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Environmental Protection  
Agency

Office of the Administrator  
Science Advisory Board  
Washington, D. C. 20460

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May 1989

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# **Report of the Environmental Effects, Transport and Fate Committee**

## **Evaluation of the Proposed Guidelines for Exposure-Related Measurements**



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF  
THE ADMINISTRATOR

May 19, 1989

The Honorable William Reilly  
Administrator  
U.S. Environmental Protection Agency  
401 M. Street, S.W.  
Washington, D.C. 20460

Dear Mr. Reilly:

The Environmental Effects, Transport and Fate Committee of the Science Advisory Board has completed its review of the Risk Assessment Forum's proposed Guidelines for Exposure-Related Measurements. The review was conducted at the request of EPA's Risk Assessment Forum, and was conducted on December 2, 1988, in Washington, D.C.

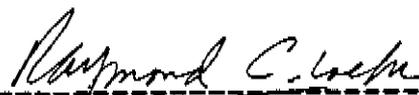
The Subcommittee recognizes these proposed guidelines as a logical complement to the previously issued Guidelines for Estimating Exposures. The prior guidelines, published and reviewed by the SAB in 1986, provide a framework for exposure assessment that may be integrated with the current guidelines resulting in a useful tool for exposure assessors. The Committee recommends that such integration take place with careful attention to the necessary linkages between measurements and modeling.

In addition to integration of the two sets of guidelines, the Committee recommends some modifications. Since the guidelines address exposure assessment for human health effects, this bias should be acknowledged. Alternatively, the guidelines, which have generic elements that can be brought to bear on effects to ecosystems, should be expanded to encompass exposure assessments in an ecological context. The focus and intended audience of the guidelines also need to be defined, and revisions made accordingly. The Committee discussed quality assurance and control stringency, the importance of exposure duration considerations, and needs concerning development and analysis of data. In addition, a recommendation was made to incorporate demographics, population dynamics, and population activity patterns into the process for assessing exposures. Finally, the Committee requests that the guidelines be amended to include references to other bodies of work that contain useful information on exposure assessment.

Independent comments were received from two members of the Indoor Air Quality and Total Human Exposure Committee. These members reviewed the Exposure Measurement Guidelines and provided a response. These independent comments are attached to the report to provide further feedback and critiques of the Guidelines.

The Subcommittee appreciates the opportunity to conduct this scientific review. We request that the Agency formally respond to the scientific advice transmitted in the attached report.

Sincerely



-----  
Dr. Raymond Loehr, Chairman  
Executive Committee  
Science Advisory Board



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Dr. Rolf Hartung, Chairman\*  
Environmental Effects,  
Transport and Fate  
Committee

ENC

cc: Dorothy Patton  
Michael Callahan  
Bill Wood  
Peter Preuss  
Donald Barnes

\* Dr. Hartung served as Chairman until December 31, 1988. Dr. Ken Dickson currently serves as Chairman of the Environmental Effects, Transport and Fate Committee. Since this review was initiated during Dr. Hartung's tenure, his efforts have seen it to completion.

U.S. ENVIRONMENTAL PROTECTION AGENCY

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\* Drs. Leaderer and Lippmann joined the Environmental, Effects Transport and Fate Committee for this review, contributing expertise in epidemiology and exposure assessment.

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**EVALUATION OF THE PROPOSED GUIDELINES FOR  
EXPOSURE-RELATED MEASUREMENTS**

**1.0 EXECUTIVE SUMMARY**

The Committee considered the draft guidelines for exposure-related measurements to provide a useful introduction to the concepts that form the basis for techniques designed to measure and estimate human exposure. The guidelines represent a logical complement to the Guidelines for Estimating Exposures that were published and reviewed by the Board in 1986. It is recommended that these guidelines be integrated into a single guideline document. The integration will require careful attention to the linkages between measurements and modeling.

The document requires a number of revisions, including a clarification of the intended audience, and an extension to explore the role of measurements for assessing exposures that detect ecosystem effects. In addition, the Committee pointed out the need for technical corrections regarding industrial hygiene measurements, and made comments on sampling design and data interpretation. The Committee also pointed out the need for increased attention to the study of variability in the context of defining uncertainty in exposure assessments.

## 2.0 INTRODUCTION

### 2.1 Request for Review

At the request of EPA's Risk Assessment Forum, the Science Advisory Board agreed to conduct a scientific review of the Proposed Guidelines for Exposure-Related Measurements. The SAB's Environmental Effects, Transport and Fate Committee performed this review with the assistance of other SAB members recognized as experts in exposure assessment.

The Committee was requested to review the adequacy of the scientific basis of the Guidelines for Exposure-Related Measurements including these specific issues: adequacy of guidance for interpreting contaminated blanks, interpretation of data at or near the limit of detection, approaches to assessing uncertainty, and the definition of specific scientific terms. In addition, the guidelines were examined in relation to previously identified Strategies for Improved Exposure Assessment<sup>a</sup>.

### 2.2 Subcommittee Review Procedures

The Environmental Effects, Transport and Fate Committee met on December 1 and 2, 1988, in Washington, D.C. On the second meeting day, Drs. Lippmann and Leaderer joined the Committee to complete the review of the exposure guidelines. Briefings were provided on the guideline formulation process, and on past SAB involvement and recommendations. An overview of the exposure guidelines was given by Michael Callahan, Director of the Exposure Assessment Group of the Office of Health and Environmental Assessment within EPA's Office of Research and Development.

Prior to receiving this briefing, the Committee was provided with a document entitled "Draft Guidelines for Exposure-Related Measurements" and dated 10-31-88. The introduction to this document is attached as Appendix A. In addition, the guidelines have been published in the Federal Register, Volume 53, Issue 232 pages 48830-48853.

Following the receipt of the draft document and the described briefings, the Committee discussed the guidelines in detail. Suggestions, conclusions, and recommendations were developed at the meeting. In addition, both general and specific written comments on the guidelines were submitted for assembly by the Chair. These comments were assembled into a draft report, which was circulated for comment and consensus, prior to issuance of this final report.

<sup>a</sup> USEPA. Science Advisory Board. 1988. Future Risk: Research Strategies for the 1990s. Appendix B: Strategies for Exposure Assessment Research. pp 20.

### **3.0 GENERAL COMMENTS**

The draft Guidelines provide a good exposition of the concepts that form the basis of exposure measurement techniques. They provide a logical and internally consistent quantification framework by which human exposure may be measured and evaluated. They represent a logical complement to the 1986 Guidelines for Estimating Exposures, and are an essential component of an overall program to insure scientific quality and technical consistency in risk assessment.

### **3.1 Integration of Exposure Guidelines**

The Committee was asked to address the integration of the proposed Guidelines with a document promulgated previously by the Agency. This document, entitled "Guidelines for Estimating Exposures," was published in the Federal Register (51 FR 34042) in 1986. The Science Advisory Board conducted a review of this document as part of its 1985 review of EPA's Risk Assessment Guidelines for Carcinogenicity, Mutagenicity, Chemical Mixtures, Developmental Effects, and Exposure Assessment.

A conclusion of the prior review was that the 1986 Guidelines for Estimating Exposures provide the framework for exposure assessment in a useful, diagrammatic way that aids overall understanding. This framework is missing from the present draft document.

The current draft Guidelines are logical correlates to the Guidelines for Exposure Assessment of September 24, 1986, which emphasized general concepts. The concepts expressed in both documents are so closely related that integration of the two is a logical step. This integration should provide a clear framework for exposure assessment.

In the process of integrating the two documents, it is important to consider previous comments made by the SAB on uses and abuses of mathematical models. These comments are detailed in a Report of the Environmental Engineering Committee entitled "Resolution on Use of Mathematical Models by EPA for Regulatory Assessment and Decision-Making" (EPA-SAB-EEC-89-012, January, 1989). The development of an integrated set of guidelines for exposure assessment will require careful attention to the linkages between measurement and modeling. Competent exposure assessments require an integrated approach that encompasses both measurements and modeling.

#### **Recommendation:**

**THE GUIDELINES FOR ESTIMATING EXPOSURES (SEPT., 1986) AND THE DRAFT GUIDELINES FOR EXPOSURE-RELATED MEASUREMENTS SHOULD BE COMBINED INTO AN INTEGRATED DOCUMENT.**

### 3.2 Scope

Contaminants entering the environment through the air, water, and soil come into contact with living organisms and materials as these contaminants move through the environment. Contact of the contaminant with the target, or exposure, can result in a variety of adverse effects. The Draft Guidelines provide a good general review of the concepts behind exposure measurement techniques, providing a useful introductory overview.

The guidelines emphasize assessment of exposure to humans. Human exposure assessment techniques play a central role in environmental epidemiology, risk assessment and risk management. In environmental epidemiology, appropriate exposure assessment methods are critical to minimizing errors, such as those caused by confounding factors and misclassification, and to improving the probability of uncovering exposure-response relationships. In risk assessment, exposure assessment provides essential information on the concentration-frequency curve (population exposed at various concentrations) for contaminant(s) in different media (water, air, soil, food), and identifies the intensity of exposure and its likely distribution. In risk management, exposure assessment helps in formulating cost effective mitigation efforts to reduce or minimize the risk associated with exposure and to then monitor progress toward the reduction of risk. Exposure assessment plays yet another role in generating questions for hypothesis testing and research. The Guidelines presented to the Committee clearly focus on exposure assessment techniques as they apply to risk assessment. This should be stated in the Guidelines to target users to appropriate applications. Some discussion of the role of exposure assessment and the modifications necessary for other applications could also be provided.

In spite of an emphasis on exposure assessments for humans, the document exhibits a general lack of understanding of the principles and practice of industrial hygiene in exposure assessment for industrial workers. Advances in this field have generated many of the approaches that are used in exposure assessments for humans; therefore, the guidance document should reflect the state of the art of this discipline.

The draft Guidelines focus on exposure assessments as part of risk assessments for human health effects. Yet, due to the general nature of the principles presented, much of the information is applicable to exposure assessment for ecological effects. The guidelines should either clearly acknowledge this bias to human effects, or they should be revised to include a more extensive framework for the assessment of exposures in an ecosystem context.

**Recommendation:**

**THE GUIDELINES SHOULD ACKNOWLEDGE THE BIAS TOWARDS EXPOSURE ASSESSMENT FOR DETERMINING HUMAN HEALTH EFFECTS, OR PREFERABLY, THE GUIDELINES SHOULD BE EXPANDED TO INCLUDE EXPOSURE ASSESSMENTS FOR THE PROTECTION OF ECOSYSTEMS.**

The Guidelines were developed with a focus on exposures to non-biological agents, such as hazardous chemicals. Therefore, the document does not apply to exposures involving agents that are biological, such as microbiological or viral agents. The exposure assessment described is not appropriate for assessing bioconcentration, species interaction or food chain interactions that may ultimately affect exposure. This focus should be explained early in the document.

In addition, the potential audience for the document is not well defined. The coverage is insufficient for a person new to the area. Are the guidelines intended to be a primer for "exposure assessors", or are they intended to provide an overview of exposure assessment for a much wider audience?

**Recommendation:**

**THE AGENCY SHOULD CLEARLY DEFINE THE FOCUS AND INTENDED AUDIENCES FOR THE GUIDELINES AND REVISE THEM ACCORDINGLY.**

**3.3 Technical Issues**

**3.3.1 Quality Assurance and Quality Control**

The sections which discuss sample plans, uncertainty, quality assurance and control, and analytical methods are reasonably well constructed and complete. Caution is advised on some of the consequences of being overly stringent on acceptance and rejection criteria. Some mention of these along with some guidance to the reader should be provided in the document. At present, the guidance is too "Black and White" with no in-between.

The accuracy and precision of exposure-related measurements, or any measurement, are a function of the accuracy and precision of all of the individual estimations that make up the measurement. Likewise, the accuracy and precision of risk assessments depend on the accuracy and precision of both hazard and exposure estimates. While one should strive to produce the best estimates possible, there may be cases where the hazard estimation is so uncertain that precise exposure estimates may not be warranted.

It is important to provide a strong statement on the need for quality assurance/quality control. Following this statement, the Guidelines need only refer to other EPA documents specifically designed to provide the detail needed.

### **3.3.2 Time Course of Exposures and Measurements**

Exposures can occur in a number of settings in which the contaminant levels vary. The duration of human contact with the contaminant also varies considerably, as does the biological response time. It is therefore important to gather exposure data on a time scale which is consistent with these factors. The identification of the health or comfort effects of concern and the environmental contaminant(s) potentially associated with that effect are vital to the selection of the exposure assessment method and sampling strategy to be used.

The draft guidelines caution that care should be exercised in applying long-term monitoring data to specific exposure assessments. The draft guidelines acknowledge the importance of population activity patterns in the case of personal monitoring. However, in general the guidelines fail to address the question of averaging times for exposure measurements. Although it is recognized that population activity patterns are important, the guidelines do not stress that chemical concentrations in the different media must be measured over time scales that are consistent with the activity of the exposed individual or sub-population that is being monitored and the biological averaging time.

### **3.3.3 Development and Analysis of Data**

Regarding the development of data, in particular the recommended soil and sediment measurements, many other properties are important in addition to pH and organic carbon content. In fact, porosity, cation-exchange capacity, or clay type may be more important than the factors mentioned. The Committee suggests omitting "pH" and "organic carbon content", or including all factors important to these processes.

The document is quite specific on the requirements for blanks, effective methodologies, the need for the measurement system to be in statistical control, limits of detection, and other tools for analysis. Such rigid specifications are essential if the analyst or the exposure assessor is not familiar with the science behind the measurement methodologies. There are, however, certain pitfalls which arise when the criteria for accepting or rejecting data are very narrow. For example, if the concentration of a pesticide is well above the limit of detection of the methodology, one may accept the measured value as long as the blank concentration is no greater than 20% of the measured value. This may be inappropriate if the concentrations in both the blank and sample are high but still within the 20% criteria, since the high blank value may be indicative of severe analytical problems and may cast doubt on all the data.

Along the same lines, one may be willing to accept a lesser degree of precision, a lesser percentage of spike recovery, etc., as concentrations decrease. Replicate measurements that are

within a factor of two may be acceptable at the  $\text{ngKg}^{-1}$  level but unacceptable at the  $\text{mgKg}^{-1}$  level.

The requirement for the measurement system to be in "statistical control" may also be inappropriate in certain circumstances. For instance, if concentrations of a chemical of interest are near the limit of detection, one may not be able to determine if the individual observations are randomly distributed around the mean. This is because one tail of the data set will be truncated due to the inability of the measurement system to detect values below a set level. Another example of the potential inappropriateness of the "statistical control" requirement is when the hazard of a chemical is extreme at very low concentrations, or when the sample size must be small (i.e., blood). In such cases, the measurement system should be optimized with less consideration being given to stability.

#### **3.3.4 Applicability of Demographics, Population Dynamics, and Population Activity Patterns to Exposure Assessments**

The Committee agrees that direct measurements of exposure reflect many sources of variability. This variability is in part due to the continual changes in activity patterns of the individuals that make up the population, and in part due to source factors and environmental factors. The discussions on pages 44-46 seem to imply that such measurements lack applicability, even though they are representative of the "real world." Instead, the draft guidelines continue to seek to justify the "maximum exposed individual" (MEI) on pages 53 and 54. The MEI concept cannot be scientifically justified as a component of exposure measurements and assessments. Whether the MEI concept has a place in risk management or policy is outside the charter of the Committee.

The Exposure Assessment Subcommittee of the Research Strategies Committee (SAB-EC-88-040B) recommended undertaking a series of steps that would improve the exposure assessments from multiple sources, and would also help to define the uncertainties in the process.

**Recommendation:**

**THE GUIDELINES MUST INCORPORATE DEMOGRAPHICS, POPULATION DYNAMICS, AND POPULATION ACTIVITY PATTERNS INTO THE EXPOSURE ASSESSMENT PROCESS.**

#### **3.3.5 Predictive Exposure Assessments**

This section (pages 47-60) is more closely related to modeling and estimating exposures in the context of the 1986 guidelines, than with exposure measurements. This section relies heavily on simplistic linear models to derive the LADE and LADD exposure equations. These are essentially extensions of Haber's Rule in toxicology without any linkage to

toxicokinetic considerations. The applicability of these models needs to be demonstrated before they can be adopted.

### **3.4 Referencing Other Sources of Information**

The Committee agrees with the Agency's approach in avoiding the development of guidelines that are "cookbooks" for specific exposure measurement technologies. However, it is important that guidance be provided to assessors that are new to the field. The Committee recommends that there be at least an acknowledgment in the Guidelines that there are some general reference texts and handbooks which can assist the new "exposure assessor" in approaching useful measurement options. Similarly, reference should be made to appropriate documents published by the Environmental Protection Agency, the Occupational Safety and Health Administration, the National Institute for Occupational Safety and Health, and the Food and Drug Administration, which contain well developed sampling and analytical protocols. The guidelines could be streamlined significantly by providing extensive references to detailed information, as long as there is assurance that this reference material is readily available to the public.

The draft guidelines contain many similarities and analogies to the concepts and guidelines developed for exposure to and dose assessment of ionizing radiation. Therefore, reference should be made to this body of work. Over 60 years ago the concept that exposure to ionizing radiation or radioactivity could have detrimental as well as beneficial effects led the international scientific community to develop an organization that would have the responsibility for developing recommendations for radiation protection, the International Commission of Radiological Protection (ICRP). Shortly thereafter, the American Roentgen Ray Society, the Radiological Society of North America, and the Radium Society joined together to establish a permanent standing committee that periodically reviews the status of developments in the field of radiation protection. This body, presently known as the National Council on Radiation Protection and Measurements (NCRP), issues reports and documents updating the development of concepts and doctrine in the areas of exposure and dose determination. Reference to these two organizations would lead the user to this important source of guidance adopted by the EPA and by all Federal Agencies.

#### **Recommendation:**

**THE GUIDELINES SHOULD REFER THE READER TO OTHER GENERAL SOURCES OF INFORMATION IN THE OPEN SCIENTIFIC LITERATURE AND IN GOVERNMENT DOCUMENTS THAT ADDRESS EXPOSURE ASSESSMENT, AS WELL AS TO THE DOCTRINE AND CONCEPTS PREVIOUSLY DEVELOPED FOR ASSESSING EXPOSURE TO IONIZING RADIATION.**

### 3.5 Glossary

The Glossary is useful, presenting many technical terms and defining them in an appropriate manner. In some cases, extensive detail in the text might be eliminated by reference to the Glossary. There are a number of terms that are presented, but not defined. Expansion is recommended to include all terms used in the Guidelines. According to two of the definitions, fate includes transport. The Committee considers this to be scientifically inconsistent. In addition, the difference between "ambient medium" and "environmental medium" is unclear.

### 4.0 SPECIFIC COMMENTS

Page 3; lines 14-16: The statements on practical significance vary because of the premises that have been adopted. They should not be "matters of opinion."

Page 6; line 30: Easier detection is only one factor, and probably not the most important one. Others include fewer confounding exposures, easier access for sample collection, more methods development and validation.

Page 7; line 19: Biological monitoring is not "usually" done for the purpose of making inferences about absorbed dose; rather, it is a technique for providing indications of either effects or exposure. The guideline values used in industry are used primarily to indicate excessive exposure.

Page 8; lines 27-32 (also see page 40, Table 3-1 and page 67; lines 9-12): Breathing zone measurements are improperly defined here and on many subsequent pages. Breathing zone measurements can only be made with fixed monitors when the worker never moves. Instead, they are generally made using personal samplers or by having a hygienist or technician hold a sampler inlet within 1 to 2 feet of a worker's nose as the worker moves about. Fixed location sampling in industry is known as General Air Sampling.

Page 12: The guidelines appropriately stress the importance of clearly defining the overall objectives of the study and the nature of the decisions that will be made from the data as the first step in the design of a study. However, the authors have not been consistent in the treatment of this issue, so that the definition of objectives has apparently a lower urgency on page 21 and 22.

Page 13; lines 12-14 (also page 17; lines 10-19): It is also important to indicate that sample averaging times are important.

Page 16; lines 3-5: It is not true that occupational exposure studies have focused more on transient exposure levels. Most are focused on chronic exposure evaluations.

Pages 18-20: Condense, with emphasis on media that account for

direct exposures, such as air, drinking water, food and soil coming into direct contact with people, especially children.

Page 19; line 10: Many factors in addition to pH and organic carbon content influence the bioavailability and other characteristics of chemicals in soils or sediments. In fact, porosity, cation-exchange capacity, or clay type may be more important in some instances than the factors mentioned. The Committee suggests omitting "pH" and "organic Carbon content", or including all factors important to these processes.

Page 21; line 9: Delete the sentence: "Frequently .... to

Page 24; par. 5: Delete the definition of "Kriging", it is too much detail for a document of this type. References to the literature dealing with data reduction and interpretation would be more useful here. The appropriate use of references here and on page 25 should lead to a condensation of the text and improve its utility.

Page 27; lines 6-8: The sampling plan should be reviewed by a good statistician. The design should be directed by a good scientist who is familiar with the problems likely to be encountered.

par. 2: Sampling duration must take the averaging time for the effect into consideration.

par. 3; line 4: The use of spiked samples should be discussed here, including the treatment of spike recovery data.

par. 6; lines 1-3: Clarify the sentence.

Page 28; lines 3-4: Delete this sentence.

Page 31; Section 2.7.: Condense with reference to other EPA documents on QA/QC.

Page 35; line 1: Natural background cannot be called contamination.

Page 41; Table 3-1: Under B.1 - Examples Col.; add: "Breathing Zone Sampling in Industry."

Under B, add a new subheading 2: "Passive Vapor Sampling."; shift existing subheadings to 3 and 4, respectively.

Under C.2 - Usually Attempts .... Column; change parenthetical entry to "may be indicative of either relatively recent exposures or long term body burden."

Pages 48-52: Condense and present concepts in narrative format.

Page 53; line 10: 20 ug/L chloroform is a more realistic concentration.

Page 58; lines 7-9: While Roach's approach is very good for occupational hygiene, it is not at all clear that it is generally applicable to community exposures.

Page 64; lines 20-22: It is not EPA's responsibility to create work for statisticians. A more appropriate statement is found on page 65, lines 7-9.

Page 68; lines 25-27: This is a definition of "Exposure-Response Assessment," it is inconsistent with earlier definitions of "Dose."

Page 69; line 22: Delete "outdoor natural."

Page 70; line 8: Expand the definition to indicate that exposure rates for air are generally characterized by concentration.

SAB REVIEW DRAFT 10-31-88

DRAFT GUIDELINES FOR EXPOSURE-RELATED MEASUREMENTS

U.S. ENVIRONMENTAL PROTECTION AGENCY

NOVEMBER 1988

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## 1. INTRODUCTION

### 1.1. Purpose of the Guidelines

In 1984, EPA organized a new program to ensure scientific quality and technical consistency in the Agency's risk assessments. Included in the program's goals was the development of Agencywide guidelines for risk assessment. The first group of five guidelines was issued in 1986 and included The Guidelines for Estimating Exposures (U.S. EPA, 1986a). The Proposed Guidelines for Exposure-Related Measurements is a companion and supplement to the Guidelines for Estimating Exposures.

The Guidelines for Estimating Exposures were developed to help avoid inadvertent mistakes of omission. They present the risk assessor with a set of questions to be considered in carrying out an exposure assessment and provide a procedural framework for estimating the degree of human contact with a chemical of concern. The Guidelines for Estimating Exposures set forth internal Agency procedures that facilitate consistency by developing common approaches to exposure assessments and by promoting the quality and accuracy of science underlying EPA exposure assessments.

As stated in the Guidelines for Estimating Exposures, "Ideally, exposure measurements are based on measured data. EPA recognizes that gaps in data will be common, but the Guidelines will nevertheless serve to assist in organizing the data that are available, including new data developed as part of the exposure assessment. In the absence of sufficient reliable data and the time to obtain appropriate measurements, exposure assessments may be based on validated mathematical models. Whenever possible, exposure assessments based on modeling should be complemented by reliable measurements." Comments received on the Guidelines for Estimating Exposures, including comments from EPA's Science Advisory Board (SAB), suggested a supplement dealing in more detail with how to make and use measurements in exposure assessment. In accord with these suggestions, the Agency prepared the Proposed Guidelines for Exposure-Related Measurements.

This document focuses primarily on chemical measurements in various physical and biological media. The guidelines are intended to help exposure assessors make informed choices regarding collection and interpretation of these types of data. Other types of exposure-related measurements (e.g., activity profiles) are not considered in detail here.

The Proposed Guidelines for Exposure-Related Measurements (hereinafter Guidelines) are not intended to serve as a step-by-step instructional guide, but to convey general principles. Rather, they represent a collection of information already refined by consensus approval. As the Agency performs more exposure assessments and incorporates various novel approaches, these Guidelines will be revised.

#### 1.1.1. Intended Audience

These Guidelines are intended to assist those who must recommend, conduct, or evaluate an exposure assessment. Exposure assessment is a multidisciplinary process that should reflect the combined input of analytical and environmental chemists, biologists, engineers, statisticians, and others as appropriate. To ensure a credible exposure assessment, the assessor must be familiar with the site or program-specific needs and the factors that affect how well these needs will be fulfilled.

Important aspects to be considered when generating new data (i.e., making measurements) include sampling plans, field activities, and analytical methodologies. Exposure assessors will enhance their expert judgment with sample designs that provide objective measurements. The purpose of sampling an environmental medium, or of sampling exposures directly for an individual, or of sampling tissues or body fluids, is to make an inference about the nature or quality of the whole medium, population, or absorbed dose. Statistics, while a useful tool, cannot alone provide the rationale for the link between the sample and the whole. It is the exposure assessor, as builder of the assessment, who must provide the explanation and justification for this link, usually through carefully laid out logic as to why the sample is accurate and representative. Statistics, and the help of a

statistician, however, are often essential parts of establishing the link between the sample and the population of inference.

When evaluating data (i.e., using exposure-related measurements) exposure assessors should carefully examine the relationship between the population on which the measurements were made and the population about which inferences are desired. Another matter to be considered and understood is the possible difference between statistical significance and practical significance. The former term relates to whether observed differences could be the result of the variability of the data used in a decision process. The latter relates to whether the difference, if real, would be of practical importance. For a given set of circumstances, measures of statistical significance should not vary from one assessor to another because they are calculated using established procedures, while statements on practical significance are very likely to vary from assessor to assessor since they are matters of opinion.

#### **1.1.2. Organization of the Guidelines**

These Guidelines consist of three parts. The introduction describes some general aspects of exposure assessment and some major sources of measurement data used in exposure assessments. The second chapter discusses the making (i.e., generation) of measurements for exposure assessments including the role of the exposure assessor, sampling plans, uncertainty analysis, quality assurance, quality control, and method selection. The third chapter describes the use of measurements in exposure assessments including evaluation of uncertainty in the use of measurements, the role of limit-of-detection values, and the use of surrogate data.

#### **1.1.3. Role of Technical Support Documents**

It is impracticable to create guidelines that give specific step-by-step instructions for every situation. The assessor should consult technical support documents, such as those referred to in these Guidelines, for more specific information.

### **1.2. Exposure Assessment**

The National Research Council (NRC) in 1983 described risk assessment as containing some or all of the following four steps:

hazard identification (the determination of whether a particular chemical is or is not causally linked to particular health effects), dose-response assessment (the determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question), exposure assessment (the determination of the extent of human exposure before or after application of regulatory controls), and risk characterization (the description of the nature and often the magnitude of human risk, including attendant uncertainty).

Once a dose-response relationship is established, and often this is done in a controlled situation such as a laboratory, one can make statements such as, "if the dose is 'x,' then the response should be 'y.'" A major problem confronting risk assessors when trying to apply the dose-response relationship to an actual "real-world" problem is the question of what dose to use as representative of the actual situation. The primary purpose of an exposure assessment is usually to estimate the real-world dose value to use in a dose-response relationship.

The EPA Guidelines for Estimating Exposure (U.S. EPA, 1986a) define exposure as the contact with a chemical or physical agent. The magnitude of this contact is determined by measuring or estimating the amount of an agent available at the exchange boundaries (i.e., lungs, gastrointestinal tract, skin) during some specified time. Once the agent is absorbed through these boundaries, the amount crossing the boundary becomes the absorbed dose. Exposure assessment is the qualitative or quantitative determination/estimation of the magnitude, frequency, duration, and route of exposure. Exposures are sometimes referred to in the literature in terms of "administered dose" or "applied dose," which describe contact with the organism, but not absorption. These terms tend to be confusing and should not be used to describe exposure if avoidable. Exposure assessments often present not only the exposures, but also the absorbed doses, which can be calculated from exposure if the absorption fraction is known (see the Glossary of Terms).

Over the last decade, exposure assessors have generally approached the evaluation of real-world exposures in three ways: by trying to measure the exposure directly while it is taking place ("the

direct measurement approach"), by trying to reconstruct an absorbed dose from evidence within an organism after the exposure and absorption have taken place ("the reconstructive approach"), or by trying to make estimates of the distribution of the chemical and the organism separately, then linking them ("the predictive approach"). All of these approaches involve measurements of some kind, and the measurements used in these approaches to determine or estimate exposure are generally termed "exposure-related measurements." This term applies to measurements taken for use in an exposure assessment, whether or not they measure actual exposures directly, or directly provide information upon which exposure will ultimately be estimated.

### 1.3. Sources of Measurement Data

This section describes some of the methods currently used to provide reliable measurements for exposure assessment needs. The methodologies discussed below focus on direct measurement of exposure, measurement of biological markers, and measurements for characterization of media for predictive assessments. These Guidelines will not discuss the collection of data on population activity patterns, although it is recognized that these data play an important role in exposure assessment.

The reader should keep in mind that the measurements discussed in sections 1.3.1 through 1.3.3 share a similarity in that for most of them, a substance or medium is being analyzed for chemical content. However, the use of the resulting measurement data is fundamentally different for the three different approaches to exposure assessment, and therefore considerations in making these measurements vary also.

#### 1.3.1. Direct Measurement of Exposure

Direct measurement of exposure measures the contact of a chemical with an organism (human or nonhuman) while it occurs, by measuring the chemical concentrations at human physical exchange boundaries (skin, lungs, etc.) as a function of time (e.g., throughout a day) to obtain an exposure profile. A number of individual profiles can be statistically aggregated to make statements about the exposure profiles for human or nonhuman populations, provided the individuals sampled have a known relationship to the entire population.

As the name implies, the direct measurement method relies essentially on measured data. The best-known example of the direct measurement of exposure is the radiation dosimeter, a small badge-like device worn in areas where exposure to radiation is possible. The dosimeter effectively measures exposures to radiation while it is taking place, then indicates when a preset level has been exceeded. Another example of direct measurement of pollutant exposure is provided by the Total Exposure Assessment Methodology (TEAM) studies (U.S. EPA, 1987a) conducted by EPA. In the TEAM studies, a small pump with a collector and absorbent is attached to a person's clothing and measures the exposures to airborne solvents or other pollutants while the exposure takes place. The absorbent cartridges are then analyzed for a variety of chemicals. A third direct measurement example is given by the carbon monoxide (CO) studies done by EPA in the 1980s, where a small CO measuring device was carried by a number of people over several days (U.S. EPA, 1984a). The device had a recording capability which allowed the assessor to analyze the exposure to CO over that time period. In all three of these examples, the key to direct measurement techniques is that the measurements must be taken at the interface between the person and the environment and measure the exposure while it is taking place.

#### 1.3.2. Biological Monitoring for Reconstructive Exposure Assessment

Another method, yielding useful measurement data for reconstructive exposure assessments, involves biological monitoring. Biological tissue or fluid measurements that reveal the presence of a chemical may indicate directly that an exposure has occurred, provided the chemical is not a metabolite of other chemicals. There has been much interest in relating biological sample levels to exposure, particularly for occupational exposure where chemical concentrations are high enough to permit easier detection.

Four types of measurements using biological monitoring can be used to evaluate the amount of a chemical in the body:

1. Measurement of the concentration of the chemical itself in various biological tissues or fluids (blood, urine, breath, hair, adipose tissue, etc.) (body burden).

2. Measurement of the concentration of one or more of the biotransformation products (metabolites) of the chemical.
3. Measurement of a biological effect that occurs as a result of human exposure to the chemical (e.g., alkylated hemoglobin) (types of biomarkers).
4. Measurement of the amount of a chemical bound to target molecules (e.g., DNA adducts or chromosome aberrations (types of biomarkers)).

The results of biomonitoring can be used to estimate the amount of chemical uptake during a specific interval if the relationship between uptake and the markers selected is known (i.e., pharmacokinetics are known) and if background levels before the exposure interval are known.

Reconstructive exposure assessment relies heavily on measured data. However, the data on body burden or biomarker values cannot be used directly for exposure assessment unless a relationship can be established between these levels and absorbed dose, and interfering reactions (e.g., from metabolism of nonrelated chemicals) can be accounted for or ruled out. Biological monitoring for exposure assessment usually involves sampling tissues or fluids for the purpose of making inferences about absorbed dose.

#### 1.3.3. Measurements for Predictive Exposure Assessment

In predictive exposure assessment, the assessor attempts to match, or link, individuals or collections of individuals with the concentrations of chemicals or agents they are contacting. Usually, the assessor addresses the characterization of the individuals or population separately from the characterization of the chemical or agent. Population characterization involves identifying those individuals who are exposed and the activities (habits) that bring them into contact with the chemical or agent. This may involve demographics, survey statistics, behavior observation, activity diaries, or other means of obtaining this information. Although population characterization may involve measurements, these measurements are fundamentally different from the chemical/media characterization discussed in these Guidelines, and therefore will not be specifically discussed further here.

Measurements employed in characterizing the chemical or agent in predictive exposure assessments are quite varied, but they all share a common purpose: to use sampling to make inferences about the distribution of chemical/agent concentrations in the media being sampled. Measurements are often used as inputs to models. Once the concentration distribution has been estimated or measured, this information can be combined with the population characterization to estimate exposure.

The following are a few examples of the types of measurements used in predictive exposure assessment to characterize the concentrations of chemicals or agents in various media. Fixed location monitoring has been used by the Agency and other groups to provide a record of pollutant concentration at one spot over some length of time. Nationwide air and water monitoring programs have been established to provide continuous monitoring of pollutant concentration so that "baseline" values in these environmental media can be documented. Measurements in environmental media can also be done in focused studies which look for specific chemicals or agents in specific places and times. Indoor air measurements simply refer to the geographic zone monitored. There are valid reasons for differentiating indoor measurements from outdoor ones, since when performing an exposure assessment, the considerable time spent indoors for most persons needs to be linked with the concentrations they are exposed to indoors. The home, office, automobile, or other defined areas are often called microenvironments, and are used in predictive exposure assessment to better link chemical concentrations with individuals or populations. Breathing zone measurements, usually associated with industrial hygiene studies of worker exposure, refer to measurements taken by a fixed location device situated at approximately head height at or near where the worker spends a substantial amount of time. Note that this differs from direct measurement, since the monitor is fixed rather than moving with the worker. Food and drinking water measurements are often made to characterize these potential exposure pathways. General characterization of these media, such as market basket studies, shelf studies (where foodstuffs are taken from store shelves and analyzed),

ATTACHMENT

Letter from Dr. Jerome J. Wesolowski to Dr. Mort Lippmann

Letter from Dr. James W. Woods to Mr. A. Robert Flaak

April 14, 1989

Dr. Mort Lippmann  
Institute of Environmental Medicine  
New York University Medical Center  
A. J. Lanza Laboratories  
Longmeadow Road  
Tuxedo, NY 10987

Dear Mort:

This responds to the request made at the March meeting of the IAQ/THE that committee members review EPA's exposure-related measurement guidelines dated October 31, 1988, and the EET & FC draft review of these guidelines dated April 1989.

It was my understanding that since the EET & FC already reviewed the guidelines and since time was of the essence, a detailed review was not required. I shall therefore make some general comments followed by specific ones which I believe will give credence to the criticisms contained in the general comments.

General Comments

- The report is poorly written. It's style is cumbersome, bureaucratic, redundant and in many parts vague. It is not clear for whom the authors intended the report. Those already knowledgeable about exposure measurements would find it tedious and minimally informative. Those new to the field would find it confusing.
- The report is replete with technical inaccuracies, and with misinformation on basic exposure concepts. Most important, the definition of exposure, which is the foundation on which the report rests, is inconsistent with that currently acceptable to most exposure experts in the scientific community, as well as with other recent EPA reports, some of which have already received SAB review and approval. This will be discussed in more detail under specific comments.

- I found the EET & FC review included many useful criticisms. However, I was surprised that the committee appeared to agree with the fundamental exposure concepts espoused in the EPA guidelines, including the definitions as given in the report and the glossary (cf. p. 14 which states "The glossary is useful, presenting many technical terms and defining them in an appropriate manner."). I also note that on p. 5, the committee states "... exposure assessment provides essential information on the concentration frequency curve (population at various concentrations)...". I maintain exposure assessment provides information on the population at various exposures. I do not wish to criticize the committee for these oversights since I do not know how much time the members had to review the guidelines and I realize that the committee review is only a draft.
- I do not recommend that these guidelines be published. I agree with the EET & FC that only one guideline be published, utilizing information in this guideline and the 1986 guideline. Further, I recommend that this be done only after the intended audience be defined, the committee's remarks as well as those in this memo be taken into account, and that an appropriate committee of SAB review the integrated document.

#### Specific Comments

- The glossary contains many definitions at variance with those commonly accepted by professional exposure assessors. The most serious discrepancy, since it lays the foundation for other definitions and for the scientific content of the entire document, is that of exposure itself (p. 69). This definition states that "Exposure is quantified as the amount of the agent available at the exchange boundaries...". The authors appear to equate exposure with dose. For example, on p. 68 "dose-response assessment" is defined as "The determination of the relationship between the magnitude of exposure and the probability of occurrence of the health effects in question", while on p. 69 they equate "administered dose" with exposure. Although EPA can define terms as suits their specific needs, I believe they should do so with internal consistency and whenever possible in concert with the scientific community outside EPA. This is not the case. For example, in the February 1988 acid aerosols issue paper, EPA repeatedly expresses acid particle exposures in units of ( $\mu\text{g}/\text{m}^3 \cdot \text{h}$ ), that is, exposure takes into account both concentration and the time an individual is exposed. On the other hand, the November 4, 1988 EPA document "Interrelation of Experimental Exposure and Ambient Air Quality Data for Comparison of Ozone Exposure Indices and Estimating Agricultural Losses" repeatedly gives exposure the units of concentration. For example, on p. 3-6 of that document the authors state "exposure should not exceed 21 ppm". Thus there is disagreement, even within EPA, on this very basic definition. Since EPA is considering the total human exposure concept as a guiding scientific principle in risk assessment and risk management, I think it critical that the agency establish one definition for this basic concept.

A committee of the National Research Council has recently completed a draft report on "Advances in Assessing Human Exposure to Airborne Pollutants". Included are suggested definitions for concepts related to exposure assessment. The committee draft report states that "Human exposure consists of contact at one or more boundary layers between the human and the environment with a contaminant(s) at a specific concentration(s) for a specified period of time. Thus the units of exposure are concentration multiplied by time.". The committee goes on to define other concepts such as total exposure, integrated exposure, dose, total dose, internal or administered dose, and biologically effected dose. I recommend that the EPA staff who rewrite the guidelines attempt to accept the recommendations of the NRC (for information as to when a draft document might be available for review I suggest calling Ray Wassel of the NRC at (202) 334-2617).

Clearly if EPA should accept this recommendation it will be necessary to make substantial revisions in the text, since the text discussion and equations all flow from the definitions in the glossary.

- p. 66 The authors state: "Indoor ambient and outdoor ambient are sometimes used to deferentiate between indoor and outdoor surroundings". I have never seen this deferentiation. Rather the most common use of the word ambient is to refer to outdoor air, which I agree is a misnomer.
- p. 67 The authors state: "Breathing zone measurements are frequently made ... by placing monitors at fixed locations ...". Breathing zone measurements are usually made using personal samplers attached to the person.
- p. 71 The authors equate the word microenvironments with "a series of areas". The definition of microenvironment is a three-dimensional space having a volume such that the concentration for the pollutant of interest can be considered constant during a specified measurement time interval. Further if properly coupled with activity pattern data, microenvironmental measurements need not be carried out sequentially.
- p. 10 Paragraph one. The statement "...dose-response assessment (the determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question) ..." shows the lack of the authors distinction between dose and exposure.
- p. 4 Second paragraph. The primary purpose of an exposure assessment is not to estimate "the real world dose", but simply to estimate exposure. Also, the authors use the Phrase "real world" a number of times during this report. What other worlds do they have in mind?
- p. 4-5 The nomenclature that the authors use to describe the three methods for measuring exposure are not as pedagogically useful as

the descriptors used by many scientists and also by the NRC committee discussed above. I recommend that exposure assessment approaches be divided into two categories; indirect methods (which combine microenvironmental measurements with activity diaries through models to obtain exposure), and the direct method. The direct method has two subcategories, personal monitoring and biological markers.

- P. 5, last par. The authors state that direct measurements are made by "measuring concentrations at human physical exchange boundaries (skin, lungs, etc.)...". Personal monitors are not placed in people's lungs. Of course the authors realize this since on the next page they give as direct measurement example, the use of a CO measuring device which is carried by people. This is just one of many cases of imprecise writing.
- p. 7, par. 2 Biological monitoring is not usually done to make inferences about adsorbed dose. Biological monitoring is used for a variety of purposes, for example, toxicological purposes, screening purposes, etc.
- p. 7, last par. In the indirect method (what the authors refer to as predictive exposure assessment) population characterization involves much more than just who is exposed and what their activities are that bring them into contact with the chemical or agent. One of the most important parameters is the activity time pattern data. These sections on the different methods for measuring exposure are vague and incomplete.
- p. 8. Indoor air measurements do not "simply refer to the geographic zone monitored". If the authors feel a need to define the term, why not say indoor measurements refer to measurements made indoors. Perhaps the intelligent reader would not require an entire sentence, but could deduce the location from the adjective "indoor".
- p.8, par. 2 The home office, etc. are not microenvironments. They are environments. See an earlier comment for the correct definition of microenvironment.
- p.8, last par. Breathing zone measurements are not taken by a fixed location device unless the worker does not move from his work location.
- p.9 The authors say that "... measurements of food and drinking water are taken as split samples simultaneously as an individual is ingesting them". This indeed must be a painful experience for the individual under test.
- p. 9, par. 1 The authors say that "Source characterization measurements usually refer to sampling to determine the rate of release of chemicals ...". Such measurements are usually referred to as source emission measurements.

- p. 9, last par. The authors state that the proof of reliability of data is embodied in the form of quality assurance and quality control. It is quality assurance that yields the "proof". Put simply, quality control is the system of procedures that is used before and during data collection to make it good data, whereas quality assurance is the system used to assure (i.e. "prove") that the data that has already been collected is indeed accurate and precise (the authors use these definitions on p. 31).
- p. 11, par. 1. The authors state "... the exposure assessors task is to obtain or estimate dose information ...". Clearly the authors do not differentiate between dose and exposure. This kind of confusion is contained throughout the report.
- p. 11, par. 1. The sentence "Since dose involves both the organism and the chemical, obtaining representative dose information involves establishing a link between the organism and the chemical" says nothing.
- p. 11, par. 2. The authors equate measurement data with samples. Data are not the same as samples.
- p. 12. The sentence "It is incumbent on the exposure assessor to be well informed and to participate in such decisions relating to the making of measurements so that the sampling process is relevant to the questions being asked to the assessor.", is another meaningless sentence.
- p. 14, last par. The authors state "... measurements are made of the actual pollutant concentrations contacting a person's body by essentially using split samples of the air breathed,...". It is unclear what the authors are referring to when they speak of splitting air samples.
- p. 17, par. 1. I think it inappropriate to state that "environmental media are primarily responsible for the wide dispersion of anthropogenic chemicals that reach the environment...". Perhaps man's activities have something to do with the wide dispersion of chemicals. It is not clear what the authors are trying to say.
- p. 46. The authors state that "... the exposure assessor is advised to consult a statistician ...". Statements about bringing statisticians occur a number of times in this report. If it is necessary to bring in this point why not also refer to the need to consult with chemists, engineers, meteorologists, toxicologists, etc., etc.,
- p. 48-57. Should the EPA accept the NRC definitions for exposure, dose etc. this entire section would have to be completely rewritten. Even now, using the definitions of the authors, there are errors in the mathematics. For example, the right side of equation (3-5) and equation (3-6) are identical. Therefore,  $T = ED$ . Yet, the authors

Dr. Lippmann  
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imply T is the time of interest, whereas, ED, is the duration of exposure over all events where exposure occurs.

- p. 56, par. 2. What do the authors mean by the statement "the Monte Carlo Method immediately uses the fact ..." that is, what is the purpose of the phrase "immediately uses"?
- p. 60, par. 3. The authors state: "Even in the case of serious flaws, data should not be discarded entirely unless better data are available". The authors would have to define the phrase "serious flaws" very carefully before I could accept this statement. Bad data is bad data and should be discarded. Put another way, garbage in, garbage out.
- I could not find a definition or reference to the important exposure metric, "integrated exposure".

I believe these specific comments adequately support my general criticisms. It is never pleasant to criticize a report, particularly so thoroughly. I also am aware that should the above recommendations be taken, the report will have to be rewritten. However, in light of the fact that EPA management is seriously considering adopting the total human exposure concept as the guiding scientific principle in carrying out the agency's mandate for risk assessment and risk management, it is critical that the exposure assessment guidelines which form the scientific foundation of the total human exposure concept be useful, readable and scientifically accurate. I compliment EPA on its foresight in embracing the total human exposure concept and in taking these first steps to develop exposure assessment guidelines. I look forward to the integrated exposure assessment guidelines.

Sincerely,

  
Jerome J. Wesolowski, Ph.D., Chief  
Air & Industrial Hygiene Laboratory

JJW:st

cc: R. Flaak  
P. Lioy  
R. Wassel

JAMES E. WOODS Ph.D., P.E.  
1235 Yale Place, #805  
Minneapolis MN 55403

22 April 1989

Mr. A. Robert Flaak, Executive Secretary  
Science Advisory Board (A-101F)  
U.S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460

Dear Bob,

The enclosed comments are submitted as requested at our IAQTHE Committee of 28-29 March 1989. These comments are based on my review of the "Draft Guidelines for Exposure-Related Measurements" of November 1988, the "Report of the Environmental Effects, Transport and Fate Committee" of April 1989, and my participation in the 28-29 March IAQTHE Committee meeting.

General Comments

1. This draft contains much useful information, and has the potential of being an important Guide for researchers and investigators. However, as indicated by the EETFC, major revisions will be required. I concur in this opinion.
2. If this document is to provide credible guidance for exposure measurement, it must clearly and authoritatively define "exposure" in measureable terminology. Only in Chapter 3 is a quantitative definition proposed. Moreover, the proposed definition is not universally accepted. If the units of exposure are to be consistently expressed as mass, then the measurements of intensity, I, and time, dt, must be clearly described. It is recommended that these terms be clearly defined and discussed in Chapter 1.
3. The three methods of "measuring" exposure are presented in a somewhat confusing manner. Does the Direct Method provide a "measure" of concentration or a measure of exposure? If it is to be exposure, is the measure in terms of mass or the integral of mass and time? The other two methods are "indirect" indicators (not measures) of exposure. If uncertainty principles are to be used, a clear distinction of measures and indicators is necessary.
4. The fact that this document is limited to discussions of measuring chemical contaminants should be clearly indicated in its objective and title.
5. I concur that this draft document should be integrated with the previously issued Guidelines for Estimating Exposures. The integrated document should then be reviewed and published.

Specific Comments

Page 2 - The focus of the document on chemical measurements, without consideration of physical (e.g., thermal, lighting, acoustic, etc) or biological (e.g., microbiological) influences of the factors, is a serious limitation.

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Page 4, par 2 - In the proposed definition of exposure, which boundaries distinguish measures of exposure from measures of dose?

Page 5, top of page - The units of measure of exposure should be defined. Also, they should be distinguished from the units of measure of dose. When assessing total exposure, how are units of measure of exposure by various pathways rationalized?

Page 5, par 1 - How can measurements of population activity or duration of exposure be neglected in a document purported to be a Measurement Guideline? These factors must be addressed.

Page 5, par 2 - Other environmental factors (e.g., physical, psychosocial, etc.) that affect exposure should be identified and measurement methods should be discussed.

Page 6, par 1 - The description of a dosimeter to measure exposure adds to the confusion between the concepts of dose and exposure. Clarification is needed.

Page 6, par 2 - "Biological monitoring" is not technically a "measure" of exposure, although it may be an "indicator". Please clarify. How biological monitoring differs from dose measurement must be clarified in terms of exchange boundaries and target organs.

Pages 6 and 7 - The "indirect" measurement methods of biological monitoring and predictive assessments should be clearly classified differently than the "direct" measurement method. In fact, is it even possible to determine total exposure by "direct measurement"? Since the "direct" method probably yields incomplete information, and the "indirect" methods require prediction to assess exposure, how can exposure be assessed without modeling and simulation? This Guideline should be rewritten integrally with the 1986 Guide.

Page 7, par 2 - The "geographic zone" of indoor air is a confusing concept. Does this refer to the difference of an indoor environment in Los Angeles and Boston, or to two adjacent rooms in the same building?

Page 12, par 1 - Why would an objective be to support a type of assessment? The "direct" and "indirect" (reconstructive and predictive) methods may be chosen to meet an objective, but they should not be objectives themselves.

Page 14, par 2 - How can methods of measuring be considered science? What is a split sample and how is it obtained? Is it real? How can a sample of air and food be split? How can these results be combined with those of a patch to get a direct measurement of total exposure? This whole concept is confusing and needs clarification.

Pages 20 - 23 - The discussion on "Setting Data Quality Objective" is very good.

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James Woods' Comments  
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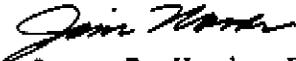
Pages 23 - 31 (Sections 2.5 and 2.6) - The discussions are primarily directed to the "predictive assessment" method. What plans and uncertainty evaluations are needed for the other methods?

Page 36, par 1; page 46, par 1; page 47, par 1 - Substitute for the term "absorbed dose". As indicated in Chapter 1 of the Guide, the term confounds the concepts of dose and exposure.

Page 48 - The dimensions of exposure (i.e., mass) in Equation 3.1 are not consistent with others generally accepted internationally (e.g., concentration x time). However, if it is assumed here that  $E = \int I dt$ , rather than  $E = \int C dt$ , then previous sections of this Guide should have extensive discussions on how to accurately and precisely measure I by direct and indirect methods. Also is E, as defined in this Section, consistent with the measures of exposure using "direct" and other "indirect" (i.e., biological monitoring) methods?

Page 51 - The Equation for dose (EQ 3.12) is not consistent with generally accepted definitions (e.g., absorption in target organ). How does the proposed definition rationalize with the more common definitions? Also, the discussion on dose goes beyond the scope of this document (EQs 3.12 to 3.14) and should be deleted.

Best regards,



James E. Woods, Ph.D., P.E.  
Member, IAQTHE Committee of SAB

cc: Dr. Morton Lippmann