feasible to perform an exposure or risk assessment, unless the assessment is restricted to a preliminary lower bound screening estimate (a lower bound risk is not likely to overestimate the true risk). In this case, if the available data describing the amount of environmental contamination suggests that exposures and risks will be unacceptable (risks that are above criteria set by regulators), plans for remediation can begin even before the extent of contamination source term is sufficiently characterized. Once the extent of contamination is more fully characterized, quantitative uncertainty analysis would be useful in guiding cost-effective measures for remediation of the contamination.

The following situations describe conditions that should justify quantitative uncertainty analyses as part of the risk assessment process:

1. A quantitative uncertainty analysis should be performed when it becomes necessary to disclose the potential bias associated with risk assessments performed using only single values for model parameters. The combination of point values, some conservative (upper 95% confidence limit) and some typical (average), yields a point estimate of exposure and/or risk that is different from a true but unknown value. The extent of this difference is unknown. For example, in many cases a risk assessor who uses federal or state guidelines to obtain parameter values or who uses computer codes with default assumptions as parameter values will not know the degree of conservatism in the calculation. At most, the assessor may have some prior knowledge that the model combines many conservative assumptions, so the result should be undoubtedly conservative. The combination of point values often yields an estimated risk that is much greater than is reasonable for a given situation. Therefore, it is imperative to disclose uncertainty in all risk assessments unless the cost of remedial action and the consequences of being wrong are low (NAS, 1994)

2. A quantitative uncertainty analysis should be performed if initial screening calculations, using conservatively biased point estimates, indicate the need for further investigation before taking action.

Conservatively biased screening calculations made with approaches similar to those recommended in NCRP Commentary No. 3 (1989) can be used to designate pathways and/or contaminants as definitely low priority when the result is clearly below a regulatory standard or concern. Pathways or contaminants classified as definitely low priority could be excluded from further analysis; however, the remaining pathways and contaminants should be studied in depth using a quantitative uncertainty analysis (Hoffman et al., 1993).

3. A quantitative uncertainty analysis should be performed when it is necessary to set priorities among sites, contaminants, exposure pathways, and toxicity or risk factors requiring further research before making final decisions. With the increased availability of inexpensive, powerful computers, sensitivity analyses can be easily performed to investigate which input variables contribute most to the overall uncertainty in the risk estimate. The input parameters with the highest priority for further investigation would be those that cause the greatest effect on the overall uncertainty of the risk. More knowledge about these parameters should effectively lower the uncertainty in the calculated risk estimate.

4. A quantitative uncertainty analysis should be performed when the consequences of an erroneous risk estimate are high. In this case, it may be useful to delay the decision, assign the assessment task to multiple independent groups for independent analyses of risk and uncertainty, and invest in the gathering of critical data needed to reduce the uncertainty in the risk estimate. For example, a quantitative uncertainty analysis should be performed when the cost of regulatory or remedial action is high and the risk of exposure is marginal. At some Superfund sites and corresponding military or weapons facilities, the anticipated costs of cleanup may exceed $100 million per facility. Such large costs require that the estimated risks, which are truly high and deserving strong interventions, be distinguished from those that have been exaggerated due to the application of sets of compounded assumptions with a conservative bias.

3. METHODS FOR UNCERTAINTY ANALYSIS

This section describes methods and examples of using error propagation techniques to quantify uncertainty in environmental and human health risk assessment. The methods involve both analytical equations for simple models and numerical approaches involving the use of a computer for more complex models. Among the numerical approaches to uncertainty analyses, Monte Carlo methods are given the most attention in this report.

For situations requiring a quantitative uncertainty analysis, an iterative approach should be used. The first step of this approach would be the use of simple bounding (or screening) calculations to determine whether further investigation is warranted before making a decision (Hoffman et al., 1993). Bounding calculations are intentionally biased to produce very high confidence that the true value is not above the calculated value or that the true value is not below the calculated value. If further studies are needed, a quantitative uncertainty analysis organized at the level of a secondary screening calculation using conservative estimates of uncertainties for each variable can be employed to indicate where studies should be focused. As new information is obtained, the analysis is repeated, each time identifying information needs until a decision is possible or until time or resource limitations force a decision. Within this iterative approach, the cost of risk reduction actions must be considered at each stage along with the alternative risks of these actions.

Please note that the examples presented in this manuscript are hypothetical. The subjective probability distributions presented in these examples are for demonstration purposes only.

3.1 LIMITING THE SCOPE THROUGH SCREENING

When taking into account the various exposure pathways for every hazardous substance found at a contaminated site, a risk assessment can become lengthy and complicated. An uncertainty analysis on every parameter involved in a scenario such as this is impractical because of the numerous pathways and contaminants involved. Therefore, the first step in any risk assessment should be to focus the scope of the problem on the primary contaminants and pathways likely to dominate the overall risk.

To limit the risk assessment problem, the objective(s) of the assessment must be clearly defined. Once the objectives have been defined, a screening procedure can be used to identify the contaminants and exposure pathways warranting a more detailed analysis (Hoffman and Gardner, 1983; Hoffman et al., 1991; NCRP, 1989). In fact, screening can be considered a first step in the approach to uncertainty analysis in that a rough estimate is provided of lower and upperbounds of risk. Upperbound estimates can be obtained from a set of conservative assumptions to produce a result that is not likely to underestimate the risk to a maximally exposed individual. Lower bound estimates can be obtained by removing the conservatism in these assumptions and producing a result that is unlikely to overestimate the risk to a maximally exposed individual. The current EPA baseline risk assessment methods are often appropriate as a conservative upperbound estimate of risk as long as the parameters are selected in a manner such that the actual risk to a maximally exposed individual will not be underestimated. This method is useful for rapidly identifying pathways and contaminants that may be given low priority for further investigation because further attempts to evaluate this situation should only produce lower risk estimates. A lower bound screening calculation, however, is useful for rapidly identifying contaminants that warrant immediate consideration for remedial action. Examples of assumptions used in the general approaches for performing conservative and nonconservative screening are provided in Table 3.1.

A situation where a screening procedure would be useful is as follows: assume that there are approximately 100 contaminants present at a site in four different environmental media, each giving rise to 5 to 10 different exposure pathways. What can be done to guide the assessment to those contaminants and exposure pathways warranting a more detailed investigation including an uncertainty analysis? Before embarking on a formal quantitative uncertainty analysis, the scope of this problem should be narrowed. This is best accomplished by performing screening calculations to aid in identifying pathways and contaminants warranting further investigation. Conservatively-based screening estimates will typically show that all but a few situations are of low priority with respect to potential health risk. Nonconservative screening estimates, however, may indicate that although no situation warrants immediate action, some contaminants may be sufficiently important to justify further investigation because limits of concern are approached.

Table 3.1. Example assumptions used for conservative and nonconservative screening (Hoffman et al., 1991)

Conservative Screening	Non-conservative Screening
Maximum or 95% UCL concentration reported for a defined location	Average of detected values reported for a defined location
Models used to estimate concentrations in various media for which samples were not taken or adequate data does not exist	Only measured concentrations in specific environmental media are considered
Reasonable estimate of maximum diet and occupancy times assumed	Estimates of diet and occupancy times are generally less than those assumed for reasonable maximum
Human receptor exposed for 70 years	Probability of exposure period being less than 70 years considered in estimates of diet and occupancy times
Multiple pathway exposure to the maximally exposed individual considered	Multiple pathway exposure to the maximally exposed individual not considered
Exposure to dredged sediment considered separately from the consumption of water, fish, and irrigated agricultural produce	Dredging of sediment not considered; use of water for irrigation not considered
Calculated exposure should not underestimate actual maximum exposures	Calculated exposure should not overestimate potential maximum exposures
Screening approach most useful for identifying definitely low priority contaminants	Screening approach most useful for identifying definitely and potentially high priority contaminants.

To distinguish between low priority, potentially high priority, and high priority contaminants and pathways, one must establish baseline screening values. These should be chosen based on a distinction between risks that are acceptable versus those that are clearly unacceptable. In most cases, this distinction may be influenced by risks permitted by current regulatory standards. An example of screening values for carcinogens is provided in Fig. 3.1, and a list for noncarcinogens is presented in Fig. 3.2 (Blaylock et al., 1991). Two primary sources that are useful for equations and parameter values to use in screening calculations are NCRP (1989; in press) for metals and radionuclides and Lyman et al. (1982) for organic chemicals.

3.2 MODEL UNCERTAINTY

The term model uncertainty is used to represent lack of confidence that the mathematical model is a "correct" formulation of the assessment problem. Model uncertainty exists if there is a possibility of obtaining an incorrect result even if exact values are available for all of the model parameters. The best method for assessing model uncertainties is through model validation (Hoffman et al., 1984), a process in which the model predictions are compared to numerous independent data sets obtained under conditions similar to those for which the risk assessment is to be performed. Model validation is often limited because of lack of data, limited experimental opportunities, and inadequate financial resources. In many instances, the endpoint of the assessment cannot be confirmed through direct measurement, as is the case with health effects at low doses.

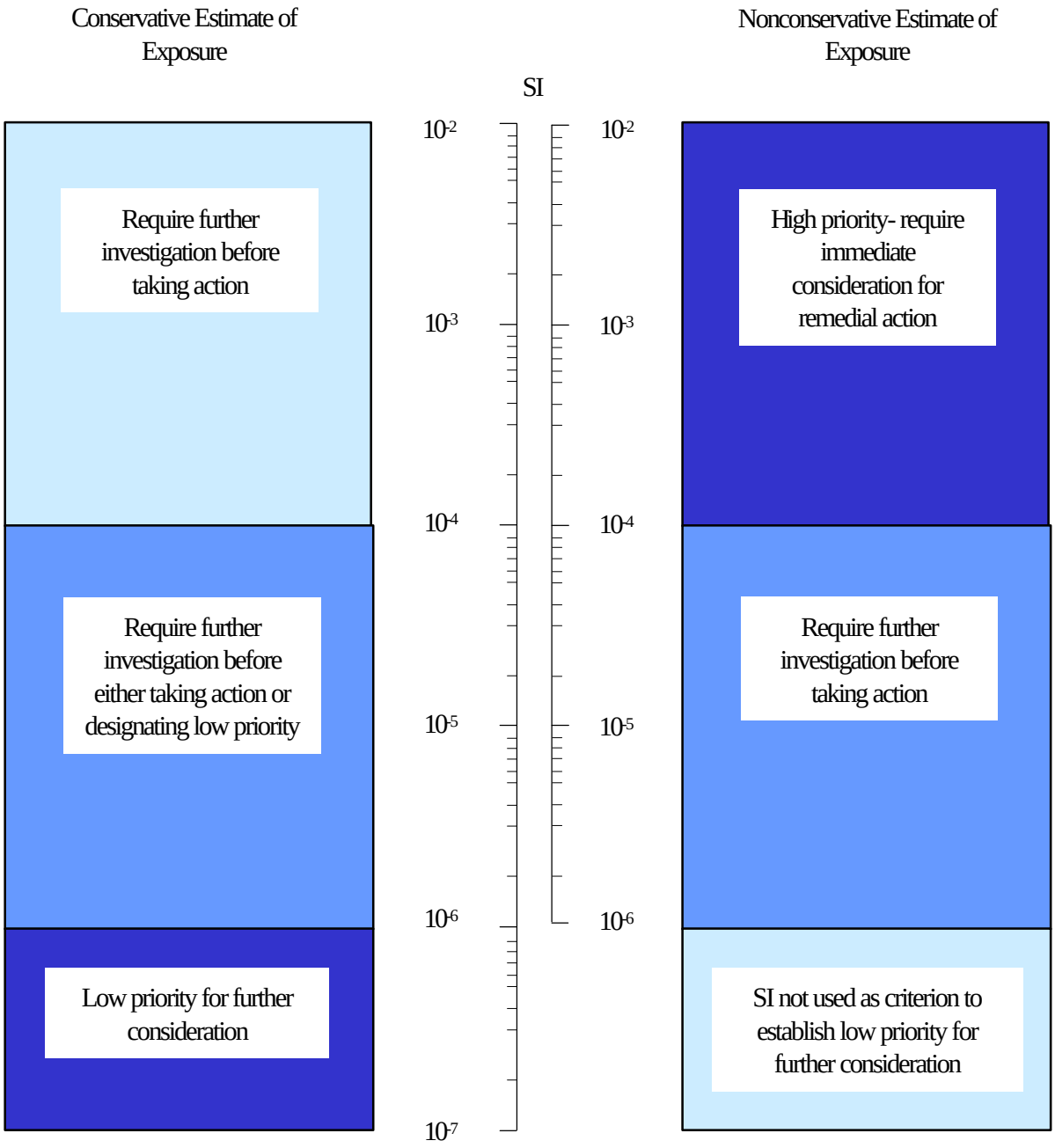
In this report, it is assumed that the uncertainty in the estimate of risk can be calculated from an estimate of uncertainty in each of the parameters used in the risk assessment equations. This approach is sometimes referred to as a "parameter uncertainty analysis" (IAEA, 1989). The technique of parameter uncertainty analysis provides a quantitative way to estimate the uncertainty in the model result assuming the structure of the model is correct. *However, if there is additional uncertainty due to model structure, this uncertainty should be examined either by alternative models or by the addition of parameters to the risk assessment model.* Many risk assessment models are built upon empirical relationships. When dealing with a model that is composed of empirical relationships, it usually can be assumed that the correct values for the model parameters will produce the correct value for the model result, provided that the conditions under which parameter values have been obtained are directly relevant to the conditions of the assessment.

For the examples presented in this report, the bounds of uncertainty for each model parameter are defined so that the unknown, true value lies within these limits. It is assumed that the correct values for the model parameters will produce the correct value for risk; therefore, no correction is made for the possibility of additional uncertainty introduced by using an incorrect model.

3.3 GENERAL APPROACH TO UNCERTAINTY ANALYSIS

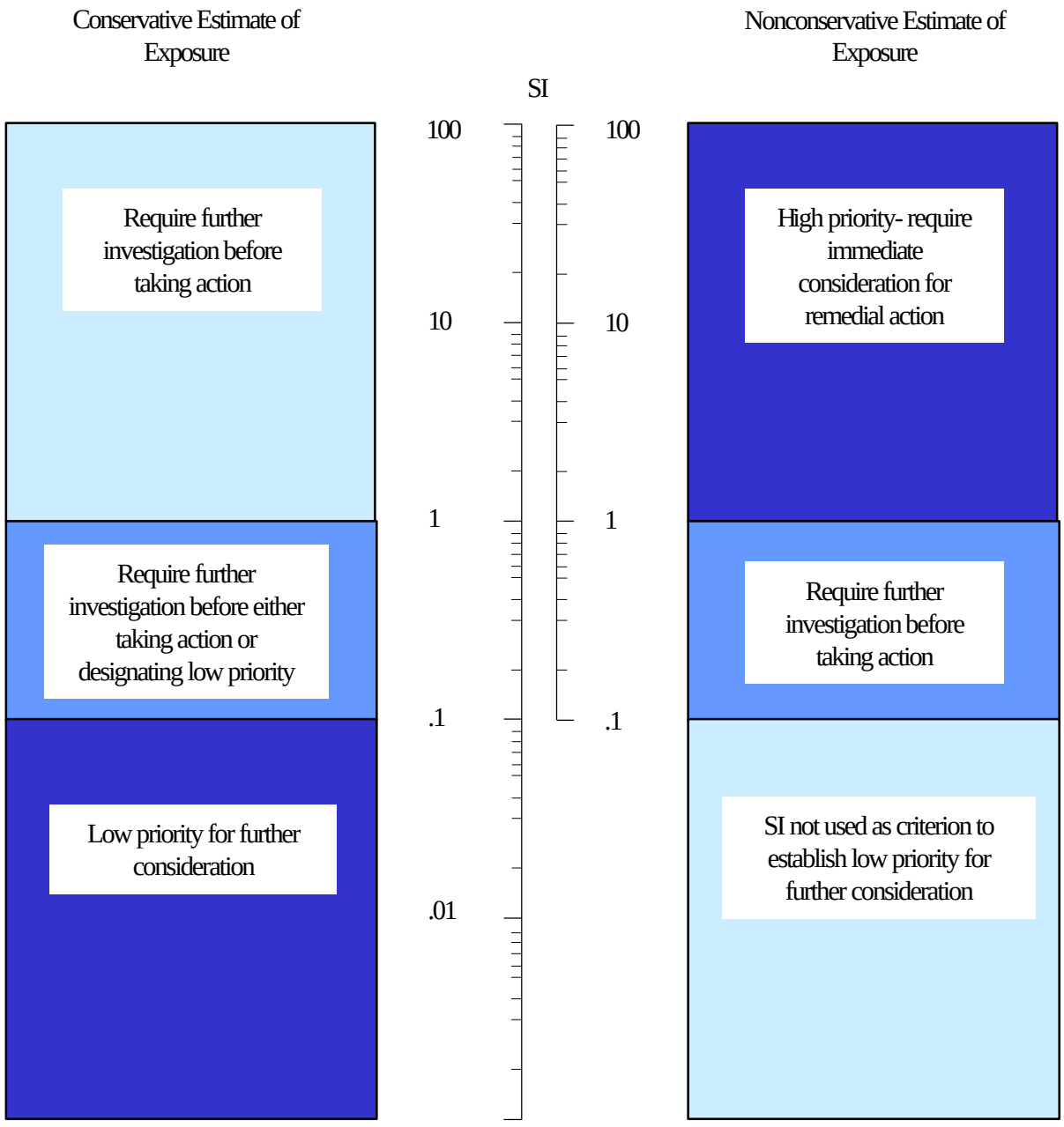
To perform parameter uncertainty analysis, one should use the following steps (IAEA, 1989):

1. Define the assessment endpoint. (For baseline risk assessments at Superfund sites, this is usually a reasonable estimate of the risk to a maximally exposed individual over a defined period of time.)



Screening index (SI) = exposure multiplied by a lifetime cancer slope factor

Fig. 3.1. Criteria for conservative and nonconservative screening of carcinogens (Blaylock et al., 1991)



Screening index (SI) = exposure divided by reference dose factor (RfD)

Fig. 3.2 Criteria for conservative and nonconservative screening of noncarcinogens (Blaylock et al., 1991)

2. List all uncertain parameters (include additional parameters if necessary to represent uncertainty in model structure).

3. Specify maximum range of potential values relevant for unknown parameters with respect to the endpoint of the assessment.

4. Specify a subjective probability distribution for values occurring within this range.

5. Determine and account for correlations among parameters.

6. Using either analytical or numerical procedures, propagate the uncertainty in the model parameters to produce a (subjective) probability distribution of model predictions.

7. Derive quantitative statements of uncertainty in terms of a subjective confidence interval for the unknown value [representing the prediction endpoint (e.g., excess cancer risk or Hazard Index)].

8. Rank the parameters contributing most to uncertainty in the model prediction by performing a sensitivity analysis.

9. Obtain additional data for the most important model parameters and repeat steps 3 through 8.

10. Present and interpret the results of the analysis.

The assessment endpoint will determine the center and spread of the probability distributions used to represent uncertainty in the parameters of the mathematical model used to perform the assessment. For example, if the assessment is targeted at a maximally exposed individual, the distributions obtained for the uncertain model parameters should be representative of individuals who are likely to be those with the highest exposure. These individuals may eat more fish, may drink more water, may live longer in the region, etc. Distributions chosen that are centered on the "average" or "typical" person might not include those who may be considered maximally exposed. In other words, if there is interest in values occurring in the extremes of a distribution, the conditions that bring about these extremes should be modeled explicitly, and the uncertainty analysis should be centered on these extreme conditions.

Steps 3 and 4 are usually accomplished by using professional judgment based on an extensive review of available literature, collected data, and interviews with experts on the parameter of interest. In addition, one can incorporate correlations among the parameters by either specifying a correlation coefficient or changing the model structure to include the additional parameters that determine interdependencies among the original parameters of interest.

After the subjective probability distributions for the model parameters are analyzed, one obtains a subjective probability distribution for the risk, using one of the methods described in the following sections of this chapter. From this qualitative expression, one can formulate a quantitative description of the risk in the form of a subjective CI in which the unknown risk should lie. The term "subjective CI" is used to denote that the probability distribution specified for the uncertain model parameters have been derived using a combination of data and judgment.

3.4 SPECIFYING PROBABILITY DISTRIBUTIONS FOR UNCERTAIN MODEL PARAMETERS

To perform a quantitative uncertainty analysis, probability distributions must be assigned to each of the uncertain parameters. The distributions may result directly from data obtained from a proper experimental design, but usually subjective judgment must be used to reflect the degree of belief that the unknown value for a parameter lies within a specified range. Where data are limited but uncertainty is relatively low (less than a factor of 10), a range may be used to specify a uniform distribution. If there is knowledge about a most likely value or midpoint, in addition to a range, a triangular distribution may be assigned. When the range of uncertainty exceeds a factor of 10, it is often prudent to assume a probability distribution of the logarithms of the parameter values; therefore, when the range of uncertainty is very large, a log-uniform or log-triangular distribution may be more appropriate than the uniform or triangular distribution. The assumption of normal, lognormal, or empirical distributions is usually dependent on the availability of relevant data. Many other distribution types are suitable for Monte Carlo analysis. A few of these other types are the gamma, beta, Poisson, Weibul, and a variety of discrete distributions (Decisioneering, Inc., 1994; Palisade Corporation, 1991).

When there is doubt about the effect of different distributions, then different distributions should be assumed and the effect analyzed. In general, as long as the mean and variance of a distribution are held constant, the exact shape of the distribution of a parameter in a risk assessment equation will have minimal effect on the mean, variance, and, to a general extent, the 90% subjective confidence interval of the model prediction (Gardner, 1988; O'Neill et al., 1981). This is particularly evident when no single parameter dominates the overall uncertainty in the model prediction and if the extent of interdependence among the model parameters is small.

The estimation of likely ranges and statistical distributions for each uncertain parameter requires a high level of expertise. Statistical information required for quantifying the uncertain parameters of interest usually cannot be obtained directly from reference material. Furthermore, published statistical distributions of data for the uncertainty analysis should be scrutinized as these data might not apply to the conditions under consideration. *Under no circumstance should a risk assessor treat an uncertain assumption or parameter as a constant* ***simply*** *because data are unavailable to define a range and distribution*. In the absence of data, it may be necessary to contact experts outside Martin Marietta Energy Systems, Inc. (MMES) and United States Department of Energy (DOE) organizations to obtain the essential data and/or for assistance in deriving uncertainty estimates. Where judgment is used to derive estimates of uncertainty, the assumptions and sources of information used should be documented.

When dealing with several different distributions, it is more efficient (easier and faster) to use numerical methods (e.g., Monte Carlo analysis) to propagate uncertainty through a risk assessment model than to use various analytical methods (algebraic equations). Analytical methods are options, however, when one has similar distributions for all of the parameters and when the risk assessment model consists of sets of fairly simple equations.

3.5 ANALYTICAL METHODS FOR UNCERTAINTY ANALYSIS

For relatively simple equations, a quantitative uncertainty analysis can be performed using analytical methods for statistical error propagation. The analytical approach most frequently used for uncertainty analysis of simple equations is variance propagation (IAEA, 1989; Martz and Waller, 1982; Morgan and

Henrion, 1990).

A simple addition model may best demonstrate an example of variance propagation. For an additive model, the mean value of the result is equal to the sum of the mean values of the model parameters; the variance of the result, assuming statistical independence among the parameters, is equal to the sum of the variances of the parameters (Hoffman and Gardner, 1983; IAEA, 1989).

$$\mu_R = \sum_{i=1}^{p} \mu_i \tag{3.1}$$

$$\sigma_R^2 = \sum_{i=1}^{p} \sigma_i^2 \tag{3.2}$$

where

p = the number of parameters in the model.

In a series of summations of uncertain parameters, the result will tend to conform to a normal distribution even if the shapes of the distributions assigned to the model parameters are other than normal (Central Limit Theorem).

However, the basic form of EPA risk assessment models is a multiplicative chain of parameters for each contaminant and exposure pathway. Multiplicative models can be reduced to additive form by logarithmically transforming the variables. This is shown in Eqs. 3.3 and 3.4.

$$Y = a \times b \times c \tag{3.3}$$

$$\ln(Y) = \ln(a) + \ln(b) + \ln(c) \tag{3.4}$$

Therefore, the distribution of Y will tend to be approximately lognormal even when the parameters a, b, and c are assigned distribution shapes other than lognormal (Hoffman and Gardner, 1983). For multiplications, the median value (or geometric mean) is simply the exponential of the sum of the mean values of the logarithms for the model parameters:

$$X_{g,R} = e^{\mu_R} \tag{3.5}$$

where

$X_{g,R}$ = the geometric mean of the result

μ_R = the (resulting) sum of the means of logarithms of the model parameters

The geometric standard deviation is found by taking the square root of the sum of the variances of the log transformed parameters and exponentiating (Hoffman and Gardner, 1983; IAEA, 1989):

$$S_{g,R} = e^{\sqrt{\sigma_R^2}} \tag{3.6}$$

where

$S_{g,R}$ = the geometric standard deviation of the result

σ_R^2 = the variance of the logarithms

The upper confidence limit is determined by multiplying the median value by the square (or some other power) of $S_{g,R}$. The lower confidence limit is obtained by dividing the median by the square (or some other power) of $S_{g,R}$. The use of the square of $S_{g,R}$ will lead to a 95% CI assuming that the distribution of the model prediction will be lognormal. Taking $S_{g,R}$ to a power of 1.65 will lead to a 90% CI for a lognormal distribution using the following equations:

$$X_{95}^R = X_{g,R} \cdot S_{g,R}^{1.65} \tag{3.7}$$

$$X_5^R = \frac{X_{g,R}}{S_{g,R}^{1.65}} \tag{3.8}$$

where

X_{95}^R = the 95% upper confidence limit of the result

X_5^R = the 5% lower confidence limit of the result.

The formula used to estimate the mean and variance of logarithms for each uncertain parameter depends on the type of (subjective) probability distribution chosen to represent the uncertain parameter. Equations describing the mean and variance of logarithms of lognormal, log-uniform, and log-triangular distributions are provided in Appendix A.

Example 3.1

Situation. Let us assume that methyl-mercury has been inadvertently released to a nearby lake. Using the technique of variance propagation, obtain a 90% CI on the hazard quotient (HQ) to a maximally exposed individual. After reviewing the literature, available data, and consulting with other experts, the (subjective) probability distributions shown in Table 3.2 are obtained for this problem.

Table 3.2. Information for Example 3.1

Parameter	Distribution	Minimum	Maximum	Mean	Standard Deviation
Fish concentration (*C*), mg/kg	Log-Normal			7.10E-2	3.43E-2
Intake (*I*), kg/d	Log-Uniform	2.00E-2	1.30E-1	6.50E-2	
Body mass (*BM*), kg	Log-Triangle	4.50E+1	1.20E+2	7.00E+1	
RfD, mg/kg-day	Log-Triangle	1.50E-4	3.00E-3	3.00E-4	

Note: The mean given for the I, BM, and RfD is the most likely value (mode). The distributions describe the uncertainty associated with estimating an unknown value for each model parameter.

Solution. The form of the equation used for this problem is as follows:

$$HQ = C \times I \times (BM)^{-1} \times (RfD)^{-1}. \tag{3.9}$$

where

HQ = hazard quotient (unitless)

C = concentration in the contaminated medium (mg/kg)

I = estimated intake rate of the contaminant for one year averaged over one year (kg/day)

BM = body mass (kg)

RfD = reference dose for the chemical of interest (mg/kg-day)

By log-transformation, Eq. 3.9 becomes:

$$\ln(HQ) = \ln(C) + \ln(I) - \ln(BM) - \ln(RfD). \tag{3.10}$$

The logarithmic mean and variance, assuming independence among the model parameters, of the HQ is found by applying Eqs. 3.1 and 3.2. The equations given in Appendix A must be used to find the mean and variance of logarithms for each of the model parameters. Equations A.1 and A.2 (Appendix A) produce a mean of the logarithms for the fish concentration of -2.75 and a variance of the logarithms for the fish concentration of 0.21.

Equations A.3 and A.4, for the log-uniform distribution, will be used to find μ (the mean of logarithms) and σ^2 (the variance of logarithms) for the intake:

$$\mu_I = \frac{\ln(0.02) + \ln(0.13)}{2} = -2.98 \tag{3.11}$$

$$\sigma_I^2 = \frac{\left[\ln\left(\frac{0.13}{0.02}\right)\right]^2}{12} = 0.29 \tag{3.12}$$

Equations A.5 and A.6, given for the log-triangular distribution, are used for the body mass and reference dose (RfD). To demonstrate, the μ and σ^2 for the body mass is calculated as follows:

$$\mu_{BM} = \frac{1}{3}[\ln(70) + \ln(120) + \ln(45)] = 4.28 \tag{3.13}$$

$$\sigma_{BM}^2 = \frac{1}{18}[(\ln(45))^2 + (\ln(120))^2 - (\ln(45))(\ln(120)) + (\ln(70))^2 - (\ln(70))(\ln(45) + \ln(120))] \tag{3.14}$$

$$\sigma_{BM}^2 = 0.04 \tag{3.15}$$

This same process is performed for the RfD, from which a mean value of -7.58 and a variance of 0.41 is obtained. The mean of logarithms and thereby the geometric mean of the HQ is calculated as follows:

$$\mu_{HQ} = (-2.75) + (-2.98) + (-4.28) + (7.58) = -2.43 \tag{3.16}$$

$$X_{g,HQ} = e^{\mu_{HQ}} = e^{-2.43} = 0.09 \tag{3.17}$$

The variance of the HQ and, consequently, the geometric standard deviation of the HQ can then be calculated:

$$\sigma_{HQ}^2 = 0.21 + 0.29 + 0.04 + 0.41 = 0.95 \tag{3.18}$$

$$S_{g,HQ} = e^{\sqrt{\sigma_{HQ}^2}} = e^{\sqrt{0.95}} = 2.65 \tag{3.19}$$

The upper and lower confidence limits for a 90% subjective CI are calculated as:

$$X_{95}^{HQ} = X_{g,HQ} \cdot S_{g,HQ}^{1.65} = (0.09)(2.65)^{1.65} = 0.45 \tag{3.20}$$

$$X_5^{HQ} = \frac{X_{g,HQ}}{S_{g,HQ}^{1.65}} = \frac{(0.09)}{(2.65)^{1.65}} = 0.02 \tag{3.21}$$

Therefore, there is high confidence (at a subjective level of 90%) that the HQ should lie between 0.02 and 0.45.

Variance propagation is a straight-forward process for simple additive and logarithmically transformed multiplicative models where the parameters are statistically independent. For more complex calculations, variance propagation techniques are more difficult to apply analytically, and in some cases their use may not be practical or possible.

3.6 NUMERICAL METHODS FOR UNCERTAINTY ANALYSIS

To overcome problems encountered with analytical variance propagation equations, numerical methods are useful in performing an uncertainty analysis. Perhaps the most commonly applied numerical technique and, as mentioned previously, the one that will be discussed most in this commentary is Monte Carlo simulation (Rubinstein, 1981). Other approaches include 1) differential uncertainty analysis (Cacuci, 1981; Worley, 1987), in which the partial derivatives of the model response with respect to the parameters are used to estimate uncertainty; 2) Monte Carlo analysis of statistical simplifications of complex models (Downing et al., 1985; Mead and Pike, 1975; Morton, 1983; Myers, 1971); 3) nonprobabilistic methods [for example: fuzzy sets, fuzzy arithmetic, and possibility theory (Ferson and Kuhn, 1992)]; and 4) first-order analysis employing Taylor expansions (Scavia et al., 1981). The last approach is based on computer implementation of the mathematical approaches used to formulate the analytical solutions to the error propagation for simple equations and is related to the first approach.

Monte Carlo analysis is usually performed using two random sampling processes: Simple Random Sampling (SRS) and Latin Hypercube Sampling (LHS) (Iman and Conover, 1980; 1982; Iman and Shortencarier, 1984; IAEA, 1989; McKay et al., 1979; Morgan and Henrion, 1990). In SRS, a random value

is sampled from each distribution specified for each uncertain model parameter, and a single estimate of the desired endpoint is calculated. This process is repeated for a specified number of samples or iterations. The result is a probability distribution of the model endpoint. Simple Random Sampling, however, is less efficient than its counterpart, LHS, when the sample size is less than a few thousand.

In standard LHS, the distribution for each parameter is divided into sections of equal probability. The number of sections equals the number of samples or iterations to be made in the Monte Carlo simulation. During the sampling, the random numbers are selected by chance within each section, but only one random number is chosen from each section. Once a random number has been selected from a section, that section is excluded from the rest of the analysis. The distributions are thereby represented more efficiently than with SRS, and it takes less sampling effort to reach a stable mean and variance of the prediction endpoint (IAEA, 1989). An alternative to standard LHS is midpoint LHS which provides an even more uniform sampling of the distributions (Morgan and Henrion, 1990). The primary difference between these techniques is that midpoint LHS chooses the median of each section instead of sampling randomly within the section.

Monte Carlo analysis may be performed in many ways. One may write a numerical code or use one of several currently available software packages. Several available Monte Carlo simulation programs are presented in the following list.

MOUSE	Klee (1986)
TAM3	Gardner (1988), Kanyar and Nielsen (1989)
PRISM	Gardner et al. (1983), Gardner and Trabalka (1985)
Crystal Ball	Decisioneering, Inc. (1994)
@RISK	Palisade Corporation (1991)
ORMONTE	Williams and Hudson (1989)
GENII/SUNS	Leigh et al. (1992)

The following example provides a more detailed description of a Monte Carlo simulation.

Example 3.2

Situation. Use the scenario presented in Example 3.1 to demonstrate the use of Monte Carlo simulation. With 90% (subjective) confidence, what is the risk to the maximally exposed individual? This example does not address dependencies among parameters; the effect of correlations among parameters will be demonstrated in Example 3.4.

Solution. To begin a quantitative uncertainty analysis, one must describe the uncertainty about each variable with a (subjective) probability distribution. This is done through judgment after extensive review of all relevant data. The information presented in Table 3.2 is used as input for a Monte Carlo simulation for this problem.

When running a Monte Carlo technique, values are selected at random from (subjective) probability distributions for each uncertain variable to produce a prediction. This procedure is repeated for a specified number of iterations and forms a distribution of predicted values. A sample of randomly selected values obtained by running 500 iterations of LHS for this problem is provided in Table 3.3.

Table 3.3. Sample of random values obtained from 500 iterations of LHS for Example 3.2

Sample number	Fish concentration (mg/kg)	Intake (kg/d)	Body mass (kg)	Reference dose (mg/kg-d)	HQ (unitless)
1	1.01E-01	3.40E-02	4.71E+01	5.25E-04	1.38E-01
2	1.14E-01	1.19E-01	7.68E+01	5.64E-04	3.15E-01
3	8.11E-02	1.05E-01	6.78E+01	1.76E-04	7.10E-01
4	6.51E-02	3.63E-02	7.50E+01	3.00E-04	1.05E-01
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
499	9.40E-02	9.21E-02	7.04E+01	2.71E-03	4.53E-02
500	8.60E-02	2.66E-02	8.15E+01	8.96E-04	3.13E-02

This process yields a (subjective) probability distribution for the HQ. Figure 3.3 contains the result for the risk after 500 iterations using LHS. From this Monte Carlo simulation, a 90% CI of [1.70E-2, 4.17E-1] is obtained and indicated by tick marks on the graph provided in Fig. 3.3. This implies that after taking into account the uncertainties on the parameters, one is highly confident (at a subjective level of 90%) that the true HQ should lie between 1.70E-2 and 4.17E-1. Since the 95% upper confidence limit is still below an HQ of 1, there is high confidence that the maximally exposed individual for this scenario is not exposed to an unacceptable level of risk, and remediation should not be warranted.

Once familiar with the Monte Carlo simulation software package, this technique becomes very efficient. Even if a risk analysis becomes more complicated, the Monte Carlo technique does not. One reason that the Monte Carlo calculations are more useful than other approaches to uncertainty analysis is that the alternative variance propagation techniques can become complicated and time consuming for more involved risk analyses. Setting up simulations to run on the computer is much more efficient and accurate than performing hand calculations. The inputs required for Monte Carlo simulations are the (subjective) probability distributions and uncertainty bounds for each parameter. To come up with these (subjective) probability distributions and uncertainty bounds, one must apply professional judgment after extensively reviewing the available literature and data. With the various input distributions, the Monte Carlo simulation program then provides a forecast of the risk in terms of a subjective probability distribution about which CIs for the risk can be obtained. A demonstration of this technique for a more complicated risk analysis situation is presented in the following example.

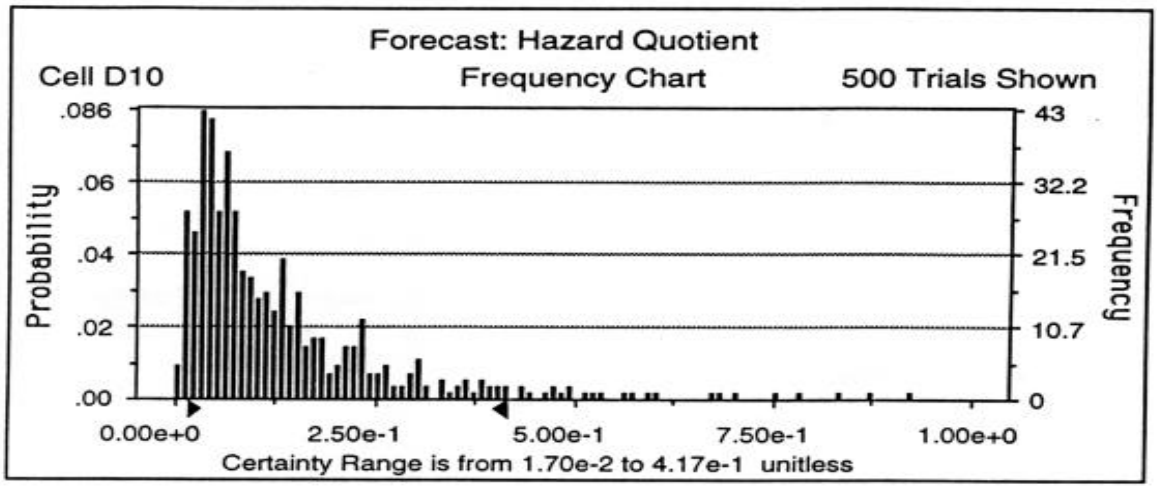


Fig. 3.3. Subjective probability distribution of the hazard quotient for Example 3.2

Example 3.3

Situation. Let us assume that as the result of waste management practices, a mixture of contaminants is released inadvertently to the environment. Through various pathways, this contamination is transported to aquatic systems such as rivers and lakes where fish and other biota are exposed. After further investigation, it is discovered that the contaminants released were Aroclor-1254, Aroclor-1260, chlordane, and methyl-mercury. Suppose that contaminated fish are caught and eaten by humans. What is the hazard index and the total lifetime cancer risk to the maximally exposed individual?

To perform this risk assessment, the HQs for chlordane and methyl-mercury will be calculated from the following equation.

$$HQ = \frac{C \cdot I}{BM \cdot RfD} \tag{3.22}$$

where

HQ = hazard quotient (unitless),

C = concentration in the contaminated medium (mg/kg),

I = estimated intake rate of the contaminant for one year averaged over one year (kg/day),

BM = body mass (kg),

RfD = reference dose for the chemical of interest (mg/kg-day).

The HQs for various chemicals are summed for each exposure pathway to obtain a hazard index for a given area (EPA, 1989). The excess lifetime cancer risk for Aroclor-1254, Aroclor-1260, and chlordane will be determined using the following equation.

$$LR = \frac{C \cdot I \cdot SF}{BM} \tag{3.23}$$

where

LR = excess lifetime cancer risk (unitless),

C = concentration in the contaminated medium (mg/kg),

I = estimated intake rate of the contaminant for thirty years averaged over a seventy year lifetime (kg/day),

BM = body mass (kg),

SF = slope factor (or cancer potency factor) for the contaminant of interest (mg/kg-day).

To quantify the uncertainty associated with each of the parameters introduced in these equations, one must derive (with the use of a considerable amount of judgment) subjective probability distributions from very limited sets of data and other relevant facts in the published literature. Once these distributions have been specified, one can use Monte Carlo techniques to obtain a probability distribution of the hazard index and the total lifetime cancer risk. From these propagated distributions, subjective CIs (90%) can be obtained for use in setting limits for decision making.

Table 3.4 contains values for the estimates of uncertainty on each of the parameters that would be used in an environmental risk assessment of Aroclor-1254, Aroclor-1260, chlordane, and methyl-mercury in the fish potentially harvested from a contaminated fresh water system.

Solution: The values given in Table 3.4 were used to find the median, the lower 5% subjective confidence limit, and the upper 95% subjective confidence limit for the noncarcinogen hazard index for chlordane and methyl-mercury and for the total cancer risk involved with the given concentrations of Aroclor-1254, Aroclor-1260, and chlordane in fish. These values (presented in Table 3.5) were obtained by using 500 iterations of the LHS Monte Carlo technique.

Table 3.4. Subjective probability distributions specified for the Monte Carlo Analysis of Example 3.3

Chemical	Parameter	Subjective Probability Distribution	Minimum	Maximum	Mean (Mode)	Standard Deviation	Units
Aroclor-1254	Fish Conc.	Log-Normal	4.00E-03	3.79E+00	5.34E-01	2.26E+00	mg/kg
	Intake	Log-Uniform	1.65E-02	8.25E-02			kg/day
	Body Mass	Log-Triangle	4.50E+01	1.20E+02	7.00E+01		kg
	Slope Factor	Triangle	0.00E+00	1.00E+01	7.70E+00		$(mg/kg\text{-}day)^{-1}$
Aroclor-1260	Fish Conc.	Log-Normal	3.19E-01	2.29E+00	9.75E-01	5.16E-1	mg/kg
	Intake	Log-Uniform	1.65E-02	8.25E-02			kg/day
	Body Mass	Log-Triangle	4.50E+01	1.20E+02	7.00E+01		kg
	Slope Factor	Triangle	0.00E+00	1.00E+01	7.70E+00		$(mg/kg\text{-}day)^{-1}$
chlordane (carcinogen)	Fish Concentration	Log-Normal	3.96E-02	3.06E-01	1.27E-01	6.98E-02	mg/kg
	Intake	Log-Uniform	1.65E-02	8.25E-02			kg/day
	Body Mass	Log-Triangle	4.50E+01	1.20E+02	7.00E+01		kg
	Slope Factor	Triangle	0.00E+00	5.00E+00	1.30E+00		$(mg/kg\text{-}day)^{-1}$
chlordane (non-carc)	Fish Concentration	Log-Normal	3.96E-02	3.06E-01	1.27E-01	6.98E-02	mg/kg
	Intake	Log-Uniform	2.00E-02	1.30E-01			kg/day
	Body Mass	Log-Triangle	4.50E+01	1.20E+02	7.00E+01		kg
	RfD	Log-Triangle	3.00E-05	1.90E-03	6.00E-05		mg/kg-day
methyl mercury	Fish Concentration	Log-Normal	2.55E-02	1.57E-01	7.10E-02	3.43E-02	mg/kg
	Intake	Log-Uniform	2.00E-02	1.30E-01			kg/day
	Body Mass	Log-Triangle	4.50E+01	1.20E+02	7.00E+01		kg
	RfD	Log-Triangle	1.50E-04	3.00E-03	3.00E-04		mg/kg-day

Table 3.5. Results obtained from Monte Carlo simulation using values in Table 3.4

Chemical	Type of Result	5% Subjective Confidence	Median	95% Subjective Confidence
Aroclor-1254	cancer risk	1.7E-05	3.4E-04	7.8E-03
Aroclor-1260	cancer risk	4.7E-04	2.5E-03	9.2E-03
chlordane	cancer risk	2.3E-05	1.0E-04	4.9E-04
Total cancer risk*		**8.6E-04**	**3.6E-03**	**1.4E-02**
chlordane	noncarcinogen HQ	6.2E-02	5.5E-01	3.3E+00
methyl mercury	noncarcinogen HQ	1.8E-02	8.8E-02	4.1E-01
Total HI*		**1.2E-01**	**6.6E-01**	**3.5E+00**

*Risks may not be directly additive due to the random sampling used in the analysis.

As shown in Table 3.5, the primary chemical contributing to the total cancer risk is Aroclor-1260, and the chemical contributing the majority of the total hazard index is chlordane. The parameter that has the most effect on the total uncertainty in the total cancer risk and the total hazard index can also be determined by performing a sensitivity analysis.

In this example, the method used for the sensitivity analysis was to square the Spearman Rank Coefficients and adjust them to 100% (Decisioneering, Inc., 1994). The approximate relative contribution of each parameter to the variance of the total cancer risk and the total hazard index was analyzed. The parameters having the greatest effect are considered to be the parameters for which additional data should reduce the amount of overall uncertainty in the results.

For the total cancer risk, the amount of fish ingestion was identified as having the most effect on the overall uncertainty in the total cancer risk contributing approximately 34.7% of the overall uncertainty. The next most important parameter is the concentration of Aroclor-1260 in the fish, contributing approximately 24.1% of the overall uncertainty. One might expect the latter result because of Aroclor-1260 contributing the majority of the risk. For the total hazard index, the sensitivity analysis showed that the two parameters that are the most significant contributors to the total uncertainty are the RfD for chlordane (contributing approximately 48.3% of the overall uncertainty) and the amount of fish ingested (contributing approximately 30.6% of the overall uncertainty).

Other methods of performing sensitivity analyses are introduced in Subsect. 3.7.

Example 3.4

Situation. The purpose of this example is to study the effect of correlation coefficients on the model result. Two scenarios are investigated.

(1) The effect of the correlation between body mass and intake on the total cancer risk and the total HI for the situation given in Example 3.3 is analyzed. First, assume that a minimum correlation of 0.3 has been determined to exist between body mass and intake, and second, compare the results with those obtained with a correlation of 0.5, 0.7, and 0.9.

(2) The effect of a correlation existing between the fish concentration and the intake on the total cancer risk and the total HI for the situation described in Example 3.3 is analyzed. This correlation would exist for those fishermen who eat only a certain species of fish. Assume that a correlation of 0.7 has been determined for this example.

Solution. (1) In this case, rank correlations are used (Decisioneering, Inc., 1994) to account for interdependencies between body mass and intake. As can be seen from Table 3.6, where the results are produced from 500 iterations using LHS, the correlation coefficients do not have a dramatic effect on the total risk. The values for the total cancer risk and the total hazard index are virtually the same. A slight difference is detected in the 5% lower confidence limit and 95% upper confidence limit values for correlation coefficients of 0.7 and 0.9. One reason that the correlation does not have an obvious effect on the results is that uncertainty in the body mass is not an important contributor to the overall uncertainty.

Table 3.6. Results obtained for correlations between body mass and intake for Part 1 of Example 3.4

		Rank Correlation Coefficient			
		0.3	0.5	0.7	0.9
Total cancer risk					
	5% LCL	9.2E-4	9.8E-4	1.0E-3	1.1E-3
	50% (median)	3.4E-3	3.4E-3	3.5E-3	3.5E-3
	95%UCL	1.4E-2	1.4E-2	1.3E-2	1.2E-2
Total HI					
	5% LCL	1.4E-1	1.4E-1	1.5E-1	1.6E-1
	50% (median)	6.7E-1	6.9E-1	6.9E-1	6.7E-1
	95% UCL	3.8E+0	3.3E+0	3.3E+0	3.1E+0

(2) Rank correlations were also used (Decisioneering, Inc., 1994) to account for interdependencies between fish concentration and intake. Table 3.7 summarizes the results obtained in Example 3.3 and presents the results obtained when accounting for a correlation coefficient of 0.7 between the fish concentrations and intake for the total cancer risk and the total HI. As can be seen from Table 3.7, the correlation coefficient has a definite effect on the lower and upper confidence limit values for both the total cancer risk and the total hazard index. The difference in the lower and upper confidence limit values that result from this correlation is because of the importance of the two correlated parameters to the overall uncertainty.

This example shows that correlation coefficients can be easily incorporated into an uncertainty analysis and should be fully considered when the effect is between important parameters or when the risk assessor is interested in the extremes of the distribution.

Table 3.7 Results obtained for a correlation between fish concentration and intake for Part 2 of Example 3.4

		No Correlation (Ex. 3.3)	0.7 Correlation
Total cancer risk			
	5% LCL	8.6E-04	6.1E-04
	50% (median)	3.6E-03	3.1E-03
	95% UCL	1.4E-02	2.1E-02
Total HI			
	5% LCL	1.2E-01	8.8E-02
	50% (median)	6.6E-01	6.7E-01
	95% UCL	3.5E+00	4.8E+00

3.7 ALTERNATIVE METHODS FOR SENSITIVITY ANALYSIS

Although not employed in Example 3.3, the use of scatter plots of the Monte Carlo samples of the input parameters against the Monte Carlo simulations of the model result is another method of identifying important parameters (Iman and Helton, 1988). For example, suppose that the risk is determined by the addition of two independent parameters, which parameter is the most important? This can be determined by graphing the 500 Monte Carlo samples of parameter 1 against the 500 simulations of the model result and comparing this graph against the same for parameter 2 as demonstrated in Fig. 3.4. As one can see, a more distinct trend exists for parameter 2 than for parameter 1. Therefore, one can conclude that the most important parameter to the overall uncertainty in the model result is parameter 2.

Many other methods are available for performing sensitivity analyses. Some of these methods include 1) simple regression (on the untransformed and transformed data) (Brenkert et al., 1988), 2) multiple and piecewise multiple regression (on transformed and untransformed data) (Downing et al., 1985), 3) regression coefficients and partial regression coefficients (Bartell et al., 1986, Gardner et al., 1981), 4) stepwise regression and correlation ratios (on untransformed and transformed data) and 5) differential sensitivity analysis (Griewank and Corliss, 1991; Worley, 1987). Other references that discuss the use of statistical regressions of the randomly selected values of the uncertain parameters on the values produced for the model predictions to determine the importance of parameters contributing to the overall uncertainty in the model result include IAEA (1989), Iman et al. (1981a; 1981b), Iman and Helton (1991), and Morgan and Henrion (1990).

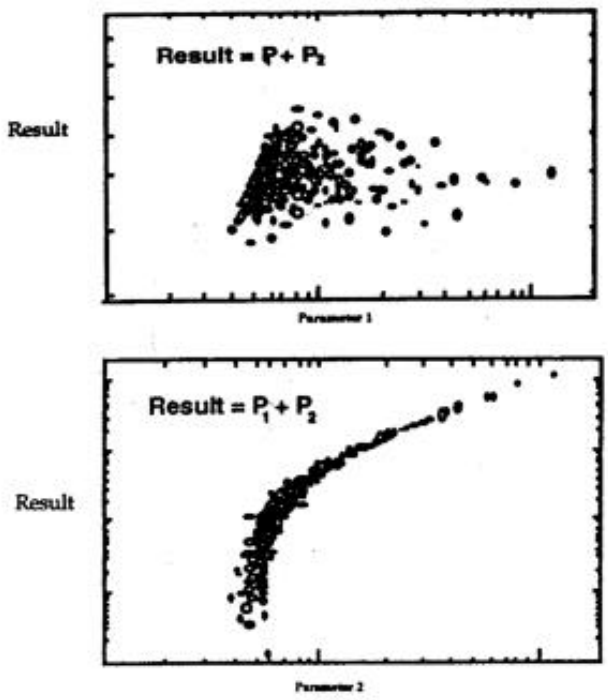


Fig. 3.4. Scatter plots of parameter 1 and parameter 2 against the model result

3.8 ADVANTAGES OF AN UNCERTAINTY ANALYSIS

One of the steps in a risk assessment is to rank the importance of the pathways and chemicals in terms of their potential contribution to the total risk. The first attempt at this is performed by screening. Screening identifies those pathways and chemicals that could be of potential concern. However, if the risk assessor attempts to rank the pathways and chemicals at this stage, the wrong conclusions may be reached because the uncertainty involved is not necessarily equal among contaminants and exposure pathways. This is best demonstrated in the following example.

Example 3.5

Situation. Upon investigation of a potentially contaminated site, it was discovered that a nearby lake and the surrounding soils were contaminated with methyl-mercury and inorganic mercury, respectively. The 95% upper confidence limit on the mean value for the concentration of the inorganic mercury in soil is found to be 700 mg/kg, and the 95% upper confidence limit on the mean value for the concentration of methyl-mercury in fish is 3.05×10^{-1} mg/kg. Considering the ingestion of soil and the ingestion of fish, which pathway is the most hazardous to the maximally exposed individual?

Solution. A summary of the values used in this example is provided in Table 3.8. The values for the HQs for the two pathways will be compared with each other for two situations: 1) by using a form of EPA's generic equations and 2) by incorporating uncertainty analysis. The exposure frequency for the soil ingestion pathway was included directly in this example because of its wide range of possible values. The exposure frequency for the fish ingestion pathway was included in the calculation of the intake parameter.

Table 3.8 Information for Example 3.5.

Parameter	Distribution	Minimum	Maximum	Mean	Standard Deviation
Fish concentration (C_F), mg/kg	Log-Normal			2.06E-1	4.22E-2
Intake of Fish (I_F), kg/d	Log-Uniform	2.00E-2	1.30E-1	6.50E-2	
Soil concentration (C_S), mg/kg	Log-Normal			3.11E+2	1.50E+2
Intake of Soil (I_S), kg/d	Log-Uniform	5.00E-5	2.00E-4	1.00E-4	
Exposure frequency (EF_s)	Log-Uniform	2.70E-1	7.00E-1	7.00E-1	
Body mass (BM), kg	Log-Triangle	4.50E+1	1.20E+2	7.00E+1	
Inorganic mercury RfD (RfD_{IM}), mg/kg-d	Log-Uniform	3.00E-4	3.00E-2	3.00E-4	
Methyl mercury RfD (RfD_{MM}), mg/kg-d	Log-Triangle	1.50E-4	3.00E-3	3.00E-4	

* Note: The mean given for the I, BM, and RfD is the most likely value (mode).

$$HQ_{SP} = \frac{C_s \cdot I_s \cdot EF_s}{BM \cdot RfD_{IM}} = \frac{(700)(1.0E-04)(0.7)}{(70)(3.0E-04)} = 2.33 \tag{3.24}$$

$$HQ_{FP} = \frac{C_f \cdot I_f}{BM \cdot RfD_{MM}} = \frac{(3.05E-01)(6.5E-02)}{(70)(3.0E-04)} = 0.94 \tag{3.25}$$

From these calculations, one would conclude that the risk to the maximally exposed individual results from the soil-ingestion pathway. However, by incorporating the uncertainties for the parameters and using Monte Carlo simulation, one obtains different results. After a Monte Carlo simulation run of 500 iterations of LHS, the 95% upper confidence limit of the HQ for the soil ingestion pathway is 0.72, and the 95% upper confidence limit of the HQ for the fish ingestion pathway is 1.20. This implies that the fish ingestion pathway is the source of most of the risk to the maximally exposed individual. The reversal of the ranking from the EPA calculations is primarily because of the large uncertainty on the RfD for inorganic mercury. If the uncertainty

of this parameter had not been taken into account, an inaccurate conclusion and, possibly, an inappropriate course of action would have resulted.

An uncertainty analysis through a quantitative description provides better direction for further investigation. If a quantitative uncertainty analysis is used routinely in risk assessment, specific areas that need further study can be determined and ranked, thereby preventing misdirected investigation and unwarranted remedial action, which in turn should result in saving limited experimental and financial resources.

3.9 BRIEF INTRODUCTION TO UNCERTAINTY ANALYSIS FOR AN ASSESSMENT ENDPOINT THAT IS A DISTRIBUTION OF VALUES AS OPPOSED TO A SINGLE VALUE

The general subject of this report to this point has coincided with uncertainty about a true but unknown value [referred to in IAEA Safety Series No. 100 (1989) as "Type B" uncertainty]. However, some risk assessments may have an endpoint defined as a stochastic variable. An example would be the variability of doses among individuals in a population whereby the individuals are selected from the population at random. An uncertainty analysis dealing with stochastic variability only is referred to as "Type A" uncertainty in IAEA Safety Series No. 100 (1989). Both "Type A" and "Type B" uncertainty occur when the assessment objective is to estimate the distribution of individual doses or risks within an exposed population group where the true shape and spread of this distribution is uncertain (i.e., unknown). The goal of this section, therefore, is to briefly describe the process of uncertainty analysis when the assessment endpoint is a stochastic variable and when there is lack of knowledge about the true distribution that describes this variable.

To distinguish between "Type A" and "Type B" uncertainty, Monte Carlo simulation must be applied in two dimensions. First, numerous sets of alternative values are obtained from marginal probability density functions (PDF_u's) representing subjective degrees of belief about quantities that are fixed but unknown with respect to the assessment endpoint (Fig. 3.5). Fixed quantities include parameters that do not vary with the assessment endpoint, such as the total amount of the contaminant released. Fixed quantities also include the mean, variance, and shape of those parameter distributions that describe variability among individuals, as well as values that describe correlations among these parameters. The alternative sets of fixed values represent "Type B" uncertainty.

Second, for each alternative set of fixed values, Monte Carlo procedures are used to simulate alternative distributions of parameter values that vary with respect to the assessment endpoint (PDF_v's) and corresponding distributions of individual risks, each with its own unique mean, variance, and shape (Fig. 3.6). Each of these distributions is an individual representation of "Type A" uncertainty. The set of alternative distributions represents "Type B" uncertainty. The alternative distributions are then used to construct confidence intervals for the unknown risk at any given fractile or for the unknown fractile at any given value of risk (Fig. 3.7). The order of importance for the parameters that contribute most to the confidence interval at a given fractile will depend on the fractile of interest (IAEA, 1989). Additional readings on this issue can be obtained from a number of authors (Bogen, 1990; Frey, in press; Helton, 1993; Hofer, 1990; Kaplan and Garrick, 1981).

When performing an uncertainty analysis where there is both stochastic variability and lack of knowledge uncertainty, correct interpretation of the results requires that these two sources of uncertainty be analyzed separately. Various distributions representing the endpoint, which are analogous to the various values obtained for the result in an uncertainty analysis where only true but unknown values are considered, are

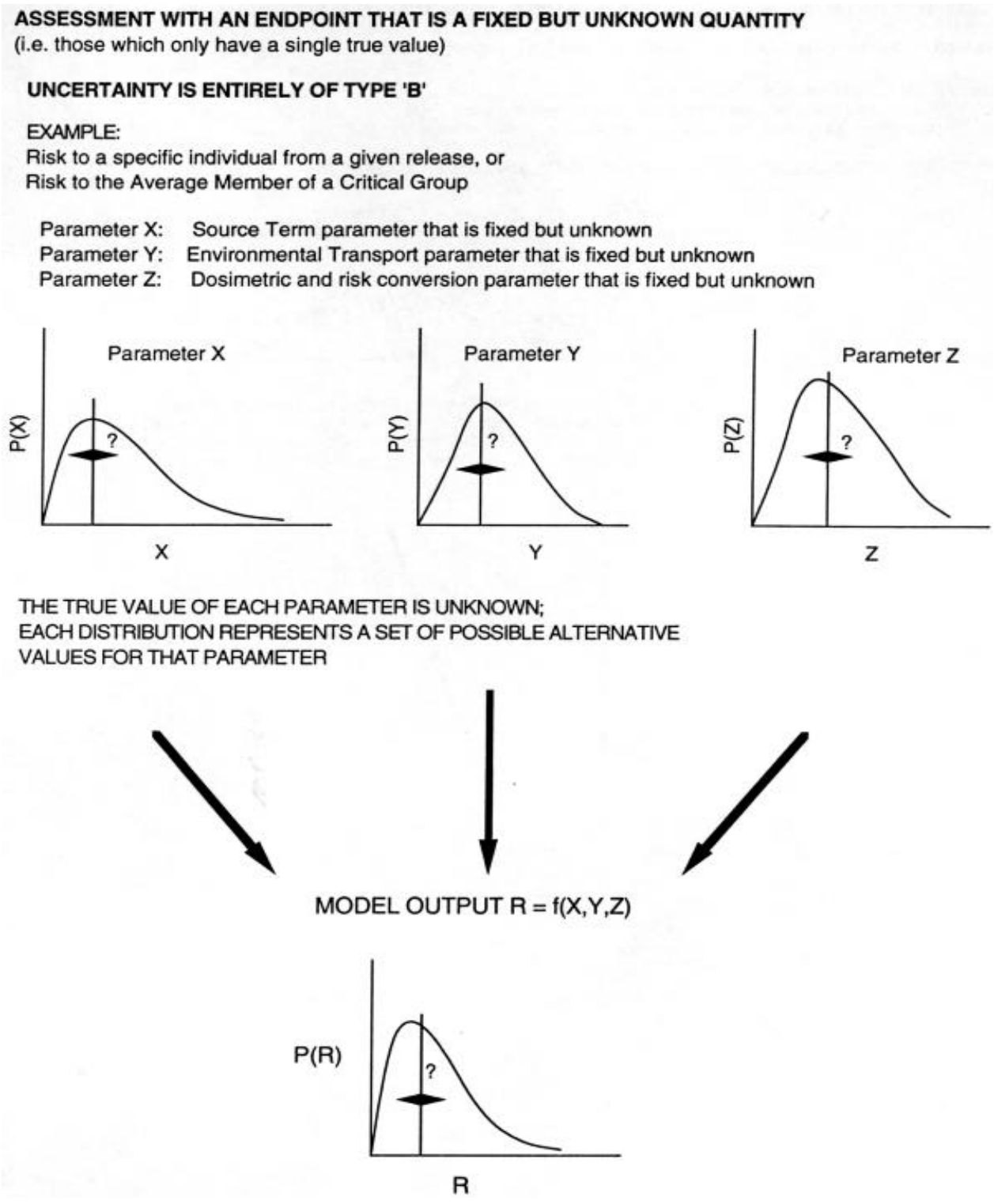


Fig. 3.5. Use of a Monte Carlo approach to estimate "Type B" uncertainty when the assessment endpoint is a fixed but unknown quantity (Hoffman and Hammonds, 1994)

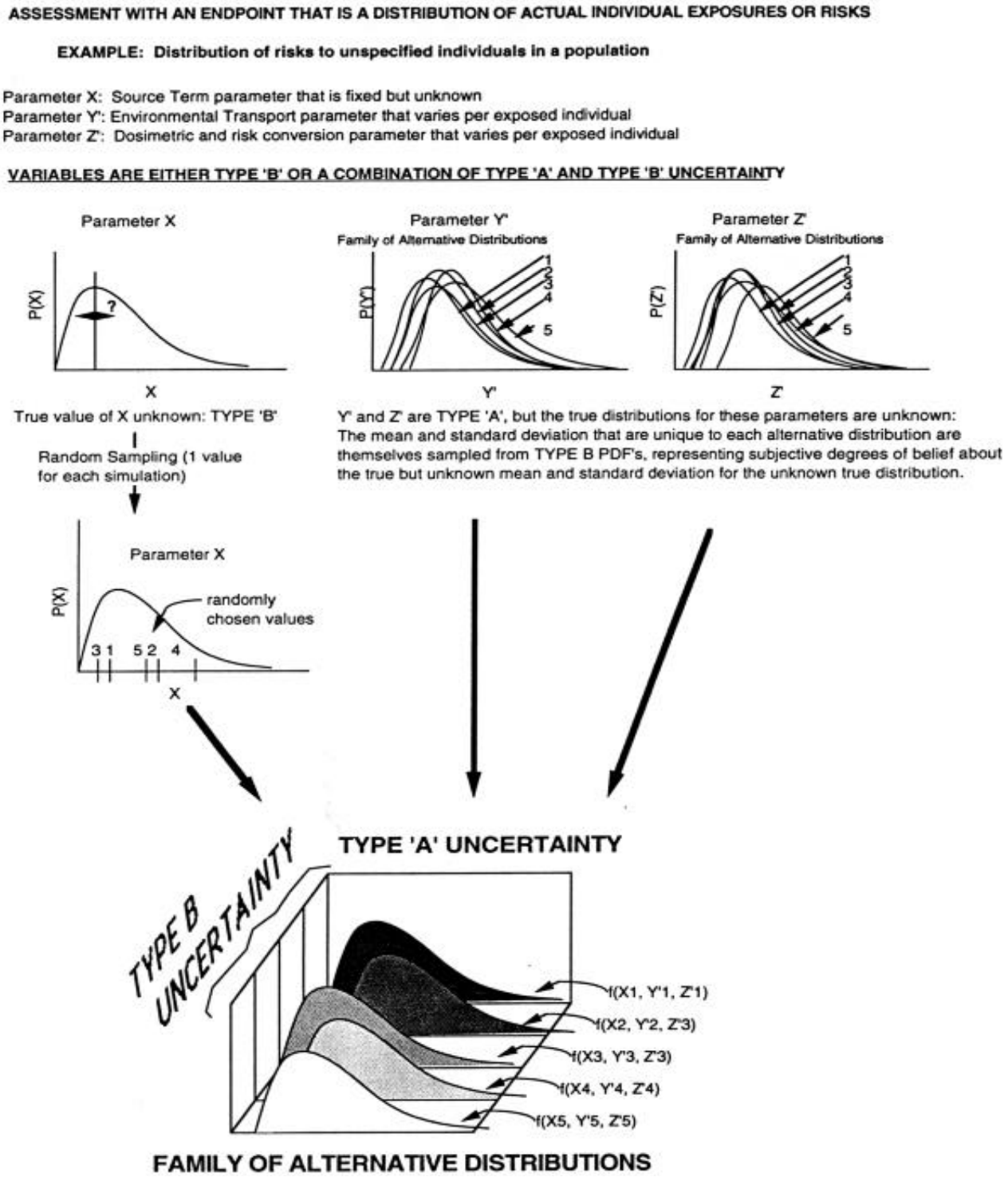


Fig. 3.6. Use of a Monte Carlo approach to distinguish between "Type A" and "Type B" uncertainty when the assessment endpoint is a true but unknown distribution of values representing variability among unspecified individuals in an exposed population (Hoffman and Hammonds, 1994)

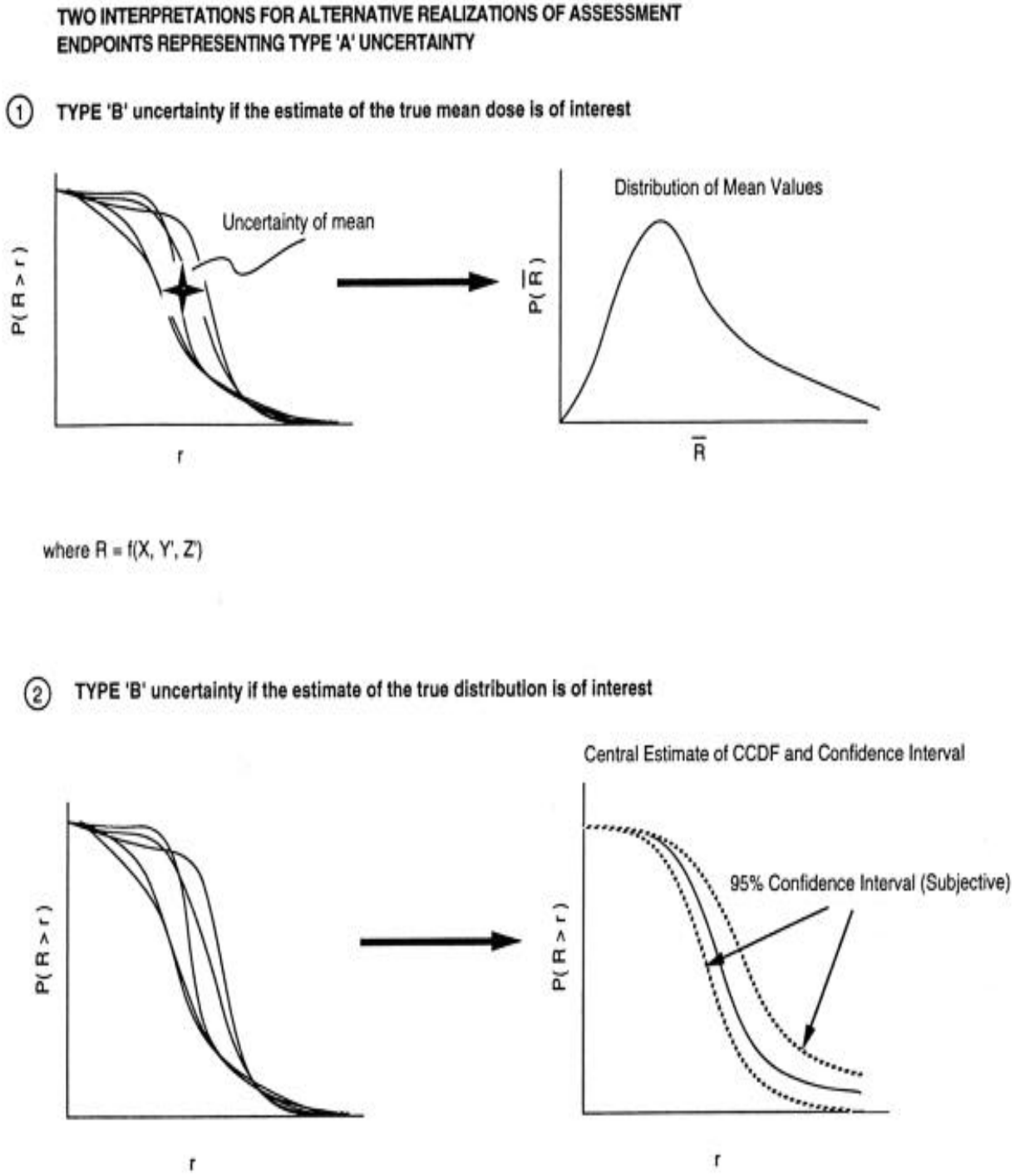


Fig. 3.7. Numerous alternative distributions produced through Monte Carlo simulation of "Type A" and "Type B" uncertainty can be used to derive confidence intervals for the mean value and any fractile of the true but unknown distribution (Hoffman and Hammonds, 1994)

obtained. The combination of these types of uncertainty analysis is facilitated using Monte Carlo simulation.

3.10 GUIDANCE FOR INTERPRETING THE RESULT OF AN UNCERTAINTY ANALYSIS

Incorporating a quantitative uncertainty analysis into a dose or risk assessment provides a major tool for decision making. A quantitative uncertainty analysis will allow the assessor to evaluate the relative importance of the contaminants and pathways more accurately. In this manner, quantitative uncertainty analysis allows the assessor to see where further study is needed or where decisions can be made in the presence of uncertainty. Not only does a quantitative uncertainty analysis allow a ranking of the pathways and contaminants that contribute most to the overall uncertainty in the result, but it also provides a subjective probability distribution about which confidence intervals can be formed to represent the uncertainty in the assessment endpoint.

The information obtained from a quantitative uncertainty analysis can be used to guide decisions. For example, if a 5% lower confidence limit is above a regulatory standard of concern, then it is likely that the standard will be violated. If the 95% upper confidence limit is below the standard, it is likely that the standard will not be violated. If the 95% upper confidence limit is above the standard, but the 50th percentile is below the standard, further study should be recommended on those parameters that dominate the overall uncertainty. However, if the 50th percentile is above the standard, further study may still be recommended, but under some circumstances one may opt to proceed with regulatory action depending on the cost-effectiveness of measures for risk reduction.

4. SUMMARY

The baseline risk assessment methods currently recommended by EPA do not explicitly account for uncertainty and may tend to produce overly conservative estimates of risk by combining, through multiplication, several conservatively biased values for parameters in the risk assessment equation. Therefore, EPA's baseline risk assessment methods should be more appropriately viewed as an initial screening tool. A more informative approach to estimating risks is to incorporate a quantitative uncertainty analysis into the risk assessment. Quantitative uncertainty analysis may be facilitated by using either analytical error propagation equations (i.e., variance propagation techniques) or by using numerical approaches with the aid of a computer (i.e., Monte Carlo simulation). The latter is more robust for varying levels of uncertainty and risk assessment models of varying levels of complexity.

Quantifying uncertainty in the risk estimate provides more information to the risk assessment and is the first step in identifying the need for additional data. The most difficult task in quantitative uncertainty analysis, however, is associated with justifying judgmental decisions that are made to obtain subjective probability distributions for the uncertain model parameters. The extent of knowledge required to exercise this judgment often exceeds the capacity of any one individual. Therefore, the judgment of several experts must often be solicited, if not formally elicited, to defensibly estimate parameter and model uncertainty.

5. REFERENCES

Bartell, S. M., Breck, J. E., Gardner, R. H., and Brenkert, A. L. 1986. Individual Parameter Perturbation and Error Analysis of Fish Bioenergetics Models. *Can. J. Fish. Aquat. Sci*. 43:160-168.

Beauchamp, John J. 1991. Personal Communication. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Blaylock, B. G., Frank, M. L., Hook, L. A., Hoffman, F. O., and Ford, C. J. 1991. DRAFT *White Oak Creek Embayment Site Characterization and Contaminant Screening Report.* ORNL/ER-81. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Bogen, K. T. 1990. *Uncertainty in environmental health risk assessment*. Garland Publishing, Inc., New York.

Brenkert, A. L., Gardner, R. H., Bartell, S. M., and Hoffman, F. O. 1988. Uncertainties associated with estimates of radium accumulation in lake sediments and biota. In: *Reliability of Radioactive Transfer Models*, G. Desmet, ed. Commission of the European Communities, Elsevier Applied Science, London. pp. 185-192.

Cacuci, D. G. 1981. Sensitivity Theory for Nonlinear Systems. Part I and II. *J. Math. Physics* 22:2794.

Decisioneering, Inc. 1994. *Crystal Ball: User's Guide.* Denver, Colorado.

Downing, D. J., Gardner, R. H., and Hoffman, F. O. 1985. An Examination of Response-Surface Methodologies for Uncertainty Analysis in Assessment Models. *Technometrics* 27:151-163.

Ferson, S. and Kuhn, R. 1992. Propagating uncertainty in ecological risk analysis using interval and fuzzy arithmetic. In, P. Zannetti (ed.). *Computer Techniques in Environmental Studies IV*: 387-401. Elsevier Applied Science, London.

Frey, H. C. in press. Separating variability and uncertainty in exposure assessment: motivations and method. *Risk Analysis*.

Gardner, R. H. 1988. *TAM3: A program Demonstrating Monte Carlo Sensitivity and Uncertainty Analysis.* Document prepared for the workshops of Biospheric Model Validation Study, BIOMOVS. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Gardner, R. H., O'Neill, R. V., Mankin, J. B., and Carney, J. H. 1981. A comparison of sensitivity analysis and error analysis based on a stream ecosystem model. *Ecol. Model.* 12:177-194.

Gardner, R. H., Rojder, B., and Bergstrom, U. 1983. *PRISM: A systematic method for determining the effect of parameter uncertainties on model predictions.* Studsvik Energiteknik AB report/NW-83/555, Nykoping Sweden.

Gardner, R. H. and Trabalka, J. R. 1985. *Methods of Uncertainty Analysis for a Global Carbon Dioxide Model.* Department of Energy Technical Report. DOE/OR/21400-4.

Griewank, A. and Corliss, H. (Eds.). 1991. *Automatic Differentiation of Algorithms: Theory, Implementation, and Application*. Philadelphia, PA. Society for Industrial and Applied Mathematics.

Helton, J. C. 1993. Risk, uncertainty in risk, and the EPA release limits for radioactive waste disposal. *Nuclear Technology* 101:18-39.

Hofer, E. 1990. On some distinctions in uncertainty analysis. In: *Methods for Treatment of Different Types of Uncertainty*, PSAC/DOC (90)11, OECD Nuclear Energy Agency, Paris.

Hoffman, F. O., Blaylock, B. G., Frank, M. L., Hook, L. A., Etnier, E. L., and Talmage, S. S. 1991. *Preliminary Screening of Contaminants in the Off-Site Surface Water Environment Downstream of the U.S. Department of Energy Oak Ridge Reservation.* ORNL/ER-9. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Hoffman, F. O., Blaylock, B. G., Frank, M. L., and Thiessen, K. M. 1993. *A Risk Based Screening Approach for Prioritizing Contaminants and Exposure Pathways at Superfund Sites*. Environmental Monitoring Assessment 28:221-237.

Hoffman, F. O. and Gardner, R. H. 1983. Evaluation of Uncertainties in Radiological Assessment Models. Chapter 11 of *Radiological Assessment: A textbook on Environmental Dose Analysis*. Edited by Till, J. E. and Meyer, H. R. NRC Office of Nuclear Reactor Regulation, Washington, D. C.

Hoffman, F. O. and Hammonds, J. S. 1994. Propagation of Uncertainty in Risk Assessments: The Need to Distinguish between Uncertainty due to Lack of Knowledge and Uncertainty due to Variability. Conference Proceedings: "When and How Can You Specify a Probability Distribution Function when You Don't Know Much?" *Risk Analysis* 14(5):707-712.

Hoffman, F. O., Miller, C. W., and Ng, Y. C. 1984. *Uncertainties in Radioecological Assessment Models.* Conference: The environmental transfer to man of radionuclides released from nuclear installations. Brussels, October 17-21, 1983.

Iman, R. L. and Conover, W. J. 1980. *Small sample sensitivity analysis techniques for computer models, with an application to risk assessment.* Commun. Stat., Part A: Theory Methods **9** (17). pgs. 1749-1842. ("Comments," pgs. 1843-1861, "Rejoinder to Comments," pgs. 1863-1874).

Iman, R. L. and Conover, W. J. 1982. A distribution-free approach to introducing rank correlation among input variables. *Commun. Stat., Part B. Simul. Comput*. **11** (3). pgs. 311-334.

Iman, R. L. and Helton, J. C. 1991. The Repeatability of Uncertainty and Sensitivity Analyses for Complex Probabilistic Risk Assessments. *Risk Analysis* 11(4):591-606.

Iman, R. L. and Helton, J. C. 1988. An Investigation of Uncertainty and Sensitivity Analysis Techniques for Computer Models. *Risk Analysis* 8:71-90.

Iman, R. L., Helton, J. C., and Campbell, J. E. 1981a. An Approach to Sensitivity Analysis of Computer Models, Part 1. Introduction, Input Variable Selection and Preliminary Variable Assessment. *Journal of Quality Technology*, 13(3):174-183.

Iman, R. L., Helton, J. C., and Campbell, J. E. 1981b. An Approach to Sensitivity Analysis of Computer Models, Part 2. Ranking of Input Variables, Response Surface Validation, Distribution Effect and Techniques Synopsis. *Journal of Quality Technology* 13(4):232-240.

Iman, R. L. and Shortencarier, M. J. 1984. *A FORTRAN 77 Program and User's Guide for the Generation of Latin Hypercube and Random Samples for Use with Computer Models.* Rep. NUREG/CR-3624. Sandia National Laboratory, Albuquerque, New Mexico.

International Atomic Energy Agency (IAEA). 1989. *Evaluating the Reliability of Predictions Made Using Environmental Transfer Models.* IAEA Safety Series 100. Vienna, Austria.

Johnson, N. L. and Kotz, S. 1970. *Continuous Univariate Distributions.* Vol. 2. pg. 64-65. Houghton Mifflin Company, Boston, Massachusetts.

Kanyar, Bela and Nielsen, Sven P. 1989. *Users Guide for the Program TAMDYN.* Document prepared for the workshops of Biospheric Model Validation Study, BIOMOVS. Technical Report 4.

Kaplan, S. and Garrick, B. J. 1981. On the quantitative definition of risk. *Risk Analysis* 1(1):11-27.

Klee, Albert J. 1986. *The MOUSE Manual.* U. S. Environmental Protection Agency, Cincinnati, Ohio.

Leigh, C. D., Thompson, B. M., Campbell, J. E., Longsine, D. E., Kennedy, R. A., and Napier, B. A. 1992. *User's guide for GENII-S: a code for statistical and deterministic simulations of radiation doses to humans from radionuclides in the environment*. Sandia National Laboratory. Albuquerque, NM. UC-721.

Lyman, W. J., Reehl, W. F., and Rosenblatt, D. H. (eds.). 1982. *Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds.* Mcgraw Hill, New York.

Martz, H. F. and Waller, R. A. 1982. Bayesian Reliability Analysis. John Wiley & Sons, New York.

McKay, M. D., Beckman, R. J., and Conover, W. J. 1979. A comparison of three methods for selecting values of input variables in the analysis of output from a computer code. *Technometrics* **21** 2. pgs. 239-245.

Mead, R. and Pike, D. J. 1975. A Review of Response Surface Methodology from a Biometric Viewpoint. *Biometrics* 31:8003-851.

Morgan, M. G. and Henrion, M. 1990. *Uncertainty, A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis*. Cambridge University Press, New York.

Morton, R. H. 1983. Response Surface Methodology. *Mathematical Scientist* 8:31-52.

Myers, R. H. 1971. *Response Surface Methodology*. Allyn and Bacon, Boston, MA.

National Academy of Sciences (NAS). 1994. *Science and Judgment in Risk Assessment*. National Research Council. National Academy Press, Washington, DC.

National Council on Radiation Protection and Measurements (NCRP). 1989. *Screening Techniques for Determining Compliance with Environmental Standards, Releases of Radionuclides to the Atmosphere.* NCRP Commentary 3. Bethesda, Maryland.

NCRP. in press. Task Group 6. NCRP Scientific Committee 64.

O'Neill, R. V., Gardner, R. H., Hoffman, F. O., and Schwarz, G. 1981. Parameter Uncertainty and Estimated Radiological Dose to Man from Atmospheric I-131 Releases: A Monte Carlo Approach. *Health Physics* 40:760-764.

Palisade Corporation. 1991. *@RISK: Risk Analysis and Simulation Add-In for Microsoft Excel; User's Guide.* Newfield, New York.

Rubinstein, R. Y. 1981. *Simulation and the Monte Carlo Method.* 278 pgs. Wiley, New York.

Scavia, D., Powers, W. F., Canale, R. P., and Moody, J. L. 1981. Comparison of First-Order Error Analysis and Monte Carlo Simulation in Time-Dependent Lake Eutrophication Models. *Water Resources Research* 17:1051-1059.

United States Environmental Protection Agency (U.S. Environmental Protection Agency). 1989. *Interim Final: Risk Assessment Guidance for Superfund. Vol. I: Human Health Evaluation Manual.* OSWER Directive 9285.7-01a. EPA Office of Emergency and Remedial Response, Washington, D.C.

United States Environmental Protection Agency. 1992. *Guidelines for Exposure Assessment.* Federal Register 57(104):22888-22938. May 29, 1992.

Williams, K. A. and Hudson, C. R. II. 1989. *ORMONTE: An Uncertainty Analysis Code for Use with User-Developed Systems Models on Mainframe or Personal Computers; A User's Guide.* ORNL/TM-10714. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Worley, Brain A. 1987. *Deterministic Uncertainty Analysis.* ORNL-6428. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

APPENDIX A

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The following distributions are suggested for subjective probability distributions in analysis of multiplicative models.

Log-Normal Distribution:

μ	=	the mean of the logarithms
σ^2	=	the variance of the logarithms

However, if you have a situation where you are given only the arithmetic mean and arithmetic variance, then μ and σ^2 can be estimated with the following equations (Hoffman and Gardner, 1983):

$$\mu = \ln\left[\frac{\bar{x}}{\left[1+\left(\frac{s}{\bar{x}}\right)^2\right]^{0.5}}\right] \tag{A.1}$$

$$\sigma^2 = \ln\left[1+\left(\frac{s}{\bar{x}}\right)^2\right] \tag{A.2}$$

where

$\bar{x}$	=	the arithmetic mean of the distribution
s	=	the standard deviation of the distribution.

Log-Uniform Distribution (Hoffman and Gardner, 1983):

$$\mu = \frac{[\ln(\min) + \ln(\max)]}{2} \tag{A.3}$$

$$\sigma^2 = \frac{\left[\ln\left(\frac{\max}{\min}\right)\right]^2}{12} \tag{A.4}$$

Asymmetrical Log-Triangular Distribution (Beauchamp, 1991; Johnson and Kotz, 1970):

$$\mu = \frac{1}{3}[\ln(H^*) + \ln(b) + \ln(a)] \tag{A.5}$$

$$\sigma^2 = \frac{1}{8}[[\ln(a)]^2 + [\ln(b)]^2 - [\ln(a)][\ln(b)] + [\ln(H^*)] - [\ln(H^*)][\ln(a) + \ln(b)]] \tag{A.6}$$

where

H^*	=	the mode of the triangular distribution,
b	=	the maximum of the triangular distribution,
a	=	the minimum of the triangular distribution.

The following distributions are suggested for use as subjective probability distributions in analysis of additive models.

Normal Distribution:

The mean value of the normal distribution is simply the value at the 50 percentile. With a normal distribution, the median, mode, and mean are the same. The variance of the normal distribution is the second central moment of the variable or the standard deviation squared.

Uniform Distribution:

$$\bar{x} = \frac{(\min + \max)}{2} \tag{A.7}$$

$$s^2 = \frac{(\max - \min)^2}{12} \tag{A.8}$$

Asymmetrical Triangular Distribution (Beauchamp, 1991; Johnson and Kotz, 1970):

$$\bar{x} = \frac{1}{3}(H^* + b + a) \tag{A.9}$$

In addition to these suggested distributions, a few more distributions that one may use are custom designed, Poisson, Weibull, gamma, beta distributions, and any number of discrete distributions (Decisioneering, Inc., 1994; Palisade Corp., 1991).

$$s^2 = \frac{1}{18}[(a)^2 + (b)^2 - (a)(b) + (H^*)^2(a+b)] \tag{A.10}$$