



Project Summary

Workshops for the Development of Methodology for Health Risk Assessment

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On September 29-30, 1982 and July 11-12, 1983, fifty environmental scientists from industry, academia, and the U.S. Environmental Protection Agency (EPA) met in Cincinnati to explore methods to assess the risks to human health from exposure to multiple chemical pollutants. In two workshops sponsored by EPA's Cincinnati-based Environmental Criteria and Assessment Office (ECAO), the scientists examined all relevant routes and durations of exposure to update and expand the single-chemical risk assessment methods developed by ECAO.

The first workshop investigated a wide range of possible approaches to assessing risks from exposure to multiple chemicals. The second workshop was limited to a discussion of five methods to evaluate risks identified in the first workshop as having the most potential for early application, including interspecies conversions, less-than-lifetime exposure, and role of pharmacokinetic data.

This Project Summary was developed by EPA's Environmental Criteria and Assessment Office, Cincinnati, OH, to announce key findings of the research project that is fully documented in three separate reports (see Project Report ordering information at back).

Introduction

The U.S. EPA's Environmental Criteria and Assessment Office (ECAO) in Cincinnati sponsored two workshops in 1982 and 1983 to bring together scientists

from government, industry, and academia to review and discuss methods for health risk assessment of chemical mixtures. An important secondary purpose of these meetings was to revise and add to the previously published health assessment guidelines (Federal Register, 1980) for assessing the chronic or lifetime health risk of single contaminants so that the more complex questions associated with exposure to chemical mixtures could be addressed.

EPA's interest in the development of risk assessment methodology for multiple chemicals stems from recognition of the nature of actual exposures. The Agency has already regulated public exposure to several mixtures including coke-oven emissions and auto and diesel exhaust. Now, with the implementation of Superfund, the Agency must develop methods for determining the risks posed by thousands of unregulated sites in order to set priorities and direct cleanup efforts. In addition, the Agency must respond to imminent hazards posed by chemical spills, and toward that goal, ECAO has developed a rapid response assessment system. Toxicity data are stored in a computer and used to make an assessment that can be provided to state or regional officials within 48 hours. Multi-chemical assessments also have a role in other emergency response and remedial action activities such as determining the reduction in risk after a cleanup of a hazardous site. All EPA programs are often dealing with mixtures rather than single pollutants.

Approaches to Risk Assessment for Multiple Chemical Exposures Workshop, September 29-30, 1982

The developing methodology for assessing risks from exposure to multiple chemicals is based on the current methodology for identifying effects of chronic exposure to a single chemical from a single route.

The ECAO in Cincinnati developed original methods for deriving ambient water quality criteria and for conducting risk assessments on a specific group of solvents. The methodology for deriving ambient water quality criteria focused on chronic exposure to a single chemical from a single route of exposure. The solvent methodology expanded this approach to consider the effects of a single chemical by all relevant routes of exposure (oral, dermal, and inhalation) and for all exposure durations (acute, short-term, subchronic, and chronic). In both methodologies, risk assessments for carcinogens associated an exposure level with a particular incidence of cancer using a nonthreshold model that is linear at low doses. Risk assessments for systemic toxicants use a threshold model deriving an estimated acceptable daily intake (ADI) by dividing the no-observed-adverse-effect level (NOAEL) by some uncertainty factors.

The new methodology examined in the first workshop, when fully developed, will be used to assess risks in specific hazardous sites. Ideally, the methodology developed will be used to estimate from the available exposure data, the types of health effects that might be expected, the incidence of these effects, and an estimate of the relative hazard of each site. Thus, some of the major areas for methodology development include a reasonable approach for multiple chemical exposures, a system for combining weighing adverse effects, and the selection of a reasonable extrapolation model for toxic effects.

These and other relevant issues were addressed during the first workshop held on September 29 and 30, 1982. As shown in the listing below, the first day of the workshop focused on the subject of "Systemic Toxicants" (noncarcinogenic effects). Presentations were made on seven aspects of this topic. Each presentation was followed by prepared critiques from other attendees and then by a discussion session. Presentations on the second day of the workshop addressed four aspects of the subject of health assessment of exposures to chemical mixtures.

Systemic Toxicants (September 29, 1982)

1. Acceptable Daily Intake
2. Interspecies Conversion of Dose and Duration of Exposure
3. Risk Assessment for Less-Than-Lifetime Exposure
4. Incidence and/or Severity of Effects
5. Route-to-Route Extrapolation and the Pharmacokinetic Approach
6. Multiple Route Exposures
7. The Impact of Carcinogens in Risk Assessment of Chemical Mixtures

Health Assessment of Exposures to Chemical Mixtures (September 30, 1982)

1. Outline of Issues and Review of Present Approaches
2. Assessment of Exposure
3. Subpopulations at Greater Risk
4. Biological Bases of Toxicant Interactions and Mathematical Models

Selected Approaches to Risk Assessment for Multiple Chemical Exposures: Progress Report on Guideline Development at ECAO-Cincinnati—Workshop, July 11-12, 1983

The primary objective of this workshop was to encourage discussions of the development and implementation of multiple chemical assessment methodology. To provide structure to these discussions, the meeting was divided into three sessions.

In Session I, specific selected approaches were proposed for five subjects discussed in the September 1982 workshop. During Session I of the July 1983 meeting, discussion focused on whether or not the approach was acceptable as stated. If not, an attempt was made to amend the approach to achieve consensus or to clearly identify remaining problems or disagreements.

The following topics were presented for consensus: interspecies conversion of dose and duration of exposure; calculation of risk for partial-lifetime exposure to carcinogens or toxicants; calculation of ADIs based on quantal, continuous, or graded response data; pharmacokinetic approaches that can be used for conversion among various exposure routes; and methods for multichemical assessment.

In Session II, several new topics were presented that had not been previously discussed or had been only touched upon in previous meetings. Presentation of brief outlines of the issues was followed by discussion to elicit comments from participants about the direction development that these issues should follow. New topics included the use of structure-activity relationships, special methods for reproductive endpoints, and use and biological justification of mathematical models.

In Session III, issues introduced at previous meetings, but needing further development, were discussed in four workgroups. Invited scientists and the ECAO staff discussed the strengths and limitations of alternative approaches in order to develop guidelines. The objectives of this session were eventual development of scientifically defensible approaches reflecting current knowledge and identification of options that reflected consensus.

The following topics were discussed in the three sessions of the July 11-12, 1983 workshop:

Consensus Topics (Session I)

1. Interspecies Conversion of Dose and Duration of Exposure—Noncarcinogenic Toxicants
2. Health Risk Assessment for Less-Than-Lifetime Exposure—Toxicants and Carcinogens
3. ADIs Based on Quantal, Continuous or Graded Data
4. Pharmacokinetic Approach for Route-to-Route Conversion
5. Multiple Chemical Assessment

Presentation of New Topics (Session II)

1. Approaches Using Structure-Activity Relationships
2. Use of Reproductive Effects as Endpoints in Risk Assessment
3. Use and Biological Justification of Mathematical Models

Workshops (Session III)

1. Consideration of High Risk (Sensitive) Subgroups in Health Risk Assessment
2. Assessment of Multiple Route Exposure
3. Ranking the Severity of Effects
4. Use of Exposure Data in Assessing Health Risk

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This Project Summary covers three separate reports, entitled:

"Approaches to Risk Assessment for Multiple Chemical Exposures," (Order No. PB 84-182 369; Cost: \$22.95, subject to change)

"Selected Approaches to Risk Assessment for Multiple Chemical Exposures: Progress Report on Guideline Development at ECAO-Cin," (Order No. PB 84-226 992; Cost: \$16.95, subject to change)

"Selected Approaches to Risk Assessment for Multiple Chemical Exposures: Appendix," (Order No. PB 84-227 008; Cost: \$16.95, subject to change)

The above reports will be available only from:

**National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Telephone: 703-487-4650**

The EPA authors can be contacted at:

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