A Framework for Risk Characterization of Environmental Pollutants

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Introduction

The EPA has recently been placing greater emphasis on environmental risk-based decision making. This emphasis applies to overall EPA strategy in addressing environmental problems and in specific EPA programs addressing specific environmental pollutants or media.

The Research Strategies Committee of the U. S. Environmental Petroleum Agency (EPA) Science Advisory Board (SAB) concluded that EPA needs to reshape its strategy for addressing environmental problems in the next decade and beyond. In addition to the current emphasis on federally-mandated controls that are put in place to clean up pollutants after they have been generated, the Agency must develop a strategy that emphasizes the reduction of pollution before it is generated. A strategic shift in emphasis from control and clean-up to anticipation and prevention is absolutely essential to our future physical, environmental, and economic health. Implementation of this concept requires a shift from “end-of-pipe” controls which were used effectively in the 1970’s under the Clean Air Act to alternative strategies.

Risk assessment will also play an important role in pollution prevention. The Pollution Prevention Act acknowledged the importance of risk assessment when it defined “source reduction” to mean any practice which:

"...reduces the hazards to public health and the environment associated with the release of such substances, pollutants, or contaminants."

Reduction in the quantity of overall pollutant discharges through substitution may actually be defeated if the new pollutants have greater toxic potential. Therefore, risk assessment is crucial in evaluating effectiveness of pollution prevention.
Risk Assessment and Risk Characterization

The National Research Council (1963) defined the four components of risk assessment: hazard identification, dose-response evaluation, exposure and risk characterization. To insure consistency, the EPA has issued guidelines on hazard identification, dose-response evaluation and exposure assessment.

Risk assessment is an interactive process between these four components as shown in Figure 1. Risk characterization is defined by both the U. S. National Academy of Sciences and the U. S. EPA as the estimation of human health risk due to harmful (i.e., toxic or carcinogenic) substances or organisms. Risk characterization studies are accomplished by integrating quantitative exposure estimates and dose-response relationships with the qualitative results of hazard identification.

Risk characterization provides the information link between risk assessment and risk management providing critical data to the risk managers. Risk management can occur at many levels, ranging from the individual (e.g., smoking) to industry to government. Risk characterization must provide useful data to allow for informed decision making.

Risk characterization can have a major impact on (and should be integral to) the risk management process. To fulfill this potential, risk characterization studies must be:

1. **Available.** Numerical risk characterization studies, as defined by the National Research Council and in the EPA Risk Assessment Guidelines Document of 1986, are relatively new and are often not available for key environmental decision at all levels.

2. **Technically defensible.** A decision-maker must be convinced that the complex technical components of a risk characterization study are based on sound scientific data. Simplifying assumptions made in the absence of scientific data should be thoroughly considered. Uncertainties in the risk estimates must be communicated to decision makers and to the public.

3. **Understandable.** Efforts to avoid simplifying assumptions to make risk estimates more realistic will inevitably lead to greater technical complexity. This complexity can increase to a point where only a handful of scientists are likely to judge the study results.

A balance between 1, 2, and 3 is therefore needed for risk characterization to be best utilized.

Based on a review of risk assessment studies, a simple predictive risk equation was developed which could be used to express most if not all of the key elements used in risk assessment. The four general equations that comprise the Predictive Risk Equation are presented in Figure 2. Representative units are shown and are useful to illustrate
dimensional consistency. Although the general equations are most relevant to carcinogenic risk assessments, they have also been modified to address noncarcinogenic effects (Pierson et al., 1991).

A Framework for Risk Characterization

The traditional Risk Assessment approaches were combined with elements of the Predictive Risk Equation to produce the Risk Characterization Framework as presented in Figure 3. It has been developed to encourage a systematic approach for analysis and presentation of risk characterization study results. This framework subdivides the four components of the risk assessment process (as defined by EPA and the National Research Council) into ten elements (Columns B through K in figure 3) to provide a refined and more systematic way of describing a very complex risk estimation process. Each of these elements is based on a term in a predictive risk equation. The equation allows independent computations of exposure, dose, lifetime individual risk, and risk to affected populations. All key assumptions in the predictive risk equation can be explicitly shown. This is important to understand the basis and inherent uncertainties of the risk estimation process. The systematic treatment of each of the ten elements in this framework aids in the difficult job of comparing risk estimates by different researchers using different methodologies. This allows for greater detail in examining the overall risk estimation process.

The four components of risk assessment are also covered in the framework. Hazard identification is covered in columns B through J of Figure 3 in a primarily qualitative manner; exposure assessment is covered by columns B through F, dose-response assessment by columns G and H, and risk characterization by columns I through K, though it actually integrates information from all previous steps. The framework has been subdivided into the four groupings of the predictive risk equation for characterizing exposure (columns C – E), dose (columns E – g), individual health effects (columns G – I) and population health effects (columns I – K). Brief descriptions of each column are described here and further described elsewhere.

Column B (Source Factors) is the starting point for the predictive risk equation. The estimation of risk can be based on the study of a single source emitting one or more pollutants of concern or the study of a pollutant or mixture that is emitted from one or more sources. Column 8, although descriptive in nature, provides information on the source(s) of the pollutant(s) under study including emission rates.

Column C (Pollutant Concentration) of the framework records the numerical data of exposure concentrations for each pollutant under study. The estimation of the pollutant concentrations will be based on different types of data depending on the focus of the study. Methods for estimating the concentration of indoor pollutants include direct measurement through sampling and analysis, modeling, analysis of biological markers, and questionnaires.
HAZARD IDENTIFICATION
(Does the agent cause adverse effects?)
- Data analysis relating chemical and exposure to disease produced.
- Characterization of chemical behavior within body.
- Inference whether toxic effects in one setting (e.g., animals) will occur in other settings (e.g., humans).

DOSE-RESPONSE EVALUATION
(What is the relationship between dose and incidence in humans?)
- A quantitative description relating the amount of exposure (or delivered dose) to the extent of injury or disease.

EXPOSURE ASSESSMENT
(What exposures are currently experienced or anticipated under different conditions?)
- A quantitative description relating the magnitude and duration of concentrations to the size and nature of the population exposed.

RISK CHARACTERIZATION
(What is the estimated incidence of the adverse effect in a given population?)
- A numerical estimate of the individual probabilities of an adverse effect based on estimated exposure and dose-response factors.
- A numerical estimate of the number of cases of the adverse effect in the exposed population.
- A discussion of assumptions and uncertainties in the risk estimate.

Figure 1: Traditional components of risk assessment.
Figure 2. Elements of the predictive risk equation.
Measurements can be taken at any location to determine a time weighted averaged concentration for a setting as a whole. Alternatively, individuals can wear personal exposure monitors (PEM) for some specified period of time. When used in combination with stationary monitors, PEMs can provide a profile of total exposure partitioned into separate microenvironments. Modeling of exposure requires data on source emission rates, ventilation and infiltration, removal by adsorption onto surfaces, mixing, volume of space in which exposure occurs, and of activity patterns of individuals in each of the environments being modeled. Models are particularly useful in making exposure estimates in temporal and spatial regimes where measured concentrations are not available and in relating exposure concentrations to particular sources. Thorough evaluation (“validation”) of new models is extremely important.

Biological makers result from the analysis of the physiological fluids of exposed persons. For example, the presence of nicotine and its major metabolite, cotinine, in biological fluids is typically a good indicator of exposure to tobacco, tobacco smoke, or environmental tobacco smoke. The determination of nicotine and cotinine in saliva, blood, or urine of active or passive smokers can be used effectively to estimate the level of exposure to these substances.

Questionnaires may also be useful tools for assessment of exposure to pollutants without specific quantitative data, especially with respect to time activity patterns of individuals in specific environments and their estimate of exposure (e.g., number of cigarettes smoked at home each day). Developing questions that elicit unambiguous replies and using replies to property make quantitative estimates of exposure are especially important.

When using averages, the selection of the appropriate averaging time can be critical to the characterization of health effects. For cancer health effects, lifetime averages are adequate. However, noncancer effects are generally tied more directly to actual exposure patterns and the associated dose than are cancer effects. As a result, greater detail is desirable for the exposure assessment. Ideally, information that should be included in column C are peak and average concentrations (either from measurement or model estimation) and, if possible, a concentration profile. For example, peak concentrations may be reported in various time increments such as hourly averages, 15-min averages, or 8-hr averages, each having different associated health effects. Averages may also prove useful in defining exposures associated with certain activities or events allowing total exposure to be calculated on the basis of number of events.

Column D (Exposure Duration and Setting) of the framework combines the identification of each environmental setting in which exposure occurs and an estimation of the time spent in that environment.

The duration of exposure is expressed differently for different health effects of concern. For carcinogenic effects, duration is typically expressed as total hours, or days of exposure during one’s lifetime. For example, if an individual is exposed every day of their
life then exposure would be 25,550 days, assuming a 70-year lifetime. For noncarcinogenic effects, health effects are more a function of duration and one is also concerned about acute health effects from short-term exposures at elevated concentrations. Short-term durations of hours or even minutes may be of equal importance. Information presented in Column D should include quantitative descriptors of any relevant time-activity patterns including duration and time of occurrence for any exposure. Information would also be included from other exposures or activities to account for synergisms or sensitivities.

Column E (Exposure) whenever possible, should expressed as the product of the concentration of pollutant to which one is exposed in a particular setting times some specific time period.

A chronic exposure is assumed to be relatively constant over a long period of time and thus, what is typically calculated is an average daily pollutant concentration to which one is exposed. This approach is standard for calculating lifetime exposures to carcinogens and assumes sources and patterns of living do not change over a lifetime. However, when dealing with less than lifetime exposures (i.e., acute or subchronic) and an array of noncarcinogenic endpoints each of which are dependent on both pollutant concentration and duration of exposure, it is important to make both Column C and Column D factors explicit.

The terms exposure and dose are sometimes used interchangeably. However, the framework distinguished between these two forms by specifically incorporating exposure duration and by providing a set of dosimetry factors that relate the estimated exposure to the dose received by an individual. As shown in Column F (Dosimetry Factor) of the framework, and previously illustrated in Figure 2, these factors include: contact rate, absorption rate, average body weight, average lifetime, regional surface area of the lung, and regional deposited dose ratio. Other factors may also be required in specific analyses.

Column G (Dose) of the framework is the product of exposure estimates and the variety of modifiers discussed above. Dose is expressed as pollutant mass per kilogram of body weight per day (mg/kg-d). For toxicological studies involving animals under controlled conditions, the pollutant dose can be directly measured. For epidemiological studies correlating human disorders with exposures, the dose must be estimated. Information presented in column G would include peak, cumulative, and average dose, and, if possible, peak cumulative and average organ burden.

Column H of the framework (Response Factor) describes the magnitude of the response of an individual to a given dose of the substance. For practical reasons, human observational data are usually available for few of the different possible chemicals and exposure routes. It is therefore necessary to derive mathematical models of the dose-
response relationship based on the best understanding of the mechanism of action of the toxic substance.

The dose-response relationship for carcinogens is usually expressed as a potency factor defined as the 95% upper confidence limit of the human excess lifetime cancer risk associated with one unit of lifetime exposure to the carcinogen measured in units of \((\text{mg/kg-day})^{-1}\). Potency factors have been estimated by EPA’s Human Health Assessment Group (HHAG) for many carcinogens. However, there are also many substances suspected of being human carcinogens for which HHAG has not estimated a potency factor due primarily to a lack of adequate data. For those compounds not yet reviewed by HHAG have not reviewed, quantitative estimates of risk may not be possible.

Methodologies to estimate the chance of one or more toxic endpoints for noncarcinogens are much less developed than carcinogenic risk assessments. The U.S. EPA has used the concept of thresholds rather than potency factors for noncarcinogenic health effects. Noncancer effects involve multiple target organs, each having its own dose-response relationship threshold, and range of effects of varying degrees of severity for each pollutant, each of which may have its own dose-response factor. Ideally, these multiple dose-response factors could be represented in column \(H\) of Figure 3.

In their simplest form, carcinogenic risks are estimated by multiplying a lifetime average daily dose (Column \(G\)) in units of milligrams per kilogram of body weight per day, by a potency factor (Column \(H\)), in units of lifetime risk per unit of exposure \((\text{mg/kg-day})^{-1}\). Column \(I\) (Individual Risk) of the framework gives estimates of the risk for an individual exposed at the given exposure. Cancer risks are usually presented as lifetime excess risk.

For noncarcinogenic agents, it is usually assumed that there is a threshold dose below which there is no effect. These thresholds differ according to the target organ and effect studied. The ratio of the exposure level to to threshold dose gives some indication of the likelihood of occurrence of the adverse health effects associated with exposure to the toxic substance. Threshold-based doses are most commonly established for chronic exposures, but may also be established for acute and subchronic exposures.

The severity of the effect, both in terms of intensity of response and in threat to the health of the overall organism is equally important in characterizing noncancer effects. Severity as a threat to the sole organism is not amenable to direct quantitative measurement though ordinal ranking schemes have been proposed to assess severity (EPA, 1990). When possible, some indication of the severity of effect should be included with the likelihood of an individual response.

Column \(J\) (Exposed Population) of the framework is provided for the types and number of affected subpopulations included in a risk analysis. A numerical estimate of the number of individuals in each subpopulation is therefore required.
subpopulation must be linked to a specific exposure scenario. Individual responses vary greatly within a population (column J of Figure 3). Especially for noncancer effects, the susceptibility of an individual to a specific adverse effect dictates the level of a response. Individual susceptibilities are believed to follow some statistical distribution within a population. Additionally, susceptibility may be rooted in personal behavior, activities, and exposures associated with those activities. Individual sensitivities are distributed among a population and can include sensitive subpopulations (e.g., children in the case of low-level lead exposure), genetic predispositions (e.g., enzyme deficiencies), other exposures (e.g., smoking), preexisting conditions (e.g., asthma), and illness. It is desirable to characterize exposed populations in column J on the basis of their sensitivities. A distribution should be obtained that incorporates variability associated with age of the population, exposure levels associated with different activity patterns and microenvironments, and the susceptibility within the population to a specific effect. Column K of the framework (Risk to Exposed Population) is typically expressed as the expected or observed number of cases in the population. Risks estimated can be determined in a deterministic fashion with a predictive risk equation as described in Figure 3. Alternatively, when sufficient human data allows, a statistical analysis of epidemiologic data can be used to obtain a risk estimate in Column K. In the latter case, exposures (Column E) related to sources (Column R) must then be ‘backward calculated’ (going from the right side of the framework to the left side) in order to suggest a cause and effect relationship.

Discussion of Uncertainties

Characterization of risk often depends on the data available and the way the analyst collects and organizes these data. The more common risk characterization estimates require a two-step procedure whereby a single point estimate is calculated for individual lifetime risk for an exposed population and point estimates aggregated across all exposed populations to get a population risk. Uncertainty in estimates of both individual lifetime risk and population risk should be addressed either qualitatively or quantitatively.

The existing methods for risk characterization are far from ideal, largely because of data limitations and incomplete knowledge of the biological mechanisms of action of toxic agents on the human body. There are four major sources of uncertainty in estimating point risks of adverse health effects:

1. Uncertainty due to statistical sampling issues;
2. Uncertainty in the exposure or dose-response models;
3. Uncertainty in the input parameters for these models; and,
4. Uncertainty due to lack of completeness in the models.

At each point in the risk characterization process where an uncertainty exists, an assumption or scientific judgement must be made in lieu of firm scientific evidence.
Specific examples of uncertainties that require the insertion of some assumption into the risk characterization process include those related to:

- Specification of an exposure scenario;
- Extrapolation from animal to human exposures;
- Extrapolation from high to low doses; and
- Extrapolation from one route of exposure to another.

Under ideal circumstances each uncertainty should be assigned individual and joint probability distributions, from which average or worst case point estimates of adverse health effects are generated. In addition, these probability distribution should be used to perform a sensitivity analysis for the point estimates for each input parameter and to generate overall probability distribution for the estimated risks.

Although considerable uncertainties exist in risk assessment methodologies and their applications, risk assessment has been adopted by government agencies in the United States and elsewhere to provide a quantitative and consistent framework for systematically evaluating environmental health risks and options for their control. The major criticisms of the methodology are that the data requirements are both time and resource intensive and that scientific judgement is often presented as scientific fact. The information needed to quantify exposure does not exist and, in some instances, the availability of data may not even support logical assumptions to be made regarding exposure. Second, scientific judgement embedded in all risk assessments needs to be understood and communicated to decision makers and other users of the risk information. This requires those knowledgeable in risk assessment to be accessible and to have access to the decision makers.

Conclusions

Risk characterization will likely play an increasingly important role in future pollution prevention programs. Reducing the quantity of waste releases may not alone be beneficial if there is not a concomitant reduction in risks to health and/or the environment, The risk characterization framework provides a methodology to evaluate and compare the effectiveness of various pollution prevention strategies. The framework provides a systematic way of describing a very complex risk estimation process. The systematic treatment of the ten elements of the framework aids in the difficult job of comparing risk estimates by different researchers or by different exposure profiles resulting from different pollution prevention methods.

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