SAB Consultation on efforts to update of
EPA's EXPOSURE ASSESSMENT GUIDELINES
September 7, 2006

The objective of this consultation is to review and comment on the approach and proposed content of the update for the Agency's Exposure Assessment Guidelines. The Agency seeks this consultation as one of several outreach efforts to identify the needs of the user community and the major relevant technical issues that should be incorporated into the update. The SAB's evaluation and recommendations will provide guidance to the Agency's Risk Assessment Forum (Forum) to ensure the update accurately reflects the state of the science for key topics and approaches. The Forum also wants to capture any additional aspects of exposure assessment that the Committee identifies as critical or important to the update. As a means to focus this consultation we have prepared several charge questions for the SAB to address during the course of their review.

Charge questions 1, 2 and 3 relate to all of the science topic summaries provided.

1. Please comment on the relevance and priority of the topics listed to the current practice and future direction of exposure assessment (both measurement and modeling).

2. Please describe any other relevant topics which should be included in the revisions, and their relationship to the topics presented and the overall guidelines.

3. What case examples or other references should we draw upon to illustrate the science and practice of exposure assessment?

Charge questions 4 and 5 relate to the content and approach for the Guidelines update.

4. How and to what extent can the current and emerging databases of human biomonitoring be used to inform exposure assessments? Please include the potential use of genomics or other biometrics to the degree they are relevant.

5. Given that guidelines are intended to provide general principles of the practice, and updated infrequently, what strategy could we explore to make (and keep) the document as relevant and up-to-date as possible?

OVERVIEW MATERIAL

Purpose and Scope of the Guidelines: The Guidelines for Exposure Assessment ("Guidelines," available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263) are intended to provide general principles, references, and an overall roadmap for designing and conducting exposure assessments. The document will provide guidance for the selection of the best information or data sources, approaches, or models. The reader will be given guidance on how to interpret the analysis and draw conclusions, e.g., how biomonitoring data may support the relationship of an exposure and an effect. While intended to be broad enough in scope to provide guidance in most uses of exposure assessment, these guidelines will not provide detailed approaches. Instead, the Guidelines will make reference to other, more specific or detailed references and their use. In addition, the Guidelines standardize terminology, outline the limits of sound scientific practice, and emphasize the scientific basis and rationale for each assessment, including identification of uncertainties, assumptions, and limitations.

The intended audience for the Guidelines is primarily EPA exposure and risk assessors, and other Agency analysts, as well as parties who either perform assessments for, or submit analyses to the Agency.

Need for Updated Guidelines: The practice of exposure assessment has been evolving rapidly and has changed significantly since the 1992 publication of the Guidelines, with the advance of the science and the publication of EPA-specific guidance in such areas as probabilistic analyses, exposure factors, aggregate exposure and cumulative risk, community-based research, and consideration for susceptible populations and life stages. The Forum received numerous comments from internal and external users of the Guidelines regarding the timeliness of an update. An update is needed to incorporate and refer to advances and changes in the theory and practice of exposure assessment. The 1992 Guidelines stated that they should be revised as practice advanced and new approaches were incorporated. In addition, the update will reflect a more current approach to exposure and risk assessment:

- beginning with planning, scoping, and problem formulation;
- then gathering data or information; and
- proceeding to analyzing the information and
- communicating the analysis and related uncertainties.

This process has become more complex, multidisciplinary, and iterative, while at the same time providing a better-informed evaluation of exposure to risk assessors and managers.

Relation to Other Guidance: It should be apparent from the preceding discussion that there has been a proliferation of guidance on specific topics, driven both by science and regulatory decision makers. The Guidelines are intentionally broad and over-arching in scope, and sufficiently general to accommodate existing guidance and understanding, while opening the door to more advanced and specific guidance and methodology. They are intended to be an integral, basic part of the risk assessment process, and complement guidance on hazard identification, risk assessment, and risk characterization.

Goals of the Updated Guidelines for Exposure Assessment: Below we have outlined some of the overall goals for the updated Guidelines, without focusing on specific topics or narrower objectives.

- To provide a "state of the science" approach to exposure assessment theory and practice.

- To lay the groundwork for production of an exposure assessment, whether it is a screening level or a data-rich, refined assessment.

- To provide sufficient technical guidance to answer most questions relating to determination of exposure.

- To provide reference to additional, more detailed resources on specific topics; including guidance documents, models, databases, standard procedures, and other tools and references both inside and outside the EPA.

- To use terminology consistent with the Agency and scientific community.

Proposed Approach to Update the Guidelines for Exposure Assessment: These objectives are intended to fulfill the goals outlined above, and to bring the document more in line with current theory and practice of exposure and risk assessment.

- Build on the solid foundation of the existing 1992 Guidelines.

- Organize the updated Guidelines to reflect current theory and practice of exposure assessment, e.g., reflect the importance of early problem formulation and planning.

- Update resources and references to reflect advances in both knowledge and technology.

- Integrate other EPA specific guidance developed since 1992 – chemical mixtures, probabilistic approaches, age groups, cumulative risk, early life stage cancer risk.

- Incorporate and expand concepts that are new or were less widely used at the time of the last writing of the Guidelines.

- More fully integrate the science and art of exposure assessment with biometrics, toxicology, epidemiology, and social sciences.

- Improve access and maintain currency of Guidelines, e.g., link to models, specific guidance documents, standard procedures, and websites such that all risk assessment sites, both Headquarters and Regions, provide complementary and consistent information.

- Harmonize, or be consistent with, accepted terminology used in the scientific community, e.g., the International Programme for Chemical Safety (IPCS).

Obtaining Input to Guidelines Content: A concerted effort has been made to solicit early and broad-based input on the planning and content of the update. To that end, there have been both internal and external meetings to gather input from various organizations within the EPA, as well as academic, governmental, tribal, commercial and non-governmental environmental entities. Efforts to date and planned opportunities for input are listed below:

- April 2005 – Forum sponsored EPA colloquium
- May 2005 – EPA Regional Risk Assessors Plenary Discussions
- November 2005 – International Society of Exposure Analysis Panel in Tucson, Arizona
- 2005 - NGO Comments
- September 2006 – SAB Consultation
- FY 2007 – Draft Guidelines update
- Late 2007 or early 2008 - Internal and External Peer Review

SUMMARY OF COMMENTS RECEIVED ON PROPOSED UPDATE

From the dialogues mentioned in the preceding section, the Agency has obtained specific comments or recommendations in a number of areas. We have attempted to put those recommendations into an outline, but this should not be construed as constituting a table of contents. These are merely topics and issues for inclusion from the various commenters.

I. Updating the Science
   A. Incorporate latest science and guidance by reference
   B. Databases
      1. National, international
   C. Aggregate and cumulative exposure
      1. When and how to aggregate
      2. Background exposures
   D. Use of health effects data (e.g., biomonitoring, epidemiology)
      1. Disease clustering
   E. Monitoring data
      1. Individual vs. population
      2. Ambient vs. personal samples
   F. Modeling exposure
      1. Model evaluation
      2. Spatial aspects
         a. Use of GIS
      3. Timing
         a. Relative to window of toxic relevance
II. Considering Special Populations
   A. Life stages – early and late
      1. Activity pattern data
      2. Age groups
   B. Tribal pathways
      1. Activity patterns
      2. Dietary differences

C. Residential and bystander exposure
D. Equity

III. Addressing Uncertainty and Communicating Risk
A. Use of probabilistic methods
B. Screening assessments
C. Community centered assessment
1. Community as resource
2. Community as client?
D. Equity – address the outliers
E. Judgment – being explicit

IV. Looking Forward – New Technology and Needs
A. Computational toxicology
B. Nanotechnology – uses and concerns
C. Genomics and microarray techniques
D. Data gaps
1. Children's exposures
2. Other populations exposure patterns

Topics to be Updated and Expanded in the Guidelines for Exposure Assessment: These specific topics have been consistently identified by representatives of the various organizations that were polled, as being either areas for expansion or updated discussion, or new and emerging areas of practice in exposure assessment. They reflect and consolidate the categories and types of comments received, as outlined above. The first four topics, collectively, address current areas of science practice where some guidance has been developed since the 1992 Guidelines were published. The fifth is a broad topic encompassing several new and emerging fields of science which could be integrated with exposure assessment practice.

Topic 1: Evaluating and Addressing Aggregate Exposure and Cumulative Risk Assessment

Topic 2: Addressing Populations, Groups, or Life Stages of Potential Concern

Topic 3: Evaluating Uncertainty and Variability, Including Probabilistic Analyses

Topic 4: Involving Communities and Communicating Results

Topic 5: Updating Exposure Assessment with New and Emerging Science: Computational Toxicology, Genomics, and other Biometrics and Social Sciences

The topics are described in the following pages.

Topic 1: Evaluating and Addressing Aggregate Exposure and Cumulative Risk Assessment

Definition: Aggregate exposure is the combined exposure of an individual (or defined population) to a specific agent or stressor via relevant routes, pathways and sources.

Aggregate exposure assessments are most often applied to estimating aggregate risk, which is the risk resulting from aggregate exposure to a single agent or stressor. The concept also applies to the developing area of cumulative risk, which addresses the combined risks from aggregate exposures to multiple agents or stressors. The Agency is currently developing guidelines for cumulative risk assessment.

How This Element Will Contribute to and Improve Existing Exposure Assessment Approaches: One of the most prominent risk-related issues routinely confronting regulatory decision-makers is the need to evaluate combined, multiple source (aggregate) exposure for human populations and ecological resources from concurrent exposure to a *single* agent or environmental stressor. Similarly, as guidelines are developed to address cumulative risk, there will be a need to address *multiple* source exposures from multiple environmental stressors. Such assessments will provide exposure estimates which more closely resemble real-world exposures to a mixture of stressors. The aggregate exposure assessment component, although more complex, would incorporate the same principles of defining the target population(s), identifying relevant sources, routes and pathways of exposure for the target population(s), determining exposure frequency and duration characteristics, and estimating the contribution of each source/medium of exposure identified from available data and other chemical-specific information.

Application/Utility: The Cumulative Risk Assessment Framework (U.S. EPA, 2003a) describes three interrelated and generally sequential phases for cumulative risk assessment: (1) planning, scoping, and problem formulation; (2) analysis; and (3) interpretation and risk characterization. The revised Exposure Assessment Guidelines approach will similarly discuss the interrelationship of the same three phases as they apply to aggregate exposure assessment and the need to integrate the principles of aggregate exposure into all phases of these assessments.

Screening-level estimates for aggregate exposure assessments are more complex than similar estimates for a single source or pathway. Both are based on making simplifying assumptions regarding timing, frequency, sequence, and magnitude of exposure levels. However, applying the principles of aggregate exposure to screening-level estimates will consider all exposure pathways thus providing greater confidence in the decision for further refinement. Screening-level estimates can also help to inform the assessor whether more data or other information is needed to determine if one or more routes, pathways and sources of exposure is significant.

Tier 2/Refined assessment – For these assessments, multiple source/route/pathway exposures are estimated based on intakes that are in the actual distribution of exposure values. EPA program office activities may employ varying combinations of central tendency and high-end values on a case-by-case basis, depending on the situation and target population(s) exposed. Aggregate exposure estimates should be evaluated to determine the degree of uncertainty associated with the estimates, if possible, as is done

with single exposure source or pathway analyses. When the degree of uncertainty is sufficiently narrow, further refinement will generally not be necessary. If not, then the data or assumptions would need to be refined, if possible given information and resource limitations.

The process of identifying life stages, populations or groups that may experience higher-than-average exposures is more complicated in an aggregate exposure assessment because of the consideration for combined exposures from all relevant routes, pathways and sources. Examples of potentially highly exposed groups are those exposed either directly or indirectly to an occupational stressor, those living, working, or playing in close proximity to major sources of a stressor, and those with activity patterns or lifestyles that bring them into greater contact with a given stressor than the "general population," e.g., children, tribal and ethnic groups.

EPA and External Guidance on Aggregate Exposure Assessment: Various statutes require assessment of cumulative risk, including the 1970 National Environmental Policy Act (NEPA) and the 1996 Food Quality Protection Act (FQPA). Statutes requiring aggregate exposure assessments are not as clearly defined. However, EPA program offices have interpreted statute language ensuring the protectiveness of its health-based criteria and standards to include the need for aggregate exposure analyses. EPA has consequently developed guidance and regulatory requirements that address this need. Examples of existing guidance that address aggregate exposure assessment include:

- Office of Water, Ground Water and Drinking Water: regulatory determination process (required by statute) and health-based Maximum Contaminant Level Goal (MCLG) development. See http://www.epa.gov/safewater/
- Office of Water, Office of Science and Technology: guidance on developing human health ambient water quality criteria. See http://www.epa.gov/waterscience/criteria/humanhealth/
- Office of Pesticides, Health Effects Division (2002): aggregate and cumulative risk guidance for evaluating chemicals with a common mode of action.

- Risk Assessment Guidance for Superfund, Part A (1992): guidance on performing aggregate exposure and risk assessments for mixtures of chemicals at sites.

- NCEA External Review Draft: considerations for developing alternative health risk assessment approaches for addressing multiple chemicals, exposures, and effect (EPA 2006a)

Topic 2: Addressing Populations, Groups, or Life Stages of Potential Concern

Definition: Populations of potential concern are those segments of the population, or particular life stages, which have increased sensitivity or have differential exposures relative to the "general population." The quotation marks reflect increasing knowledge and acceptance of the variability in exposure, which can reflect diverse behavioral, developmental, cultural, geographic, or intrinsic genetic attributes.

How This Element Will Contribute to and Improve Existing Exposure Assessment Approaches: Assessing variability and sensitivity of exposure in groups will help make exposure assessments more accurate and allow better informed risk management decision making. Discussion of this topic in the 1992 Guidelines is limited to identification of highly susceptible or highly exposed subgroups, where possible, but states that sufficient data to do so is generally lacking. The updated Guidelines will in part consolidate, as well as reference, the recent Agency guidance on assessing the possible unique exposure of special subgroups, including lifestages, of concern.

Application/Utility: In many cases, initial or screening level exposure assessments do not currently consider sensitive or differentially exposed populations or lifestages. Identifying special subgroups of concern should clearly start in the planning and scoping phase prior to conducting an exposure assessment. As part of this process, a dialog should be established between exposure assessors and health effects scientists to try to identify any groups which should be specifically characterized and assessed. Refined assessments should include risk estimates for any identified subgroups.

Some programs are required by statute to consider children or other sensitive populations (e.g., Food Quality Protection Act of 1996 (FQPA)) and such an approach will make the assessment more protective of the general population as well. In addition to statutory requirements, various independent scientific and academic organizations (e.g., IOM, 1990; NEJAC, 2004; EPA Tribal Science Council, 2005) have advocated that assessments consider the data available on the population at risk, making the exposure estimates more "real." Using location or population-specific data or models may make estimates more accurate, but they can be more or less conservative than assessments using default exposure factors.

In 1993, the National Academy of Sciences released Pesticides in the Diets of Infants and Children, which highlighted important differences between children and adults with respect to risks posed by pesticides. Some of the principles in the report provided the foundation for the FQPA and Executive Order 13045, "Protection of Children from Environmental Health Risks and Safety Risk." One of the provisions of the FQPA requires that children's aggregate exposure be considered when establishing pesticide tolerances (legal limits for residues in food). Executive Order 13045 also broadened consideration of impacts on children by stating that "each Federal agency: shall ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks."

The 1990 Institute of Medicine report, *Towards Environmental Justice*, examined research and policy issues of environmental justice concerns that poor and minority populations are burdened with more than their share exposures to toxic waste, pesticide runoff, and other hazardous environmental exposures. IOM recommended identifying environmental hazards and assessing risk for populations of varying ethnic, social, and economic backgrounds, and the development of assessment methodologies that uniquely suit the populations at risk. In 2004, the National Environmental Justice Advisory Council (NEJAC) published, *Ensuring Risk Reduction in Communities with Multiple Stressors: Environmental Justice and Cumulative Risks/Impacts*, which provided many recommendations on how to involve communities in exposure and risk assessment, and how to emphasize a "bias for action" in environmental assessments.

EPA and External Guidance on Addressing Sensitive Groups: Since 1992, EPA has released other Agency-wide guidance and other tools to aid scientists in the assessment of sensitive or differentially exposed groups and life stages:

- Guidelines for Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (U.S. EPA, 2005a).

- Exposure Factors Handbook (U.S. EPA, 1997a). A summary of the available statistical data on various factors used in assessing human exposure.

- Standard Operating Procedures (SOPs) for Residential Exposure Assessments (U.S. EPA, 1997c). Procedures designed for those who assess exposure to pesticides in a residential setting.

- Technical workshop on issues associated with considering developmental changes in behavior and anatomy when assessing exposure to children (U.S. EPA, 2000a)

- Child-Specific Exposure Factors Handbook (Interim Report) (U.S. EPA, 2002). A summary of the available and up-to-date statistical data on various factors assessing children exposures.

- EPA OIG. EPA needs to consistently implement the intent of the executive order on environmental justice. 2004-P-00007. (March 1, 2004).

- Ensuring Risk Reduction in Communities with Multiple Stressors: Environmental Justice and Cumulative Risks/Impacts. EPA - National Environmental Justice Advisory Council (NEJAC, 2004).

- Framework for Assessing Risks of Environmental Exposure to Children (U.S. EPA, 2003b) External peer review of the framework and approach is in progress.

- Paper on Tribal Issues Related to Tribal Traditional Lifeways, Risk Assessment, and Health and Well Being: Documenting What We've Heard. National EPA-Tribal Science Council (U.S. EPA 2006b).

Issue 3: Evaluating Uncertainty and Variability, Including Probabilistic Analyses

Definition: Uncertainty and variability exist in all risk assessments. Thus, it is important that the risk assessment process handle uncertainties in a predictable way that is scientifically defensible, consistent with the Agency's statutory mission, and is responsive to the needs of decision makers (NRC, 1994). EPA has increasingly evaluated the potential for evaluating uncertainty and variability in risk assessments using techniques such as qualitative assessments and quantitative probabilistic risk assessments.

Uncertainty is defined as a lack of precise knowledge and can be reduced with additional research. Uncertainty is addressed either quantitatively or qualitatively. The National Research Council (NRC, 1994) identified two broad categories: parameter uncertainty and model uncertainty.

Variability refers to the inherent heterogeneity across space, in time, and among individuals. It cannot be reduced with additional investigation, only better understood or characterized. Human variability refers to person-to-person differences in biological susceptibility or in exposure or the variability of exposure for an individual person with time and location. Although both human variability and uncertainty can be characterized as ranges or distributions, they are fundamentally different concepts. Uncertainty can be reduced by further research that supports a model or improves a parameter estimate, but human variability is a reality that can be better characterized, but not reduced, by further research.

How This Element Will Contribute to and Improve Existing Exposure Assessment Approaches: In general, EPA's approach to variability has focused on exposure. Fuller, or more complete understanding of the ranges of exposures in an assessment, based on analysis of the variability and uncertainty, will aid the risk manager in the decision making process. The Guidelines will assist the exposure assessor in evaluating the available data in light of the goals of the assessment, e.g., what to consider, deciding when and how to use single data points, distributions of data, or sampling of data. Various types of models exist representing a range of methods focusing on frequency as well as expert judgment.

Application/Utility: The probabilistic risk assessment that addresses either uncertainty and/or variability in exposure and ultimately in the risk characterization is primarily a higher tiered or more refined assessment. However, the planning for the application of this technique may begin in the screening level assessment through a sensitivity analysis to identify the key parameters that contribute to the uncertainty. The information on the key parameters may then be used in the refined assessment.

As described above, the potential use of probabilistic risk assessment techniques to characterize exposure variability should be considered in the planning and scoping so that costs, resources, peer-review where appropriate, and time necessary to conduct the probabilistic risk assessment may be included in the estimates for the assessment. Sensitivity analyses are useful tools to identify which parameters in the exposure assessment are the key parameters for further probabilistic analysis. As the risk assessment progresses further refinements in the probabilistic risk analysis may be necessary based on information learned from the earlier stages of the assessment.

EPA and External Guidance on Evaluating Uncertainty and Variability: Since 1992, EPA's Risk Characterization Policy provided more direction for describing uncertainty in risk estimates. For probabilistic analysis specifically, EPA made significant efforts in recent years to use probabilistic techniques to characterize uncertainty; these include the 1997 Guiding Principles for Monte Carlo Analysis (USEPA, 1997b), the May 1997 Policy Statement (U.S. EPA, 1997d), and the December 2001 Superfund document Risk Assessment Guidance for Superfund: Volume III – Part A, Process for Conducting Probabilistic Risk Assessment (U.S. EPA, 2001a). Extensive literature exists regarding uncertainty and variability. Examples of documents include: books on application of probabilistic techniques (Cullen and Frey, 1999; Morgan and Henrion, 1990); case studies (Finley and Paustenbach, 1994); exposure models

(Maddalena et al, 2002); and the application of this technique in decision making (NRC 1994, Finkel 1990).

Topic 4: Involving Communities and Communicating Results

Definition: Public involvement encompasses the full range of activities that EPA uses to engage the American people in the Agency's decision-making processes. Public involvement is a progression that starts with outreach to build awareness and interest. It evolves to information exchange, through collaboration and recommendation to agreement and decision-making (http://www.epa.gov/publicinvolvement/intro.htm). Communication of exposure and risk assessment information involves the development of a sense of trust and credibility with the community so that the information is effectively exchanged with interested communities.

How This Element Will Contribute to and Improve Existing Exposure Assessment Approaches: Community participation is important in assuring the relevance and accuracy of the planning and scoping phase of an exposure and risk assessment, and in the communication of the risk analysis results. The 1992 Guidelines highlighted the importance of: communicating results of a risk assessment to the risk manager, establishing a communication strategy, presenting the results of the exposure assessment in a report, and reviewing the resulting exposure/risk assessment. Since that time, EPA developed a Public Involvement Policy (2003f) and associated homepage that outlines methods and tools to aid in involving the community and establishing trust and credibility with the community. Building on the trust and credibility within a community it is possible to work with the community to identify potential routes of exposure, duration and frequency of exposure, and community-specific exposure activities and practices to assure the exposure assessment reflects geographic-specific practices. The new guidelines will highlight sources of information on communication of exposure information and community involvement to aid the exposure assessor in assessing potential risks within the community.

Application/Utility: EPA recognizes the community may be aware of unique activities or practices that may result in higher or lower exposure assumptions than the standard defaults exposure assumptions used in risk assessments. Through community involvement practices and communication it is possible to work with the community to identify sources of this exposure information. For example, community members may be aware of past actions at a landfill, be aware of population-specific information on food consumption, activities within a specific geographic area, and be aware of locations of potential exposure (i.e., a specific exposure area where children play). Identifying this site-specific information will improve the exposure assessment. This site-specific exposure information is important in establishing exposure areas for media-specific sampling or identifying exposure routes, frequencies and durations. The establishment of trust and credibility with the community provides additional opportunities to obtain site-specific exposure information. This information is essential to meeting Data Quality Guidelines (EPA 2002c) and improving the transparency of the exposure assumptions and ultimately building trust and credibility with the community. The identification of exposure information is important in communicating with the community recommendations to reduce exposures.

Since the 1992 Guidelines were published, EPA has gathered a great deal of information regarding communication of risk information, both in theory and in practice. The new guidance will highlight the need for community involvement consistent with recent guidance documents. The update will include additional information regarding new theories of communication of risk assessment information, updates to the guidance documents originally listed, and provide additional information on presenting ranges of risk such as those developed in a probabilistic risk assessment. The assessment will also provide information on risk comparisons.

The communication of exposure and risk information begins early in the risk assessment process so that the community can learn about the principles and practice of risk assessment. Following completion of the risk assessment challenges still exist regarding how to appropriately communicate this information in a format that is understandable to both the risk managers and the community and other interested parties. The updated Guidelines will provide links to guidance on developing audience appropriate exposure assessment documents including: summaries, detailed reports, graphics, and formal presentations at meetings and public availability sessions. In cases where probabilistic risk assessment is used, there are additional challenges to providing risk information to the community and these challenges and suggested approaches regarding communication will also be identified. An important portion of this process is to assure the exposure and risk information are explained in a clear and transparent manner consistent with EPA's Risk Characterization guidance.

EPA and External Sources of Guidance on Community Involvement and Communication: Extensive literature exists regarding community involvement and risk communication. EPA guidance documents are available at: http://www.epa.gov/stakeholders and http://www.epa.gov/publicinvolvement/policy2003/index.htm). Guidance on risk communication is also available (U.S. EPA, 1994, 1999, 2000a, 2000b, 2001a, 2003c, 2006c). These homepages include information for the exposure assessor to consider including: Agency policy, manuals, tools, guidance from other federal agencies, and public involvement techniques. These references provide an important, centralized pointer to information to consider before conducting an exposure assessment. In addition, there is an extensive published literature on risk communication and public involvement (Covello, 1987; Deisler, 1988; Fischhoff, 1995, 1997, and 1998); Hora, 1992; Ibrekk and Morgan, 1987; Johnson and Slivic, 1995; Kaplan, 1992; Morgan et al., 1992; Ohanian et al., 1997, and Thompson and Bloom, 2000). Other resources include the Pan American Health Organization training course on public involvement and risk communication (available at: http://www.cepis.ops-oms.org/tutorial6/i/index.html). The International Association of Public Administration also has information on public involvement available at: http://www.iap2.org/displaycommon.cfm?an=4. ATSDR. A Primer on Health Risk Communication Principles and Practices. Available online at: http://www.atsdr.cdc.gov/HEC/primer.html

Topic 5: Updating Exposure Assessment with New and Emerging Science: Computational Toxicology, Genomics, and Other Biometrics and Social Sciences

Definition: It is impossible to completely separate consideration of exposure and potential dose from consideration of internal dosimetry and response. Advances in

exposure measurement methods with a commensurate understanding of the time location activity patterns continue to reduce the gap between exposure and dose. Molecular toxicology, biomonitoring, epidemiology, the "-omic" sciences (genomics, metabonomics, proteomics) and social sciences have the potential to improve our ability to estimate exposure and its relationship to dose and health effects.

Description of How This Element Will Contribute to and Improve Existing Exposure Assessment Approaches: The 1992 Guidelines focused on environmental measurements to estimate exposure directly or indirectly defined as the concentration of the agent at the individual ("boundary of receptor"). Advances in exposure monitoring technology, biological monitoring and dosimetry provide tools to estimate exposure with greater precision and accuracy, especially when coupled with human activity and behavior data. Expanding this linkage to advances in molecular toxicology, epidemiology, and -omic sciences may provide a means to improve our ability to reconstruct exposure events from biological markers or early indicators of disease. The Guidelines will summarize these advances and describe how these tools can be incorporated into exposure assessments.

Application/Utility: In conducting the hazard and dose-response characterization portion of a risk assessment, the assessor must consider critical windows within development that may result in greater vulnerability to toxic effects. These windows are provided by the exposure assessment based on age, gender, behaviors (crawling, mouthing), activities (locations, product use, diet), and physiological factors (oxygen requirements, caloric requirements) that may lead to particularly high levels of exposure.

Likewise, human activities can be responsible for dramatic exposures. Many of these activities have been classified and categorized as time location activity patterns or exposure factors. Available data suggest that these patterns may be dependent on age, socioeconomic status, or cultural practices. Because human behavior can be highly variable and difficult to quantify, consideration is being given to developing better quantitative measures of the behavioral determinants of exposure. Research is required to identify, evaluate and apply tools developed in the social science arena by specialists in child development and environmental anthropology to characterize and classify behaviors that are major determinants of exposure. Recent field studies of adult and child behavior patterns (e.g., videography) indicate a need for more research, but field monitoring may improve our ability to characterize and classify various groups based on their potential to be exposed to environmental contaminants.

Dosimetry information can indicate the level of temporal resolution needed in exposure data and modeling. The fate of the agent (including half-life in the body) should be related to temporal patterns (continuous vs. intermittent) and standard measures (e.g., frequency and duration) of exposure.

The development of -omic technologies has evolved into three scientific disciplines: genomics, the study of genes and their function; proteomics, the study of the full set of proteins encoded by a genome; and metabonomics, the study of the total metabolite pool. The recent technological advances in these areas have led to the development of the field of toxicogenomics in which the effects that chemicals have on living organisms and/or the environment can be examined using genomic, proteomic, and metabonomic methods

(U.S. EPA, 2003d). These emerging tools in molecular biology may provide the potential to develop cellular and molecular indicators of exposure that can be used to assess the vulnerability of humans and wildlife to environmental stressors. Toxicogenomic tools provide the potential to improve identification and interpretation of early effects resulting from low-dose exposures. Better understanding of genomic expression will also provide insight into factors impacting differences in susceptibility to chemical exposure that is seen in the human population (Oberemm et al., 2005).

Ultimately, integrated research in genetics and genomics may elucidate specific altered molecular processes associated with genotypes representative of sensitive or vulnerable subpopulations. These data may then be incorporated into dosimetry models to reduce the uncertainties associated with assuming populations are homogeneous regarding toxic response to stressors. Indicators of susceptibility obtainable from body fluids may also be developed to provide simple methods to characterize population composition (U.S. EPA, 2003d).

EPA and External Guidance on New and Emerging Science: The Agency has generated guidance documents on the application of this technology to exposure and risk assessment:

- EPA's Science Policy Council Genomics Task Force Workgroup: Potential Implications of Genomics for Regulatory and Risk Assessment Applications at EPA (2004). http://www.epa.gov/osa/pdfs/EPA-Genomics-White-Paper.pdf

- EPA's Computational Toxicology Program: Home Page: http://www.epa.gov/ncct/index.html

- EPA draft guidance on use of microarray data (internal review); poster: http://www.epa.gov/ORD/scienceforum/2006/poster_abstracts/disease_susceptibility/DS_Gallagher.pdf

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