

**Summary Minutes of the
U.S. Environmental Protection Agency (EPA)
Science Advisory Board (SAB)
Metals Risk Assessment Framework Review Panel Meeting
February 1-3, 2005 Washington, D.C.**

Panel Members: See Panel Roster – Appendix A

Date and Time: Tuesday, February 1, 2005, 9:00 A.M. – 5:30 P.M.; Wednesday, February 2, 8:30 A.M. – 5:30 P.M.; Thursday, February 3, 8:30 A.M. – 1:00 P.M.

Location: SAB Conference Center, 1025 F Street, N.W., Suite 3705, Washington, D.C.

Attendees: Chair: Dr. Deborah Swackhamer

Panel Members:

- Dr. Max Costa
- Dr. David Dzomak
- Dr. Kevin Farley
- Dr. Ivan Fernandez
- Dr. Bruce Fowler
- Dr. Andrew J. Friedland
- Dr. A. Jay Gandolfi
- Dr. Joshua Hamilton
- Dr. Kim Hayes
- Dr. Robert Hudson
- Dr. Thomas La Point
- Dr. Samuel Luoma
- Dr. Glenn Miller
- Dr. James Shine
- Dr. Katherine Squibb
- Dr. William Stubblefield
- Dr. Bernard Weiss
- Dr. John Westall
- Dr. Herbert Windom
- Dr. Judith Zelikoff

EPA SAB Staff:

- Thomas Armitage, Designated Federal Officer
- Vanessa Vu, Director, EPA Science Advisory Board Staff Office
- Anthony Maciorowski, Associate Director, EPA Science Advisory Board Staff Office

Other EPA Staff:

- Edward Bender, EPA Office of Research and Development

William Farland, EPA Office of Research and Development
Erin Koch, EPA Office of General Counsel
Pamela Noyes, EPA National Center for Environmental Assessment
Keith Sappington, EPA National Center for Environmental Assessment
Randall Wentsel, EPA Office of Water
William Wood, EPA National Center for Environmental Assessment

Others Participating:

William Adams, Rio Tinto, NAMC
John Arnett, Copper and Brass Fabricators Council
Nancy Beck, U.S. Office of Management and Budget
Kevin Bromberg, U.S. Small Business Administration
Khouane Dittarong, King and Spalding, LLP.
Larry Kaputska, Ecological Planning and Toxicology, Inc.
M. Keener, CRWI
James Laity, Office of Management and Budget
Debra Littleton, U.S. Department of Energy
Jane Luxton, King and Spalding, LLP
Margaret MacDonell, Argonne National Laboratory
Ann Smith-Reiser, Asincorp.
Ron Wellson, PMA

Meeting Summary

The discussion followed the issues and timing as presented in the meeting agenda (Appendix B)

Tuesday, February 1, 2005

Convene Meeting, Call Attendance

Dr. Thomas Armitage, Designated Federal Officer (DFO) for the SAB Metals Risk Assessment Review Panel opened the meeting at 9:00 A.M. He stated that the Science Advisory Board (SAB) is a chartered federal advisory committee whose meetings are public by law. He reviewed Federal Advisory Committee Act (FACA) requirements, the Panel's compliance with federal ethics and conflict-of-interest laws, and the panel formation process. Dr. Armitage stated that, as DFO he would be present during Panel business and deliberations. Records of Panel discussions are maintained and summary minutes of the meeting will be prepared and certified by the Panel Chair. Dr. Armitage then asked the Panel members to identify themselves and their affiliations.

Dr. Vanessa Vu, Director of the EPA Science Advisory Board Staff Office, welcomed the meeting participants and thanked them for providing advice to EPA on the draft Framework for Inorganic Metals Risk Assessment

Purpose of the Meeting and Review of the Agenda

Dr. Deborah Swackhamer, Panel Chair thanked the Panel members for serving and reviewed the charge questions to the Panel and meeting agenda. She stated that the purpose of the meeting was to respond to EPA's charge questions concerning the draft document, *Framework for Inorganic Metals Risk Assessment*. She noted that after initial overview presentations from EPA, the entire Panel would discuss responses to the first two charge questions and part of the third charge question. Panel members would then break into three assigned groups (environmental chemistry and fate, human exposure and health effects, and ecological exposure and effects/bioaccumulation) to develop responses to the remaining charge questions. The Panel would then reconvene as a whole to hear reports from each of the breakout groups and deliberate on integrated responses to each of the charge questions. Dr. Swackhamer noted that the Panel would hear public comments after the overview presentations from EPA.

Background Presentation on Development of EPA's Framework for Inorganic Metals Risk Assessment (the Framework)

Representatives from EPA's Office of Research and development provided a background presentations addressing: 1) why EPA developed the draft document, *Framework for Inorganic Metals Risk Assessment*, 2) how the document was developed, 3) public comments on the document, and 4) an overview of the contents of the document (presentations are provided in Appendix C). The first presentation focused on why EPA developed the document and how it was developed. It was stated that there has been considerable interest in EPA's assessments of metals and metal compounds. It has become clear that the development of cross-Agency guidance for assessing metal and metal compounds should be a priority for EPA. The Agency therefore decided to initiate a process to address issues associated with metals and develop the *Framework for Inorganic Metals Risk Assessment*. Several examples of controversial science issues associated with metals risk assessment were identified, including use of BCFs/BAFs, use of human data to characterize bioaccumulation potential, and extent to which bioavailability and chemical speciation should be addressed in Agency assessments.

The Agency described the risk assessment context as an important organizing component of the framework, as it is a major factor in determining the type of analysis conducted. Specifically, the framework principles for metals are discussed in the context of three general categories of risk assessment: 1) national ranking and categorization; 2) national level assessments; and 3) site-specific assessments. These assessments can vary in detail from relatively simple screening analyses to complex definitive assessments. The programmatic challenges associated with metals risk assessment were briefly discussed.

Some of these challenges include both the unique properties of metals and the varying statutory requirements and assessment goals of EPA programs

The goals of developing cross-Agency guidance for metals risk assessment and the multi-step development process were described. The draft Framework is a part of a comprehensive effort by EPA to evaluate hazard and risk issues for metals and metal compounds. The metals work has been devised and implemented by a three-phased approach under the Metals Action Plan (MAP). It has included the development of white papers to articulate science issues specific to metals risk assessment, followed by the framework for metals risk assessment, and, if need be, the development of methodology to characterize and risk metals based on their relative hazard and risk.

The review process and opportunities provided for public comment on the draft Framework were described. The public was provided an opportunity to comment on the Metals Action Plan, the Science white papers developed as precursors to the Framework, and an external review draft of the Framework. In addition, a peer consultation workshop was held with external scientists from across EPA programs, other government agencies, academia, and the private sector to review an early draft of the framework, in which the public was also invited to comment.

The role of the Framework was described. It was noted that the Framework is not specific to a particular Agency program, but it is intended to provide recommendations concerning methods, models, and approaches that can be applied in different assessment contexts (i.e., ranking/categorization, national-scale, site specific assessments) across EPA programs. The intended audience of the Framework was described. It was noted that the primary audience is EPA risk assessors and risk managers, but the Framework is also intended to inform the public and stakeholders interested in understanding EPA's approach to the assessment of metals.

Panel members asked a number of questions about the purpose of the Framework document. Panelists asked who would use the document. EPA representatives responded that it is intended primarily for those who conduct risk assessments for EPA. Panelists asked whether EPA had much dialogue with Regional Offices in developing the document. EPA representatives responded that input was provided through EPA Regional risk assessors. Panelists asked EPA to define the intent of the research needs assessment in the Framework. EPA representatives responded that the research needs section of the Framework was developed to identify gaps in knowledge that need additional research. Panelists questioned whether the SAB would be asked to review a final Framework document. EPA representatives stated that typically the Agency will take SAB advice in developing a final product but the document will not go to SAB again unless this is requested.

Highlights of Public Comments on the Framework for Inorganic Metals Risk Assessment

EPA representatives presented highlights of public comments received on the Framework. EPA provided a 30-day public comment period on the draft Framework in anticipation of the SAB review. Comments were received from 11 individuals/organizations. Comments were received on terminology in the document including: accumulation, tolerance, biomagnification, and bioavailability. EPA also received requests to expand and correct text in several areas of the document. EPA received comments stating that the term bioaccumulation does not apply to human health assessment. Those who commented stated that bioaccumulation, applies to ecological assessment. Comments were also received stating that BAFs/BCFs should not be used as generic threshold criteria for the hazard potential of metals.

Panelists asked how BAFs and BCFs are now used by the Agency. EPA representatives responded that the Agency uses BAFs and BCFs in assessing field data. They are also used by EPA in establishing national criteria that support discharge limits.

Overview of EPA's Framework for Inorganic Metals Risk Assessment

EPA representatives provided an overview of the Framework document. The document was developed to provide a consistent set of principles to be considered in assessing risks posed by inorganic metals and to identify available methods, models, and approaches for use in metals assessments.

The purpose of the framework was described. It was stated that the Framework does not set forth a step-by-step process for metals risk assessment. The Framework addresses inorganic metals and metal compounds, including metals mixtures. The document does not address methyl mercury, although the document describes transformation processes for organometallics. Other Agency groups are addressing methyl mercury.

The contents of the various sections of the Framework were described. The Introduction sets forth the purpose, scope and regulatory context. Section 2 of the document, "Problem Formulation and Metals Principles," sets forth the major principles underlying metals analysis, provides guidance on how to set up the conceptual model, and provides guidance on the scope of risk assessments. Section 3 of the document provides recommendations for risk assessors in the form of bullet points. Section 4 of the document, "Metal Specific Topics and Methods," provides supporting material for the recommendations that are contained in Section 3. It is divided into parts according to subject matter: environmental chemistry, human health exposure pathway analysis and effects, and ecological exposure pathway analysis and effects. Section 5 of the document, "Research Needs," identifies specific research needs for each topic addressed.

Panelists asked a number of specific questions about the document. Panelists asked how EPA had balanced the objective of not being prescriptive with the need to foster consistent application of methods and applications for risk assessment. EPA representatives responded that it was the Agency's intent to develop the Framework for use across multiple EPA programs, with the possibility that EPA programs may need to develop more specific guidance to fit individual program needs. Panelists asked whether

the Framework is the forerunner to one or more guidance documents. EPA representatives responded that EPA Program offices typically use framework documents such as this one to develop their own more specific guidance. The Risk Assessment Guidance for Superfund was mentioned as an example. Panelists asked questions about the compounds addressed in the Framework. Panelists asked whether it was EPA's intent to address any assessment of organometallic compounds in the document. EPA representatives responded that it was not the Agency's intent to address assessment of these compounds in the framework. Panelists discussed the extent to which transformation of metals should be covered in the Framework. Panelists asked questions about the Unit World Model and who developed it. EPA responded that the Unit World Model was developed at the University of Delaware.

Following the EPA presentations the Chair recessed the meeting for a 15-minute break until 10:45.

Presentation of Issue Papers on Inorganic Metals Risk Assessment

The Panel heard an overview presentation from Dr. Lawrence Kapustka of Ecological Planning and Toxicology, Inc., on the Issue Papers that were developed to provide information for the Framework.

The charge and challenges in developing the issue papers were described. The papers focus on the unique properties of metals that should be considered in metals risk assessment. The Issue Papers describe the state of the science without being exhaustive, discuss special considerations related to regulatory requirements, suggest draft language for the Framework, and identify research topics.

Dr. Kapustka described the topic covered in each issue paper and the process used to review the issue papers. The five issue paper topics developed were: Environmental Chemistry, Bioavailability/Bioaccumulation, Exposure, Ecological Effects, and Human Health Effects (topics covered in the issue papers are provided in the presentation material in Appendix C).

Panelists asked questions about the issue papers. A panelist noted that there may be some lack of objectivity in the issue papers because physical transport modeling was not discussed. Panelists and EPA representatives discussed how the lists of research needs in the issue papers were generated and how the issue papers were reviewed. It was noted that 33 public groups provided comments on the issue papers.

At the conclusion of the discussion of the issue papers the Chair stated that the floor would be open for public comment.

Public Comments

Comments were presented at the meeting by the following individuals:
Dr. William Adams, Rio Tinto

Ms. Debra Littleton, U.S. Department of Energy
Dr. Margaret MacDonell, Argonne National Laboratory

Dr. Adams stated that his comments were presented on behalf of the North American Metals Council, an unincorporated group of 31 metals-producing and using associations and companies. Dr. Adams commented on the use of BCFs and BAFs as discussed in the Framework document. Dr. Adams stated that BCFs and BAFs should be used with care because tissue concentrations are inversely related to exposure conditions for inorganic metals and organometallic compounds. Dr. Adams stated that BCFs and BAFs should not be used for either screening level hazard assessments or for hazard ranking of metals or metal substances. Dr. Adams also stated that BCFs and BAFs reflect site-specific exposure conditions. He stated that when the relationship between exposure and tissue concentration of metals is understood, BAFs and BCFs can be used for site-specific assessments or predictions. Dr. Adams also commented on the use of Kd values as discussed in the Framework document. He stated that the Framework should indicate that there is no one partition coefficient that reflects distribution between dissolved and sorbed phases for a given metal. In addition, Dr. Adams provided comments on the applicability of the concept of bioaccumulation to risk assessment for metals in humans. He noted that because of the complexity of the distribution of metals among various target organs and differences in retention time between different metals, the concepts of bioaccumulation and persistence are of questionable applicability in risk assessment for metals in humans.

The text of Ms. Littleton's comments is provided in Appendix D below. Ms. Littleton commented that the term bioaccumulation does not apply to human health assessment. She stated that it applies specifically to ecological assessment.

Dr. Margaret MacDonell offered comments in support of Ms. Littleton's statement.

Panelists asked Dr. Adams and Ms. Littleton a number of questions. Panelists asked questions concerning the costs of collecting site-specific data to assess the partitioning of metals and the appropriate use of Kd values. Panelists also asked questions concerning use of the term bioaccumulation versus accumulation in metals risk assessment for humans.

At 12:00 p.m., following the public comment period, the Chair recessed the Panel for lunch. The Panel was reconvened at 1:00 p.m. to begin discussing the responses to the charge questions (provided in Appendix E below)

Panel Discussion of Framework Scope and Assessment Categories (Charge Question 1)

The Chair reconvened the Panel at 1:00 P.M. to discuss the response to charge question 1 (addressing the Framework scope). Panelists discussed a number of issues concerning the scope. Several panelists stated that the Framework had a "mixed personality." Panelists stated that the Framework has some aspects of a guidance document and some

aspects of a summary of the science. Panelists noted that the document does not appear to adhere to either approach consistently. Panelists noted that if the primary audience of the document is risk assessors, additional specific guidance may be needed. Panelists discussed at length whether the Framework provided an appropriate balance between a science summary and a guidance document. EPA staff stated that the document was developed to focus on risk assessment concerns that are unique to metals. The Framework is not intended to cover all aspects of risk assessment. Some panelists stated that they supported developing a document to initiate changes in the way EPA may be conducting risk assessments for metals.

Panelists discussed the question of whether the Framework was “too academic” and not focused on practical concerns. A panelist noted that the quality of writing in parts of the document could be improved but that it was important not to confuse the quality of writing with the issue of whether the document meets the stated purpose. Panelists noted that the Framework addresses the complexity of metals and important issues associated with metals risk assessment. Panelists recommended that section 5 discussing research needs should be removed and is beyond the document scope.

Discussion of Unique Aspects of Metals in the Framework

Panelists noted that some aspects of metals risk assessment could be more clearly covered in the document. Some panelists noted that the discussion of trophic transfer could be expanded. Other panelists noted that it is not clear in the Framework how EPA defined “metals and metal compounds.” Panelists noted that, although EPA stated that the document was not intended to address metals acting like organic compounds, parts of the document do in fact cover metal compounds that are organic. Panelists suggested that the document should more clearly articulate how inorganic metals are different from organic compounds.

Discussion of Categories of Risk Assessment Covered in the Framework

Panelists discussed the utility of the categories of risk assessment covered in the Framework. In general, panelists stated that they thought the categories of risk assessment were useful. Panelists discussed the question of whether the three categories of risk assessment in the document should be expanded to five categories. Panelists noted that much of the Framework was written from a site-specific risk assessment perspective. Panelists stated that the document could be revised to improve the discussion of risk assessment at a national scale. Panelists stated that in some places the Framework attempts to discuss both site specific and national scale risk assessments and that this is confusing. Panelists discussed whether the Unit World and metalloregion concepts of risk assessment should be further developed or revised in the Framework.

Some panelists stated that they found the presentation of risk assessment categories in the Framework to be useful, but they noted that there is a paucity of information in the document on endpoints or criteria that could be used for national ranking. Panelists stated that additional examples addressing national scale risk assessment would be useful.

Some panelists expressed the opinion that a separate section is needed to cover national scale ranking.

Panel Discussion of Problem Formulation, Metals Principles, and the Conceptual Model (charge question 2)

Panelists commented on whether the discussion of inorganic metals assessment principles is clearly articulated in the Framework, and whether the discussion is objective and has utility. Some panelists noted that atmospheric processes were not considered in the Framework document. Some panelists stated that a number of the principles in the Framework are not well formulated and articulated. Panelists compared the Framework to EPA's previous *Metals Assessment Plan* and noted that the Framework is not as easy to understand as the *Metals Assessment Plan*. Panelists commented at length on the Framework discussion of natural background concentrations of metals. EPA noted that the discussion of background concentrations of metals provides information to point out how site-specific risk assessment is different from a national evaluation. The Panel discussed a number of changes that could clarify the discussion of background concentrations of metals.

Some panelists noted that many of the principles in the Framework may be more applicable to national assessments not site-specific assessments. Panelists identified a number of issues that should be discussed in greater depth in the Framework. These issues included: sediment bioavailability and toxicity, trophic transfer, and sources of metals. Panelists noted that a discussion of biogeochemical cycles is missing from the Framework. Panelists discussed the importance of considering biogeochemical cycles in metals risk assessment. Panelists noted that parts of the text in the Framework addressed "toxicity testing" but did not move beyond this to address issues such as trophic transfer. A panelist noted that the document should address the issue of metals mixtures in more detail, particularly mixtures of metals and organic compounds. A panelist noted that this is particularly important in conducting human health risk assessments of metals inhaled with other gases.

Panelists discussed how the Framework addresses routes of exposure, noting that some key questions do not appear to be discussed in the document. A panelist noted that the discussion of essentiality in the Framework should provide more specific definitions. Panelists also discussed how acclimation is addressed in the Framework. A panelist noted that the discussion of acclimation in Section 4 of the Framework does not "come forward" into Section 2.

Conceptual Model

The Panel discussed the presentation of the conceptual model in the Framework. Panelists noted that the model lacks coverage of some important elements. These included feedbacks to biogeochemical cycles and transport. Panelist noted that the linkage between the conceptual model and various parts of the Framework is not clear. A number of possible clarifications in the figures depicting the conceptual model and the

level of detail required in the model were discussed. The Panel also discussed possible reorganization of the Framework structure to clarify the discussion of the conceptual model.

Following the discussion of metals principles, problem formulation and the conceptual model, the Chair stated that the panel would recess for a break and reconvene in three breakout groups to discuss the remaining charge questions. At 3:00 p.m. the Chair recessed the Panel for a break.

Breakout Group Discussion

The Chair reconvened the Panel at 3:15 p.m. and provided instructions for the breakout group discussion. The Chair stated that the Panel would meet in breakout groups for the remainder of the day and during the morning on the following day. The Chair reminded the panelists that they had been assigned to one of the following three breakout groups: 1) Environmental Chemistry/Fate and Transport, 2) Human Exposure and Health Effects, and 3) Ecological Exposure and Effects/Bioaccumulation. The Chair identified the charge questions to be discussed by each group: Charge questions 3.1 – 3.4 (all three breakout groups), Charge questions 3.5 – 3.7 (Environmental Chemistry breakout group), Charge questions 3.8 – 1.10 (Human Exposure and Health Effects breakout group), Charge questions 3.11 – 3.14 (Ecological Exposure and Effects). The Chair asked whether any members of the Panel had questions about assignments or remaining charge questions. There were no questions, so the Chair identified the rooms where the breakout sessions would be held and asked the panelists to meet as breakout groups and reconvene as a whole at 1:00 p.m. the following day to report on the breakout group deliberations. Breakout groups met for the remainder of the day and the morning of the following day to deliberate on assigned charge questions.

February 2, 2005

Breakout group deliberations continued from 8:30 a.m. until 1:00 p.m. when the Panel reconvened as a whole to discuss the responses to the charge questions.

Reports of Breakout Group Deliberations

The Chair reconvened the Panel as a whole at 1:00 p.m. to hear reports from each of the breakout groups and discuss integrated responses to the charge questions.

Environmental Chemistry Breakout Group

The environmental chemistry breakout group reported the results of its deliberation on the charge questions. In response to charge question 3.1, the group provided a number of comments on how well the recommendations in Section 3 of the Framework are supported by the detailed information in Section 4. The group stated that environmental chemistry recommendations are distributed throughout Section 3 of the Framework, particularly in Sections 3.2.1 and 3.3.1. The group provided specific comments on each

of the recommendations. In general, the group found that the environmental chemistry recommendations in Section 3 are supported by the discussion in Section 4. However, the group found that it was difficult to determine which parts of Section 4 correspond to particular recommendations in Section 3. The group stated that, in order to better assess the support for the recommendations, it would be helpful for EPA to provide a section identifier indicating the sources of the supporting information.

The group found that the environmental chemistry recommendations in the Framework lack some consistency with respect to scope. Some recommendations were found to be broad statements that may be of little practical use to a risk assessor, while others provide more specific statements. The group noted that, instead of providing a non-hierarchical list of recommendations, it would be useful for EPA to organize recommendations with respect to importance or specificity. The group also found that it may be useful to combine the discussion of soil and sediment into one section.

The group noted that the focus of many of the environmental chemistry recommendations in the Framework is on modeling. However, the group noted that little information is provided in the document on activities related to model validation or other empirical data collection efforts. The group also noted that many of the recommendations at the end of Section 3.3.1 of the framework are very specific, and that it is unclear whether this level of specificity is appropriate for a Framework document.

In response to charge question 3.2, the group noted that the breadth of coverage in the Framework of available tools for risk assessment and methods for metals analysis is impressive. The group found that more discussion should be provided on critical evaluation of available models and on model uncertainty. The group also noted that limitations of chemical speciation models and the difficulty associated with applying speciation-transport models should be addressed in more detail. The group noted that the coverage of certain topics in the Framework is unbalanced. The group identified a number of areas where more or less information would be appropriate. The group noted that the issue of binding to dissolved organic carbon is not specifically covered, and that marine environments are not discussed. The group also noted that biogeochemical cycles and their role in affecting the fate of metals in the environment should be acknowledged and discussed in the Framework.

In response to charge question 3.3, the group noted that numerous tools in the form of models and analytical methods are listed and discussed in the Framework. The group noted that analytical tools to measure inorganic metals species should be discussed in more detail in the Framework. The group noted that all of the discussions in the Framework that are related to speciation would benefit from consistent use of related terms. The group stated that research needs in the Framework were not addressed at a similar level of detail. The group provided supplementary material to concerning speciation and recommended that it be included in the Framework.

In response to charge question 3.4, the group noted that the tables in Appendix A-1 of the framework should be cross-referenced to the text. The group noted that tables do not

lend themselves well to discussion of complex topics and thus the utility of tables in this context remains in question. However, the group stated that it did not want to discourage the development of alternative table methods for summarizing appropriate information.

In response to charge question 3.5, the group concluded that the application of the Hard Soft Acid Base (HSAB) concept to the stability of metal complexes in the general context of risk assessment is presented in an unbiased manner. However, the group found that the clarity and completeness of the presentation could be improved by expanding the introduction to make users aware that quantitative calculations depend on thermodynamic data such as stability constants and solubility products. The group also found that the text should be clarified to note that the extent of the toxic response of bound metals is not addressed by the HSAB concept.

In response to charge question 3.6, the group noted that a practicing atmospheric chemist was not on the Panel. Review of the document by an atmospheric chemist was recommended to ensure that there are no gaps in coverage. The group pointed out several revisions to improve the completeness of the atmospheric chemistry section (e.g., addressing nanoparticles and long scale transport of metals).

In response to charge question 3.7, the group identified several limitations of models that should be clarified.

Human Exposure and Health Effects Breakout Group

The group found that there are some major issues that should be addressed before the Framework is finalized. The group strongly recommended that the Framework not distinguish between the term “bioaccumulation” to describe metal concentration in aquatic and terrestrial organisms and the term “accumulation” of metals for humans.

In response to charge question 3.1, the group provided a number of specific comments on the individual recommendations in the Framework document. These comments include suggested changes to amend or delete recommendations.

In response to charge question 3.2, the group noted that the information in Section 4 of the Framework concerning human health effects is not complete and contains errors. The group identified a number of key items that need to be addressed. The group recommended that the Framework include: consideration of nanoparticles and their associated metal content; further discussion of mercury speciation; revisions with regard to metal accumulation in humans, plants, and animals; discussion of toxicity at low doses; and discussion of the interactions between metals and other organic chemicals as applied to the problem of mixtures.

In response to charge question 3.3, the group noted that tools are available for measuring speciation and they are improving. The group noted that the Framework should not recommend specific tools. It should discuss the importance of determining speciation in environmental media and human biomonitoring samples. The group noted the need to

place the discussion of metal speciation in one location in the Framework. The group provided several additional revisions to improve the discussion of metal speciation in the Framework.

In response to charge question 3.4, the group noted that tables are a good way to summarize important points presented in the Framework. The group provided a number of specific recommendations to make the tables more useful.

In response to charge question 3.8, the group strongly recommended that EPA use the term “ambient” or “ambient levels” rather than “background.” The group provided specific glossary definitions for “ambient levels,” body burden,” and “human biological monitoring.”

In response to charge question 3.9, the group noted that for some metals there may be an apparent discrepancy between recommended daily intakes and calculated reference doses or reference concentrations. The group pointed out the need for a definition of essentiality that demonstrated the role of metals in essential physiological or biochemical processes. The group identified a number of revisions needed in tables in the Framework and pointed out the need to restrict the treatment of essentiality to humans.

In response to charge question 3.10, the group noted that the discussion of mixtures in the Framework is limited and needs clarification and expansion. A number of recommendations were provided in this regard.

Ecological Exposure and Effects Breakout Group

In response to charge question 3.1, the ecological exposure and effects breakout group provided specific comments concerning the recommendations in the Framework. The group recommended that: recommendations be separated from statements; recommendations be categorized to indicate whether they are useful for hazard evaluation national scale risk assessments, site specific risk assessments, complex, or screening level risk assessments; indication be included on whether recommendations address present or future utility, and the recommendations are supported in the Framework. The group noted that the recommendations in the Framework should be revised to make them more concise and to eliminate redundancy. The group stated that references to parts of the Framework should be added to the recommendations, and that references to the general literature should be moved from the recommendations to other parts of the Framework. The group also stated that there is a lack of parallelism between the aquatic and terrestrial parts of the Framework.

In response to charge question 3.4, the group recommended the use of tables to highlight recommendations, categorize, and summarize information. The group noted that the tables need reorganization and provided a suggested format.

In response to charge question 3.11, the group noted that there a deficiency in the discussion of dietary uptake and pointed out that it is important to recognize the

bioavailable fraction of metals. The group also noted that bioaccumulation is important for metals; however, bioconcentration factors are not useful for national assessments. The group recommended that trophic transfer be discussed in more detail in the document. The group also provided recommendations concerning the treatment of acclimation.

In response to charge question 3.12, the group commented that it would be important to discuss assessment tools that could replace bioconcentration factors and bioaccumulation factors. The group also noted that in the Framework, EPA should consider trophic transfer and the potential to transform into bioavailable organometals. The group stated that the Hard Soft Acid Base concept is appropriate for helping to estimate potential toxicity. The group further noted that bioaccumulation factors and bioconcentration factors are more appropriate for site-specific assessments. The group pointed out that a biodynamic approach and not a fixed ratio approach is most appropriate.

In response to charge question 3.13, the group pointed out that, if bioaccumulation dynamics are used, the variance and uncertainties are lessened. The group recommended that trophic transfer be used to bound the uncertainties, and recommended that a bioenergetics approach be used. The group also pointed out that the BAF/BCF (bioaccumulation factor/bioconcentration factor) ratio is not a valid approach for national scale assessments.

In response to charge question 3.14, the group pointed out that there is considerable debate on the use of SEM-AVS (simultaneously extracted metals – acid volatile sulfides) and BLM (biotic ligand) methods. This debate is not captured in the Framework. The group also pointed out that the Framework does not provide important information on the empirical use of correlational data for sediments. The group also noted a number of limitations associated with use of the BLM.

Following the breakout group reports the Chair recessed the Panel for a break and reconvened at 3:15 to for a discussion of integrated responses to the charge questions.

Development of Integrated Responses to the Charge Questions

The Chair stated that the Panel would discuss the responses to the Charge questions developed by each of the breakout groups and identify issues that should be resolved to reach agreement on an integrated response. Panel members discussed responses to the charge questions and deliberated on the responses developed by the breakout groups.

Members first discussed the use of tables such as those presented in the Appendix of the Framework. Panel members agreed that it would be useful to provide tables in the Framework, but that revisions were necessary. The panel discussed an example format for the tables.

Panel members next discussed the response to charge question 3.1. Members of the Panel noted that it was an enormous task for the Panel to determine where the

recommendations were located in the Framework. The Panel agreed that better “mapping of the recommendations” was needed. It was agreed that the number of recommendations in the Framework should be reduced. Members noted that this could be accomplished by combining redundant recommendations. In addition recommendations that were not stated as recommendations could be eliminated. Panelists also discussed the need to eliminate recommendations that were too prescriptive

Members discussed the responses to charge question 3.3. The Panel discussion focused on tools that are missing from the Framework. A panelist noted that the discussion is unbalanced throughout much of the Framework. It was noted that a discussion of uncertainties must be provided. It was noted that an organized and systematic way to deal with the uncertainties associated with each tool is needed.

The Panel discussed a number of points in the responses to charge question 3.3. It was noted that the research section of the Framework does not consistently address research needs. Some panelists suggested that this section be removed from the Framework. Panelists noted that it might be possible to expand upon the research needs in other parts of the Framework. There was some discussion of the Unit World Model and how it was presented in the Framework. It was noted that the model should be discussed in the Framework but the discussion should be balanced. It was suggested that Section 3 of the Framework could be reorganized to clearly identify tools that are ready for use now and those that need further development. A panelist suggested eliminating Section 3 and moving the recommendations to the end of Section 4. Other panelists noted that it would probably not be appropriate to eliminate Section 3 completely. Panelists discussed the need to reorganize parts of the Framework to improve the clarity of the document.

The Chair reminded the Panel that it would be important to develop much of the text of the SAB report as possible by the end of the face-to-face meeting. There was some discussion of whether the Framework should be reviewed a second time by the SAB. Panelists stated that the document would benefit from a second review after it has been revised.

Members of the environmental chemistry breakout group noted that they would like to provide a number of overarching recommendations to improve the Framework (in addition to the responses to the specific charge questions). A list of suggested overarching recommendations was provided to the Panel by the environmental chemistry breakout group. The overarching recommendations included: the need for greater clarity in organization of the Framework, the need to include additional discussion of geochemistry, the need to discuss categories of metals that can be modeled using the same model, the need to reduce the number of recommendations and increase consistency of recommendations, the need to deal with the “dual personality “ of the Framework (i.e., it is not clear whether it is a framework or a guidance document).

At the conclusion of the discussion, the Chair asked the Panel to continue the discussion of the integrated responses the following morning. The Chair stated that she wanted to provide some additional time the following morning for breakout groups to complete the

development of their responses to the charge questions. The Chair asked the breakout groups to complete their writing assignments by 9:30 the following morning. She stated that from 9:30 – 12:00 the Panel would complete the discussion of integrated responses. The chair then assigned individuals on the panel lead responsibilities for incorporating changes into integrated responses to charge question 1 and 2. The Chair asked these individuals and the breakout group leads to develop responses to all of the charge questions and provide them to the entire panel by 9:30 a.m. on the following day. The Chair then adjourned the meeting at 5:30 p.m.

February 3, 2005

Panel breakout groups and members with lead assignments for charge questions 1, 2, and 3 met from 8:30 a.m. – 9:30 a.m to complete development of responses to the charge questions.

The Chair convened the Panel as a whole to discuss any remaining issues associated with integrated responses. Copies of all the responses to the charge questions, and the overarching comments, were provided to panel members for the discussion. The Chair stated that she wanted to discuss any additions or changes needed in the responses.

The Chair asked for additional Panel comments on the overarching recommendations that had been distributed. A panelist noted that the nature and type of source and route of exposure is an important issue to be considered in the overarching recommendations. Another panelist noted that an overarching recommendation should be to define the term speciation. The Environmental Chemistry group had provided an IUPAC definition of speciation. The panelist who provided the definition offered to clarify it. Another panelist suggested that an overarching recommendation should address data quality and data needs in the Framework. The panelist offered to provide a bullet. A panelist raised the issue of biogeochemical cycling. The panelist stated that an overarching comment should recommend that EPA include a discussion of biogeochemical cycling in the Framework. Panelists also discussed overarching recommendations concerning modifications needed to clarify the tables in Section 3 of the Framework.

The Chair thanked the panelists for their comments and asked if there were any comments on the integrated response to charge question 1. Panelists stated that it was important to recommend that the Framework more clearly differentiate between those parts of the document that represent the framework, and those parts that represent specific guidance for risk assessors. The Director of the Science Advisory Board Staff Office described three types of EPA documents that are produced by the Agency, overarching Agency framework documents, specific program guidance, and standard procedures. Panelists further discussed the risk assessment categories in the Framework and indicated that the three categories could be described as five categories.

The Chair thanked the panelists for their comments and asked for additional comments on charge question 2. A panelist stated that the “principles” should be renamed. It was suggested that the principles be called “factors to be considered.” Panelists discussed

factors that should be further addressed in the Framework. These factors included routes of exposure, trophic transfer, and biogeochemical cycling. Panelists discussed the differences between metals and organic compounds and noted that careful definitions were needed in the Framework in this regard. Figure 2.3 of the Framework was discussed and panelists noted that it was a unifying graphic for Section 2. Panelists noted that Figure 2-3 should cross-reference other parts of the Framework. The Panel discussed whether the concept of metal specific ecoregions should be addressed in the Framework. Some panelists stated that this concept is useful and should be included in the Framework. The Panel discussed uncertainty associated with metalloregions. There was general agreement that, although there is uncertainty associated with the concept, it should be expanded in the Framework because it can potentially be very useful.

The Chair thanked the panelists for their comments and asked for additional comments on the integrated responses to all parts of charge question 3. There was further discussion of the Framework text addressing “background” concentrations of metals. Panelists stated that the term “ambient” should be used in the Framework, and that this should be interpreted to include both naturally occurring and anthropogenic metals. The Panel further discussed whether the term “bioaccumulation” applies to metals in humans. Panelists stated that bioaccumulation does apply to metals in humans. The Panel discussed the response to charge question 3.9. Panelists noted that revision of the essentiality table in the Framework was needed because some of the metals are not essential for humans. The Panel also discussed the need to include a table of reference doses and recommended daily allowances in the Framework. Panelists noted that the table should identify metals that are essential for humans. Panelists provided additional comments on the responses to charge questions 3.1 – 3.4. Panelists noted that the Framework should provide additional information on the analytical methods used to characterize speciation. Reorganization of the Framework was also discussed.

The Chair noted that several Panel members had to depart early and stated that she wanted to discuss the next steps in developing the Panel report before completing the discussion of the integrated responses. The chair stated that she wanted the breakout group chairs and leads for charge questions 1 and 2 to develop draft responses to the charge questions and submit them to the DFO within two weeks. The DFO and the Chair would develop a draft Panel report and send it to the Panel for review and discussion on a teleconference. The Panel discussed possible dates for the teleconference and tentatively decided on March 15. The Chair stated that after the teleconference the report would be revised and sent to the Panel for approval before transmittal to a quality review committee of the SAB. The final report would be reviewed and approved by the SAB after approval of the quality review committee.

The Chair then asked for additional comments on charge questions 3.8 – 3.10. Panelists noted that the response to charge question 3.10 should recommend expansion of the discussion of mixtures. Several panelists had additional comments on the response to charge question 3.5. It was noted that the Hard Soft Acid Base concept was presented in the Framework in the context of toxicity assessment. It was noted that revision of the Framework was needed to more clearly state the limitations of the Hard Soft Acid Base

concept. The Panel also discussed the need to provide alternatives to the use of the BAFs and BCFs

The Chair asked for additional comments on the integrated responses to charge questions 3.11 – 3.14. Panelists noted that there is a lack of parallelism between the part of the Framework addressing soil and that part addressing the aquatic environment. Panelists stated that BAFs and BCFs should be used to make site-specific decisions not national assessments. The need to consider dietary uptake of metals was further discussed.

The Chair then asked panelists if they had any additional comments on any of the integrated responses to the charge questions. There were no additional comments. The Chair then thanked the panelists for a productive meeting. She asked for revised integrated responses to the charge questions within two weeks and adjourned the meeting at 12:00 p.m.

Respectfully Submitted:

Certified as True:

/Signed/

/Signed/

Thomas M. Armitage, Ph.D.
Designated Federal Officer

Deborah L. Swackhamer, Ph.D.
Panel Chair

APPENDICES

Appendix A: Roster of SAB Metals Risk Assessment Framework Review Panel

Appendix B: Teleconference Agenda

Appendix C: EPA Presentations

Appendix D: Public Statements at Panel Meeting

Appendix E: Charge Questions to the Panel

APPENDIX A - Panel Roster

U.S. Environmental Protection Agency Science Advisory Board Metals Risk Assessment Framework Review Panel

CHAIR

Dr. Deborah Swackhamer, Professor, School of Public Health, University of Minnesota, Minneapolis, MN

MEMBERS

Dr. Max Costa, Professor and Chairman, Department of Environmental Medicine, New York University School of Medicine, New York, NY

Dr. David Dzombak, Professor, Department of Civil and Environmental Engineering, Carnegie Mellon University, Pittsburgh, PA

Dr. Kevin Farley, Professor, Department of Civil and Environmental Engineering, Manhattan College, Riverdale, NY

Dr. Ivan Fernandez, Professor, Department of Plant, Soil, and Environmental Sciences, University of Maine, Orono, ME

Dr. Bruce Fowler, Assistant Director for Science, Division of Toxicology, Agency for Toxic Substances and Disease Registry, Atlanta, GA

Dr. Andrew J. Friedland, Professor and Chair, Environmental Studies Program, Dartmouth College, Hanover, NH

Dr. A. Jay Gandolfi, Assistant Dean for Research and Graduate Studies, College of Pharmacy, University of Arizona, Tucson, AZ

Dr. Joshua Hamilton, Professor, Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH

Dr. Kim Hayes, Professor and Director, Environmental and Water Resources Engineering Program, University of Michigan, Ann Arbor, MI

Dr. Robert Hudson, Associate Professor, Department of Natural Resources and Environmental Science, University of Illinois at Urbana-Champaign, Urbana, IL

Dr. Thomas La Point, Professor and Director, Department of Biological Sciences, University of North Texas, Denton, TX

Dr. Samuel Luoma, Senior Research Hydrologist, U.S. Geological Survey, Menlo Park, CA

Dr. Glenn Miller, Director, Center for Environmental Science and Engineering, University of Nevada, Reno, NV

Dr. James Shine, Assistant Professor of Aquatic Chemistry, Department of Environmental Health, School of Public Health, Harvard University, Boston, MA

Dr. Katherine Squibb, Associate Professor, Department of Epidemiology and Preventative Medicine, University of Maryland School of Medicine, Baltimore, MD

Dr. William Stubblefield, Senior Environmental Toxicologist, Parametrix, Inc., Albany, OR

Dr. Bernard Weiss, Professor of Environmental Medicine, University of Rochester Medical Center, Rochester, NY

Dr. John Westall, Professor, Department of Chemistry, Oregon State University, Corvallis, OR

Dr. Herbert Windom, Professor, Skidaway Institute of Oceanography, Savannah, GA

Dr. Judith Zelikoff, Associate Professor, Department of Environmental Medicine, New York University School of Medicine, Tuxedo, NY

SCIENCE ADVISORY BOARD STAFF

Dr. Thomas Armitage, Designated Federal Officer, US EPA Science Advisory Board (1400F), 1200 Pennsylvania Avenue, NW, Washington, DC 20460

B APPENDIX B – Meeting Agenda

SCIENCE ADVISORY BOARD
Metals Risk Assessment Framework Review Panel
SAB Conference Center
1025 F Street, N.W., Suite 3705, Washington, D.C. 20004

February 1-3, 2005, Public

AGENDA

Tuesday, February 1, 2005

- 9:00 - 9:10 a.m. **Meeting Convened by the Designated Federal Officer**
Dr. Thomas Armitage
- 9:10 - 9:15 a.m. **Welcoming and Introductory Remarks**
Dr. Vanessa Vu, Director, EPA Science Advisory Board
Staff Office
- 9:15 - 9:30 a.m. **Purpose of the Meeting and Review of Agenda**
Dr. Deborah Swackhamer, Chair
- 9:30 – 10:30 a.m. **Highlights of EPA’s Framework for**
Inorganic Metals Risk Assessment
Dr. William Farland, Acting EPA Assistant Administrator
for Science

Dr. William Wood, EPA National Center for
Environmental Assessment

Dr. Randall Wentsel, EPA Office of Water
- 10:30 – 10:45 a.m. **BREAK**
- 10:45 – 11:15 a.m. **Issue Papers on Inorganic Metals Risk Assessment**
Dr. Lawrence Kapustka, Ecological Planning and
Toxicology, Inc.
- 11:15 – 12:00 p.m. **Public Comments**
- 12:00 – 1:00 p.m. **LUNCH**

- 1:00 – 2:00 p.m. **Panel Discussion of Framework Scope and Assessment Categories (Charge Question 1)**
Dr. Deborah Swackhamer and Panel
- 2:00 – 3:00 p.m. **Panel Discussion of Metals Principles and Problem Formulation (Charge Question 2)**
Dr. Deborah Swackhamer and Panel
- 3:00 – 3:15 p.m. **BREAK**
- 3:15 – 3:45 p.m. **General Discussion of Charge Question 3 and Instructions for Breakout Group Sessions**
Dr. Deborah Swackhamer, Chair
- 3:45 – 5:30 p.m. **Concurrent Breakout Group Meetings**
(Panel will meet in breakout rooms to develop responses to the charge questions)
-- Environmental Chemistry/Fate and Transport
-- Human Exposure and Health Effects
-- Ecological Exposure and Effects/Bioaccumulation
- 5:30 p.m. **RECESS FOR THE DAY**

Wednesday, February 2, 2005

- 8:30 – 8:45 a.m. **Summary of Previous Day and Expectations for Today**
Dr. Deborah Swackhamer, Chair
- 8:45 – 10:30 a.m. **Concurrent Breakout Group Meetings (continued)**
(Panel groups will meet in breakout rooms to develop responses to the charge questions)
-- Environmental Chemistry/Fate and Transport
-- Human Exposure and Health Effects
-- Ecological Exposure and Effects/Bioaccumulation
- 10:30 – 10:45 a.m. **BREAK**
- 10:45 – 12:00 a.m. **Concurrent Breakout Group Meetings (continued)**
(Panel groups will meet in breakout rooms to develop responses to the charge questions)
-- Environmental Chemistry/Fate and Transport
-- Human Exposure and Health Effects
-- Ecological Exposure and Effects/Bioaccumulation
- 12:00 – 1:00 p.m. **LUNCH**

1:00 – 3:00 p.m. **Reports of Breakout Group Deliberations**
Dr. Deborah Swackhamer and Panel

3:00 - 3:15 p.m. **BREAK**

3:15 – 5:30 p.m. **Panel Develops Integrated Responses to the Charge Questions**
Dr. Deborah Swackhamer and Panel

5:30 p.m. **RECESS FOR DAY**

Thursday, February 3

8:30 – 8:45 a.m. **Expectations for the Day**
Dr. Deborah Swackhamer, Chair

8:45 – 9:15 a.m. **Review of Draft Responses to Charge Question 1**
Dr. Deborah Swackhamer and Panel

9:15 – 9:45 a.m. **Review of Draft Responses to Charge Question 2**
Dr. Deborah Swackhamer and Panel

9:45 – 10:45 a.m. **Review of Draft Responses to Charge Question 3**
Dr. Deborah Swackhamer and Panel

10:45 – 11:00 a.m. **BREAK**

11:00 – 1:00 p.m. **Review of Draft Responses to Charge Question 3**
(continued)
Dr. Deborah Swackhamer and Panel

1:00 p.m. **ADJOURN MEETING**

Framework for Inorganic Metals Assessment

William Farland, Ph.D.
Acting Deputy Assistant Administrator for Science
Office of Research and Development

Background

- ❑ **There has been considerable interest in the Agency's assessments on metals and metal compounds as illustrated by recent events surrounding promulgation of the Toxics Release Inventory (TRI) lead rulemaking and development of the Agency's Waste Minimization Prioritization Tool.**
- ❑ **As a result of discussions within the Agency, with external stakeholders and with Congress, it became clear that the development of cross-Agency guidance for assessing metal and metal compounds should be a priority for EPA.**
- ❑ **The Agency therefore decided to initiate a process to address the issues associated with metals that will provide opportunities for external input, peer review and cross-Agency involvement. Responsibility was assigned to the Science Policy Council with technical support from the**

Examples of Controversial Science Issues

- ❑ **Application to metals of the criteria in the Agency's PBT chemical rule to characterize the persistence and bioaccumulation of toxic chemicals.**
- ❑ **Comparison of BCF/BAF data to numerical criteria for the purpose of determining a metal's bioaccumulation potential.**
- ❑ **The appropriate use of human data in characterizing a metal's bioaccumulation potential.**
- ❑ **The extent to which bioavailability and chemical speciation should be addressed in national rulemaking.**
- ❑ **Whether the consideration of persistence has any relevance to metals.**



EPA Legislation Addressing Metals

- ❑ Metals and metalloids in the environment are of concern to almost all EPA programs.**
- ❑ Examples include:**
 - Clean Air Act**
 - Clean Water Act**
 - Safe Drinking Water Act**
 - CERCLA and RCRA**
 - EPCRA (TRI Program)**

Types of Assessments Conducted by the Agency

- ❑ **Site-specific Assessments** conducted to inform decisions concerning a particular , e.g., a Superfund site.
- ❑ **National Regulatory Assessments** conducted to set media standards or to develop guidance, e.g., Maximum Contaminant Levels, National Air Quality Standards, ambient water quality criteria, Superfund soil screening levels, and national release and/or treatment standards for industrial categories.
- ❑ **Ranking or Characterization** for purposes such as priority setting, information



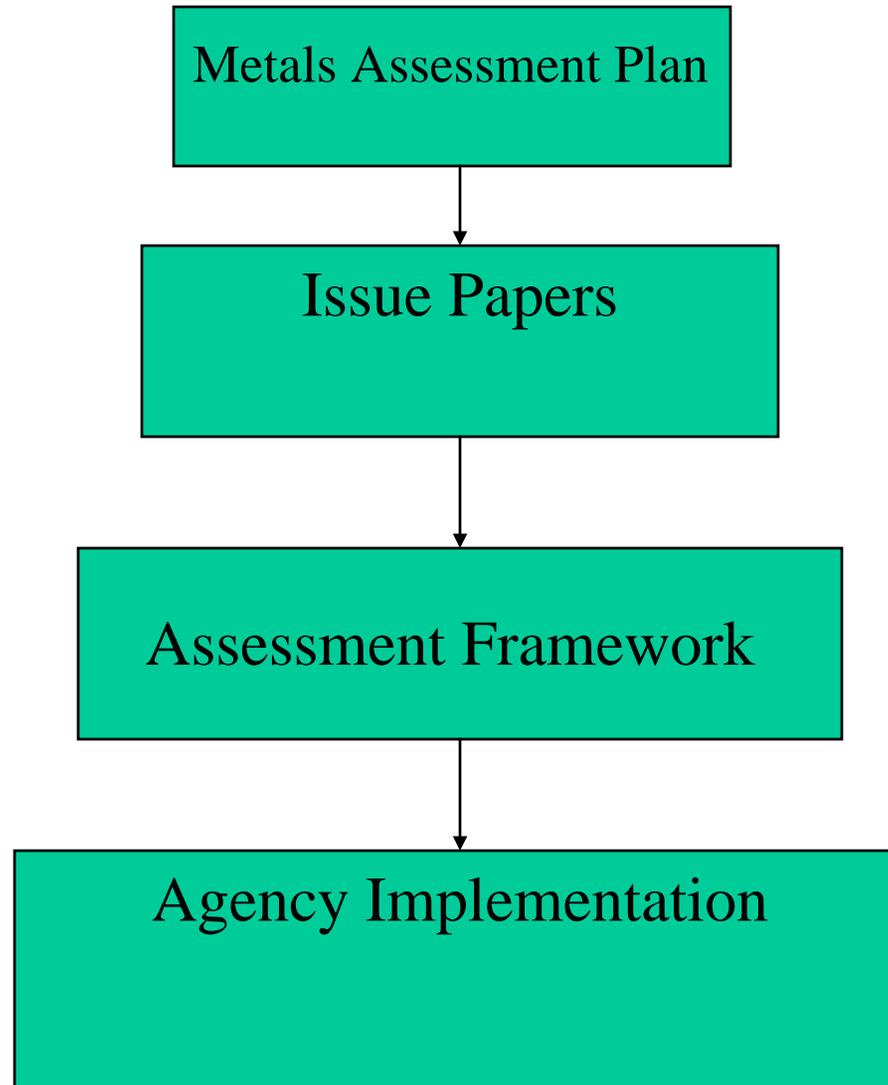
Programmatic Challenges

- ❑ Difficult to develop a single approach for all programs based on available science**
- ❑ All programs acknowledge the unique properties of metals that make assessment difficult**
- ❑ Programs have different ways of dealing with the unique features of metals due to:**
 - statutory requirements and assessment goals**
 - availability of exposure and effects data**
 - degrees of conservatism**
 - ways of dealing with uncertainties**

Overall Goal of the Metals Assessment Project

The goal of this cross-Agency guidance will be to articulate a **consistent approach** for assessing the hazards and risks of metals and metal compounds, based on application of all available data to a **uniform and expanded characterization framework**. Such an assessment **would involve reviewing a broad range of physico-chemical properties** that may go beyond those encompassed in the Lead TRI Rule and **may suggest more of a case-by-case (i.e., metal by metal) approach** to evaluating metals and metal compounds. This guidance on approaches to characterizing metals and metal compounds will benefit many of our programs.

Multi-step Development Process



Participation by the Public, Stakeholders, and the Scientific Community

- Opportunities provided for the public to comment on the Action Plan, Science Issue Papers, and Framework.**
- Convening of two public meetings to facilitate dialogue.**
- Involvement of internal and external scientific experts in developing the Science Issue Papers and review of an early draft of the Framework.**
- SAB review of the Action Plan and the Framework.**

Role of the Framework

The Framework's role is to articulate a consistent set of principles and conceptual model for assessing the hazards and risks of metals and metal compounds that can be applied across the variety of assessments conducted by the Agency. Meant to avoid errors of omission.

The Framework is not specific to a particular Agency program but is intended to make recommendations as to methods, models, and approaches that can be applied in different assessment contexts.

The Framework can provide the basis for future development of science policy and program specific guidance as needed.

INTENDED AUDIENCE

- **The Intended Audience for the Framework :**
 - **primary audience is EPA risk assessors, risk managers, and others who perform assessments for the Agency.**
 - **also intended to inform the public and stakeholders interested in understanding EPA's approach to the assessment of metals.**

Next Steps

- The Agency will begin work to incorporate SAB recommendations based on discussions at this meeting and will make final revisions after receiving official SAB recommendations. Goal is to finalize Framework this summer.
- Agency programs have already begun to examine their current practices and science policy positions vis-à-vis the Framework's recommendations. Programmatic decisions to make any changes will follow SAB's final recommendations.
- SPC will determine based on discussions with program offices whether additional Agency-wide guidance is needed to facilitate implementation by the programs.

Highlights of Public Comments on Framework for Inorganic Metals Assessment

William P. Wood, Ph.D.
Executive Director
Risk Assessment Forum
Office of Research and Development

Background

- EPA provided a 30 day public comment period on the draft Framework in anticipation of the SAB review.**
- All comments received have been forwarded to SAB staff for consideration by SAB panel members.**
- Comments have been received from 11 individuals/organizations.**
- Many of the commenters provided comments previously on the Action Plan, the Issue Papers, and/or an early draft of the Framework.**
- Overall, commenters had positive things to say about the openness of the process and the quality of document.**
- Those who have commented before acknowledge that many of their comments have been addressed.**
- Still some issues remain. These generally represent some of the more controversial issues.**

Public Comments

- **Terminology-related comments**
 - Accumulation (in humans) and bioaccumulation (in ecological receptors)
 - Tolerance reflects concepts of acclimation and adaptation
 - Biomagnification
 - Bioavailability versus bioaccessibility

Public Comments (cont.)

- **Requests to expand/correct discussions in several areas:**
 - Inclusion or lack of inclusion of metals (e.g., Mg, U, Va, Cd, Ni)
 - Further discussion about plant uptake factors and reference to some recent metals assessments
 - Analytical methods data gaps for metals species
 - Validation and implementation issues surrounding Biotic Ligand Model (BLM)
 - Refinement of generic conceptual model
 - Dermal pathway of exposure

Public Comments (cont.)

- **Comments that bioaccumulation does not apply to human health assessment.**
 - Rather, it applies to ecological assessment, notably related to indications of PBT for organic metals.
 - Recommend that the human health discussion should state that PBT factors are not appropriate for use in addressing hazard ranking for humans.
 - No current methodology exists for evaluating human bioaccumulation or determining if one substance is more bioaccumulative than a second substance.
 - Emphasize PBPK/PBPD models in understanding the toxicokinetics of metals in humans (no simple metric presently available for looking at the behavior of metals in humans).

Public Comments (cont.)

- **Comments that bioaccumulation does not apply to human health assessment (cont'd).**
 - Explain that bioaccumulation, defined as the net accumulation of a metal in a tissue of interest or a whole organism, may be of limited value in humans, for most metals, since body compartments are in dynamic equilibrium with differing turnover rates.

Public Comments (cont'd)

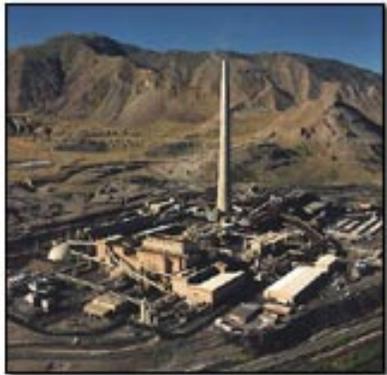
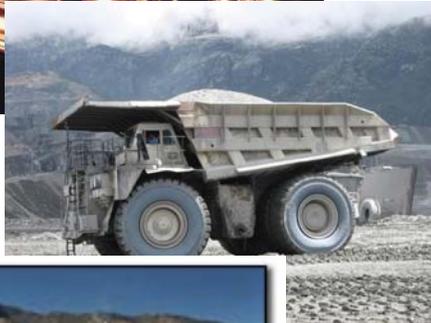
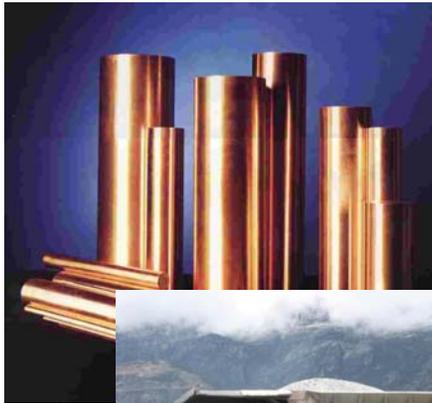
- BAFs/BCFs
 - Comments generally support recommendation that BCFs/BAFs should not be used as generic threshold criteria for the hazard potential of metals.
 - However, comments state that further clarification of the role and applications of BCFs/BAFs in metals assessment is needed. In particular, their use in ranking/ priority setting.

Framework for Inorganic Metals Risk Assessment

Randall Wentzel and Anne Fairbrother
U.S. EPA
Science Advisory Board Review
February 1, 2005

Metals Framework

Charge:



- ❑ **Develop a comprehensive framework that could be the basis of future Agency actions**
- ❑ **Provide a consistent set of basic principles to be considered in assessing risks posed by inorganic metals**
- ❑ **Identify available methods, models, and approaches for use in metals assessments**

Framework Purpose



- ❑ **Science-based document**
 - Addresses the special attributes of inorganic metals and metal compounds when assessing their human health and ecological risks
- ❑ **Provides currently available **tools** and **recommended approaches****
 - Addresses modifications for particular **regulatory contexts**

Framework Purpose (cont.)

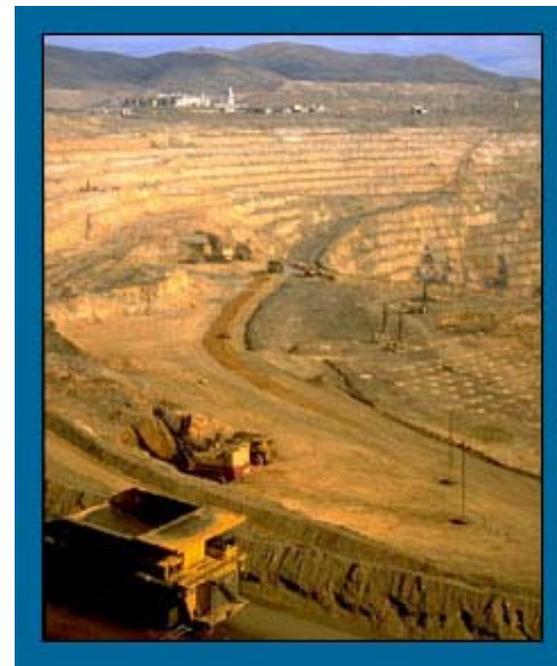


- ❑ Framework **does not** put forward a step by step process
 - Works within current risk assessment guidelines to guide assessors on the **unique properties** of metals and metal compounds
- ❑ Framework **is not** proscriptive for how any particular type of assessment should be done within a USEPA program office

Framework Purpose (cont.)

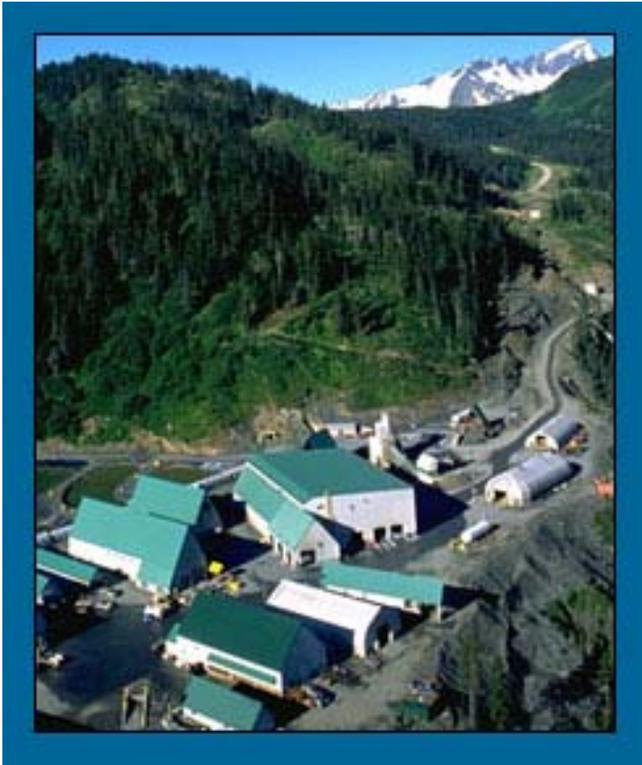
- ❑ Focuses on issues associated with **inorganic metal compounds**
 - However, describes transformation processes for organometallics
 - Methyl mercury not included because other Agency groups are actively addressing issues

- ❑ Meets SAB request to stress importance of **environmental chemistry and mixtures**



Framework Outline

Section 1 - Introduction



- ❑ **Sets out the purpose, scope, and regulatory contexts**
 - **National criteria**
 - **Screening and detailed**
 - **Ranking and Classification**
 - **Site specific assessments**
 - **Screening and detailed**

Framework Section 1

Introduction

- 1.1. Purpose and Audience
 - Guidance to risk assessors on inorganic metals
- 1.2. Framework Scope
 - Science-based on special attributes of inorganic metals
- 1.3. Risk Assessment Framework
- 1.4. Metals Assessment Context
 - National Ranking and Categorization
 - National-Level Assessments
 - Site-Specific Assessments
- 1.5. Organization of Framework

Framework Section 2

Problem Formulation & Metals Principles

To account for **metals-specific differences** in risk analysis –



- ❑ States the **major principles** underlying metals analysis
- ❑ Provides guidance on how to set up the **conceptual model**
- ❑ Provides guidance on the **scope of the assessment**

Framework Section 2

Problem Formulation & Metals Principles

□ 2.1. Principles of Metals Risk Assessment

Environmental Background Concentrations

Because metals are naturally present in the environment, it is important to consider the background concentrations of metals when conducting risk assessments.

Essentiality

Some metals are essential to maintaining proper organism health and may cause adverse effects when present at deficient or excess amounts. The influence of metals essentiality on exposure and effects of the metal(s) of concern should be addressed to the extent practicable in the assessment.

Environmental Chemistry

The environmental chemistry of metals strongly influences their fate and effects on human and ecological receptors.

Framework Section 2

Problem Formulation & Metals Principles

□ Principles Continued

Bioavailability

The bioavailability of metals and, consequently, the associated risk vary widely according to the physical, chemical, and biological conditions under which an organism is exposed. To the extent that available data and methods allow, factors that influence the bioavailability of a metal should be explicitly incorporated into assessments. In situations where data or models are insufficient to address bioavailability rigorously, the assumptions made regarding bioavailability should be clearly articulated in the assessment as should the associated impact on results.

Bioaccumulation and Bioconcentration

Organisms bioaccumulate metals through multiple mechanisms of uptake, distribution, metabolism, and elimination. The highly complicated and specific nature of metals bioaccumulation substantially hinders the ability to accurately predict bioaccumulation and extrapolate results across species and exposure conditions, particularly when simplified models are used (e.g., BAF/BCF).

Framework Section 2

Problem Formulation & Metals Principles

□ Principles Continued

Acclimation, Adaptation, and Tolerance

Metals naturally occur at a range of environmental concentrations and are influenced by local biogeochemical controls on metal cycling. Within limits, organisms have developed mechanisms for coping with excess metals exposure.

Toxicity Testing

Owing to limitations in available data and test methods, application of laboratory-derived toxicity data often requires extrapolation of results across test species, metal compounds, and exposure conditions that affect bioavailability. Toxicity data should be expressed in a manner comparable to environmental exposure estimates, thus accounting for bioavailability, tolerance (acclimation and/or adaptation), and species-response effects.

Mixtures

Metals frequently occur as mixtures owing to their natural abundance in the environment and the dietary essentiality of some metals for normal physiological functioning. Metals may interact either synergistically, additively, or antagonistically in various ways, depending on the combinations of metals and their relative amounts.

Framework Section 3

Risk Assessment Recommendations

- ❑ Succinct “**bullet points**” for risk assessors
- ❑ Directed toward **risk assessors** in EPA
 - Program offices, Regional offices
- ❑ Application to various **types of risk assessments**
 - Site-specific, national criteria, ranking or categorization
 - The degree of application will depend on the type and level of the assessment (e.g. screening or detailed)
 - Not all recommendations apply to all types of risk assessments
- ❑ Additional supporting text, etc. in **Section 4** and in the **Issue Papers**

Framework Section 3

Risk Assessment Recommendations

□ 3.1. Human Health

- 3.1.1. Fate and Transport
- 3.1.2. Exposure Assessment: background; air, dietary, water pathways, integrated approaches, bioavailability
- 3.1.3. Effects Analysis: PBPK/PBPD models, essentiality, toxicity, mixtures, sensitive subpopulations/life stages

□ 3.2. Aquatic Environment

- 3.2.1. Fate and Transport
- 3.2.2. Water Column Exposure, Bioavailability, and Effects
- 3.2.3. Background
- 3.2.4. Bioaccumulation
- 3.2.5. Trophic Transfer, Biomagnification, and Dietary Toxicity
- 3.2.6. Sediment Exposure and Effects
- 3.2.7. Metals mixtures

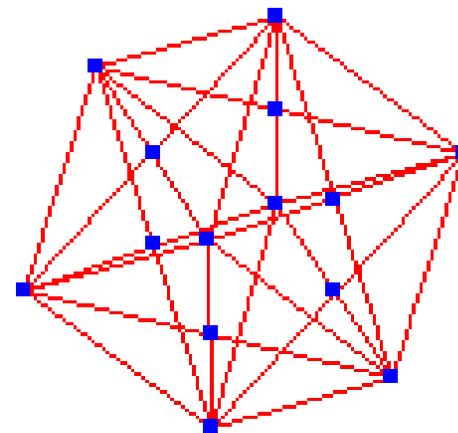
□ 3.2. Terrestrial Environment

- 3.3.1. Fate and Transport: Atmospheric chemistry; soil mobility and transformations
- 3.3.2. Exposure Assessment: Background; soil invertebrates & plants; wildlife; food chain modeling; bioaccumulation;
- 3.3.3. Toxicity Assessment: Adaptation & acclimation; essentiality; metals mixtures; toxicity testing; extrapolation of effects

Framework Section 4

Metal Specific Topics and Methods

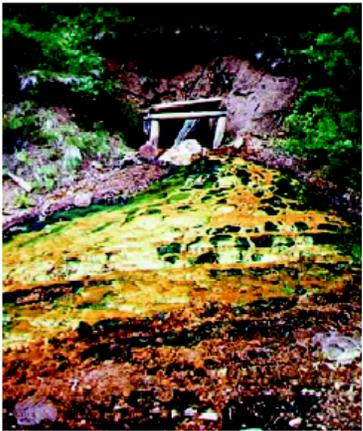
- ❑ **Provide supporting material for Section 3 recommendations**
 - Not meant to be an exhaustive review
- ❑ **Focus is on attributes specific to inorganic metals**
- ❑ **Divided by subject matter (Environmental Chemistry, Human Health and Ecological)**



Framework Section 4

Metal Specific Topics and Methods

- 4.1. **ENVIRONMENTAL CHEMISTRY**
 - Reviews Metal Chemistry
 - Discusses Media Specific Chemistry
 - Discusses methods for K_d , aging, soil metal transfer to plants and metal speciation
- 4.2. **HUMAN EXPOSURE PATHWAY ANALYSIS**
 - Presents the Applications and Limitations for Models and Methods
 - Discusses Routes of Entry and Integrated Exposure Approaches
 - Reviews Modeling Approaches (e.g. Toxicokinetics and PBPK)
- 4.3. **HUMAN HEALTH EFFECTS**
 - Presents Tools and Methods
 - Discusses Essentiality Versus Toxicity
 - Reviews the Toxic and Essential Properties of Metals
 - Reviews Variations in Susceptibility



Framework Section 4

Metal Specific Topics and Methods

- **4.4. ECOLOGICAL EXPOSURE PATHWAY ANALYSIS**
 - Presents Models and Methods
 - Reviews Aquatic and Terrestrial Transport Pathways
 - Discusses Routes of Exposure to Aquatic and Terrestrial Species
- **4.5. CHARACTERIZATION OF ECOLOGICAL EFFECTS**
 - Presents Applications and Limitations of Tools and Methods
 - Reviews Background, Acclimation/ Adaptation, Essentiality, and Mixtures Issues
 - Discusses Bioavailability and BAF/BCF Issues in Terrestrial and Aquatic Systems
 - Reviews Sediment, Soil, and Wildlife Toxicity Issues

Framework Section 5

Research Needs



- ❑ On-going EPA and external research
- ❑ Specific needs for each topic area
- ❑ Discussion of Unit World model
 - Evolving approach for calculating critical loads
 - Currently under development for aquatic compartment
 - Water column & sediment
 - Future work for terrestrial systems

Core Technical Panel

Co-leads:

Anne Fairbrother	ORD/NHEERL
Randall Wentzel	OW/OST

Steering Committee:

Stephen Devito	OEI/OIAA
Alexander McBride	OSWER/OSW
David Mount	ORD/NHEERL
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SCIENCE ADVISORY BOARD
Metals Risk Assessment Framework Review Panel
SAB Conference Center

Issue Papers on Inorganic Metals Risk Assessment

1 February 2005

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Issue Papers

- Langmuir, D; Chrostowsk, P; Vigneault, B; Chaney, R. (2004). Issue paper on the environmental chemistry of metals. September 2004.
- McGeer, J; Henningsen, G; Lanno, R; Fisher, N; Sappington, K; Drexler, JW. (2004). Issue paper on the Bioavailability and Bioaccumulation of Metals. September 2004.
- Newman, MC; Diamond, GL; Menzie, C; Moya, J; Nriagu, J. (2004). Issue paper on metal exposure assessment. September 2004.
- Kapustka, LA, Clements, WH; Ziccardi, L; Paquin, PR; Sprenger, M; Wall, D. (2004). Issue paper on the ecological effects of metals. September 2004.
- Goyer, RA; Golub, M; Choudhury, H; Hughes, M; Kenyon, E; Stifelman, M. (2004). Issue paper on the human health effects of metals. September 2004.

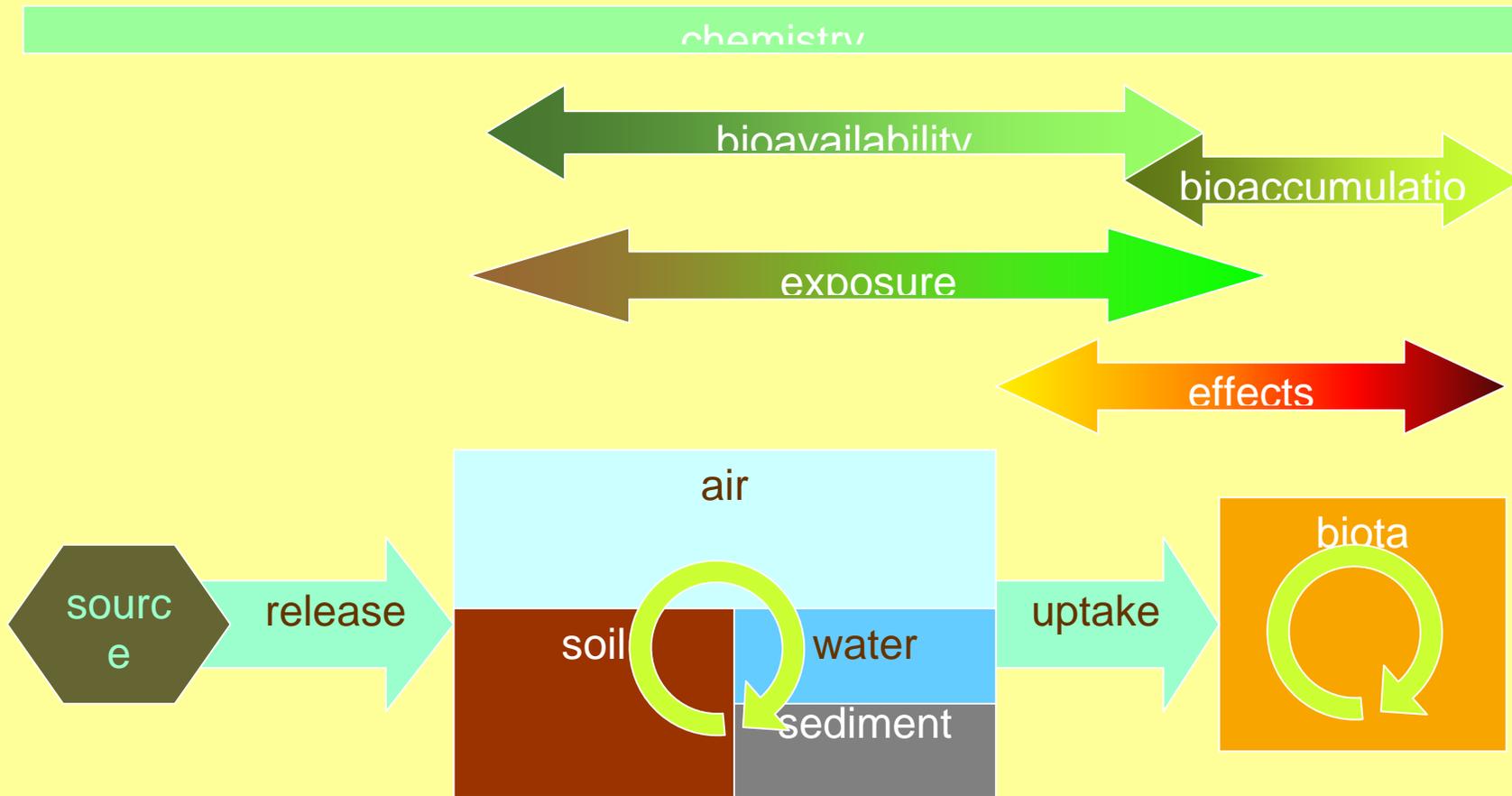
Charge and Challenges

- Focus on unique properties of metals as addressed in risk assessment
- Describe the “state-of-the-science” without being exhaustive -- reference key literature
- Discuss special considerations related to regulatory requirements (i.e., across range from hazard ranking to site-specific assessments)
- Project likely future developments
- Suggest draft language for the *Framework*
- Identify research topics

Reviews/Responses

- 33 individuals/organizations plus US EPA supplied comments
- Many reviewers wanted expanded text, many more references
- Flagged redundancies, contradictions
- Reconciliation/response table >650 pages
- Selectively expanded text, shifted some subsections among papers
- Harmonized terminology

Basis for "Redundancies"



Redundancies

- Biotic Ligand Model (BLM) discussed in each paper
 - BLM provides a way of organizing the array of physical, chemical, and biological information that helps predict toxic responses to metals
- Essentiality, background, bioavailability, bioaccumulation, transformations, effects touched on in each issue paper
- Determination regarding inclusion of “redundancies” largely left to lead authors
 - Different degrees of emphasis
 - Transitional passages included to improve readability and flow (considered better than calling out specific references to the respective companion papers)
 - Recognition that chemists would likely read the chemistry paper before diving into the other issue papers; ...

Environmental Chemistry

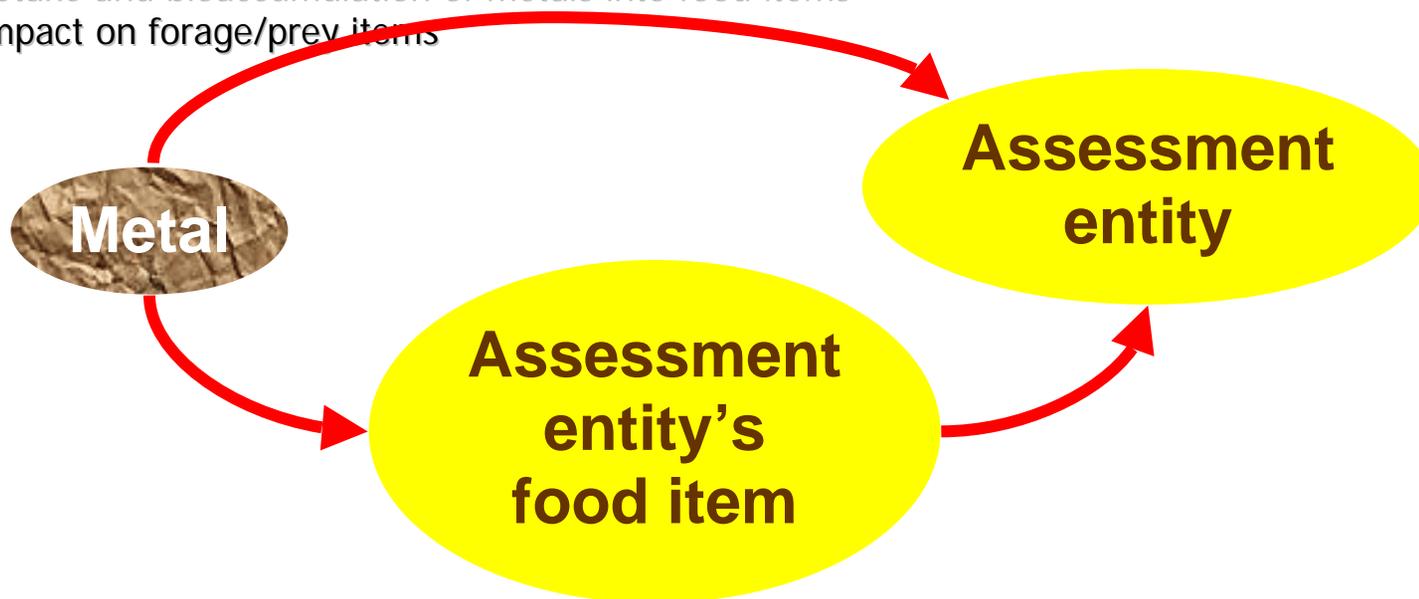
- Introduction
 - listing of the metals of concern identified by the Agency
 - the natural occurrence of metals in the environment
 - concepts of baseline or background concentrations are defined
 - geographic distribution of metals are described
 - sources of data and maps are identified
- Subtopics
 - metal speciation and metal complexes
 - classification of metals into hard and soft acids and bases
 - importance of pH amply illustrated with activity curves for the various metal species
 - (adsorption controls)
 - (solubility controls)
 - bioavailability and transfers to plants and livestock couched in terms of chemical properties
 - Biotic Ligand Model (BLM) -- focused on features of metal speciation modeling
 - atmospheric chemistry of metals
 - metal speciation in waters and soils

Bioavailability/Bioaccumulation

- Define (bioaccessibility, bioavailability, and bioaccumulation)
- Transformations of metals (speciation) in environmental media influences accessible to biota
 - largely physico-chemical processes
 - several biochemical reactions
- Upon contacting a living membrane, biochemical and physiological activities effect transfer across the membrane and into the cells
- Various metabolic processes distribute the metals into different tissues or organs in the organism
- Some metals in some biota accumulate (occasionally to very high concentrations relative to the environmental media)

Exposure

- Bridge between the abiotic and the biotic media (aquatic receptors, terrestrial receptors, human health receptors)
- Subtopics
 - pathways
 - fate and transport
 - hard and soft acids and bases
 - speciation
 - bioavailability
 - effects
- Exposure assessment typically includes ingestion of food, water, and soil/sediment
 - uptake and bioaccumulation of metals into food items
 - Impact on forage/prey items



Ecological Effects

- Subtopics
 - essentiality
 - physiological responses
 - mechanisms of toxicity
 - toxicity test methods
- Special emphasis
 - individual-based (organism-based) features of metal toxicity
 - ecological consequences, (i.e., those occurring at the population-level or higher)
 - acclimation
 - adaptation
 - microbial functions
- extrapolation issues
 - across chemical forms
 - among species
 - lab-to-field

Human Health Effects

- Subtopics
 - essentiality,
 - extrapolation from animal model species
 - interactions between metals
 - dietary exposure pathways
 - cancer and non-cancer endpoints are considered
- Special emphasis on target tissue/organ effects (As, Cd, Hg, Pb)
 - measured or modeled distribution of metals within the body
 - retention of and excretion of metals
 - specific end organ effects
- Pharmacokinetic/Pharmacodynamic models
- Specific attention given susceptibility groups
 - age
 - gender
 - genetically determined variability

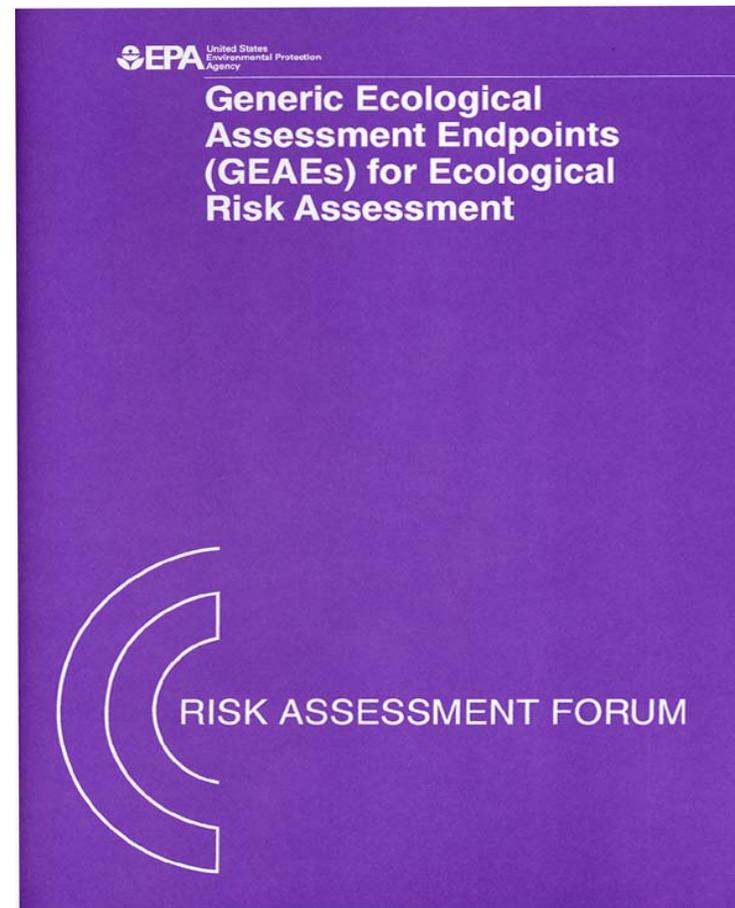
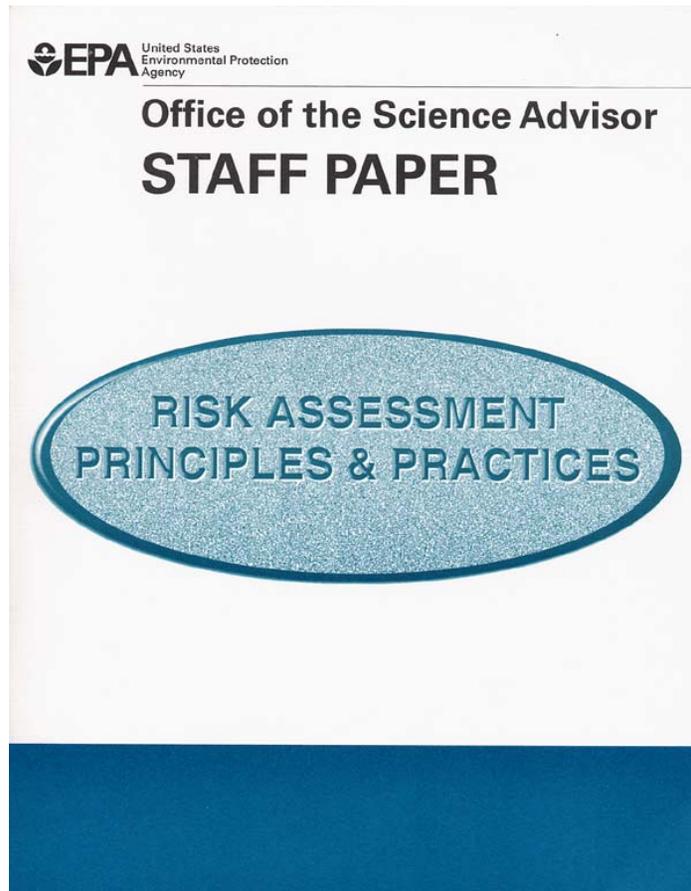
Issue papers as Reference Documents

Paper	References
Chemistry	~ 150
Bioavailability/bioaccumulation	> 200
Exposure	> 200
Ecology	~ 250
Human Health	> 75

Unresolved Matters

- Research agendas, though not contradictory among issue papers, have not been ranked as a single list
- Unit World Model was not prominent among the issue paper authors
 - Limited technical experience among authors
 - Healthy skepticism awaiting more results
- Marked differences between HHRA and EcoRA
 - Segregation of the practices (guidance; personnel)
 - Different endpoints (i.e., organism versus population)

Underlying split between ecological and human health risk assessment -- Recent US EPA Documents



G. W. Suter *et al.* 2004. *Individuals versus Organisms versus Populations in the Definition of Ecological Assessment Endpoints.* SETAC Poster

Precedent for Organism Attribute Endpoints

Attributes of an	Human Health Risk Assessment	Ecological Risk Assessment
Individual Organism	Probability of death or injury	Seldom used
Population of Organisms	Frequency of death or injury or Numbers dying or injured	Frequency of mortality or anomalies

Precedent for Population Attribute Endpoints

Attributes of an	Human Health Risk Assessment	Ecological Risk Assessment
Individual Population	Not used	Extirpation, Production, or Abundance
Set of Populations	Not used	Seldom used (e.g., extinction rate)

APPENDIX D - Public Statements at the Panel Meeting

Public Statement for the Science Advisory Broad's Metals Risk Assessment Framework Review Panel –February 1, 2005

*Debra Jo Littleton, U.S. Department of Energy
Office of Fossil Energy, Office of Planning and Environment*

The Department of Energy (DOE) and the Small Business Administration (SBA) have been extensively involved with the development of the Environmental Protection Agency's Metals Assessment Framework over the last several years. We believe that this Framework is a much needed and valuable document, and it contains a great deal of sound scientific information relevant to inorganic metals. The SBA and DOE have both filed comments on this draft Framework that have been provided to the SAB for consideration during this peer review, and I refer you to those comments for the specific areas in the report that need clarification. Today I would just like to highlight one primary comment from each of the DOE and SBA comments. There is language that appears throughout the document that may be misconstrued by those who have not closely followed the iterative development of this report – and which must be corrected so that possible scientific misinterpretations do not occur during human health assessments. The primary comment relates to clarifying the distinction between bioaccumulation and accumulation terminology for ecological and human health assessments. This could be addressed specifically under Charge Question 2.1.

The Framework focuses on *human and ecological* assessment of *inorganic* metals. Although used in various sections of this report as a general term, the term *bioaccumulation* **does not apply to human health assessment**. It applies specifically to *ecological* assessment, notably related to indications of “persistent, bioaccumulative, and toxic” (PBT) for organic metals. In a number of places, EPA has taken care to be specific about usage of the word bioaccumulation, and it is important to revise the content elsewhere throughout the document where the distinction between bioaccumulation in ecological species and accumulation in humans is unclear, beginning with the Executive Summary.

Understanding that the EPA commissioned the issue papers in an effort to provide state-of-the-art expert information on these topics for the Framework, we encourage including valuable text from the August 2004 Human Health Effects Issue paper regarding this topic in response to Charge Question 3.1. The issue paper cautioned that “[a]ccumulation in this context [accumulation of metals in organs that results from chronic exposure to metals] refers to the capacity-limited sequestration of metals in a specific organ or tissue and not in the sense of bioaccumulation or biomagnification discussed in the Bioavailability and Bioaccumulation Issue paper.” The issue paper further noted that “the concepts of bioaccumulation and persistence are questionable when it comes to metals risk assessment for humans for a number of reasons” and that “[t]he concept of PBT (persistence, bioavailability (sic), and chronic toxicity, discussed in the Bioavailability

and Bioaccumulation Issue paper) regarding metals in environmental media may not be a valid way to predict chronic toxicity in humans because of the complexity of distribution between various target organs, and differences in retention time between different metals.” *August 2004 Issue Paper section 7.1, p. 18*. Incorporating these statements in the human health discussion of the Framework would parallel the clear discussion in the analogous section on aquatic ecology, Section 3.2. “The latest scientific data on bioaccumulation do not currently support the use of BCF and BAF values when applied as generic threshold criteria for the hazard potential of inorganic metals (e.g., for classification as a “PBT” chemical).” *Framework section 3.2.4*.

Thus, I would ask the SAB to review both DOE and SBA comments, which include examples of sections and wording throughout this important Framework, that need correction or further clarification to limit possible confusion regarding *accumulation* vs. *bioaccumulation*. For example, the human health sections 4.2 and 4.3 should emphasize that based on current science, PBT factors are not appropriate for use in hazard ranking for humans. The text should further state that there is no current consensus methodology for evaluating human bioaccumulation or determining if one inorganic substance is more bioaccumulative than another.

To illustrate the importance of this clarification to avoid further misapplication, a recent EPA final rule preamble stated that lead is known to bioaccumulate in bone. This type of misrepresentation or inappropriate use of terminology can be avoided in the future if clear language is provided in this strong Framework.

On a related note, it would be helpful if two other terms could be used more consistently. *Bioavailability* is sometimes used when the discussion seems to be addressing *bioaccessibility*, as defined in this document. Reflecting clear and consistent definitions in this Framework, and in the supporting Issue Papers, will help limit confusion so risk assessors will use these terms more appropriately in the future. (Some examples of where the terminology seems confusing are included in the DOE Comments.)

I have one final point from our comments that I would like to bring to the SAB’s attention as you develop your report. DOE has reviewed many drafts of the Framework, and many of us at the July 2004 Peer-Input Workshop found that the concept of example tables, as an appendix or in the Recommendations Section 3, to illustrate points across the three categories of assessment was very valuable. We hope the SAB will seriously consider the usefulness of these tables when addressing charge question 3.4. These tables could serve as excellent, practical guides for risk assessors implementing this Framework across a variety of programs. They could effectively synthesize key information from the “applications” sections, as balanced by useful points made in the “limitations” sections. (Note that those companion sections are not provided in the Framework for all main topics, so presenting such information in these tables would help fill that current context gap.) We believe that providing a full set of these tables would further enhance the significant contributions this document will make to the practice of inorganic metals risk assessment.

The Framework is an excellent and well-documented product that will serve EPA and other users for years to come. It is important that the Framework be as comprehensive as possible, and we have worked hard for many years towards that goal. I thank you for allowing me to highlight a couple of concerns from the comments of DOE and SBA today. I would also like to compliment EPA once more for their sustained dedication and outstanding efforts in developing this valuable report.

APPENDIX E – Charge Questions to the Panel

Framework for Inorganic Metals Risk Assessment

Charge to the Panel

Background

Many U.S. Environmental Protection Agency (EPA) programs face decisions on whether and how to regulate metals. These decisions range from controlling releases to the environment, to establishing acceptable levels in environmental media, to setting priorities for programmatic or voluntary activities. A basic input to the decision-making process for most EPA programs is an assessment of the potential hazards or risks posed by metals or metal compounds to human health and the environment.

The Agency recognizes that inorganic metals present unique issues and the added challenge of addressing the complexity of these issues in a consistent manner across the Agency's programs. The Framework for Inorganic Metals Risk Assessment reflects an EPA effort to develop cross-agency guidance for assessing metals (within all programs and regions). The overarching goals of the framework are to outline key inorganic metal-specific scientific principles and approaches in metals risk assessment, based on the best currently available science. As such, the framework provides recommendations, including applications and limitations of currently available tools and methods, for conducting inorganic metals risk assessment. These recommendations are designed to supplement current Agency human health and ecological risk assessment guidance.

Given the complexity of issues surrounding inorganic metals risk assessment, to engage the external scientific community, the Agency commissioned external experts to lead the development of a series of papers on metal-specific issues, including environmental chemistry, exposure, human health effects, ecological effects, and bioavailability and bioaccumulation. Some individual EPA experts contributed specific discussions on topic(s) for which he or she has scientific expertise or knowledge of current Agency practice. The framework relies heavily on these issue papers. Development of the framework has involved extensive consultation with the scientific community, stakeholders, and intended users. Throughout the development process, the Agency has held stakeholder meetings and made the issue papers open for public comment. Likewise, the Agency has made the framework open for public comment, and has consulted with other federal agencies as part of interagency review.

Charge to the SAB Peer Review Panel

EPA is seeking comment from the SAB on the scientific soundness of the framework's synthesis of the state of the science. Specifically, the Agency seeks comment on: the overall objectivity and utility of the recommendations and supporting

tools, methods, and models to its primary audience, EPA risk assessors, and the public; and whether there are any additional research needs that warrant inclusion or further discussion in the framework. To facilitate SAB review, please refer to definitions of pertinent terminology (i.e., objectivity, utility) in OMB's Information Quality Guidelines for guidance, summarized here as follows:

- Objectivity – A focus on whether the disseminated information is being presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased.
- Utility – The usefulness of the information to its intended users, including the public.

Specific Charge Questions

Question 1: Section 1 - Framework Scope and Assessment Categories

- 1.1 Please comment on the overall framework scope and whether it is sufficiently encompassing to allow for the consideration of the broad spectrum of physical and chemical properties, exposures, and effects among inorganic metals and metal compounds.
- 1.2 The context of the regulatory application (e.g., contaminated site clean-up, national regulation, or programmatic decision) is a major factor in determining the type of analysis that is appropriate for a particular assessment. The framework identifies three general categories of assessments, including site-specific assessments, national scale assessments, and national ranking and categorization. With the understanding that screening and detailed assessments occur within the assessment categories, please comment on the utility of these categories in setting the context for discussion of metals assessment.

Question 2: Section 2 - Problem Formulation, Metals Principles, and Conceptual Model

- 2.1 Please comment on whether the discussion of inorganic metals assessment principles is clearly articulated, objective, as defined above, and has utility.
- 2.2 Please comment on how well the conceptual model presents key metal processes and whether (or not) it is complete.

Question 3: Sections 3, 4, and 5 – Recommendations, Tools/Methods, and Research Needs

Questions 3.1 – 3.4 address the recommendations, data, tools, methods, and research needs discussed in sections 3, 4, and 5 of the guidance document. Questions 3.5

– 3.14 focus specifically on distinct topics in environmental chemistry, human exposure and health effects, or ecological exposure and effects.

- 3.1 Please comment on how well the recommendations under Section 3 are supported by the detailed information in Section 4. Are there other recommendations that should be included? Are there any inorganic metals or metal compounds for which any of the recommendations would not apply?

Note: Recommendations pertaining to environmental chemistry are distributed throughout Section 3, particularly under Sections 3.2.1 and 3.3.1 presenting recommendations on environmental fate and transport.

- 3.2 Please comment on the objectivity and utility of the data, tools, and methods discussed in Section 4. Identify any scientific or technical inaccuracies, or any emerging areas or innovative applications of current knowledge that may have been overlooked or warrant a better discussion of uncertainty, including areas needing further research.
- 3.3 Please comment on the state of the science (i.e., data, tools and methods) to address inorganic metals speciation in all environmental compartments for any given inorganic metal from the point of environmental release to the point of toxic activity as discussed in the document. Please comment on whether the framework identifies appropriate research needs to overcome any limitations in the state of the science. Please address these questions separately for each of the three types of assessments presented (i.e., site-specific, national level, and ranking and categorization.)
- 3.4. In an earlier draft of the framework, EPA had included three Summary Recommendation Tables in Section 3 on human health, aquatic, and terrestrial risk assessment, covering the three general assessment categories (i.e., site-specific, national level, and ranking and categorization). An example of this table is included as Appendix A in the draft provided to the SAB. To minimize confusion for users of the framework, the initial idea behind the recommendations and adjoining table was to have concise recommendations on the science, followed by a separate accounting of how these recommendations could then be applied to the different assessment categories. Reviews have been mixed on the utility of these tables as a sufficient communication tool. Please comment on whether tables of this type would be useful for inclusion in the final version of the framework. Does the panel have alternative suggestions for effectively communicating how the recommendations can be considered for each of the three assessment levels?

Environmental Chemistry (Sections 3.3.1, 4.1)

- 3.5 Please comment on the objectivity of the Hard Soft Acid Base concept to applications of stability of metal complexes in toxicity assessments. See Section 4.1.2.

- 3.6 Please comment on the objectivity of the atmospheric metal chemistry discussion and its application to exposure assessments. See Sections 3.3.1.1 and 4.1.7.
- 3.7 Please comment on the objectivity of the metal chemistry and environmental parameters incorporated in the various metal surface complexation and partition coefficient models and their applications to exposure assessments. See Sections 3.3.1.2 and 4.1.4.1.

Human Exposure and Health Effects (Sections 3.1, 4.2, 4.3)

- 3.8 Please comment on the objectivity of the discussion and recommendations on natural background of metals. See Sections 3.1.2.1 and 4.2.2.1.
- 3.9 Please comment on the objectivity of the discussion of essentiality versus toxicity, including the relationship between Recommended Daily Intakes (RDAs) and thresholds such as Reference Doses (RfDs) and Reference Concentrations (RfCs). See Sections 3.1, 4.3.2, and 4.3.3.
- 3.10 Please comment on the objectivity of the discussion and recommendations presented for assessing toxicity of mixtures, including how to assess additivity versus departure from additivity. See Sections 3.1.3.4 and 4.3.6.

Ecological Exposure and Effects (Sections 3.2, 3.3, 4.4, 4.5)

- 3.11 Please comment on the objectivity of the discussion and recommendations concerning natural background, bioavailability, bioaccumulation, biomagnification, and trophic transfer in both aquatic and terrestrial environments. See Sections 3.2.2 to 3.2.4, 3.3.2, 4.4.3, 4.5.4, and 4.5.6 to 4.5.9.
- 3.12 Please comment on the objectivity of the framework statement that the latest scientific data on bioaccumulation do not currently support the use of bioconcentration factor (BCF) and bioaccumulation factor (BAF) values as generic threshold criteria for hazard classification of inorganic metals (see recommendation on page 3-17, lines 27-29 of the document). By this, the framework means that various assumptions underlying the BCF/BAF approach, including the independence of BCF/BAF with exposure concentration and the proportionality of hazard with increasing BCF/BAF do not hold true for the vast majority of inorganic metals assessed. Please comment on the framework's acknowledgement that the appropriate use of BCFs/BAFs to evaluate metal bioaccumulation, including the degree to which BCFs/BAFs are dependent on exposure concentrations, needs to consider information on bioaccessibility, bioavailability, essentiality, acclimation/adaptation, regulation of metals (uptake and internal distribution), detoxification and storage, dependence on exposure concentration, and background accumulation. While the ability to quantitatively address all these factors may be limited at the present time, the framework states that their potential impacts should at least be qualitatively addressed. See Sections 3.2.4, 3.3.2.5, and 4.5.8.

- 3.13 Given the variety of organism responses to inorganic metals exposure, based on factors such as bioaccessibility, bioavailability, essentiality, uptake/excretion mechanisms, and internal storage/regulation, as described in Section 3.2.4, the framework states that BAFs/BCFs should be derived using mathematical relationships that represent the concentration in the organism or tissue as a function of the bioavailable concentration in the exposure medium/media for each set of exposure conditions. Please comment on whether this is the best approach based on the current state of the science or if there are alternative approaches that are more appropriate that can be routinely applied. See Sections 3.2.4, 3.3.2.5, and 4.5.8.
- 3.14 Please comment on the objectivity of the information and recommendations pertaining to the use of the acid-volatile sulfide-simultaneously extracted metals (AVS-SEM) approach and the biotic ligand (BLM) model. Are additional recommendations warranted? If yes, what are they? See Sections 3.2.6, 4.4.2.3, and 4.5.10.