Principles of Risk Assessment: Overview of the Risk Assessment Process

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There are three different approaches to chemical risk assessment which will be considered in this paper. The U.S. Environmental Protection Agency (EPA) Cancer Risk Assessment includes some of the approaches used by the International Agency for Research on Cancer (IARC). The Agency for Toxic Substances and Disease Registry (ATSDR) effort is an evaluated database approach similar to that used in the National Institute for Occupational Safety and Health (NIOSH) Criteria Documents and in the documentations prepared by the Occupational Safety and Health Administration (OSHA) for the Permissible Exposure Limits (PELs) and those of the American Conference of Governmental Industrial Hygienists (ACGIH) for the Threshold Limit Values (TLVs). A third approach is used by the Committee on Toxicology.

Introduction

Although risk assessment, as it is known today, is less than 20 years old, it is derived from that part of toxicology called hazard evaluation which is almost as old as toxicology itself. There are differences, however, between what was done in hazard evaluation and what is done today in risk assessment.

Traditionally, hazard evaluation has been a judgmental decision based on information concerning the agent, the subject, and the exposure. The first step in hazard evaluation is to characterize the toxicity of the agent; this is accomplished by identifying all of the potential adverse effects that can result from either acute or chronic exposure to the agent and by establishing the dose–response relationship for each of these adverse effects. The next step is to determine whether the tox database obtained with the test species is appropriate for the subject or target species and for the actual exposure conditions.

In those cases where the tox data are relevant and where there is a threshold or no-effect level for the specific adverse effect of interest, then the tolerance can be established by simply dividing the No-Observed-Effect Level (NOEL) by an appropriate safety factor. The goal in this approach is to predict a "safe" dose for the target species and, except for those adverse effects for which thresholds cannot be clearly demonstrated, this continues to be the most practical and widely used approach for protecting the health of the public, workers, and military personnel against the adverse effects of exposure to chemicals.

During the early 1970s, there was growing concern about cancer and mutagenesis. Coupled with the creation of the EPA and the growing ability of chemists to detect vanishingly small amounts of environmental contaminants, this concern led to demands for a new approach to risk assessment. Along with many other groups, the National Academy of Sciences/National Research Council (NAS/NRC) was involved in this effort and subsequently issued two reports that had a major impact in this area. One of these was the 1977 report of the Safe Drinking Water Committee, which was sponsored by the EPA, and the other was the 1983 report on Risk Assessment in the Federal Government, which was sponsored by the Food and Drug Administration (FDA). In the second chapter of the first Drinking Water Report, a subcommittee presented an analysis of risk assessment which was "state of the art" at that time. They defined the following four general principles for risk assessment:

1. Effects in animals when properly qualified are applicable to humans.
2. Methods do not exist to establish thresholds for some long-term effects.
3. Use of the maximum tolerated dose (MTD) is a necessary and valid approach to detect carcinogens.
4. Materials should be assessed in terms of their risk rather than as "safe."

These principles plus the recommendations in the report concerning high- to low-dose extrapolation provided the scientific basis for this new approach to risk assessment and set the stage for the second report, which focused on policy and procedures for managing the process of Risk Assessment in the Federal Government. This second report clearly divided risk management from risk assessment and then subdivided risk assessment into four steps: hazard identification, dose–response assessment, exposure assessment, and risk characterization. The latest topic to be added to this classification is risk communication which has also been addressed by a NAS/NRC committee, a Council on Environmental Quality report, and numerous other workshop and

conference reports.

The evolution of risk assessment methodology will undoubtedly continue. At this point in time, there are four areas that should be carefully examined and evaluated.

1. The two approaches to risk assessment — the threshold approach and the extrapolation approach — should be considered to be complementary rather than competing methodologies. The existence or lack of a threshold should determine which approach to use in risk assessment.
2. To improve the threshold approach to risk assessment, safety factors should be used that include appropriate adjustments for differences in kinetics and sensitivity between the test and target species. The concept of a "safe" dose should be replaced with an indication of actual risk.
3. To improve the nonthreshold approach to risk assessment, best estimates rather than upper-bound limits of risk should be provided, and the worst-case assumptions currently used in this approach should be replaced with actual data derived from the target species. The use of kinetic data in this approach is a good first step; however, we must also ensure that the model is capable of dealing appropriately with the relevance of the animal data to the target species and that it addresses such issues as the lack of a dose–response, species differences in susceptibility, and the like.
4. One of the major problems, if not the major problem, with the current state of risk assessment is lack of credibility. Since we often consider some of our predictions to be better than others, we need to develop a good system for communicating this information to the public in a logical and understandable fashion. We need to be able to explain why we are more concerned about Agent A than Agent B even though they have identical Q* values or GRAS status. We need to convince the public and our peers that it is not the chemical but the dose that determines the risk. It would also help if risk assessors would focus on areas of consenus rather than on confrontation, since the public is confused and justifiably angered when they are sent mixed signals. A good place to start would be to compare the toxicological and epidemiological predictions because these are the two disciplines that contribute most directly to assessing risk from chemical exposure. In those situations where toxicology and epidemiology are giving us different answers, we need to determine why the answers are different and, if possible, to reconcile the difference. In order to accomplish this, we will need to identify and defend all of the assumptions and uncertainties that we have used; we will also need to provide adequate documentation so that the next investigator can replicate the process. If we can do this in a way that is readily understood by the public, we will help them decide whether the risk assessment is a "whitewash" or a "witch hunt."

In conclusion, there is a quote by Albert Einstein that sums it up well. "The right to search for truth implies a duty: One must not conceal any part of what one recognizes to be true."