Alceon
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Technical and Policy Memorandum

To: The File
From: David E. Burmaster
Subject: Computations Illustrating Variability and Uncertainty

Introduction

Quantitative risk assessments are, fundamentally, simple algebraic equations that use a large number of variables to compute a single numerical output. Risk assessors gather data, or use default values, representing a host of exposure and dose-response factors -- how long someone lives somewhere, how toxic some substance is, etc. -- and combine those numbers to determine an estimate of risk. This process is typically deterministic; that is, it takes a single point value for each of the input variables, and thus yields a single point output.

Much attention has been devoted in the last few years to the methods and the value of performing probabilistic health risk assessments, i.e., assessments in which ranges of input variables are combined to yield a range of risk. The purpose of this appendix is to explain what probabilistic risk assessments are, how they work, and what their strengths and limitations are.

The Deterministic Approach

A number of guidance documents present the values that are widely quoted and used as inputs to health risk assessments under the deterministic approach. For example, the US EPA's Exposure Factors Handbook (US EPA, 1989) provides that each adult weighs 70 kilograms, ingests 2 liters per day of drinking water, breathes 20 to 24 cubic meters per day of air, and lives in the same residence 30 years. The Agency chose most of the values as "conservative" or upper bound values and chose the others as typical or average values.

While these numbers are simple to memorize and easy to apply, it is important to realize that they are wrong. People vary in many attributes. Not everyone has the same weight, has the same diet, or lives in a home as long as 30 years. Furthermore, the values for other assumptions such as soil ingestion rates are simply unknown.

These problems represent a challenge to health risk assessments -- dealing with the large variability and the large uncertainty inherent in the exercise:

> Variability represents true heterogeneity in the biochemistry or physiology (e.g., body weight) or behavior (e.g., time spent showering) in a population which cannot be reduced through further measurement or study. For example, different children in a population ingest different amounts of tap water each day. Thus variability is a fundamental property of the exposed population and or the exposure scenario(s) in the assessment. Variability in a population is best analyzed and modeled in terms of a full probability distribution, usually a first-order parametric distribution with constant parameters.
>
> Uncertainty represents ignorance -- or lack of perfect knowledge -- about a phenomenon for a population as a whole or for an individual in a population which may sometimes be reduced through further measurement or study. For example, although we may not know much about the issue now, we may learn more about certain people's ingestion of whole fish through suitable measurements or questionnaires. In contrast, through measurements today, we cannot now eliminate our uncertainty about the number of children who will play in a new park scheduled for construction in 2001. Thus, uncertainty is a property of the analyst performing the risk assessment. Uncertainty about the variability in a population can be well analyzed and modeled in terms of a full probability distribution, usually a second-order parametric distribution with nonconstant parameters.

Variability and uncertainty have different ramifications for decision making. In one situation, for example, the decision maker may select a risk management program designed to reduce high-end exposures in the population. In another example, the decision maker may elect to collect more information to illuminate future issues.

As a result of variability and uncertainty, most if not all of the inputs to a health risk assessment are really random variables; that is, variables that can take any one of a range or distribution of values, with a certain probability of occurrence. The range of values that a variable can take, and the probability of those values, are usually codified in a mathematical function called the probability distribution for that random variable. In practice, analysts can capture the range and probabilities in either of two (interchangeable) mathematical functions. The most well-known is the "probability density function" (PDF), which for Normal (or Gaussian) distributions is the familiar bell-shaped curve. The second is called the "cumulative distribution function" (CDF), and is usually S-shaped. The CDF is the integral of the PDF, so the two functions contain identical information.

Most risk assessments now contain only a few paragraphs of text acknowledging the variabilities and uncertainties in the methods and results. Some risk assessments go further and include some sensitivity analysis -- that is, performing several single-point calculations of the same result, choosing different values for one variable from within the range of the variability or the uncertainty applicable to it, while holding all others constant. Sensitivity analyses reveal the degree to which the outcome is affected by a given change in a given input -- large changes in some variables may have little effect on the result, whereas small changes in others may greatly change the outcome. A sensitivity analysis might indicate that the risk estimate is sensitive to the rate of fish ingestion and may suggest that a survey of the affected population might refine the risk estimate.

Risk assessments may also include some information on model uncertainty; i.e., the uncertainty inherent in the models used for exposure assessment, dose-response assessment, or risk characterization.

These sorts of steps are worthwhile, but they represent only partial attempts to address the consequences of variability and uncertainty.

The Probabilistic Approach

The essence of probabilistic risk assessment is that it incorporates variability and/or uncertainty into the risk calculation, to estimate a distribution of risk that contains more information than the single-point output of the deterministic approach. George Box, a

famous statistician, once said that "All models are wrong, but some are useful." The goal of probabilistic risk assessment is to yield results that are more useful to risk managers and to the public.

As just discussed, most variables in health risk assessment are truly random variables that can take any value in a range with different probabilities. For example, we all know that all adults do not weigh 70 kilograms. How much people weigh is well-documented, however, and so one can readily develop a simple (but realistic) probability function for body weight by saying it is described as a LogNormal distribution with a mean of 70 kilograms and standard deviation of 10 kilograms.

Instead of using the 70 kilogram point value for body weight specified in the US EPA's Exposure Factors Handbook, a probabilistic risk assessment uses a random variable to represent body weight -- that is, it inserts the probability function for body weight into the risk assessment equation to capture the known and well measured inter-individual variability among people in a population. Where a particular input is characterized by uncertainty (for example, the distribution for the number of days a person goes swimming in a local pond), the risk assessor will construct and insert into the equation a function that reflects his or her best judgment of the possible distribution for that input, so that the random variable will capture the unknown or poorly measured inter-individual behavior in a population.

While most people know how to multiply several point values to create a new point value, few people know how to multiply several random variables to create a new random variable (distribution) for the output variable. Even though multiplication of probability distributions is mathematically well defined, the calculation is tedious and involved. With the advent of powerful desktop computers, however, commercial software packages can perform the mathematical operations among random variables by a process called Monte Carlo simulation. The computer can estimate the output distribution by iteratively sampling from the input distributions some 10,000 or more times and then assembling a list of the answers into an output distribution.

The logical consequence of this approach, and the most instructive feature of probabilistic risk assessment, is that if some or all of the input variables in a risk assessment are random variables, then the output variable -- the estimated risk -- is also a random variable. In other words, the estimated risk for a situation is not a point

value but a range or distribution of values. The importance of this result is at least two-fold: it allows one to see (literally as well as figuratively) the likelihood of any particular result, and it also allows one to judge the acceptability of the risk by more than a single yardstick. While risk management in deterministic paradigm consists of comparing a point value for estimated risk to a point value for acceptable risk as so called "bright line test," risk management in the probabilistic paradigm now consists of comparing a distribution of estimated risk to an acceptable distribution of risk. The following example illustrates these concepts.

Comparison of Deterministic and Probabilistic Approaches

Deterministic Approach

To give a numerical example, we estimate the increased lifetime cancer risk (ILCR) for a group of adults who (unwittingly) drank water from a contaminated well at a vacation property, first using the standard deterministic approach, and then using a probabilistic approach with an uncertainty analysis.

In the deterministic case, we estimate the average daily dose over a lifetime by using point values: the adults weighed 70 kilograms, drank 2 liters per day of water, and visited the vacation property 2 days per week for 10 weeks per year. These adults visited the house for 20 years. Using the "Land Method" to estimate a conservative point value for the exposure point concentration (US EPA, 1992, EPC), a local hydrologist estimated that the well water contained 130 micrograms per liter of chemical B (a known human carcinogen). We use this formula:

$$<ADD>_{life} = \frac{Conc \bullet IngR \bullet CF}{BW} \bullet \frac{D}{7} \bullet \frac{W}{52} \bullet \frac{Y}{70},$$

where:

$<ADD>_{life}$	=	average daily dose, averaged over a lifetime, $(\frac{mg}{kg \bullet d})$
Conc	=	concentration in drinking water (µg/l)
IngR	=	ingestion rate (l/d)
CF	=	conversion factor (mg/µg)
BW	=	body weight (kg)
D	=	number of days of exposure per week

W	=	number of weeks of exposure per year
Y	=	number of years of exposure in lifetime of 70 yr

Substituting the values with CF = 10^{-3}, we find $\langle ADD \rangle_{life} \sim 5.85 \bullet 10^{-5} \frac{mg}{kg \bullet d}$. Next, we multiply the average daily dose by the cancer slope factor (CSF) for chemical B by the ingestion route ($0.0289 \frac{kg \bullet d}{mg}$). The result, $\sim 1.69 \bullet 10^{-6}$, is the estimated point value for the incremental lifetime cancer risk (ILCR)

Probabilistic Approach for Variability

As discussed above, the fixed values just used over-simplify the history for this population. After talking with the people and doing some further field testing, some of the variables in the equations are better represented as probability distributions than as point values, precisely because variability was an intrinsic part of both the people's behavior and also of the aquifer from which they drank ground water. With this new information, we find that these probability distributions describe the population better than do the point values that they replace:

- The variability in Conc (concentration) is well described by a Triangular probability distribution with a minimum of 80, a mode of 85, and a maximum of 125, in units of μg/l;

- The variability in IngR (ingestion rate) is well described by a Normal or Gaussian probability distribution with a mean of 1.60 and a standard deviation of 0.20, in units of l/d;

- The variability in BW (body weight) is well described by a LogNormal or Gaussian probability distribution with an arithmetic mean of 70 and an arithmetic standard deviation of 10 in units of kg;

- The variability in D (days per week) is well described by a Uniform probability distribution with a minimum of 1.0 and a maximum of 2.5;

- The variability in W (weeks per year) is well described by a Uniform probability distribution with a minimum of 7 and a maximum of 11; and

- The variability in Y (years of exposure in a lifetime) is well described by a Triangular distribution with a minimum of 14, a mode of 16, and a maximum of 20.

All the other variables and conversions in the equation have the same point values as before. This example illustrates a common occurence: the "Land Method" often estimates an EPC (point value) that exceeds all measurments and the range.

With this new knowledge, we use a commercial software package to multiply the probability distributions and the point values in the equations for estimating $<ADD>_{life}$ and ILCR. Figure 1 shows the results of the convolution (as done by 500 repetitions of a Monte Carlo simulation in the software package). The estimated probability density function (PDF) and the estimated cumulative distribution function (CDF) in Figures 1A and 1B, respectively, now express the variability inherent in the population as a range of incremental lifetime cancer risk (ILCR) from ~$2.1 \cdot 10^{-7}$ to ~$2.0 \cdot 10^{-6}$. These graphs follow the format recommended by Ibrekk and Morgan (1983) by using dots to show the location of the arithmetic mean (~$6.6 \cdot 10^{-7}$) The point estimate calculated earlier (~$1.69 \cdot 10^{-6}$) occurs well above the 99^{th} percentile of the estimated distribution. These graphs convey much more information than did the point value calculated earlier.

Given an estimated distribution for risk, the risk manager(s) might use decision rules along these lines to render an opinion on the acceptability of the estimated risk: (i) is the median of the risk distribution less than 1 in a million? (here, yes); (ii) is the average of the distribution less than 1 in 100,000? (here, yes); and/or (iii) is the 95th percentile of the risk distribution less than 1 in 10,000? (here, yes). If the answer to all three of these questions is yes, the risk manager(s) might decide the distribution of risk is acceptable. In other words, the risk manager(s) may only look at selected percentiles or summary statistics when deciding if a risk is acceptable for a population.

The probabilistic paradigm is built on the fundamental definition of risk as the probability of adverse outcome. And it reestablishes the now blurred lines between risk management and risk assessment. Thus, in our view, the probabilistic assessment follows the two defining tenets of risk assessment, while the deterministic paradigm violates them both.

Probabilistic Approach for Variability including Uncertainty

Figures 2A and 2B, respectively, illustrate two types of uncertainty in this example.

First, each of these figures shows two solid lines, the first repeating the curve from its corresponding panel in Figure 1 and the second depicting the curve from a second (independent) simulation of n = 500 iterations. The small differences between the two solid lines gives the risk assessor and the risk manager a measure of the inherent stability of using only 500 iterations in the simulation. If anyone thinks that the difference between the two solid curves is unacceptably large, the risk assessor make the difference as small as desired by re-running the simulations with a greater number of iterations.

Second, each of these figures also shows two dashed lines that "bracket" the estimated distribution of ILCR from above and below. Figure 2B clearly shows how the dashed curves bracket the solid curves. What do the dashed curves represent?

After completing the analyses leading to Figures 1A and 1B, the risk assessor talked further with the hydrologist who had estimated the exposure point concentration for the concentration of chemical "B" in the ground water. This hydrologist emphasized the considerable uncertainty in his/her earlier results since it is so difficult to "backcast" ground water flows and concentrations. Upon reflection, the hydrologist stated that the distribution for variability in Conc (i) could have been as small as a Triangular probability distribution with a minimum of 40, a mode of 75, and a maximum of 100, in units of μg/l; but (ii) could have been as large as a Triangular probability distribution with a minimum of 90, a mode of 100, and a maximum of 150, in units of μg/l. Using this information on the uncertainty in the variability in Conc, the risk assessor calculated two sensitivity analyses to show this uncertainty as the two bracketing (dashed) curves in Figures 2A and 2B.

With additional information on the uncertainty in the variability in exposure factors, the risk assessor could complete a full uncertainty analysis of the variability in the population's exposure by having the software compute (hundreds of other combinations of uncertain distributions) and then draw graphs like Figures 2A and 2B showing all the lines (or probabilistic contours of the envelope of lines). These techniques go beyond the present example, but are well within the state of the art.

See, for example: Cullen & Frey, 1997; NCRP, 1996; Brattin et al, 1996; Cohen et al, 1996; Henrion, 1996; Frey & Rhodes, 1996; MacIntosh et al, 1994; Rai et al, 1996; Burmaster & Wilson, 1996; Burmaster & Thompson, 1996; Hattis & Barlow, 1996; Price et al, 1996; Hammonds et al, 1994; McKone, 1994; Hoffman, 1993; Frey, 1992; Finkel, 1990.

Given these bounding distributions for risk, the risk manager(s) can assess the value of collecting additional information to reduce the uncertainties (see, for example: Graham & Hartwell, 1997; Dakins et al, 1996; Thompson & Graham, 1996; Dakins, Toll & Small, 1994; Hammitt & Cave, 1991; Finkel, 1990; Evans, Hawkins & Graham, 1988; Finkel & Evans, 1987).

Discussion and Conclusions

An old adage in computer science holds that "The purpose of computation is insight."

For too long, risk assessors and risk managers -- and the American people -- have been crippled by US EPA's stubborn insistence that all risk assessments must use simplistic point values and 8th-grade mathematics that compound conservatisms beyond credulity. With risk assessors forced to use methods that systematically distort the analyses, risk managers have no insights into the many sources of variability in Nature and the many sources of uncertainty in human knowledge. Blinded to the insights that more powerful methods reveal, US EPA's risk managers cannot understand and manage the many competing risks that are inherent in all environmental issues. We will never live in a zero-risk world, and all interventions and substitutes have risks inherent in them. It is now time for the Agency to accept computational methods in use in many other disciplines for more than 50 years.

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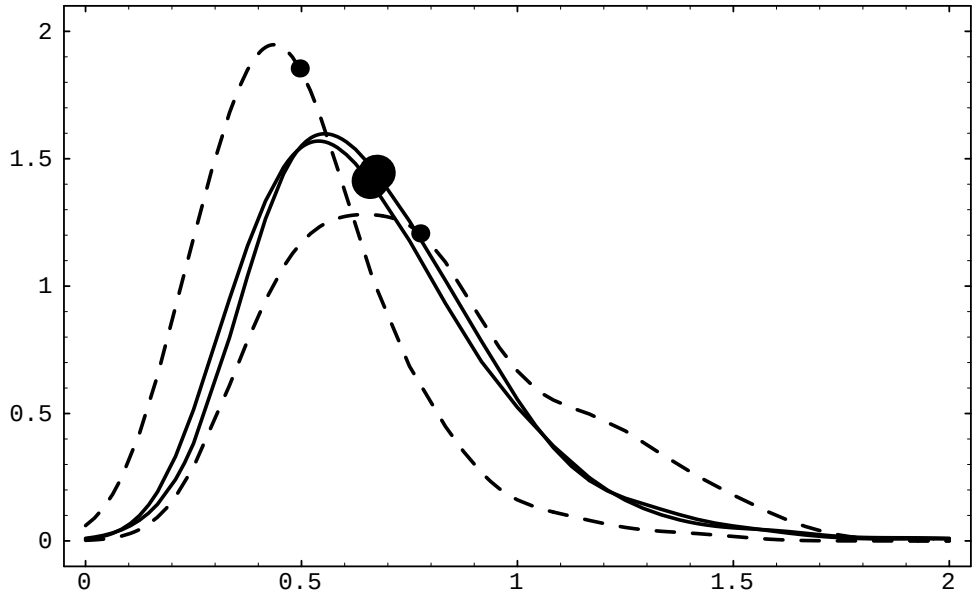

Figure 2A -- Estimated PDFs for ILCR showing AMeans as a Dots

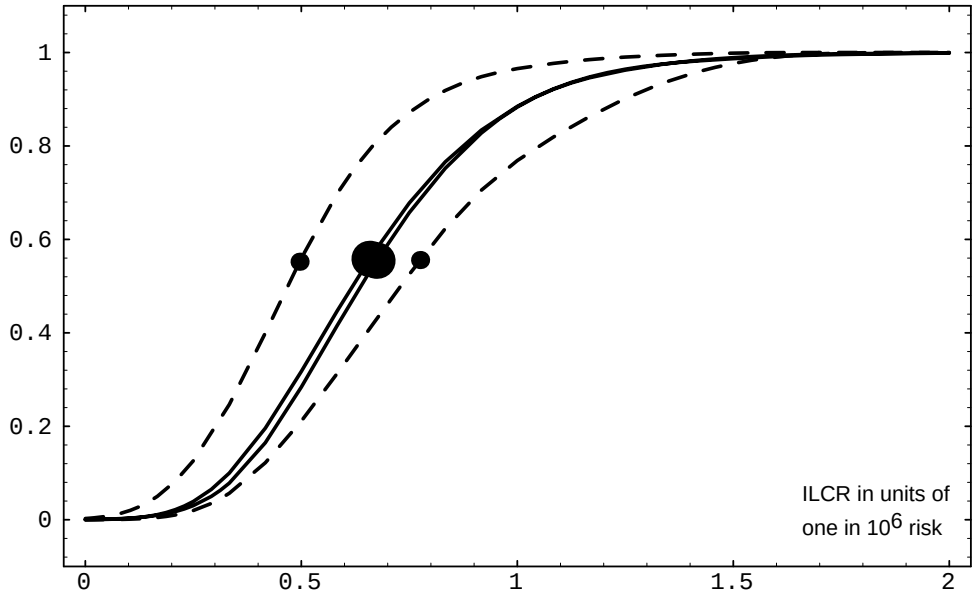

Figure 2B -- Estimated CDFs for ILCR showing AMeans as a Dots

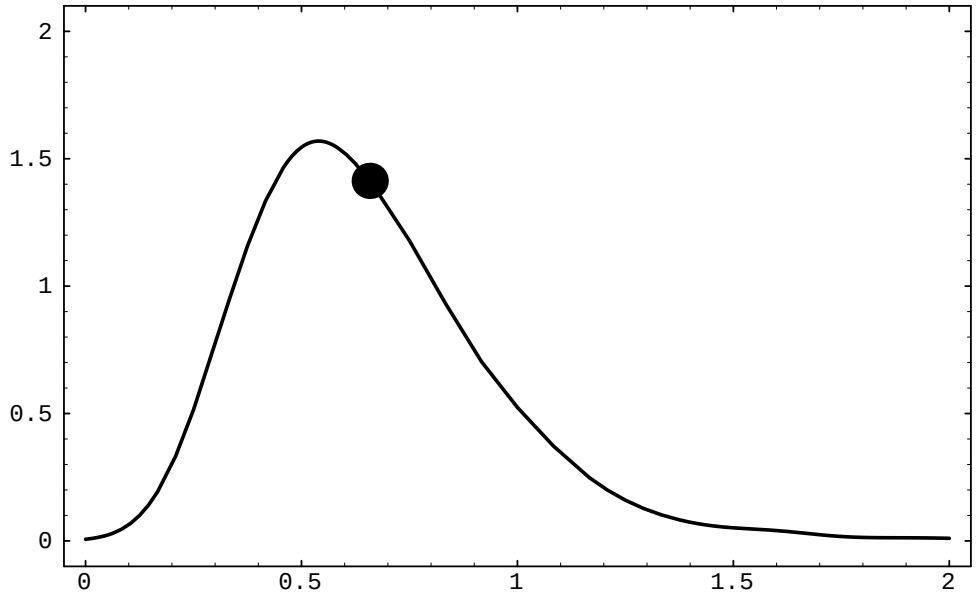

Figure 1A -- Estimated PDF for ILCR showing AMean as a Dot

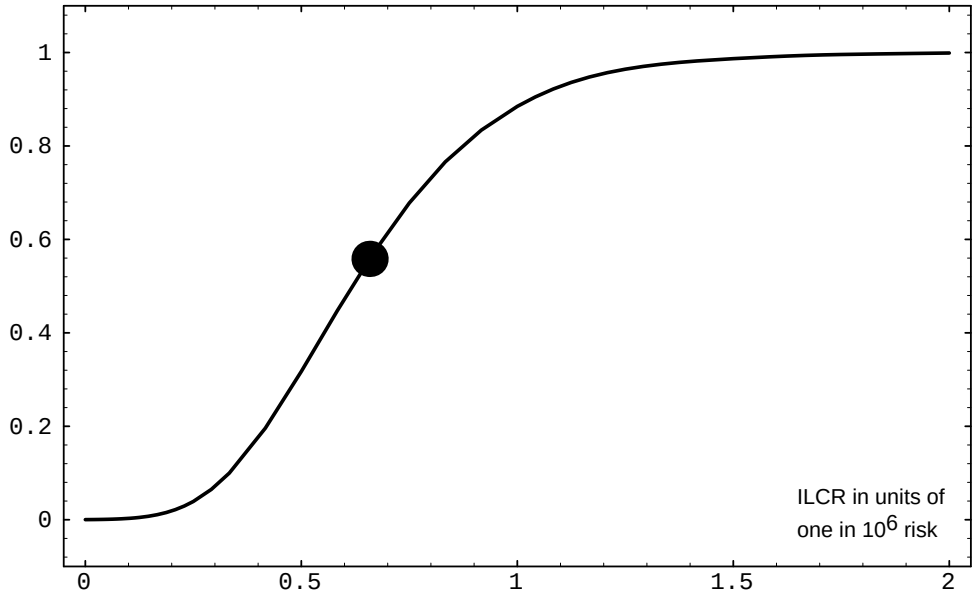

Figure 1B -- Estimated CDF for ILCR showing AMean as a Dot