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

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OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Review of Metals Action Plan; An EPA Science Advisory Board Report

Dear Governor Whitman:

On September 10-12, 2002, the Metals Assessment Panel of the EPA Science Advisory Board reviewed the EPA's plans for development of a Framework for Metals Risk Assessment and a Guidance for Characterization and Ranking of Metals. With this letter, we are submitting the Panel's review.

In the Metals Action Plan, the EPA has put forward the key scientific issues important for assessing the hazards and risks of metals in general. The Panel understands that in future documents, the EPA will put forward approaches for evaluating or ranking the risks and hazards of metals in specific applications. Accordingly, in this review, the Panel addressed the broad scientific issues underlying the assessment of metals hazards and risks, and not specific parameters that might or might not be used in particular applications. The SAB looks forward to continuing to be involved as this work proceeds from general scientific principles to guidelines for specific applications.

Overall, the Panel agrees that metals should be assessed differently from organic pollutants in a number of contexts. The Panel also agrees that the issues of chemical speciation, bioavailability, bioaccumulation, and toxicity are key issues in assessing the hazards of metals.

However, in developing an overall framework, the Panel recommends that these scientific issues be considered broadly, with consideration of all the relevant processes, rather than narrowly considering these issues merely as parameters or fixed values. In particular, the Panel recommends that:

a) speciation be considered broadly in terms of the environmental chemistry that determines speciation and transformation under various conditions; that

b) bioaccumulation be considered broadly, as determined by a set of processes that are related to the processes of bioavailability; and

c) the temporal characteristics of the risks and hazards of metals be considered not merely as a persistence parameter, but broadly in terms of the underlying chemical, biological and physical processes.

These recommendations are consistent with a previous SAB Review of "An Integrated Approach to Metals in Surface Waters and Sediment" (EPA-SAB-EPEC-00-005), which recommended that the EPA develop a "conceptual model that incorporates all partitioning phases and routes of exposure in order to guide the Agency's long-term efforts." By considering the scientific issues broadly in development of an overall framework, EPA can develop a scientific foundation to support appropriate simplifications in particular applications.

The Panel commends the EPA for seeking advice on the Action Plan at an early stage. We look forward to reviewing the Framework and Guidance when they are developed. Please contact us if we may be of further service.

Sincerely,

/ Signed /

Dr. William Glaze, Chair
EPA Science Advisory Board

/ Signed /

Dr. Valerie Thomas, Chair
Metals Assessment Panel
EPA Science Advisory Board

SAB REVIEW OF THE METALS ACTION PLAN

1. EXECUTIVE SUMMARY

The draft Action Plan initiates the development of a Framework for Metals Assessment and a Guidance for Characterizing and Ranking of Metals (henceforth, the Action Plan, Framework, and Guidance, respectively). At this stage, the role of the EPA Science Advisory Board (SAB) review is not to approve or evaluate scientific conclusions, but rather to provide a preliminary response to the activities proposed in the Action Plan.

The Panel commends the EPA for seeking advice on the Action Plan at an early stage. Based on the current status of the Action Plan, the Panel has the following comments and suggestions:

a) The Panel agrees that metals should be assessed differently from organic pollutants in a number of contexts. Metals are elements and, while they do not degrade, they undergo complex environmental chemistry. Metals are naturally occurring; some are essential for living organisms.

b) The Panel agrees that the issues of chemical speciation, bioavailability, including bioaccumulation, and toxicity are key issues in assessing the hazards of metals, with the following qualifications:

   i) The Panel recommends that metal speciation be considered broadly under the umbrella of environmental chemistry. Understanding chemical speciation with regard to the most toxic forms is clearly important to assessing hazard and risk. But also important to this assessment are processes occurring at environmental interfaces (including organisms) and/or in different environmental compartments which regulate the rate of formation, stability and prevalence of these metal species. These reactions likewise control the chemical speciation of metals that enhance or restrict their transport in the environment, and to and within organisms.

   ii) The panel recommends that bioaccumulation be considered broadly under the umbrella of bioavailability. Understanding bioaccumulation is clearly important. To develop a broader framework for understanding, the processes determining both bioavailability and bioaccumulation should be considered as an integrated concept. Bioaccumulation encompasses not only the net result of the competing processes of chemical uptake and elimination by an organism, but also the distribution of the chemical within organisms. Bioaccumulation processes are related to bioavailability processes, both because bioavailability is a measure of chemical uptake by an organism, and because the bioaccumulation of a chemical by one organism may make it bioavailable to another organism.

iii) The Panel recommends stability and environmental residence time as more appropriate variables or terms than persistence for characterizing the temporal dynamics of metals. All metals are persistent. Characteristics such as stability of the toxic species or the environmental residence time, and overall environmental chemistry, determine the temporal characteristics of the hazard.

c) The Panel recommends greater emphasis on the combined effects of metals, including nutritional and toxicological considerations. The scientific foundation for such assessments is under development and EPA should begin to think about these considerations.

d) The Panel recommends that the differences between assessments for ecological systems and assessments for human health be clarified and highlighted in the Framework and Guidance. The emphases in human health assessments are often quite different from those in ecological system assessments. Key differences include: the focus of the assessment (humans or ecological populations); exposure pathways; receptors and endpoints; data availability and quality; uncertainty requirements; metrics, and criteria for defining acceptable risks.

e) The Action Plan is inconsistent and somewhat confusing in its use of the words hazard and risk. EPA needs broadly and fundamentally to rethink where and how hazard and risk differ, when it is or is not appropriate to use either, and apply that perspective consistently throughout the Framework and Guidance documents. Hazard deals with inherent properties of substances; risk adds the critical exposure element, which is necessary to accurately gauge safety or danger in a given use and exposure scenario. A hazard ranking of metals would produce a different end-result than a risk ranking, as the latter weighs the context of exposure.

f) In evaluating risk, exposure must be considered. The Panel recommends greater emphasis on exposure in the Framework. EPA should examine approaches to incorporate public health, environmental, and ecological system surveillance data in the metals risk assessment process.

The Panel recommends extensive consultation with the scientific community, the public, stakeholders, and intended users, including risk assessors in other federal and state agencies when developing the Framework and Guidance.

2. INTRODUCTION AND PROCEDURAL HISTORY

In response to a request from EPA, the EPA Science Advisory Board formed a specialized Metals Assessment Panel to review the draft Metals Action Plan. In doing so, the staff used the new panel formation process, approved by the SAB's Executive Committee May 8, 2002 and described in *EPA Science Advisory Board (SAB) Panel Formation Process: Immediate Steps to Improve Policies and Procedures - An SAB Commentary* (EPA-SAB-EC-COM-02-003) available at http://www.epa.gov/sab/pdf/ecm02003.pdf.

The Panel met by public conference call meetings on August 8, 15 and 29, 2002. At those meetings, the Panel heard briefings on Federal ethics rules and regulations, and on the document to be reviewed; listened to invited presentations from outside experts; provided opportunities for public comment; and presented and discussed preliminary responses to the charge questions. Panelists circulated revised responses before the September 10-12, 2002 face-to-face meeting.

In addition to the "Draft Action Plan for the Development of a Framework for Metals Assessment and Guidance for Characterizing and Ranking Metals" (EPA/630/P-02/003A, June 2002), EPA provided the Panel with public comments on that plan and a number of background documents. Public commenters also provided written text and documents.

At the face-to-face meeting, the panelists heard an additional briefing from EPA and two public comments. The chief activity of the Panel was the preparation and approval of its report for subsequent consideration by the Executive Committee. The Panel approved its report September 12, 2002. The Executive Committee considered this report at its October 1-2, 2002 meeting.

Each charge question appears below in its entirety followed by the Panel's response.

3. RESPONSE TO THE CHARGE

Charge Question # 1

Please comment on the soundness of the proposed organizing principles suggested by the public that are reflected in the draft Action Plan for the ``Framework for Metals Assessment and Cross-Agency Guidance for Assessing Metals-Related Hazard and Risk.'' (The proposed organizing principles, listed in section 1 of the draft Action Plan, include the following: providing a basis for identifying and prioritizing among metals, metal alloys and other metal compounds with respect to hazard and risk, use of sound science, use of a tiered approach, recognition of the influence of bioavailability on toxicity, and initially focus on hazard assessment as a screening tool.)

The organizing principles suggested in the Action Plan are generally sound and address a number of issues for inclusion in a long term EPA strategy.

Specifically, the plan for identifying and prioritizing metals, metalloids, metal alloys, organo-metallic and other metal compounds (henceforth referred to as metals) is critical with respect to distinguishing assessment of hazard and risk. This process is important since those metals of greatest interest to public health or the environment will vary over time. Therefore a flexible process is needed that can accommodate changing priorities and new science. The Panel recommends that EPA retain the general tenets common to ecological and human health risk assessments in the Framework but separate them in the Guidance to delineate specific differences between ecosystems and human health. Clarification of the scope of both the Framework and Guidance would be helpful, with respect to which metals are included as well as a range of other issues.

Development of credible environmental regulations requires the use of sound data and current state-of-the-art science. These regulations need to take advantage of modern scientific tools that incorporate mechanistic data. While some of these methods will require validation with time and experience, inclusion of a narrative commentary on their potential application to regulatory approaches for metals will enhance the utility of the Framework and Guidance over time. As some of these newer methods (e.g., biomarkers) are validated, they can be incorporated into future versions of the Framework. Mechanistic approaches that integrate metal- induced effects across the molecular, cellular and whole organism levels of biological organization will reduce uncertainty. Such approaches would enhance the sensitivity of any National Hazard or Risk Assessments and ultimately lead to a mechanism-based regulatory process. The latter will add further scientific credibility to any derived regulations. Including mechanistic data in the discussed tiered approach could also be very useful in interpreting findings and predicting risk in complex mixture situations such as Superfund sites.

Bioavailability exerts a major influence on bioaccumulation and toxicity. In aqueous systems, factors such as salinity, complexation with humics and methylation by bacteria are examples of processes that will influence uptake/toxicity by organisms living in different environments. In terrestrial environments, complexation of toxic elements with respirable particles in soil may vary as a function of soil pH, and bacterial populations. Metal binding to respirable particles may also vary as a function of incineration temperatures. The revised Action Plan would be strengthened by a more detailed inclusion of such factors beyond those currently incorporated. The intracellular handling of metals in target cell populations is a topic which is not addressed in the current Action Plan beyond the paragraph on page 14 in relation to the toxic potential of metals to aquatic species. The potential role of these compartments as factors influencing the bioaccumulation of metals in some edible species should be further developed in the Framework and Guidance.

Finally, the focus on hazard assessment as an initial screening tool could be strengthened by delineating differences between hazard and risk and consideration of other critical factors. The Panel strongly recommends that EPA clearly distinguish between hazard and risk assessments and apply the most appropriate approach in a given situation. Hazard and risk assessment approaches would be strengthened by inclusion of a number of factors. Aggregate and cumulative risks as well as metal-metal mixtures must be considered. Dose is only one factor in assessing hazard/risk. Duration and frequency of exposure are major variables critical to chronic low dose exposures. The issue of most appropriate toxic endpoints for a given organism or toxic element must be addressed. The issue of sensitive sub-populations and species should be discussed. Developing organisms (e.g., larvae of crustacea or fetal/newborn mammals) are recognized as highly sensitive life stages. Susceptibility of geriatric populations is also of increasing concern and should be considered in these processes as the world population ages. Nutritional status should also be considered since this factor can influence susceptibility to metals.

Charge Question #2

Are the issues raised in the Action Plan--chemical speciation, bioavailability, bioaccumulation, persistence, and toxicity--the major issues of concern for improving EPA's scientific assessments of the hazards and risks of metals?

Chemical speciation, bioavailability, including bioaccumulation, and toxicity are relevant scientific issues identified in the Action Plan but the Panel recommends that **environmental chemistry** should be an umbrella issue embracing and expanding the issue of **chemical speciation**. Understanding chemical speciation with regard to the toxicity is clearly important to assessing their hazard and risk. But also important to this assessment, are processes occurring at environmental interfaces (including organisms) and/or in different environmental compartments which regulate the rate of formation, stability and prevalence of these metal species. These reactions likewise control the chemical speciation of metals that enhance or restrict their transport in the environment, and to and within organisms.

The Panel believes that **persistence** is a problematic scientific issue for assessing metals hazards and risks. In the case of synthetic organic contaminants, persistence refers to their environmental stability relative to degradation, thus providing a metric of exposure. As the Action Plan points out, metals do not degrade so that “persistence” relative to their environmental fate has little meaning. The Panel suggests that for metals, persistence is addressed better within the context of **environmental chemistry** in terms of stability of chemical species, residence times and attenuation within environmental media.

While bioaccumulation data can be useful for site specific assessment of risk, bioaccumulation metrics such as BCF/BAF measures can be problematic for assessing generic metal hazard ranking. In general, bioaccumulation data are less straight forward to evaluate for hazard and risk assessment due to the essentiality of some metals, the various methods organism have adapted to regulate and detoxify (and therefore expunge) metals, natural occurrence and the variation of background metal levels, and the known inverse relationship of metal exposure to accumulation to living systems to name a few issues. The panel recommends that bioaccumulation be considered broadly under the umbrella of bioavailability. Understanding bioaccumulation is clearly important. To develop a broader framework for understanding, the processes determining both bioavailability and bioaccumulation should be considered as an integrated concept. Bioaccumulation encompasses not only the net result of the competing processes of chemical uptake and elimination by an organism, but also the distribution of the chemical within organisms. Bioaccumulation processes are related to bioavailability processes, both because bioavailability is a measure of chemical uptake by an organism, and because the bioaccumulation of a chemical by one organism may make it bioavailable to another organism.

Considering the scientific issues broadly in the development of the Framework will provide a more robust basis for determining appropriate simplifications that will be needed for specific applications.

Charge Question # 3

Has EPA adequately characterized the issues and do the summaries adequately capture the key scientific uncertainties that will need to be addressed by the Framework and the Guidance?

The Panel agrees that speciation (under the umbrella of environmental chemistry), bioavailability including bioaccumulation, and toxicity are key scientific issues but that persistence should not be considered a key issue (Charge Question 2). Have these issues been adequately characterized in the Action Plan? The Panel reached the following conclusions:

The broader scientific issues of environmental chemistry of metals should be part of the Framework. In the context of environmental chemistry of metals, additional scientific issues that were missing include stability, transformation processes (physical, chemical, biological speciation transformation dynamics), background metal levels, frequency of occurrence and monitoring, and important transport pathways into the environment and within different media (air, water, solid). A major concern with respect to uncertainty in speciation and environmental chemistry issues of metals is the extrapolation of data from model to natural systems to assess environmental risk. This should be emphasized as well.

The sections on bioavailability and toxicity adequately characterize the basis for including these as primary scientific topics in the Framework. However, extrapolation from model systems (e.g., the use of surrogate species) to assess bioavailability and toxicity for ecological system or human receptors involves uncertainties that need to be addressed.

The issue of persistence was adequately addressed. The Panel believes that persistence is inherently part of the environmental chemistry of metals and included in the context of species environmental residence times, transformation rates and the predominance under a specified set of environmental conditions (e.g., pH, redox conditions, and ligand concentrations). In the case of metals, persistence may be protective rather than detrimental and this aspect should be recognized.

The background section illustrates in some instances (e.g., bioaccumulation) that metals should be treated differently than organics in the context of assessment of risk and hazard. The Panel concludes that metals, in many contexts, need different criteria for characterizing hazard compared to organics, and that the Framework should consider this possibility from the outset.

Better supporting information should be provided on the numbered Summary Issues in the Action Plan. Many of the numbered summary issues (except for those provided in the bioaccumulation section) were inadequately characterized and did not follow logically from the discussion provided. The Panel liked the organization of the Bioaccumulation section in which supporting information was provided for each numbered summary issue. If other sections had been similarly structured, the numbered summary issues would have been much more useful to the Panel. These questions raised in the numbered summary issues should be reconsidered in the Framework when a more in-depth review of the major scientific issues is undertaken.

Charge Question # 4

Can the SAB suggest priorities within the list of issues based on (a) the potential impact on the assessment of risk or hazard and (b) the state-of-the-science and the feasibility of developing guidance in the near term?

Determination of priorities can be done in many ways (e.g., “use-exposure-properties” approach, or evaluation of rank, based on one or several of the issues – e.g., toxicity, bioavailability). The Panel can not prioritize the issues presented without a context. Evaluating the state-of-the-science and providing guidance without context is a fruitless undertaking. Once the supporting white papers are developed, the state of the science can be evaluated. Available scientific information varies widely by organism and key issue (environmental chemistry, bioavailability, toxicity) of interest. Conceptually, a systematic approach to evaluating information (e.g., developing a matrix) is necessary. A matrix can be generated with key issues on one axis and organism/trophic level on another. Assessment of the supporting science (little, some, sufficient) can be used to identify gaps in the science/knowledge base, or areas suitable for investigation.

Charge Question # 5

Are there specific recommendations for the Framework or for the “Guidance for Characterization and Ranking of Metals" (including methods and models) for addressing these issues that are not captured by EPA's Action Plan?

Models and methods – A number of models and methods are available for estimating speciation, bioavailability, bioaccumulation, and exposure and toxicity. Few were described in the Action Plan. At this stage in the process it is appropriate not to include specific models. However, several aspects related to modeling should be made more transparent in the Framework, including: what data needs exist for modeling or setting criteria, the relative uncertainties of data and how uncertainty will be addressed.

Clarity on receptors – The Framework discussion should delineate ecological system and human health risks. The Panel suggests that the Guidance address ecological and human health issues separately. Although the Panel recognizes that an integrated, human health and ecological perspective is the desired end-product, there are substantial differences, including the audience to warrant separate documents. Risks to human and ecological receptors vary widely by metal. Key differences include: the focus of the assessment (humans or ecological populations); exposure pathways; receptors and endpoints; data availability and quality; uncertainty requirements; metrics (e.g., RfD vs NOEC), and criteria for defining "acceptable risks." Major issues in the Framework also have different connotations to human health and ecological risk assessors. For example, in the outline, principles to determine sensitive sub-populations that receive significant exposure of concern were presented under the heading "Assessment of Endpoint Selection," (section 2.4). Human health risk assessors tend to interpret endpoint in the context of toxic conditions (e.g., neurological, reproductive, and developmental effects, etc.) and not the various receptors in the ecological system. The term "sensitive sub-population" means sensitive species (i.e. biological sensitivity) to ecological risk assessors, while sensitive sub-population in human terms can be defined based on a number of parameters (e.g., age, gender, genotype, exposure strata, etc.).

Surveillance data – The Action Plan briefly mentions natural metal background levels in the bioavailability section. In most cases, site-specific background levels of metals in groundwater were discussed. Human biomonitoring provides integrated measures of exposure and in the case of metals, natural background burdens may be captured in these integrated measures. Ongoing exposure surveillance programs such as the NHANES/NCEH surveillance program are intended to establish such population baseline exposure levels. A large number of metals are included on the list of analytes in the NHANES (1999) study.[1] These data may be used in the context of national risk assessment and ranking when they become available. There are also a number of extant environmental monitoring data for metals[2] but the Action Plan makes no mention of these resources and their utility in metal risk ranking and assessment. The US Geological Survey has a program called NASQAN (National Stream Quality Accounting Network) that measures chemicals including some metals, nutrient ions and pesticides in rivers across the United States (http://water.usgs.gov/nasqan)[3]. In the development of the Framework and Guidance, EPA should examine approaches to incorporate public health, environmental and ecological system surveillance data.

Metal mixtures -- The Action Plan does not address the issue of metal mixtures and the possible types of interactions (additive, synergistic, antagonistic) among metals. Also, environmental mixtures should be evaluated in the context of prevailing body burdens (including body burden of essential metals and dietary intake) in living organisms (Mertz, 1993). Superfund sites frequently contain elemental mixtures. The Framework and Guidance should address this issue, even if it is only in a generic way that would allow for more sophisticated analyses as the science develops. A growing number of investigators and other Federal agencies such as ATSDR are taking an active interest in this area. This means that in the near future, the

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[1] http://www.cdc.gov/nceh/dls/nhanes.htm (accessed 4/30/02)

[2] USEPA's (1992) Inventory of Exposure-Related Data Systems Sponsored by Federal Agencies provides descriptions of databases and contact for other sources of exposure data, with a focus on environmental concentrations. (EPA/600/R-92/078)

[3] Other relevant programs include NOAA's National Status and Trends Program and EPA's EMAP Program (Environmental Monitoring and Assessment Program).

database on metal-metal interactions will become more robust and it will be easier to incorporate new data into a regulatory framework that has already considered this issue. A discussion of metal mixtures from this perspective will indicate a current awareness and facilitate inclusion of interaction data as they are published.

CHARGE QUESTION # 6

Please comment on the feasibility of the proposed process for drafting the Framework and the Guidance. Will the timeline allow for the scientific issues to be adequately addressed? Are the measures being taken to involve the scientific community and the public adequate?

The Action Plan provides only a superficial description of the Guidance, which presumably will be designed to provide the criteria for application. Furthermore, the Action Plan does not address how the Guidance is going to be used by risk assessors. To be useful and comprehensive, the Framework should present the principles and methods for metals assessment so that they relate directly to the risk assessor's responsibilities.

The Action Plan provides little information on how the Framework and Guidance are to be coordinated. Figure 1 of the Action Plan indicates somewhat parallel paths, offset by a few months, but the specifics of how the two efforts are to be completed are not articulated. The Panel is concerned that the Framework and Guidance might diverge in content without a deliberate *a priori* plan for integration. Writing the Framework to facilitate the preparation of the Guidance will prove useful and serve as a model for further EPA initiatives.

The schedule laid out in the Action Plan, if the Guidance is adopted on the basis of the Framework, may require some modification, requiring earlier action on the former rather than the latter. Even without pursuing integration between the two documents, the schedule appears to be ambitious. The timeline for developing white papers by the start of Workshop #1 (November 2002) will be difficult to achieve. The succeeding steps should be feasible if the initial part of the schedule is performed on time.

The proposed steps for involving the public and scientific community are reasonable although fairly conventional. The panel considered whether novel forms for involving the public could be undertaken. These might include interactive web-based surveys and communications. (Weiss, 2001) The Panel recommends extensive outreach in the development of both the Framework and the Guidance to the scientific community, the public, stakeholders, and to intended users of the Guidance including risk assessors in other federal and state agencies.

CHARGE QUESTION # 7

Please comment on the outline for the Framework and the description of the Guidance. Is it clear and all-inclusive?

Aligning Regulatory Functions with Tiered Risk Assessment

The proposed Framework (Section 1.1.3 "Tiered Approach") relates the tiered approach for risk assessment to three regulatory functions: National Hazard/Risk Ranking and Characterization, National Regulatory Assessments, and Site-Specific Assessments. The tiered approach is a broadly-accepted paradigm which recognizes the value of systematic and graduated assessments of risk based upon data availability, and needs for accuracy and/or the reduction of uncertainty. The Action Plan implies that these regulatory functions parallel tiered risk assessment in terms of these needs. The Panel questions whether the three regulatory functions consistently follow the same logic and pattern and will always "fit the mold" of tiered assessment.

Regulatory functions such as the three described in the proposed Framework are designed and implemented to comply with specific statutory requirements dictated by law. They may or may not follow sound principles or processes for conducting risk assessment. Legislative or judicial mandates may require the collection of certain effects or exposure data that are not necessary for risk assessment. Conversely, legal requirements for data collection may be inadequate to enable thorough risk assessment. The Guidance should not, for example, imply: that National Regulatory Assessments always require less data and precision than Site-Specific assessments; that screening level assessments cannot be performed on a site (indeed, soil screening levels are designed to do just that); or that National Hazard Characterizations can be conducted on the basis of screening level risk assessment using data readily at hand.

Distinguishing Between Hazard and Risk

The Action Plan is inconsistent and somewhat confusing in its use of the words hazard and risk. The phrase "hazard and risk" are used repeatedly throughout the document, as if synonymous and interchangeable. Hazard deals with inherent properties of substances; risk adds the critical exposure element that is necessary to accurately gauge safety or danger in a given use and exposure scenario. A hazard ranking of metals would produce a different end-result as a risk ranking, than the latter weighs the context of exposure. EPA needs to broadly and fundamentally rethink where and how hazard and risk differ, when it is, or is not, appropriate to use either, and apply that perspective consistently throughout the Framework and Guidance documents.

In the Framework, the key process of Risk Characterization particularly needs to be further developed. Under Section 4.0 (p. 37), "Characterization of Exposure and Effects", there is no mention of when and how effects and exposure data for metals can be integrated into the fundamental metric of risk. Relevant questions include: How should risk be calculated for metals? When are quotient methods acceptable versus a distributional (e.g., probabilistic) analysis of risk? How does one treat background or reference levels of metals in the environment, unique from synthetic organic chemicals? How can the risks of both metal deficiencies as well as intoxication be recognized, as indicated by the U-shaped dose-response curve of essential metals?

The Action Plan also distorts hazard and risk in the description of the Guidance, which would seem to primarily relate to hazard ranking. If so, it should not refer to "risk prioritization", which is best accomplished by procedures which weigh both effects and exposure information (e.g., comparative risk analysis). Generic and simplistic ranking of metals (e.g., Hg, Pb, Cd, Cu, Zn) without consideration of exposure, may compromise the risk assessment process and could lead to regulations and practices which are scientifically unsound, if not dangerous. For example, a broadly-discharged or poorly managed substance with relatively low toxicity may pose greater risk than a highly toxic but well-managed substance. If a risk ranking exercise is attempted, consideration should be given to factors such as: uses of metals, the availability of surveillance data, and the context of exposure (e.g., extraction of minerals; refining; chemical processing and manufacturing; industrial uses as catalysts, etc.; consumer uses, by product sectors; agricultural uses).

Guidance for Characterization and Ranking of Metals

There is simply too little information offered in the description of this Guidance (i.e., four paragraphs on p. 38) to ascertain whether it will be "clear and all-inclusive."

CHARGE QUESTION # 8

Are there any additional actions, beyond those proposed in the Action Plan that could improve EPA's scientific assessments of the hazard and risks of metals?

EPA's scientific assessments would be improved by an evaluation of how impaired function in an organ system, organism or ecological system will predispose that system, and other systems, to adverse effects of metals. In human populations, the very old and the very young as well as those with impaired immune systems are examined for that reason. Infants rely on immature, inadequate mechanisms to eliminate chemicals with toxic properties. For example, high nitrate levels in drinking water can pose a special risk for infants because their low stomach acidity facilitates bacterial conversion of nitrate into nitrite and leads to methemoglobinemia. In ecological systems, elevated levels of acids, ozone or other toxins, or temperature or moisture stress, can predispose the system to adverse effects of metals. Whether the system is a human being suffering malnutrition or disease, or an ecological system suffering effects of air pollution, global warming or insect infestation, it is probable that effects of metals would be exacerbated by the predisposing agent. The amount of exacerbation and the circumstances facilitating adverse effects of metals are poorly known.

In stressed systems such as those in proximity to a smelter, exposure to metals can come from air, water and soil simultaneously. Multiple sources and cumulative and aggregate exposure should be considered in the Framework. The Panel believes that airborne exposures to metal particulates should receive more attention in the Framework and Guidance than currently contemplated. For example, fine metal dust inhaled by susceptible individuals enhances sensitization to common allergens (Peden, 1997; Carter et al., 1997; Lambert et al., 2000). Such adjuvant effects, which may have both positive and negative consequences, are exemplified by aluminum. In addition, recent findings indicate transport into the brain by ultrafine particles, including metals, underline the role of inhalation exposures in evaluating total exposure (Oberdörster and Utell, 2002)

Finally, since some metals are plant and human essential trace elements, both too little and too much exposure present risks. The Framework should carefully note the non-monotonic dose-response functions characteristic of many metals.

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Dr. Bruce Fowler, Agency for Toxic Substances and Diseases Registry, Atlanta, GA

Dr. Andrew Friedland, Dartmouth College, Hanover, NH

Dr. Kim Hayes, University of Michigan, Ann Arbor, MI

Dr. Mary Kay O'Rourke, University of Arizona, Tucson, AZ

Dr. Nga L. Tran, Exponent, Washington, DC

Dr. Bernard Weiss, University of Rochester Medical Center, Rochester, NY

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

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* Members of this SAB Panel consist of: a) SAB Members: Experts appointed by the Administrator to serve on one of the SAB Standing Committees. b) SAB Consultants: Experts appointed by the SAB Staff Director to a one-year term to serve on ad hoc Panels formed to address a particular issue. c) Liaisons: Members of other Federal Advisory Committees who are not Members or Consultants of the Board. d) Federal Experts: The SAB charter precludes Federal employees from being Members of the Board. "Federal Experts" are federal employees who have technical knowledge and expertise relevant to the subject matter under review or study by a particular panel.

Brief Bios of the Metals Assessment Panel

Dr. Bruce A. Fowler Ph.D., Fellow A.T.S. received a B.S. degree in Fisheries (Marine Biology) from the University of Washington in 1968 and a Ph.D. in Pathology from the University of Oregon Medical School in 1972. He was a staff scientist at the National Institute of Environmental Health Sciences from 1972 until 1987 when he became Director of the University of Maryland System -wide Program in Toxicology and Professor of Pathology at the University of Maryland School of Medicine. In 2001, he became Professor and Director of the Laboratory of Cellular and Molecular Toxicology in the Department of Epidemiology at the University of Maryland School of Medicine. In August 2002, he will go on an IPA assignment as a Senior Research Advisor to the Agency for Toxic Substances and Diseases Registry (ATSDR) in the Division of Toxicology.

Dr. Fowler, who is an internationally recognized expert on the toxicology of metals has served on a number of State, National and International Committees in his areas of expertise. These include the Maryland Governor's Council on Toxic Substances (Chair), National Academy of Sciences / National Research Council Committees on Toxicology, Toxicology Information Committee, Committee on Women in Science and Engineering, Measuring Lead in Critical Populations (Chair), Biological Markers of Urinary Toxicology, Committee on the Evaluation of Augmenting Potable Water Supplies with Reclaimed Water, and the Subcommittee on Arsenic in Drinking Water of the Committee on Toxicology. He has also served as a temporary advisor to the World Health Organization (WHO) and the International Agency for Research Against Cancer (IARC). Dr Fowler has been honored as a Fellow of the Japanese Society for the Promotion of Science (1990), a Fulbright Scholar and Swedish Medical Research Council Visiting Professor at the Karolinska Insititute , Stockholm , Sweden (1994 -1995) and elected as a Fellow of the Academy of Toxicological Sciences (2000). He currently serves as Chairman of the Scientific Committee on the Toxicology of Metals under the International Commission on Occupational Health (ICOH), as a consultant to the USEPA Science Advisory Board and a member of the Fulbright Scholarship review committee for Scandinavia (1999-, Chair, 2000-2001). He is a member of the AAAS Recruitment and Screening Committee for the Court Appointed Scientific Experts (CASE) Demonstration Project 2000.

Dr. Fowler is the author of over 195 research papers and book chapters dealing with molecular mechanisms of metal toxicity and biomarkers for early detection of metal-induced cell injury. He has been the editor or co-editor of 4 books or monographs on metal toxicology and mechanisms of chemical – induced cell injury. His current research is focused on the toxicology of chemical mixtures involving metals, particularly in relation to semiconductors, lead, cadmium, arsenic mixtures and the role(s) of lead – binding proteins in mediating the toxicity of this ubiquitous metal to the kidney and brain. He serves on the editorial boards of a number of scientific journals in toxicology and environmental health. Dr. Fowler has peer-reviewed research funding from the EPA STAR Grant Program and the National Institutes of Health.

Dr. Andrew J. Friedland is Professor and Chair of the Environmental Studies Program at Dartmouth College. His research has focused on understanding the effects of atmospheric deposition of pollutants on elemental cycling processes in high-elevation forests of New England and the Northeastern United States. He has examined the processes and behavior of trace elements such as lead, copper, zinc, nickel and cadmium and major elements such as nitrogen and calcium on vegetation, soils and water. In a number of related projects, he has described the decline of red spruce in the mountains of New England and has examined water relations in conifers during winter. Friedland has published approximately 40 peer-reviewed articles on these topics. He has written one book, co-authored with biologist Carol Folt, Writing Successful Science Proposals (Yale University Press, 2000). Dr. Friedland has received funding from the National Science Foundation, the US Forest Service, the Environmental Protection Agency and private foundations.

Dr. Friedland has taught introductory and advanced environmental science courses as well as soil science, forest biogeochemistry and an interdisciplinary course on science and literature. He was a member of the Citizens Advisory Panel of the Strategy for Vermont's Third Century, an environmental risk assessment program conducted by the State of Vermont and the U.S. EPA. From 1995-1998, he chaired the College Board Advanced Placement Environmental Science development committee. This committee designed the first Advanced Placement course in environmental science that was offered nationwide for the first time in 1998. Approximately 25,000 students took the most recent AP Environmental Science exam earlier in 2002. Dr. Friedland is a member of the Soil Science Society of America, the Ecological Society of America and the American Association for the Advancement of Science. He is currently on the editorial boards of the *Journal of Sustainable Forestry* and *Science of the Total Environment*. Friedland has B.A.s in Biology and Environmental Studies (double major) (1981) and a Ph.D. in Geology (1985), all from the University of Pennsylvania.

Dr. Kim Hayes is Professor and Program Director of the Environmental and Water Resources Engineering Program in the Department of Civil and Environmental Engineering at the University of Michigan.

Professor Hayes' research focuses on the effects of interfacial properties on transport and transformation processes of environmental contaminants, with more than 20 years of experience in conducting experiments on the sorption of heavy metal ions and radionuclides to soil and sediment mineral constituents. His recent research activities include surface spectroscopic investigations of metal ion sorption reactions; impact of trace metal sorption processes on organic pollutant transformation rates; reductive dechlorination by reduced mineral surfaces in anaerobic environments, investigation of nanostructured particles for remediation of metal contaminated groundwaters, sequestration of metals in the subsurface through precipitation and sorption processes; and the study of binders and barriers materials for nuclear waste containment. Support for this work has been provided by the Environmental Protection Agency, the National Science Foundation, Department of Energy, and National Institute for Environmental Health Sciences.

Professor Hayes is presently serving as a reviewer of a National Research Council report on the "Bioavailability of Contaminants in Soils and Sediments." He recently served as a member of a peer-review panel for the Strategic Environmental Research and Development Program (SERDP) to evaluate proposals on "In-Situ merits of Sequestration Enhancement and Engineered Bioavailability Reduction of Metals in Soils." He has also participated on a variety other workshop and review panels for the Environmental Protection Agency, National Science Foundation, and Department of Energy related to metal ion speciation, sequestration and mobility. Professor Hayes is currently a member of the Board of Director's and an Executive Officer of the Association of Environmental Engineering and Science Professors as well as a member of the Technical Advisory Board of the Great Lakes Protection Fund for the state of Michigan.

Professor has more than 100 publications in peer-reviewed manuscripts, book chapters, technical reports, and proceedings detailing work on environmental chemistry and interfacial processes for contaminant remediation. Professor Hayes was awarded a National Science Foundation Presidential Young Investigator Award earlier in his career (1989-1994). His research group has been selected 4 times for American Chemical Society Environmental Chemistry paper awards (1992, 1996, 1997, 1999).
Professor Hayes obtained his BS degree in Chemistry (1980), MSE in Environmental Engineering (1980), MSE Chemical Engineering (1982), a Ph.D. in Environmental Engineering (1987), all from Stanford University.

Dr. Mary Kay O'Rourke is an Associate Professor of Public Health Research and Medicine at the University of Arizona in the Environmental and Community Health Division. She has conducted interdisciplinary environmental research relating environmental exposure to human health for over 22 years. O'Rourke holds degrees in geology (B.A. Alfred University) and geosciences (M.S. Ph.D. The University of Arizona) with minors in the biosciences.

Her current research addresses exposures *to Coccidioides immitis*, arsenic and other metals and pesticides. She has directed several exposure assessment surveys investigating metal, pesticide, VOC and PAH exposures. She directed two surveys examining pesticide exposure among children in Yuma Co. Arizona and a pesticide exposure in the Gila River Indian Community. She was Co-Principal Investigator of the National Human Exposure Assessment Survey and the Arizona Border Survey. These studies utilize multimedia and multipathway approaches to exposure assessment. She has extensive experience in designing and implementing exposure assessment field surveys, quality assurance programs and the data processing protocols for large studies. Prior to joining the College of Public Health, she evaluated human symptom response to bioaerosols (pollen, fungi, house dust mites) using the tools of exposure assessment in a cross-sectional population of the Pima County (AZ) work force. Projects have been funded by the Environmental Protection Agency, National Cancer Institute, Centers for Disease Control, the Arizona Disease Control Research Commission, and Arizona Department of Health Services.

Dr. O'Rourke has served on several panels and workshops for NIEHS and EPA; these include: "Technical Workshop on Issues Associated with Considering Developmental Changes in Behavior and anatomy when assessing Exposure to Children," Example Exposure Scenarios," "Lessons Learned from the National Human Exposure Assessment Survey," and " Fat Intake Analysis." Dr. O'Rourke was a Councilor for the International Society of Exposure Analysis and a past Secretary-Treasurer of the Pan-American Aerobiology Association (1989-1993). O'Rourke served as the Secretary General of the International Association for Aerobiology (IAA) from 1990-1994 and as an IAA councilor from 1994-98. She is a past member of the review boards of Grana and Aerobiologia.

Dr. Charles A. Pittinger is an environmental toxicologist with broad experience in risk assessment and risk management and technical policy development. He is currently Principal Scientist with the Cadmus Group, Inc., a multi-disciplinary consulting firm specializing in ecological risk assessment, air and water issues, energy efficiency and global climate processes. He previously served as Director of Research for SoBran, Inc., managing a division of some 50 people supporting federal environmental research contracts with USEPA ORD Laboratories, including contracts with NERL and NHEERL. The majority of Dr. Pittinger's professional career was spent with Procter & Gamble, where he served as Section Head and Principal Scientist for their corporate Human & Environmental Safety Division for 17 years.

Dr. Pittinger has conducted and managed R&D programs involving extensive field monitoring, assessment and laboratory studies for private companies and trade associations, has led peer reviews, conducted regulatory policy development and negotiations for industry and government. His regulatory experience in the U.S. and abroad extends to consumer product ingredients and industrial chemical registrations; site contamination and remediation; natural resource management; and effluent permitting.

Dr. Pittinger has diverse experience in a range of technical areas including: ecological risk assessment; hazard and risk management; risk communications; pollution prevention; life-cycle analysis; ecological indicators of sustainability; persistent, bioaccumulative and toxic substances; and high production volume chemicals.

Dr Pittinger's work has required close coordination among internal business sectors and external regulatory (e.g., USEPA OPPTS, ORD and the Science Advisory Board (SAB), Organization for Economic Cooperation and Development), trade (e.g., American Industrial Health Council, American Chemistry Council, Soap & Detergent Association, Alliance for Chemical Awareness), non-profit (e.g., The John F. Heinz III Center, International Life Sciences Institute), academic and professional scientific organizations (e.g., Society for Environmental Toxicology and Chemistry, Society for Risk Analysis). He is currently a member of the SAB's Ecological Processes and Effects Committee.

Dr. Pittinger earned his doctorate in zoology (environmental toxicology) from Virginia Polytechnic Institute and State University. He received a Master's Degree in Ecology from The University of Tennessee, and a Bachelor's Degree in Biology from the University of Notre Dame.

Dr. Valerie M. Thomas

Current Position: Research Scientist, Princeton Environmental Institute, Princeton University

Educational Background: Ph.D., Theoretical Physics, Cornell University; B. A. (High Honors), Swarthmore College

Area of Expertise: Sources, emissions and fate of pollutants, including lead, cadmium, mercury, and dioxin. Industrial ecology. End-of-life management of products. Use of quantitative methods for environmental policy.

Research Activities: Current research projects include: Phase-out of leaded gasoline in Africa. The content of lead, cadmium, and mercury in electronic products. Electronic and optical tags for product end-of-life management. Economics of second-hand markets. Sources of dioxin. Development of research agendas for industrial ecology.

Service on other advisory committees, professional societies, especially those associated with issues under discussion in this review
Member, U.S. EPA Science Advisory Board (SAB), Environmental Engineering Committee, appointed October 2000. Co-chair, Subcommittee on Industrial Ecology.
Consultant, U.S. EPA Science Advisory Board, 1995-2000.

- 2000: Review of *EPA Dioxin Reassessment.*
  Review of *Residual Risk Case Study* (for Clean Air Act residual risk assessments)
- 1996-99:*Integrated Risk Project*. Human Exposure and Health, and Steering Committee.
- 1997: Review of *EPA's Report to Congress on Mercury*. Chair, sources working group.
- 1995: Review of *EPA Dioxin Reassessment*: Exposure Panel.

Consultant on use and sources of cadmium, New York Academy of Sciences, New York-New Jersey Harbor Industrial Ecology Project. 2002.

US Director, Russian Lead Project. Participants from a range of Russian NGO, scientific, industry, and governmental organizations, and with participants from the Johns Hopkins School of Hygiene and Public Health, and the International Lead Management Center. 1997-2000.

New Jersey Comparative Risk Project, NJ Department of Environmental Protection (DEP):
Ecosystem Technical Working Group, and Project Team. 1999-2001.

Consultant to Environmental Defense, on vehicle emissions, 2000.

Co-Organizer (with R. Socolow and C. Andrews). NSF-sponsored Workshop on Industrial Ecology and Policy, White House Conference Center, April 1998.

Technical Expert to US Delegation, OECD Workshop on Lead Products, Toronto, Sept. 1994.

Sources of recent grant and/or contract support
AT&T Foundation
US Environmental Protection Agency
National Science Foundation
New York Academy of Sciences
New Jersey Department of Environmental Protection
US Agency for International Development (pending)

Dr.Nga Tran is a Senior Managing Scientist at Exponent's Food & Chemicals practice, and is based in Washington, DC. Dr. Tran has more than 15 years of experience in environmental and occupational health risk assessment and management in the private and public sectors and academia. Dr. Tran has worked on a wide range of issues, including health surveillance strategy at the Department of Defense (DOD) cleanup sites, chemical and radiation risk harmonization at the Department of Energy's (DOE) cleanup sites, methodology for assessing and prioritizing environmental health threats to military personnel deployed overseas, environmental insurance risks, probabilistic exposure/risk assessment, dietary exposure assessment, product stewardship, industrial hygiene and epidemiology. Prior to joining Exponent Dr. Tran was a faculty member at the Johns Hopkins University, Bloomberg School of Public Health where she conducted research and taught exposure and risk assessment, risk prioritization, and risk harmonization. Dr. Tran remains an Adjunct Assistant Professor at the university.

Dr. Tran had served as a Special Assistant to the Assistant Secretary for Environment, Safety and Health at DOE where she was an active participant in the inter-agency efforts to coordinate risk assessment, cost-benefit analysis and regulatory reform issues. She advised the Assistant Secretary on risk policy decisions as they relate to cleanup efforts at DOE sites. Dr. Tran is also a Certified Industrial Hygienist with experience in developing and implementing cost-effective health and safety and product stewardship programs. As a Corporate Public Affairs Manager, she had successfully implemented risk communication programs, counseled and trained facility managers on effective community relations, implemented an industry community outreach initiative (the Chemical Manufacturing Association-Community Awareness/Emergency Response, (CMA-CAER), consulted facility managers on media relations, advised corporate officers on public policy matters, and worked with the Company's lobbyists to develop legislative position/strategy on issues critical to the business operations.

Dr. Tran has served on a number peer review panels sponsored by the EPA, including "Comparative Dietary Risks: Balancing the Risks and Benefits of Fish Consumption" (2000), "National Human Exposure Analysis Survey (NHEXAS) Data Analysis Strategy" (1999), "Water Quality Criteria Methodology: Human Health – Federal Register Notice" and "Ambient Water Quality Criteria Derivation Methodology Human Health – Technical Support Document" (1999). Dr. Tran is a member of the American Industrial Hygiene Association, Risk Assessment Committee (1996-) and the Technical Advisory Committee for the development of EPA's Aggregate and Cumulative Exposure and Risk Assessment Model (Lifeline™ Project) (1999-).

Dr. Tran was a Kellogg Fellow in the Doctor of Public Health program at the Johns Hopkins University, Bloomberg School of Public Health. Her dissertation was on U.S. food safety policy and pesticide risks.

Credentials and Professional Honors
Dr.P.H., Johns Hopkins University, Bloomberg School of Public Health, 1995
M.B.A., DePaul University, 1991
M.P.H., Yale University, Department of Epidemiology and Public Health, 1985
B.A., Biology, Whitman College, 1982

Sources of recent grant and/or contract support
National Academy of Sciences/National Research Council (2002)
3M (2002)
FMC (2002)
AIG Environmental (2001-2002)
U.S. Department of Defense (2000-01; 1996-98)
U.S. Department of Agriculture (1999-2000)
U.S. EPA and The Environment Law Institute (1997-2000)
The Pew Charitable Trusts (1999-2001)

Dr. Bernard Weiss is Professor of Environmental Medicine and Pediatrics at the University of Rochester School of Medicine and Dentistry, where he has been a member of the faculty since 1965. Before coming to Rochester, he served on the faculty of the Johns Hopkins School of Medicine, and, earlier, held an appointment at the U.S. Air Force School of Aviation Medicine. He earned a B.A. in psychology at New York University and a Ph.D. from the University of Rochester also in Psychology.

Dr. Weiss has served as a member of many committees and panels devoted to toxicology and environmental health, including those organized by the U.S. Environmental Protection Agency's Science Advisory Board (for example, the Dioxin Reassessment Review Panel and the subcommittee on human testing of pesticides, and earlier served as chair of the Subcommittee on Metals), and the National Academy of Sciences (for example, the recent Committee on Air Quality in Passenger Aircraft). He is especially concerned with risk assessment issues arising from the effects of environmental chemicals on brain development and brain aging. He is the editor or co-editor of seven books and monographs and author or co-author of over 200 articles. His special interests and publications lie primarily in areas that involve chemical influences on behavior; these include the neurobehavioral toxicology of metals such as lead, mercury and manganese; endocrine disruptors such as dioxin; solvents such as toluene and methanol; drugs such as cocaine; and air pollutants such as ozone. Current and recent grant support have been provided by NIH (specifically, the National Institute of Environmental Health Sciences) and ATSDR (Agency for Toxic Substances and Disease Registry).

Dr. Herbert Windom is a geochemist at the Skidaway Institute of Oceanography where he has been employed since 1968. He was Acting Director from 1/94 until 3/2001 at which time he became an Emeritus Professor. He is also an Adjunct Professor at the University of Georgia and at Georgia Tech from which most of his graduate students come. Over the past thirty plus years his research has focused the transfer and fate of trace elements in riverine, estuarine and coastal marine environments and the contamination of these systems from land-based sources. And to understand how such things as watershed characteristics, climatology and human intervention affect processes, he has conducted studies in various parts of the world from the Russian Arctic to the Asian tropics and has studied heavily impacted as well as relatively pristine systems. This research has been/is funded by NSF, NOAA, EPA, ONR, DOD and other State and Federal agencies. Past national and international service includes the United Nations sponsored Group of Expert on the Protection of the Marine Environment (Chairman), several environmental committees of the International Council for the Exploration of the Seas and UNESCO and several review committees and panels for National and State environmental programs. Present service includes EPA's Board of Scientific Councilors, the Coastal Advisory Council for the State of Georgia and several additional State, private and professional boards, panels and committees Dr. Windom received his BS from Florida State University and MS and Ph.D degrees from the University of California, San Diego (Scripps Institution of Oceanography)

NOTICE

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