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Project Summary

Methodology for Characterization of Uncertainty in Exposure Assessments

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Virtually all exposure assessments except those based upon measured exposure levels for a probability sample of population members rely upon a mathematical model to predict exposure. Whenever a model that has not been validated is used, an uncertainty associated with the exposure assessment may be present. The primary characterization of uncertainty is partly qualitative, i.e., it includes assumptions inherent in the model. Sensitivity of the exposure assessment to model formulation can be investigated by replicating the assessment for plausible alternative models.

When an exposure assessment is based upon directly measured exposure levels for a probability sample of population members, uncertainty can be greatly reduced and described quantitatively. In this case, the primary sources of uncertainty are measurement errors and sampling errors. A thorough quality assurance program should be designed into the study to ensure that measurement errors can be estimated. The effects of all sources of random error should be measured quantitatively by confidence interval estimates of parameters of interest, e.g., percentiles of the exposure distribution. Moreover, the effect of random errors can be reduced by taking a larger sample.

Whenever the latter is not feasible, it is sometimes possible to obtain at least some data for exposure and model input variables. This substantially reduces the amount of quantitative uncertainty for estimation of the distribution of exposure.

This Project Summary was developed by EPA's Office of Health and Environmental Assessment, Washington, DC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

This document is written for the professional who is actively involved in the performance of exposure assessments. It is intended to facilitate use of the latest statistical methods for characterizing uncertainty for exposure assessments.

The introductory chapter of the full report discusses the nature of an exposure assessment which serves as a point of reference for the remainder of the report. An overview of the characterization of uncertainty for exposure assessments at various stages of refinement is also presented.

Exposure Assessment

An exposure assessment quantitatively estimates the contact of an affected population with a substance under investigation. Typically, the magnitude, duration, and/or frequency of contact are estimated. The U.S. Environmental Protection Agency has prepared a draft handbook to provide guidance pertinent to performing an exposure assessment. In addition, the

Office of Science and Technology and the National Research Council have also developed valuable sources of information with regard to the methodology of exposure assessments.

An integrated exposure assessment quantifies the contact of population members with the substance under investigation via all routes of exposure (inhalation, ingestion, and dermal) and all pathways from sources to exposed individuals (e.g., from manufacturing plants to plant workers and/or consumers of manufactured products). It also estimates the size of population affected by each exposure route. Since an integrated exposure assessment is often needed to enable regulaboratory decisions, characterization of uncertainty is addressed in this context.

The overall uncertainty associated with both the exposure assessment and the dose-response relationships must be addressed by risk assessments. Characterization of uncertainty for exposure assessments is addressed in the full report; other comparable documents address characterization of uncertainty for risk assessments *per se*. The primary purpose of an exposure assessment is to enable risk assessment and possible selection of a regulatory option. Regulatory decisions must be capable of withstanding close scrutiny (perhaps even in a court of law). Therefore, the characterization of uncertainty for an exposure assessment should be very thorough and based upon state-of-the-art quantitative methods to the extent possible.

The type of exposure (internal dose, external dose, etc.) investigated by an integrated exposure assessment depends upon the input needed to enable risk assessment. In most cases an exposure assessment should ideally quantify the dose of the substance under investigation that is absorbed by individual body organs in order to enable the most reliable estimates of health effects. Presently it is practical to quantify absorbed organ-specific doses only in certain circumstances—e.g., when the affected organ is the skin (dermal route) or when exposure is due to radiation. Moreover, the absorbed whole-body dose often cannot be quantified. Instead, indicators of the absorbed dose are often used by necessity in exposure assessments. These indicators of absorbed doses may be either environmental exposure or body burden. Environmental exposure refers to the levels of the substance under investigation contacted through the air, water, food, soil, etc. Body burden refers to levels of the substance in body fluids or tissues, e.g., blood, urine, breath, fatty tissues, hair, nails, etc.

An integrated exposure assessment generally partitions the affected population into subpopulations such that all members of a subpopulation are affected by the same sources of exposure. For each source, there can be one or more pathways by which the substance under study travels from the source to the affected population. For each source and pathway, a population member can be exposed via one or more of three absorption routes: inhalation, ingestion, and dermal. An integrated exposure assessment often begins by estimating exposure for a subpopulation via a specific combination of source, pathway, and route. Exposure is then aggregated across pathways and sources to estimate exposure via a particular route for subpopulation members.

An exposure assessment addresses the exposures experienced by the subjects (human or nonhuman) of a specified population. The most complete characterization of these exposures is the population distribution of individual exposures. If the population distribution of exposure was known, then all parameters of the distribution would also be known.

Characterization of Uncertainty

Since it is uncertainty of the predicted output that is of interest, the probability distribution of the output variable and the variance of this distribution are advocated as primary characterizations of the uncertainty associated with the predicted output. Within this context, the estimated distribution of exposures could be regarded as a characterization of the uncertainty with regard to the prediction of an individual population member's exposure level. However, estimation of the population distribution of exposures is the primary goal of an exposure assessment, and it is the uncertainty with regard to this estimated distribution of exposures that must be addressed.

The determination of which methods are appropriate for characterizing the uncertainty of an estimate depends upon the underlying parameters being estimated, the type and extent of data available, and the estimation procedures utilized. As a result, a great deal of the full report actually addresses estimation procedures for exposure assessments. The methodology considered most appropriate for characterizing the uncertainty associated with an exposure assessment is then discussed with regard to each estimation procedure. For example, when the population distribution of exposure is being estimated, characterization of uncertainty addresses the possible differences between the estimated distribution of exposures and the true population distribution of exposures.

An exposure assessment is often based on one or more exposure scenarios and associated mathematical models. An exposure scenario ideally considers all potential sources of the substance that could come in contact with population subjects. Exposure prediction models based upon transportation and fate of the substance would then be used to describe the pathways from sources to contact with population members. These models may be very complex, using data on levels of the substance at sources and/or ambient monitoring sites and the geographic distribution of the target population to estimate the population distribution of exposures. Alternatively, these models can be relatively simple models that predict an individual population member's personal exposure as a function of several input variables.

The initial exposure assessment for a substance is often based upon a very limited amount of data. Under such conditions, the primary characterization of uncertainty may be qualitative. Exposure assessments based upon limited data are discussed in Chapter 2 of the full report.

Chapter 3 discusses assessments based upon the estimated joint probability distribution of model input variables, given a model that predicts personal exposure as a function of the input variables. Depending upon the extent of data available to validate the model as well as the input variable distributions, this type of assessment has the potential for reducing uncertainty relative to the methods discussed in Chapter 2. It also has the potential for a more quantitative characterization of the uncertainties.

The uncertainties associated with an exposure assessment can potentially be reduced further by basing the assessment on measured values of model input variables for a sample of population members, given a model that predicts personal exposure as a function of the input variables, as discussed in Chapter 4. Chapter 5 discusses exposure assessments based on measured exposure levels for a sample of population members, which has the potential for minimizing the uncertainties associated with an assessment.

When the exposure levels experienced by individual population subjects are measured, they generally reflect the total exposure across all sources and pathways, and if possible across all routes as well. However, when the modeling approach is employed for an exposure assessment, a model often predicts an individual population member's exposure due to a specific combination of source, pathway, and route. Methods for combining estimated exposure distributions over sources, pathways, and routes are discussed in Chapter 6. Finally, Chapter 7 of the full report discusses combining the estimated exposure distributions over disjointed subpopulations to produce an estimate of the exposure distribution for the total population. Methods for characterizing the uncertainties associated with these estimated exposure distributions are also discussed in Chapters 6 and 7.

A hypothetical example of a subpopulation exposure assessment that progresses through several stages of refinement is presented in Appendix A of the full report. The sections of the example in Appendix A correspond directly to the sections of the first five chapters of the full report and are numbered accordingly.

Summary

Virtually all exposure assessments except those based upon measured exposure levels for a probability sample of population members rely upon a model to predict exposure. The model may be any mathematical function, simple or complex, that estimates the population distribution of exposure or an individual population member's exposure as a function of one or more input variables. Whenever a model that has not been validated is used as the basis for an exposure assessment, the uncertainty associated with the exposure assessment may be substantial. The primary characterization of uncertainty is at least partly qualitative, i.e., it includes a description of the assumptions inherent in the model and their justification. Sensitivity of the exposure assessment to model formulation can be investigated by replicating the assessment for plausible alternative models.

When an exposure assessment is based upon directly measured exposure levels for a probability sample of population members, uncertainty can be greatly reduced and described quantitatively. In this case, the primary sources of uncertainty are measurement errors and sampling errors. A thorough quality assurance program should be designed into the study to ensure that the magnitude of measurement errors can be estimated. The effects of all sources of random error should be measured quantitatively by confidence interval estimates of parameters of interest, e.g., percentiles of the exposure distribution. Moreover, the effect of random errors can be reduced by taking a larger sample.

Whenever the latter is not feasible, it is sometimes possible to obtain at least some data for exposure and model input variables. These data should be used to assess goodness of fit of the model and/or presumed distributions of input variables. This substantially reduces the amount of quantitative uncertainty for estimation of the distribution of exposure and is strongly recommended. It is recognized, however, that it may not always be feasible to collect such data.

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The complete report, entitled "Methodology for Characterization of Uncertainty in Exposure Assessments," (Order No. PB 85-240 455/AS; Cost: $17.50, subject to change) will be available only from:
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