



Review of EPA's Draft Framework for Inorganic Metals Risk Assessment

A Report by
The Science Advisory Board Metals Risk
Assessment Framework Review Panel

-- DRAFT 3/29/05 do not cite or quote --

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

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March 29, 2005

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Note to the Reader:

This document, *Review of EPA's Draft Framework for Inorganic Metals Risk Assessment*, is a draft Science Advisory Board (SAB) report still undergoing deliberation by the SAB Panel. It has not received the final concurrence/approval of the Panel or the SAB. For further information, please contact:

Thomas Armitage, Ph.D.,
Designated Federal Officer
Science Advisory Board (1400F), U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460
(202) 343-9995 Fax: (202) 343-0643 E-Mail: armitage.thomas@epa.gov



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3 *DFO Note to the SAB Panel: This letter is a rough draft that needs further*
4 *discussion by the Panel*

5
6 Stephen L. Johnson
7 Acting Administrator
8 U.S. Environmental Protection Agency
9 1200 Pennsylvania Avenue, N.W.
10 Washington, D.C. 20460

11
12 Subject: Review of EPA’s Draft Framework for Inorganic Metals Risk Assessment
13

14 Dear Acting Administrator Johnson:

15 A Panel of the EPA Science Advisory Board (SAB) met on February 1-3, 2005 to review the
16 Agency’s Draft Framework for Inorganic Metals Risk Assessment (Framework). The
17 Framework was developed to supplement previous Agency guidance for use in risk assessment
18 activities related to metals. The Framework is based on a set of issue papers that discuss key
19 topics pertaining to metals risk assessment. The enclosed SAB report addresses EPA’s charge
20 questions to the Panel regarding the Framework, and provides recommendations for
21 improvements.

22 The SAB commends EPA for initiating the development of a risk assessment framework that
23 will guide the Agency and others in evaluating metals in ecological and health risk assessments.
24 The Agency is commended for the breadth of most issue papers developed to discuss key
25 scientific topics pertaining to the Framework. The issue papers and Framework cover a broad
26 spectrum of topics related to human health and ecological risk concerns from exposure to toxic
27 metals and metalloids. The unique attributes of managing metals were clearly identified.
28 However, the SAB believes that a number of major issues must be addressed, and that significant
29 revision of the Framework is needed, before the document is published in final form in order to
30 make it of more current and long-term value to EPA. In this regard the SAB finds that:

- 31 • The Framework appears to have a “dual personality.” In some sections, the Framework
32 provides background information on the state of the science and general

1 recommendations of “basic principles” that need to be considered for risk assessments of
2 metals. In other sections, the Framework appears to serve as a practical guide for risk
3 assessors, offering specific recommendations of methods and tools (often with
4 insufficient justification for the specific selection). The SAB recommends that the
5 purpose of the Framework be reviewed to remove any sense of contradiction in the
6 intended purpose. In addition, the Framework document, and particularly all
7 recommendations, should be carefully reviewed and revised to ensure that they are
8 consistent with the intended purpose.
9

- 10 • The overall clarity of expression, precision of wording, and inconsistent coverage leave
11 the perception of insufficient objectivity. Aspects of the synthesis in the document do not
12 sufficiently capture the state of the science described in the issue papers. The SAB finds
13 that the current Framework is unclear and disorganized, and that significant revision and
14 reorganization are required. Many of the SAB’s specific comments clarify the main
15 technical issues that need to be addressed.
16
- 17 • The overall document provides fairly comprehensive coverage of available tools for risk
18 assessment and methods for metals analyses. However, the human health and ecological
19 subsections of the Framework are incomplete syntheses of the science. In many instances
20 critical evaluations of the tools and methods are not provided and the justification for
21 many recommendations is not clear. The SAB therefore recommends the Framework be
22 focused on the strengths, weaknesses, and limitations of the various methods and tools.
23 Where appropriate, comparative assessment of competing approaches should be
24 provided.
25

26 In summary, the SAB commends EPA for initiating the development of this risk assessment
27 framework to improve current risk assessment practice by addressing human health and
28 ecological risk concerns associated with exposure to toxic metals and metalloids. The SAB
29 strongly urges EPA to continue developing the Framework and provides recommendations to
30 improve the document. Because of the scope of revisions recommended, the SAB believes the
31 revised Framework would benefit from a second external peer review. The SAB is willing to
32 provide such a review.
33

34 Sincerely,
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39 Dr. M. Granger Morgan, Chair
40 EPA Science Advisory Board
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Dr. Deborah L. Swackhamer
Metals Risk Assessment
Framework Review Panel
EPA Science Advisory Board

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NOTICE

This report has been written as part of the activities of the EPA Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to the problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use. Reports of the EPA Science Advisory Board are posted on the EPA website at <http://www.epa.gov/sab>.

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

CHAIR

Dr. Deborah L. Swackhamer, Professor, Division of Environmental Health Sciences, School of Public Health, and Co-Director, Water Resources Center, University of Minnesota, Minneapolis, MN

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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

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

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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, Washington, DC

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2 *DFO Note to the Panel: This executive summary is a rough draft that needs*
3 *further discussion.*

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6 **1. EXECUTIVE SUMMARY**

7
8 The U.S. Environmental Protection Agency (EPA) Science Advisory Board (SAB) Metals
9 Risk Assessment Framework Review Panel has reviewed EPA’s draft *Framework for Inorganic*
10 *Metals Risk Assessment* (the Framework). This report transmits the SAB’s comments and
11 recommendations. Many EPA programs face decisions on whether and how to regulate metals.
12 These decisions range from setting standards or permitting for environmental releases to
13 establishing safe levels in different environmental media, to setting priorities for programmatic
14 or voluntary efforts. EPA developed the draft *Framework for Inorganic Metals Risk Assessment*
15 to supplement previous Agency guidance for use in site-specific risk assessments, criteria
16 derivation, and other similar Agency activities related to metals.

17
18 EPA sought comment from the SAB on the scientific soundness of the Framework’s synthesis
19 and representation of the state of the science. Specifically, EPA sought comment on: the overall
20 objectivity and utility of the recommendations and supporting tools, methods, and models to its
21 primary audiences, EPA risk assessors, and the public, and whether there were any additional
22 research needs that warrant inclusion or further discussion in the Framework. EPA defined
23 objectivity as: “a focus on whether the disseminated information is being presented in an
24 accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate,
25 reliable, and unbiased.” EPA defined utility as: “the usefulness of the information to its intended
26 users, including the public. The EPA gave the following fourteen charge questions to the SAB
27 panel.

28
29 *Question 1: Section 1 - Framework Scope and Assessment Categories*

30 1.1 Please comment on the overall framework scope and whether it is sufficiently
31 encompassing to allow for the consideration of the broad spectrum of physical and
32 chemical properties, exposures, and effects among inorganic metals and metal
33 compounds.

34 1.2 The context of the regulatory application (e.g., contaminated site clean-up, national
35 regulation, or programmatic decision) is a major factor in determining the type of
36 analysis that is appropriate for a particular assessment. The framework identifies three
37 general categories of assessments, including site-specific assessments, national scale
38 assessments, and national ranking and categorization. With the understanding that
39 screening and detailed assessments occur within the assessment categories, please
40 comment on the utility of these categories in setting the context for discussion of metals
41 assessment.

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

43 2.1 Please comment on whether the discussion of inorganic metals assessment principles is

1 clearly articulated, objective, as defined above, and has utility.

2 2.2 Please comment on how well the conceptual model presents key metal processes and
3 whether (or not) it is complete.

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

5 3.1 Please comment on how well the recommendations under Section 3 are supported by the
6 detailed information in Section 4. Are there other recommendations that should be
7 included? Are there any inorganic metals or metal compounds for which any of the
8 recommendations would not apply?

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

12 3.2 Please comment on the objectivity and utility of the data, tools, and methods discussed in
13 Section 4. Identify any scientific or technical inaccuracies, or any emerging areas or
14 innovative applications of current knowledge that may have been overlooked or warrant a
15 better discussion of uncertainty, including areas needing further research.

16 3.3 Please comment on the state of the science (i.e., data, tools and methods) to address
17 inorganic metals speciation in all environmental compartments for any given inorganic
18 metal from the point of environmental release to the point of toxic activity as discussed in
19 the document. Please comment on whether the framework identifies appropriate research
20 needs to overcome any limitations in the state of the science. Please address these
21 questions separately for each of the three types of assessments presented (i.e., site-
22 specific, national level, and ranking and categorization.)

23 3.4. In an earlier draft of the framework, EPA had included three Summary Recommendation
24 Tables in Section 3 on human health, aquatic, and terrestrial risk assessment, covering the
25 three general assessment categories (i.e., site-specific, national level, and ranking and
26 categorization). An example of this table is included as Appendix A in the draft provided
27 to the SAB. To minimize confusion for users of the framework, the initial idea behind
28 the recommendations and adjoining table was to have concise recommendations on the
29 science, followed by a separate accounting of how these recommendations could then be
30 applied to the different assessment categories. Reviews have been mixed on the utility of
31 these tables as a sufficient communication tool. Please comment on whether tables of
32 this type would be useful for inclusion in the final version of the framework. Does the
33 panel have alternative suggestions for effectively communicating how the
34 recommendations can be considered for each of the three assessment levels?

35 *Environmental Chemistry (Sections 3.3.1, 4.1)*

36 3.5 Please comment on the objectivity of the Hard Soft Acid Base concept to applications of
37 stability of metal complexes in toxicity assessments. See Section 4.1.2.

38 3.6 Please comment on the objectivity of the atmospheric metal chemistry discussion and its

1 application to exposure assessments. See Sections 3.3.1.1 and 4.1.7.

2 3.7 Please comment on the objectivity of the metal chemistry and environmental parameters
3 incorporated in the various metal surface complexation and partition coefficient models
4 and their applications to exposure assessments. See Sections 3.3.1.2 and 4.1.4.1.

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

6 3.8 Please comment on the objectivity of the discussion and recommendations on natural
7 background of metals. See Sections 3.1.2.1 and 4.2.2.1.

8 3.9 Please comment on the objectivity of the discussion of essentiality versus toxicity,
9 including the relationship between Recommended Daily Intakes (RDAs) and thresholds
10 such as Reference Doses (RfDs) and Reference Concentrations (RfCs). See Sections 3.1,
11 4.3.2, and 4.3.3.

12 3.10 Please comment on the objectivity of the discussion and recommendations presented for
13 assessing toxicity of mixtures, including how to assess additivity versus departure from
14 additivity. See Sections 3.1.3.4 and 4.3.6.

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

16 3.11 Please comment on the objectivity of the discussion and recommendations concerning
17 natural background, bioavailability, bioaccumulation, biomagnification, and trophic
18 transfer in both aquatic and terrestrial environments. See Sections 3.2.2 to 3.2.4, 3.3.2,
19 4.4.3, 4.5.4, and 4.5.6 to 4.5.9.

20 3.12 Please comment on the objectivity of the framework statement that the latest scientific data
21 on bioaccumulation do not currently support the use of bioconcentration factor (BCF) and
22 bioaccumulation factor (BAF) values as generic threshold criteria for hazard classification
23 of inorganic metals (see recommendation on page 3-17, lines 27-29 of the document). By
24 this, the framework means that various assumptions underlying the BCF/BAF approach,
25 including the independence of BCF/BAF with exposure concentration and the
26 proportionality of hazard with increasing BCF/BAF do not hold true for the vast majority
27 of inorganic metals assessed. Please comment on the framework's acknowledgement that
28 the appropriate use of BCFs/BAFs to evaluate metal bioaccumulation, including the degree
29 to which BCFs/BAFs are dependent on exposure concentrations, needs to consider
30 information on bioaccessibility, bioavailability, essentiality, acclimation/adaptation,
31 regulation of metals (uptake and internal distribution), detoxification and storage,
32 dependence on exposure concentration, and background accumulation. While the ability to
33 quantitatively address all these factors may be limited at the present time, the framework
34 states that their potential impacts should at least be qualitatively addressed. See Sections
35 3.2.4, 3.3.2.5, and 4.5.8.

1 3.13 Given the variety of organism responses to inorganic metals exposure, based on factors
2 such as bioaccessibility, bioavailability, essentiality, uptake/excretion mechanisms, and
3 internal storage/regulation, as described in Section 3.2.4, the framework states that
4 BAFs/BCFs should be derived using mathematical relationships that represent the
5 concentration in the organism or tissue as a function of the bioavailable concentration in
6 the exposure medium/media for each set of exposure conditions. Please comment on
7 whether this is the best approach based on the current state of the science or if there are
8 alternative approaches that are more appropriate that can be routinely applied. See
9 Sections 3.2.4, 3.3.2.5, and 4.5.8.

10
11 3.14 Please comment on the objectivity of the information and recommendations pertaining to
12 the use of the acid-volatile sulfide-simultaneously extracted metals (AVS-SEM) approach
13 and the biotic ligand (BLM) model. Are additional recommendations warranted? If yes,
14 what are they? See Sections 3.2.6, 4.4.2.3, and 4.5.10.

15
16 In this report, the SAB provides specific recommendations and comments in response to each of
17 these charge questions.

18
19 The SAB notes that the Framework will be an important document. It will be used by EPA to
20 develop risk assessment guidance, and it will be used by both EPA and the external community
21 as an authoritative compilation of the state of science regarding metals in the environment. The
22 SAB commends EPA for initiating the development of a risk assessment framework for metals
23 that covers a broad spectrum of topics related to human health and ecological risk concerns
24 associated with exposure to toxic metals and metalloids. However, the SAB believes that a
25 number of major issues within the Framework document need to be addressed, and that
26 significant revision of the Framework is required, before the document is published in final form
27 in order to make it of long-term value to EPA. A major weakness in this version of the
28 Framework is the lack of consistency in identity, vacillating inconsistently from a description of
29 basic principles to a methods manual. The SAB recommends substantial revision of the
30 Framework to reorganize the document, include additions and corrections, and remove
31 redundancies. The SAB finds the Human Health section of the Framework, in particular, to be
32 incomplete, lacking in important details, and containing inaccuracies that need to be addressed
33 before the document can be produced in a final form. The ecological subsections of the
34 Framework should more fully reflect the state of the science (i.e., they leave the perception of
35 not being objective). The bioaccumulation and bioavailability sections need to treat the routes of
36 exposure (diet and dissolved metals) in an integrated fashion. This could be accomplished by
37 organizing the discussion around the bioavailability conceptual model. The toxicity testing
38 section needs to discuss uncertainties of particular importance to metals: lack of dietary exposure
39 is a good example. Discussions of sediment contamination all but ignore major aspects of this
40 field such as bioavailability from oxidized sediments and the National Oceanic and Atmospheric
41 Administration's (NOAA) effects range median (ERM) and effects range low (ERL) approach
42 (Long & Morgan, 1990; 1991). The discussion of simultaneously extracted metals – acid
43 volatile sulfides (SEM-AVS) does not capture the controversies surrounding this approach; nor
44 does the discussion of the biotic ligand model (BLM) capture the limits of the approach or its
45 early state of development. The SAB provides recommendations for improvements in the
46 Framework to make it more useful to EPA and other intended audiences. Because of the scope

1 of revisions recommended, the SAB believes the revised Framework would benefit from a
2 second external peer review. The SAB is willing to provide such a review.

3
4 *Presentation*

5
6 The overall clarity of expression, precision of wording, and balance in coverage among topics
7 in the Framework must be greatly improved. Many of the SAB’s comments focus on the main
8 technical issues that need to be addressed specifically. However, the SAB finds that sections of
9 the current Framework are unclear and disorganized and that revision is needed to develop a
10 document that is of high quality.

11
12 *Title*

13
14 The title of the Framework is awkward: metals are inorganic by definition, and thus the use of
15 the adjective “inorganic” in front of metals is redundant. Although the SAB realizes that the
16 adjective “inorganic” was probably used in the original title to exclude organometallics,
17 especially methyl mercury, it detracts from the clarity of the title. A better title would be
18 “Framework for Assessment of Risk of Metals and Metalloids in the Environment.” The
19 specific exclusion of organometallics should be addressed in the beginning of the report.

20
21 *Purpose*

22
23 The SAB finds that the Framework has a “dual personality.” At times, the Framework
24 provides background information on the state of the science and general recommendations of
25 “basic principles” that need to be considered for risk assessments of metals. At other times, the
26 report appears to serve as a practical guide for risk assessors, offering specific recommendations
27 of methods and tools (often with insufficient justification for the specific selection). This dual
28 nature of the report stems largely from its intended purpose (as stated on pages 1-1 and 1-2) to
29 serve as a “statement of policy” while at the same time “provide recommendations and foster
30 consistent application” across EPA. The SAB recommends that the purpose of the Framework
31 be reviewed and revised accordingly to remove any sense of contradiction in its intended
32 purpose. In addition, all recommendations in the Framework should be carefully reviewed and
33 revised to ensure that they are consistent with its intended purpose. As such, the
34 recommendations should focus on the key issues that need to be considered in metals
35 evaluations. Specific methods and tools should be cited accordingly to highlight the current state
36 of the science. EPA, however, should refrain from making final recommendations of specific
37 methods and tools until a full evaluation of the strengths and weaknesses of each method/tool is
38 performed.

39
40 *Restructuring of Framework Document*

- 41
42 • Section 3 of the Framework should be reorganized and rewritten to provide more
43 comparability among the human health effects, aquatic effects, and terrestrial effects. The
44 SAB recommends that the aquatic section be modeled on the terrestrial section.
45 Recommendations should be highlighted by minimizing textual justification and cross-
46 referencing justification to Section 4 of the Framework.

- Section 4 of the Framework should be reorganized to mirror the organizational structure used in Section 3.
- Section 5 of the Framework, “Research Needs”, should be removed from the document because the research needs presented are not supported with interpretative text (see discussion below).

Critical Evaluation of Supporting Information

The SAB commends EPA for providing extensive coverage of available tools for risk assessment and methods for metals analyses in some sections of the Framework. In many instances however, critical evaluations of the tools and methods are not provided and the justification for many recommendations is not clear. The SAB therefore recommends that more information be presented on the strengths, weaknesses, and limitations of the various methods and tools, and where appropriate, comparative assessment of competing approaches should be provided.

Illustrative Examples

The SAB finds that illustrative examples would be useful throughout the document. Examples of how certain recommendations might be implemented would greatly improve the utility of the document.

Discussion of Uncertainties and Data Quality

Discussion of uncertainties of the tools, methods and data is generally lacking and inconsistent throughout the document. Data quality is a large concern for metals, particularly for measurement of dissolved metals. Historic data must be considered with a critical eye, as the data were often generated before clean-room and trace-level measurement techniques were adopted. The need to critically consider data quality should be explicitly stated throughout the document wherever the use of analytical data is discussed.

Use of the term “Bioaccumulation” versus “Accumulation” to Describe Metals Concentrations

As part of this SAB review, public comments were received concerning use of the terms “bioaccumulation” and “accumulation.” Public commenters have suggested use of the term “bioaccumulation” to describe the concentration of metals in aquatic and terrestrial organisms, and use of the term “accumulation” of metals for humans. EPA sought SAB advice regarding these comments. It is the opinion of the SAB that there should not be a distinction between the term “bioaccumulation” to describe metal concentration in aquatic and terrestrial organisms and the term “accumulation” of metals for humans. This is not an accepted distinction in the scientific community. In humans as in other terrestrial animals, the steady-state body burden of many metals is under homeostatic control that balances intake and excretion. However, for certain metal compounds bioaccumulation can occur, which can be defined as either a persistent increase in individual steady-state levels that is correlated with higher prior exposure, and/or a progressive increase in body burden as a function of exposure time or age, that is above normal

1 steady-state levels and which may involve selective bioaccumulation of the metal in certain
2 tissues.

3
4 The SAB believes it important to recognize that some metals do bioaccumulate in the tissues
5 of humans and that this bioaccumulation is related to their toxicity. The rate at which this
6 process occurs depends upon the balance between the accumulation and elimination of the metal
7 in the tissues of concern and, thus, is dependent upon the concentration of the exposure dose and
8 the frequency of exposure. Pharmacokinetic models can be used to estimate the extent to which
9 metals bioaccumulate in tissues. The SAB recommends that the definition of the term
10 “bioaccumulation” in the glossary of this document be modified to read as follows:

11
12 Bioaccumulation: The net accumulation of a metal in a tissue of interest or the whole
13 organism that results from exposure to all environmental sources, including air, water,
14 solid phases (i.e., soil, sediment) and diet, *and that represents a net mass balance*
15 *between uptake and elimination of the metal.*

16
17 *Bioconcentration Factors (BCF) and Bioaccumulation Factors (BAF) as Measures of Relative*
18 *Ecological Hazard*

19
20 An important conclusion of the Framework seemed to be that BCF and BAF are not
21 universally useful measures of the relative ecological hazard of metals. The SAB agrees that
22 conclusion is justified. Unfortunately, discussion of the topic was particularly scattered, and the
23 recommendations were contradictory. This could be resolved by clearly stating the uses of these
24 measures that are justified, and the uses that are not; and building recommendations accordingly.
25 If the Framework is going to eliminate BCF as a consideration, it needs to discuss alternative
26 measures of relative hazard beyond toxicity. The Framework’s explicit elimination of trophic
27 transfer potential for consideration is particularly unfortunate. Trophic transfer potential varies
28 widely among metals/metalloids and is an important source of uncertainty in toxicity
29 determinations.

30
31 *Metal-specific Reference Values (RfD/RfC) and/or Cancer Potency Factors*

32
33 The SAB recommends that, in introducing the Human Health Effects Section, EPA should set
34 the context by explaining that human health risk assessors start their analysis with a metal-
35 specific reference value (RfD/RfC) and/or cancer potency factor that has been developed through
36 a process separate from the risk assessment. The role of the human risk assessor is to
37 appropriately integrate the reference values and potency factors with the exposure assessment.
38 Thus, the risk assessor needs an understanding of the toxicological endpoints and mechanisms of
39 action that underlie the derivation of these values to ensure that, for example, the appropriate
40 population and life stages are addressed, appropriate dietary aspects are taken into consideration,
41 and the appropriate exposure pathways are considered. For metals, frequency and duration of
42 exposure, as well as exposure concentrations, are important parameters to be considered for
43 accurate dose assessments. The Framework should focus on advising human health risk
44 assessors on how to take these considerations into account in constructing the risk assessment.

45
46 *Background Versus Ambient Concentration*

1
2 The term background is often incorrectly assumed to connote “natural” and therefore “safe”
3 or of no significant human or ecological health concern. However, ambient levels can vary, or
4 can be inherently high enough to represent a potential health concern by themselves. They can
5 also represent a total concentration from a combination of natural and anthropogenic sources,
6 some of which may be historical or unknown. For metals in particular, the concept of
7 background concentrations as described in the Framework document is complicated by several
8 factors, which include the sometimes highly variable natural concentrations of metals in soils,
9 sediments, air and water, various historical anthropogenic sources, atmospheric deposition from
10 distal anthropogenic sources. This is discussed in detail in the response to charge question 3.8
11 below.

12 13 *Chemical Speciation*

14
15 Among risk assessors and scientists working on metals, the concept of “chemical species” and
16 “chemical speciation” is fundamental. In the Framework, there are certain instances where the
17 terms are used incorrectly. In addition to correcting these instances, the SAB recommends that
18 the speciation concept be introduced in the environmental chemistry part of Section 2,
19 specifically in the “Environmental Chemistry” principle section, and in the environmental
20 chemistry part of Section 4. Appendix A of this SAB report contains text that is adapted from
21 recent International Union of Pure and Applied Chemistry (IUPAC) recommendations
22 (Templeton et al., 2000). The SAB believes that this material would serve as a suitable starting
23 point for discussions in Section 4 of the Framework.

24
25 The SAB also recommends that greater care be taken in distinguishing general descriptions of
26 solid-water “partitioning” processes and the specific term “partition coefficient.” In this context,
27 “partitioning” refers to a general set of processes that controls the distribution of metal among
28 dissolved and solid phases, whereas “partition coefficient” is one specific descriptor of the
29 empirical distribution which is based on the ratio of solid phase to dissolved metal.

30 31 *Metals Mixtures*

32
33 The SAB notes that in virtually all settings, individual metals exist as components of
34 mixtures. Even in their natural settings, metals of concern to a risk assessor are typically
35 mingled with other metals. When the question of risk is posed from the standpoint of pollution
36 episodes, the principle still holds; that is, metals are usually presented to ecological receptors and
37 to humans as a mixture with other metals and/or organics. In all instances and settings, then, the
38 assessor must be aware of the additional materials present in that particular environment when a
39 metal is studied as a potentially hazardous pollutant. These “mixed exposures” can have
40 dramatic effects on the toxic potential of the metal.

41 42 *Mimicry*

43
44 The SAB notes that structural similarities of metals, such as similar ionic radii, may result in
45 competition for essential receptors, thus, disrupting normal functions. Examples may include
46 chromate substituting for sulfate or phosphate, Pb replacing Ca or Zn, and Cd substituting for Zn

1 or Ca on important regulatory proteins or enzymes. The degree to which these ionic
2 substitutions may occur in target cell populations is dependent upon a number of factors
3 including cellular uptake/excretion of toxic metals, intracellular complexations with metal-
4 binding proteins such as metallothionein or lead-binding proteins and sequestration in lysosomes
5 or inclusion bodies. In this regard, the limited discussion of metal-binding proteins in the
6 Framework could be expanded to include more recent references on all of these potential
7 intracellular metal sequestration depots since they will determine the extent to which
8 molecular/ionic mimicry actually occurs *in vivo* (see response to charge question 6.3.10).

9 10 *Balance of Coverage – Metal Speciation*

11
12 The SAB commends the EPA for emphasizing approaches that employ a relatively
13 sophisticated understanding of metal speciation in the context of metals risk assessment. While
14 there is an adequate discussion in the Framework of the use of models to estimate metal
15 speciation in water, soil and sediments, there is insufficient discussion of analytical tools to
16 measure the speciation of a metal. A fuller description of the currently available tools to
17 quantify metal speciation in environmental samples, including the strengths and weaknesses of
18 each technique, would be of great benefit to a risk assessor in determining the form and potential
19 effects of metal contamination at a given site, and which tools are most appropriate for a given
20 assessment.

21 22 *Balance of Coverage – Data Collection*

23
24 The SAB finds that the Framework contains insufficient information on data collection.
25 Recommendations and supporting information should be presented on the type of field data that
26 are needed (including metal speciation and concentrations, and related system parameters such as
27 pH, redox conditions, organic carbon concentrations, iron concentrations, or acid volatile
28 sulfides), and on the appropriate time and space scales for data collection. Revised procedures
29 and processes that are needed to evaluate the adequacy and quality of the data being used for the
30 metals risk assessment should be discussed.

31 32 *Biogeochemistry*

33
34 The SAB notes that a key difference between the fate and transport of metals compared to
35 organic compounds is in the relationship of metals to biogeochemical cycles. For organic
36 compounds, the coupling to natural biogeochemical cycles is essentially unidirectional, i.e., the
37 major biogeochemical cycles affect the fate and transport of organic compounds, but not vice
38 versa. Metals interact with the cycles of more elements (especially sulfur and other metals) than
39 organic compounds. In addition, metals can be limiting nutrients, toxicants, or both with respect
40 to organisms that can determine the rates and character of the major biogeochemical cycles (e.g.,
41 higher plants, phytoplankton, bacteria). The SAB finds that the role of metal biogeochemical
42 cycling is not adequately addressed in the conceptual model for the risk assessment framework,
43 or in subsequent sections of the Framework.

44 45 *Modeling*

46

1 The SAB notes that the Framework accurately reflects the fact that modeling the
2 environmental fate and transport of metals differs in significant ways from modeling organic
3 compounds. However, descriptions of a number of models are included in the Framework with
4 little or no information presented on: requirements for adapting existing models for metals
5 applications, for developing new metals-specific models for risk assessment, for establishing
6 data requirements for model calibration, or for determining suitable techniques for estimating
7 parameter values (and associated uncertainties). Further guidance will need to be developed.
8

9 *Removing Section on Metal Research Needs*

10
11 The SAB feels that the identification of research needs should not be within the scope of the
12 current Framework. There has not been a thorough review of all research areas and it is not
13 appropriate in the given context to highlight and identify specific research needs for the future.
14 Therefore, the SAB recommends that the research needs section (Section 5) of the Framework be
15 removed.
16

17 *Recommended Revision of Specific Sections of the Framework*

- 18
19
- 20 • The “principles” provided in Section 2.1 of the Framework are not fundamental
21 principles. The term should therefore be replaced with a more appropriate term. The SAB
22 also finds a lack of uniformity in the quality and/or clarity of writing among the
23 subsections in Section 2 . It is noted that the well-written report of the SAB’s 2002
24 Metals Assessment Plan (MAP) review (EPA Science Advisory Board, 2002) addressed
25 many of the same issues. It is therefore recommended that SAB MAP report be revisited
26 prior to revision of Section 2 in order to improve the quality and clarity of the writing.
 - 27 • The recommendations in Section 3 of the Framework should be rewritten to clearly
28 express them as recommendations rather than statements.
 - 29
 - 30 • The number of recommendations in Section 3 of the Framework should be reduced by
31 omitting statements and condensing similar or redundant recommendations.
32 Recommendations should also be organized by importance or specificity
33
 - 34 • Revised recommendations in Section 3 of the Framework should not be proscriptive, but
35 suggest options or examples.
 - 36
 - 37 • Tables such as those provided in A-2 of the Framework should be included in an
38 appendix. Recommendations for improvements to the tables are provided below.
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40
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1 **Review of EPA’s Draft Framework for Inorganic Metals Risk Assessment**

2
3 **A Report by the Science Advisory Board Metals Risk Assessment**
4 **Framework Review Panel**

5
6 **2. INTRODUCTION**

7
8 The U.S. Environmental Protection Agency (EPA) Science Advisory Board (SAB) Metals
9 Risk Assessment Framework Review Panel has reviewed EPA’s draft *Framework for Inorganic*
10 *Metals Risk Assessment* (Framework). This report transmits the SAB’s comments and
11 recommendations. Many EPA programs face decisions on whether and how to regulate metals.
12 These decisions range from setting standards or permitting for environmental releases, to
13 establishing safe levels in different environmental media, to setting priorities for programmatic
14 or voluntary efforts. EPA developed the draft *Framework for Inorganic Metals Risk Assessment*
15 to supplement previous Agency guidance for use in site-specific risk assessments, criteria
16 derivation, and other similar Agency activities related to metals.

17
18 EPA has followed a stepwise process to develop the draft Framework. A Metals Action Plan
19 (MAP) was first developed to establish a process for application of scientific principles to metals
20 risk assessment. In September 2002, the SAB reviewed the MAP and provided comments to
21 EPA (U.S. EPA SAB, 2002). EPA then developed metals issue papers addressing the following
22 topics: environmental chemistry of metals, bioavailability and bioaccumulation of metals, metal
23 exposure assessment, human health effects, and ecological effects (U.S. EPA, 2004). The draft
24 Framework was then completed and a peer consultation workshop was held in July, 2004 to seek
25 input on the document from scientists in the field of metals risk assessment. The draft
26 Framework was revised based on comments received from the peer consultation workshop and
27 inter-Agency review, and the document was provided to the SAB for review.

28
29 The SAB commends EPA for recognizing the need to carefully analyze the differences
30 between metals and organic chemicals in site specific and national risk assessments.
31 Specifically, the SAB congratulates EPA for initiating the development of a risk assessment
32 framework for metals that covers a broad spectrum of topics related to human health and
33 ecological risk concerns from exposure to toxic metals and metalloids. The SAB’s comments
34 are directed to the EPA to help develop a strong final document that will help guide Agency risk
35 assessors for a number of years into the future.

36
37 **3. CHARGE TO THE REVIEW PANEL**

38
39 EPA sought comment from the SAB on the scientific soundness of the Framework’s synthesis
40 and representation of the state of the science. Specifically, EPA sought comment on: the overall
41 objectivity and utility of the recommendations and supporting tools, methods, and models to its
42 primary audience, EPA risk assessors, and the public, and whether there are any additional
43 research needs that warrant inclusion or further discussion in the Framework. EPA defined
44 objectivity as: “a focus on whether the disseminated information is being presented in an
45 accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate,
46 reliable, and unbiased. EPA defined utility as: “the usefulness of the information to its intended

1 users, including the public. The EPA gave the following fourteen charge questions to the SAB
2 panel.

3
4 *Question 1: Section 1 - Framework Scope and Assessment Categories*

5 1.1 Please comment on the overall framework scope and whether it is sufficiently
6 encompassing to allow for the consideration of the broad spectrum of physical and
7 chemical properties, exposures, and effects among inorganic metals and metal
8 compounds.

9 1.2 The context of the regulatory application (e.g., contaminated site clean-up, national
10 regulation, or programmatic decision) is a major factor in determining the type of
11 analysis that is appropriate for a particular assessment. The framework identifies three
12 general categories of assessments, including site-specific assessments, national scale
13 assessments, and national ranking and categorization. With the understanding that
14 screening and detailed assessments occur within the assessment categories, please
15 comment on the utility of these categories in setting the context for discussion of metals
16 assessment.

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

18 2.3 Please comment on whether the discussion of inorganic metals assessment principles is
19 clearly articulated, objective, as defined above, and has utility.

20 2.4 Please comment on how well the conceptual model presents key metal processes and
21 whether (or not) it is complete.

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

23 3.1 Please comment on how well the recommendations under Section 3 are supported by the
24 detailed information in Section 4. Are there other recommendations that should be
25 included? Are there any inorganic metals or metal compounds for which any of the
26 recommendations would not apply?

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

30 3.2 Please comment on the objectivity and utility of the data, tools, and methods discussed in
31 Section 4. Identify any scientific or technical inaccuracies, or any emerging areas or
32 innovative applications of current knowledge that may have been overlooked or warrant a
33 better discussion of uncertainty, including areas needing further research.

34 3.3 Please comment on the state of the science (i.e., data, tools and methods) to address
35 inorganic metals speciation in all environmental compartments for any given inorganic
36 metal from the point of environmental release to the point of toxic activity as discussed in
37 the document. Please comment on whether the framework identifies appropriate research
38 needs to overcome any limitations in the state of the science. Please address these

1 questions separately for each of the three types of assessments presented (i.e., site-
2 specific, national level, and ranking and categorization.)

3 3.4. In an earlier draft of the framework, EPA had included three Summary Recommendation
4 Tables in Section 3 on human health, aquatic, and terrestrial risk assessment, covering the
5 three general assessment categories (i.e., site-specific, national level, and ranking and
6 categorization). An example of this table is included as Appendix A in the draft provided
7 to the SAB. To minimize confusion for users of the framework, the initial idea behind
8 the recommendations and adjoining table was to have concise recommendations on the
9 science, followed by a separate accounting of how these recommendations could then be
10 applied to the different assessment categories. Reviews have been mixed on the utility of
11 these tables as a sufficient communication tool. Please comment on whether tables of
12 this type would be useful for inclusion in the final version of the framework. Does the
13 panel have alternative suggestions for effectively communicating how the
14 recommendations can be considered for each of the three assessment levels?

15 *Environmental Chemistry (Sections 3.3.1, 4.1)*

16 3.5 Please comment on the objectivity of the Hard Soft Acid Base concept to applications of
17 stability of metal complexes in toxicity assessments. See Section 4.1.2.

18 3.6 Please comment on the objectivity of the atmospheric metal chemistry discussion and its
19 application to exposure assessments. See Sections 3.3.1.1 and 4.1.7.

20 3.7 Please comment on the objectivity of the metal chemistry and environmental parameters
21 incorporated in the various metal surface complexation and partition coefficient models
22 and their applications to exposure assessments. See Sections 3.3.1.2 and 4.1.4.1.

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

24 3.8 Please comment on the objectivity of the discussion and recommendations on natural
25 background of metals. See Sections 3.1.2.1 and 4.2.2.1.

26 3.9 Please comment on the objectivity of the discussion of essentiality versus toxicity,
27 including the relationship between Recommended Daily Intakes (RDAs) and thresholds
28 such as Reference Doses (RfDs) and Reference Concentrations (RfCs). See Sections 3.1,
29 4.3.2, and 4.3.3.

30 3.10 Please comment on the objectivity of the discussion and recommendations presented for
31 assessing toxicity of mixtures, including how to assess additivity versus departure from
32 additivity. See Sections 3.1.3.4 and 4.3.6.

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

34 3.11 Please comment on the objectivity of the discussion and recommendations concerning
35 natural background, bioavailability, bioaccumulation, biomagnification, and trophic
36 transfer in both aquatic and terrestrial environments. See Sections 3.2.2 to 3.2.4, 3.3.2,
37 4.4.3, 4.5.4, and 4.5.6 to 4.5.9.

1 3.12 Please comment on the objectivity of the framework statement that the latest scientific data
2 on bioaccumulation do not currently support the use of bioconcentration factor (BCF) and
3 bioaccumulation factor (BAF) values as generic threshold criteria for hazard classification
4 of inorganic metals (see recommendation on page 3-17, lines 27-29 of the document). By
5 this, the framework means that various assumptions underlying the BCF/BAF approach,
6 including the independence of BCF/BAF with exposure concentration and the
7 proportionality of hazard with increasing BCF/BAF do not hold true for the vast majority
8 of inorganic metals assessed. Please comment on the framework's acknowledgement that
9 the appropriate use of BCFs/BAFs to evaluate metal bioaccumulation, including the degree
10 to which BCFs/BAFs are dependent on exposure concentrations, needs to consider
11 information on bioaccessibility, bioavailability, essentiality, acclimation/adaptation,
12 regulation of metals (uptake and internal distribution), detoxification and storage,
13 dependence on exposure concentration, and background accumulation. While the ability to
14 quantitatively address all these factors may be limited at the present time, the framework
15 states that their potential impacts should at least be qualitatively addressed. See Sections
16 3.2.4, 3.3.2.5, and 4.5.8.

17 3.13 Given the variety of organism responses to inorganic metals exposure, based on factors
18 such as bioaccessibility, bioavailability, essentiality, uptake/excretion mechanisms, and
19 internal storage/regulation, as described in Section 3.2.4, the framework states that
20 BAFs/BCFs should be derived using mathematical relationships that represent the
21 concentration in the organism or tissue as a function of the bioavailable concentration in
22 the exposure medium/media for each set of exposure conditions. Please comment on
23 whether this is the best approach based on the current state of the science or if there are
24 alternative approaches that are more appropriate that can be routinely applied. See
25 Sections 3.2.4, 3.3.2.5, and 4.5.8.

26
27 3.15 Please comment on the objectivity of the information and recommendations pertaining to
28 the use of the acid-volatile sulfide-simultaneously extracted metals (AVS-SEM) approach
29 and the biotic ligand (BLM) model. Are additional recommendations warranted? If yes,
30 what are they? See Sections 3.2.6, 4.4.2.3, and 4.5.10.

31 32 **4. REVIEW PROCESS**

33
34 To establish the Metals Risk Assessment Framework Review Panel, the EPA Science
35 Advisory Board Staff Office published a Federal Register notice requesting nominations, and
36 identified a subset of nominees for consideration as panelists. The final panel was selected after
37 requesting public comments on the nominees and further evaluating them against EPA Science
38 Advisory Board selection criteria. The members of the review panel included scientists with
39 expertise in: the environmental chemistry of metals, environmental fate and transport of metals,
40 bioavailability of metals, routes of exposure of aquatic and terrestrial species to metals, routes of
41 human exposure to metals, human health effects of exposure to metals, and ecological effects of
42 exposure to metals.

43
44 The SAB review was conducted by a public teleconference and a two and one half day
45 public face-to-face meeting of the SAB Panel. During the public conference call, EPA answered
46 questions from the Panel about the draft Framework and the review charge. At the public

1 meeting, the Panel heard presentations from EPA on the Framework and deliberated on the
2 charge questions. The Panel met in the following three working groups to develop responses to
3 the charge questions: 1) Environmental Chemistry/Fate and Transport, 2) Human Exposure and
4 Health Effects, and 3) Ecological Exposure and Effects/Bioaccumulation. Responses of the three
5 working groups were integrated by the Panel to develop the final SAB report.

6 7 **5. OVER-ARCHING COMMENTS AND RECOMMENDATIONS**

8
9 The SAB provides a number of broad over-arching comments and recommendations to
10 improve the Framework. The SAB notes that the draft Framework is an ambitious attempt to
11 survey the major issues involved in the assessment of human health and ecological effects of
12 metals and metalloids, and should be a source of pride for EPA once it is rigorously evaluated
13 and produced in a final form. In this regard, the SAB believes that the following major issues
14 within the Framework document need to be addressed before the document is published in final
15 form in order to make it of more current and long-term value to EPA.

16
17 The SAB recommends substantial revision of the Framework to reorganize the document,
18 include additions and corrections, and remove redundancies as detailed in the responses to the
19 charge questions below. Because of the scope of recommended revisions, the SAB believes the
20 revised Framework would benefit from a second external peer review. The SAB is willing to
21 provide such a review. The SAB finds the Human Health section of the Framework, in
22 particular, to be incomplete, lacking in important details, and containing inaccuracies and
23 grammatical errors that need to be addressed before the document can be produced in a final
24 form. Some critical references are missing, a number of the references cited in Section 4 are
25 outdated, and more recent references should be included. The ecological subsections of the
26 Framework should more fully reflect the state of the science (i.e., they leave the perception of
27 not being objective). The bioaccumulation and bioavailability sections need to treat the routes of
28 exposure (diet and dissolved metals) in an integrated fashion. This could be accomplished by
29 organizing the discussion around the bioavailability conceptual model. The toxicity testing
30 section needs to discuss uncertainties of particular importance to metals: lack of dietary exposure
31 is a good example. Discussions of sediment contamination all but ignore major aspects of this
32 field such as bioavailability from oxidized sediments and the National Oceanic and Atmospheric
33 Administration's (NOAA) effects range median (ERM) and effects range low (ERL) approach
34 (Long & Morgan, 1990; 1991). The discussion of simultaneously extracted metals – acid
35 volatile sulfides (SEM-AVS) does not capture the controversies surrounding this approach; nor
36 does the discussion of the biotic ligand model (BLM) capture the limits of the approach or its
37 early state of development.

38
39 The following comments and recommendations are discussed in more detail in the responses
40 to the charge questions below.

41 42 *Presentation*

43
44 The overall clarity of expression, precision of wording, and balance in coverage among topics
45 in the Framework must be greatly improved. Many of the SAB's comments below focus on the
46 main technical issues that need to be addressed specifically. However, the SAB finds that

1 sections of the current Framework are unclear and disorganized and that revision is needed to
2 develop a document that is of high quality.

3
4 *Title*

5
6 The title of the Framework is awkward: metals are inorganic by definition, and thus the use of
7 the adjective “inorganic” in front of metals is redundant. Although the SAB realizes that the
8 adjective “inorganic” was probably used in the original title to exclude organometallics,
9 especially methyl mercury, it detracts from the clarity of the title. A better title would be
10 “Framework for Assessment of Risk of Metals and Metalloids in the Environment.” The
11 specific exclusion of organometallics should be addressed in the beginning of the report.

12
13 *Purpose*

14
15 The SAB finds that the draft Framework has a “dual personality.” At times, the Framework
16 provides background information on the state of the science and general recommendations of
17 “basic principles” that need to be considered for risk assessments of metals. At other times, the
18 report appears to serve as a practical guide for risk assessors, offering specific recommendations
19 of methods and tools (often with insufficient justification for the specific selection). This dual
20 nature of the report stems largely from its intended purpose (as stated on pages 1-1 and 1-2) to
21 serve as a “statement of policy” while at the same time “provide recommendations and foster
22 consistent application” across EPA. The SAB recommends that the purpose of the Framework
23 be reviewed and revised accordingly to remove any sense of contradiction in its intended
24 purpose. In addition, all recommendations in the Framework should be carefully reviewed and
25 revised to ensure that they are consistent with its intended purpose. As such, the
26 recommendations should focus on the key issues that need to be considered in metals
27 evaluations. Specific methods and tools should be cited accordingly to highlight the current state
28 of the science and to serve as examples. EPA, however, should refrain from making final
29 recommendations of specific methods and tools until a full evaluation of the strengths and
30 weaknesses of each method and tool is performed.

31
32 *Critical Evaluation of Supporting Information*

33
34 The SAB commends EPA for providing fairly comprehensive coverage of available tools for
35 risk assessment and methods for metals analyses. In many instances however, critical
36 evaluations of the tools and methods are not provided and the justification for many
37 recommendations is not clear. The SAB therefore recommends that more information be
38 presented on the strengths, weaknesses, and limitations of the various methods and tools, and
39 where appropriate, comparative assessment of competing approaches should be provided.

40
41 *Tiered Recommendations in the Framework*

42
43 The SAB recommends that the recommendations in the Framework should be tiered, with the
44 most critical recommendations (those with the greatest impact) presented first, followed by
45 specific recommendations that would be of value to the assessor. This would help focus the
46 different sections of the Framework to ensure that the most important issues are addressed.

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Illustrative Examples

Illustrative examples would be useful through the document. Examples of how certain recommendations might be implemented would greatly improve the utility of the document.

Discussion of Uncertainties and Data Quality

Discussions of uncertainties of the tools, methods and data are generally lacking and inconsistent throughout the document. Data quality is a large concern for metals, particularly measurement of dissolved metals. Historic data must be considered with a critical eye, as the data were often generated before clean-room and trace-level measurement techniques were adopted. The need to critically consider data quality should be explicitly stated throughout the document wherever the use of analytical data is discussed.

Terminology and Additions to the Glossary

As discussed in the detailed responses to the charge questions, and in the recommendation concerning the definition of bioaccumulation below, the SAB recommends revision of several definitions in the glossary to make them consistent with current science and reduce confusion to the reader.

Use of the term “Bioaccumulation” versus “Accumulation” to Describe Metals Concentrations

As part of this SAB review, public comments were received concerning use of the terms “bioaccumulation” and “accumulation.” Public commenters have suggested use of the term “bioaccumulation” to describe concentration of metals in aquatic and terrestrial organisms, and use of the term “accumulation” of metals for humans. EPA sought SAB advice regarding these comments. It is the opinion of the SAB that there should not be a distinction between the term “bioaccumulation” to describe metal concentration in aquatic and terrestrial organisms and the term “accumulation” of metals for humans. This is not an accepted distinction in the scientific community. In humans as in other terrestrial animals, the steady-state body burden of many metals is under homeostatic control that balances intake and excretion. However, for certain metal compounds bioaccumulation can occur, which can be defined as either a persistent increase in individual steady-state levels that is correlated with higher prior exposure, and/or a progressive increase in body burden as a function of exposure time or age, that is above normal steady-state levels and which may involve selective bioaccumulation of the metal in certain tissues.

The SAB believes it important to recognize that some metals do bioaccumulate in the tissues of humans and that this bioaccumulation is related to their toxicity. The rate at which this process occurs depends upon the balance between the accumulation and elimination of the metal in the tissues of concern and, thus, is dependent upon the concentration of the exposure dose and the frequency of exposure. Pharmacokinetic models can be used to estimate the extent to which metals bioaccumulate in tissues. The Panel recommends that the definition of the term “bioaccumulation” in the glossary of this document be modified to read as follows:

1
2 Bioaccumulation: The net accumulation of a metal in a tissue of interest or the whole
3 organism that results from exposure from all environmental sources, including air, water,
4 solid phases (i.e. soil, sediment) and diet, *and that represents a net balance of uptake versus*
5 *elimination of the metal.*
6
7

8 *Metal-specific Reference Values (RfD/RfC) and/or Cancer Potency Factors*

9

10 The SAB recommends that, in introducing the Human Health Effects section, EPA should set
11 the context by explaining that human health risk assessors start their analysis with a metal-
12 specific reference value (RfD/RfC) and/or cancer potency factor that has been developed through
13 a process separate from the risk assessment. The role of the human risk assessor is to
14 appropriately integrate the reference values and potency factors with the exposure assessment.
15 Thus the risk assessor needs an understanding of the toxicological endpoints and mechanisms of
16 action that underlie the derivation of these values to ensure that, for example, the appropriate
17 population and life stages are addressed, appropriate dietary aspects are taken into consideration,
18 and the appropriate exposure pathways are considered. For metals, frequency and duration of
19 exposure, as well as exposure concentrations, are important parameters to be considered for
20 accurate dose assessments. The discussion in the Framework should focus on advising human
21 health risk assessors on how to take these considerations into account in constructing the risk
22 assessment.
23

24 *Background Versus Ambient Concentration*

25

26 The term background is often incorrectly assumed to connote “natural” and therefore “safe”
27 or of no significant human or ecological health concern. However, ambient levels can vary, or
28 can be inherently high enough to represent a potential health concern in and of themselves. They
29 can also represent a total level from a combination of natural and anthropogenic sources, some of
30 which may be historical or unknown. For metals in particular, the concept of background levels
31 as described in the Framework document is complicated by several factors, which include the
32 sometimes highly variable natural levels of metals in soils, sediments, air and water, various
33 historical anthropogenic sources or activities, air deposition from distal anthropogenic sources.
34 This is also discussed in detail in the response to charge question 3.8 below.
35

36 *Chemical Speciation*

37

38 Among risk assessors and scientists working on metals, the concept of “chemical species” and
39 “chemical speciation” is fundamental. In the Framework, there are certain instances where the
40 terms are used incorrectly. The SAB recommends that, in addition to correcting these instances,
41 the speciation concept be introduced in the environmental chemistry part of Section 2,
42 specifically in the “environmental chemistry” principle section, and in the environmental
43 chemistry part of Section 4. Appendix A of this SAB report contains text that is adapted from
44 recent IUPAC recommendations (Templeton et al., 2000). The SAB believes that this material
45 would serve as a suitable starting point for discussions in Section 4 of the Framework.
46

1 The SAB also recommends that greater care be taken in distinguishing general descriptions of
2 solid-water “partitioning” processes and the very specific term “partition coefficient.” In this
3 context, “partitioning” refers to a general set of processes that controls the distribution of metal
4 among dissolved and solid phases, whereas “partition coefficient” is one specific descriptor of
5 the empirical distribution which is based on the ratio of solid phase to dissolved metal.

6
7 *Metals Mixtures*
8

9 The SAB notes that in virtually all settings, individual metals exist as components of
10 mixtures. Even in their natural settings, metals of concern to a risk assessor are typically
11 mingled with other metals. When the question of risk is posed from the standpoint of pollution
12 episodes, the principle still holds; that is, metals are usually presented to ecological receptors and
13 to humans as a mixture with other metals and/or organics. In all instances and settings, then, the
14 assessor must be aware of the additional materials present in that particular environment when a
15 metal is studied as a potentially hazardous pollutant. These “mixed exposures” can have
16 dramatic effects on the toxic potential of the metal.

17
18 *Mimicry*
19

20 The SAB notes that structural similarities of metals, such as similar ionic radii, may result in
21 competition for essential receptors, thus, disrupting normal functions. Examples may include
22 chromate substituting for sulfate or phosphate, Pb replacing Ca or Zn, and Cd substituting for Zn
23 or Ca on important regulatory proteins or enzymes. The biological degree to which these ionic
24 substitutions may occur in target cell populations is dependent upon a number of factors
25 including cellular uptake/excretion of toxic metals, intracellular complexations with metal-
26 binding proteins such as metallothionein or lead-binding proteins and sequestration in lysosomes
27 or inclusion bodies. In this regard, the limited discussion in the Framework of metal-binding
28 proteins could be expanded to include more recent references on all of these potential
29 intracellular metal sequestration depots since they will determine the extent to which
30 molecular/ionic mimicry actually occurs *in vivo* (see response to charge question 6.3.10).

31
32 *Balance of Coverage – Metal Speciation*
33

34 The SAB commends the EPA for emphasizing approaches that employ a relatively
35 sophisticated understanding of metal speciation in the context of metals risk assessment. While
36 there is an adequate discussion in the Framework of the use of models to estimate metal
37 speciation in water, soil, and sediments, there is insufficient discussion of analytical tools to
38 measure the speciation of a metal. A fuller description of the tools that are currently available to
39 quantify metal speciation in environmental samples, including the strengths and weaknesses of
40 each technique, would be of great benefit to a risk assessor in determining the form and potential
41 effects of metal contamination at a given site, and which tools are most appropriate for a given
42 assessment.

43
44 *Balance of Coverage – Data Collection*
45

1 The SAB finds that the Framework contains insufficient information on data collection.
2 Recommendations and supporting information should be presented on the types of field data that
3 are needed (including metal speciation and concentrations, and related system parameters such as
4 pH, redox conditions, organic carbon concentrations, iron concentrations, acid volatile sulfides,
5 etc.), and on the appropriate time and space scales for data collection. Revised procedures and
6 processes that are needed to evaluate the adequacy and quality of the data being used for the
7 metals risk assessment should be discussed.

8 9 *Biogeochemistry*

10
11 The SAB notes that a key difference in the fate and transport of metals as compared to
12 organic compounds is in the relationship of metals to biogeochemical cycles. For organic
13 compounds, the coupling to natural biogeochemical cycles is essentially unidirectional (i.e., the
14 major biogeochemical cycles affect the fate and transport of organic compounds, but not vice
15 versa). Metals interact with the cycles of more elements (especially sulfur and other metals) than
16 organic compounds. In addition, metals can be limiting nutrients or toxicants to organisms that
17 drive the major biogeochemical cycles (e.g., higher plants, phytoplankton, bacteria). The SAB
18 finds that the role of metal biogeochemical cycling is not adequately addressed in the conceptual
19 model for the risk assessment framework, and in subsequent sections of the report.

20 21 *Modeling*

22
23 The SAB notes that the Framework accurately reflects the fact that modeling the
24 environmental fate and transport of metals differs in significant ways from modeling organic
25 compounds. However, descriptions of a number of models are included in the Framework with
26 little or no information presented on: requirements for adapting existing models for metals
27 applications, for developing new metals-specific models for risk assessment, for establishing
28 data requirements for model calibration, or for determining suitable techniques for estimating
29 parameter values (and associated uncertainties). Further guidance will need to be developed.

30 31 *Recommended Revision of Specific Sections of the Framework*

- 32
- 33 • The “principles” provided in Section 2 of the Framework are not fundamental principles.
34 The term, “principles,” should therefore be replaced with a more appropriate term such as
35 “factors” or “key issues.” The SAB also finds a lack of uniformity in the quality and/or
36 clarity of writing among the parts of Section 2. It is noted that the well-written report of
37 the SAB’s 2002 Metals Assessment Plan (MAP) review (EPA Science Advisory Board,
38 2002) addressed many of the same issues. It is therefore recommended that the SAB
39 MAP report be revisited prior to revision of Section 2 in order to improve the quality and
40 clarity of the writing.
 - 41
42 • Section 3 of the Framework should be reorganized to provide more comparability among
43 the parts of the section. Recommendations should be highlighted by minimizing textual
44 justification and cross referencing justification to Section 4.
- 45

- 1 • The recommendations in Section 3 of the Framework should be rewritten to clearly
2 express them as recommendations rather than statements.
- 3
- 4 • The number of recommendations in Section 3 of the Framework should be reduced by
5 omitting statements and condensing similar or redundant recommendations.
6 Recommendations should also be organized by importance or specificity.
- 7
- 8 • Revised recommendations in Section 3 of the Framework should not be proscriptive, but
9 suggest options or examples.
- 10
- 11 • Tables such as those provided in A-2 of the Framework should be included in an
12 appendix. Recommendations for improvements to the tables are provided below in the
13 response to charge question 3.4.
- 14
- 15 • Section 4 of the Framework should be reorganized to mirror the organizational structure
16 used in Section 3.
- 17
- 18 • Section 5 of the Framework, “Research Needs”, should be removed from the document
19 because the research needs are not supported with interpretative text (see discussion
20 below). A separate, follow-up document identifying and prioritizing research needs
21 would be helpful if it were done in a comprehensive manner.
- 22

23 **6. RESPONSE TO THE CHARGE QUESTIONS**

24 **6.1.1 Charge question 1.1. Please comment on the overall framework scope and whether** 25 **it is sufficiently encompassing to allow for the consideration of the broad spectrum** 26 **of physical and chemical properties, exposures, and effects among inorganic metals** 27 **and metal compounds.** 28

29
30 The SAB believes the overall framework scope is sufficiently broad and provides an
31 appropriate level of flexibility in addressing issues of concern. The SAB feels that the following
32 four specific issues deserve attention in answering charge question 1.1.

33 *Balance Between Science and Guidance*

34
35
36 The Framework document has features of both a state-of-science document and a technical
37 guidance document. The prevailing view of the SAB is that the document should retain both of
38 these features but care should be given so that the document does not restrict or prescribe *specific*
39 methods or tools for risk assessment that may become obsolete over time.

40 *Treating Human and Ecosystem Health Risk Assessment in One Document*

41
42
43 The SAB agrees that both human and ecosystem health risk assessment need to be in one
44 framework document since the uniqueness of metals compared to organic compounds is germane
45 to both. However, the document needs to achieve better balance in quality and depth of coverage
46 in the sections on human and ecosystem health. Better integration of the human health and

1 ecosystem health sections with the environmental chemistry section is also needed.

2
3 *Expanding and Clarifying the Definition of Metals*

4
5 The SAB feels that the use of the term “metals and metal compounds” is confusing and does
6 not accurately capture the types of metals EPA intends to cover in the document. The SAB
7 recommends that the introduction section of the Framework provide a definition and
8 nomenclature that is inclusive of metals that do not behave like organic compounds but also
9 delineates the groups and classes of metals covered by this document, including metalloids.

10
11 *Removing Section on Metal Research Needs*

12
13 The SAB feels that the identification of research needs should not be within the scope of the
14 current Framework. There has not been a thorough review of all research areas and it is not
15 appropriate in the given context to highlight and identify specific research needs for the future.
16 Therefore, the SAB recommends that the research needs section (Section 5) of the Framework be
17 removed.

18
19 **6.1.2 Charge question 1.2. The context of the regulatory application (e.g., site specific**
20 **contaminated site clean-up, national regulation, or programmatic decision) is a**
21 **major factor in determining the type of analysis that is appropriate for a particular**
22 **assessment. The framework identifies three general categories of assessments,**
23 **including site-specific assessments, national scale assessments, and national ranking**
24 **and categorization. With the understanding that screening and detailed assessments**
25 **occur within the assessment categories, please comment on the utility of these**
26 **categories in setting the context for discussion of metals assessment.**

27 In general, the SAB agrees that the risk assessment categories listed in the Framework are an
28 appropriate context to cast the relevant issues of metals in comparison to organic compounds.
29 The Framework document needs to consider the important properties of metals in these
30 regulatory contexts.

31
32 The SAB, however, recommends that the scope of the categories be more clearly defined at
33 the beginning of the document. For example, the SAB believes that the three categories
34 delineated in the document may actually represent five different aspects of assessment (national
35 screening level assessment, national ranking assessment, national complex assessment, site scale
36 screening assessment and site scale complex assessment). The assessments differ by both scope
37 and complexity. Under national ranking and categorization, single metal properties or regional
38 site features can be used. Similarly, at the national level assessment, a single parameter can be
39 utilized or the assessment can incorporate site-specific information. At the site-specific
40 assessment level, however, the approach is more focused.

41 Examples of the types of risk assessment that span the range of complexities referred to above
42 include: national level that can be either 1) screening (e.g., comparing ambient water
43 concentrations to water quality criteria), 2) ranking (e.g., a contaminant candidate list for the
44 Safe Water Drinking Act); or 3) complex such as criteria documents. They can also include
45 more site-specific screening such as that required prior to completing an environmental impact

1 statement; and site specific complex assessments such as are required for Superfund.

2 The SAB feels that the sections in the Framework following the introduction largely concern
3 site specific assessment issues. The SAB recommends that the subsequent sections of the
4 document be edited to represent more balance among the different types of assessment. In
5 addition, these sections should include focused discussions and mapping to relevant issues at
6 each level of assessment.

7 **6.2.1 Charge question 2.1. Please comment on whether the discussion of inorganic metals**
8 **assessment principles is clearly articulated, objective, as defined above, and has**
9 **utility.**

10
11 *Articulation of the Inorganic Metals Assessment Principles*

12
13 Section 2 of the Framework is entitled Problem Formulation and Principles. This suggests
14 that Section 2 will provide a concise overview of the Framework. The SAB finds that some
15 changes are needed to make this view of the Framework consistent with recommendations in
16 Section 3 and the detail in both Section 4 and EPA's *Papers Addressing Scientific Issues in the*
17 *Risk Assessment of Metals* (Issue Papers) (EPA, 2004). A primary issue that arises in
18 concerning the utility of the material in Section 2 is how applicable it is at local, regional, and
19 national scale risk assessments. It is the judgment of the SAB that most of the detailed material
20 in Section 2, and indeed throughout the Framework is relevant to site-specific risk assessment.
21 However, the general descriptions of the "principles" are relevant to larger-scale risk
22 assessments as well as site-specific assessments.

23
24 The topics listed in Section 2 of the Framework are not principles, but rather are factors to be
25 considered. For example, bioaccumulation is a process; the relevant principle is fugacity. The
26 SAB recommends that the terminology in the Framework be changed. It is recommended that
27 EPA drop use of the word "principles" and instead use "factors to be considered" or "factors".
28 The SAB supports the inclusion of the "key questions" listed under several, but not all, of the
29 factors in the Framework. It is recommended that "key questions" be listed in the front of the
30 subsections for all factors included. This will result in parallel construction and to help justify
31 the selection of metal-unique topics to focus on in Section 3. The key questions should identify
32 why factors are important and uniquely needed for metal risk assessment.

33
34 The SAB finds a lack of uniformity in the quality and/or clarity of writing among the
35 subsections in Section 2 of the Framework. It is noted that the well-written report of the SAB's
36 2002 Metals Assessment Plan (MAP) review (EPA Science Advisory Board, 2002) addressed
37 many of the same issues. It is therefore recommended that SAB MAP report be revisited prior to
38 revision of Section 2 in order to improve the quality and clarity of the writing in some
39 subsections. Some of the material in the SAB MAP report may be used in Section 2.

40
41 The SAB finds that Section 2 of the Framework also has an imbalance of coverage among the
42 factors considered. For example, the subsections on environmental chemistry and toxicity
43 testing are very brief. It is recommended that the extent of the discussion in the subsections be
44 reviewed and made more uniform. Suggestions for specific revisions in this regard are provided
45 below (see especially the recommendations for subsections 2.1.4, 2.1.5, and 2.1.6).

1
2 In the context of risk assessment, the factors included in the Framework comprise a fairly
3 complete list, but some important factors are omitted and should be added to the text. These are:
4 the nature and type of source, and the route of exposure. These factors should be added to the
5 list in the Framework and text should be developed to a level of detail that is consistent with the
6 other factors presented. While the two factors above are relevant for all contaminants, there are
7 unique aspects of metals sources and routes of exposure that a risk assessor will have to address.
8 Two important processes that should be discussed under route of exposure are trophic (dietary
9 and/or food web) transfer, and atmospheric transport to receptors. In the explanation of trophic
10 transfer, it should be noted that the concentration in the water is not predictive of the
11 concentrations at the highest trophic levels. With regard to atmospheric transport, it should be
12 noted that most metals occur almost exclusively as particles in the atmosphere, and this affects
13 how exposure occurs and the types of effects exerted on receptors.
14

15 *Objectivity and Utility of Inorganic Metals Assessment Principles*

16

17 Section 2 of EPA’s Framework provides an overview of the risk assessment framework for
18 metals, including the conceptual model representing the various components of the process and
19 their interlinkages. The SAB finds Section 2 to be of high utility for understanding the context
20 of the recommendations in Section 3 and the importance of the detailed process component
21 descriptions in Section 4. However, the SAB provides the following recommendations to
22 improve the utility, objectivity, and clarity of the document.
23

- 24 • The introductory paragraphs of Section 2 on page 2-1 emphasize the need for risk
25 assessments at scales ranging from site specific to national. It would be useful to note
26 the risk assessment factors that are unique to metals. It would be helpful to clearly
27 discuss how the complex properties and reactivity of metals present unique challenges in
28 risk assessment.
29
- 30 • The terms used to describe the various factors introduced in Section 2 also need to be
31 carefully defined. For example, the term “essentiality” is vaguely defined in
32 comparison to the level of detail in text boxes defining “background” and
33 “bioavailability”. A more precise definition of essentiality that should be included in the
34 document is “a metal that participates in and is required for some basic biological
35 process with positive consequences for the organism.” Similarly, “bioaccumulation and
36 bioconcentration” could be defined in a text box that incorporates the definitions of
37 bioconcentrate, bioaccumulate and biomagnify that are presently in the text. A
38 definition of trophic transfer should also be included in this text box. The SAB also
39 notes that the definition of bioavailability given on page 2-6 and in the glossary suggests
40 the units of a rate constant in an uptake equation. This does not fit the intended
41 definition of the term.
42
- 43 • The discussion of “background” in subsection 2.1.1 includes references to both naturally
44 occurring and anthropogenically-introduced metals. To some reviewers, the subsection
45 seemed to imply that risk assessments should focus on metals present above natural
46 system concentrations. The SAB therefore recommends that in this subsection EPA

1 place greater emphasis on the potential for naturally occurring metals to pose as much or
2 more risk than anthropogenic metals. The SAB notes that arsenic, for example, is
3 naturally occurring but still needs to be regulated. It should be more clearly emphasized
4 in the Framework that background concentrations are not necessarily acceptable
5 concentrations. The SAB also notes that consideration of background is substantially
6 different for risk assessments conducted at local, regional, and national scales.
7

- 8 • The SAB notes that involvement of metals in biogeochemical cycles should be
9 emphasized in the Framework document in the discussion under the factor
10 “environmental chemistry.” At the ecosystem scale, metal biogeochemical cycling
11 considerations are different for metals than for organic compounds. Since metals do not
12 biodegrade, they are recycled in the environment. Metal cycles are often coupled with
13 nutrient cycles. This has important implications for risk assessment since metal
14 contaminants may not pose a risk in the current environmental scenario under
15 consideration, but they may pose a future risk if their chemistry (e.g., oxidation-
16 reduction conditions) changes. In this context, there may not be any single value of
17 “bioavailable fraction” (page 2-2, lines 3-4) of a metal that applies to its fate once
18 discharged to the environment. In the environmental chemistry section, metal fate,
19 transport, and bioavailability should be discussed in the context of biogeochemical
20 cycles.
21
- 22 • The environmental chemistry section of the Framework document currently focuses on
23 speciation. The SAB believes that additional issues should be included in this section of
24 the document. Other issues that involve unique considerations for metals include
25 processes affecting metals in sediments, and reactions that incorporate metals in organic
26 compounds, thus rendering their behavior more like organic than inorganic compounds.
27
- 28 • The “bioavailability” subsection of the Framework (2.1.4) is much longer and more
29 detailed than the other sections. To improve the utility of this part of the Framework, the
30 SAB recommends the following revisions. The conceptual
31 bioaccessibility/bioavailability model shown in Figure 2-2 should be moved to Section 4,
32 as should the “bioaccessibility”, and “bioavailability” sections. The first italicized
33 sentence in section 2.1.5 “Bioaccumulation and Bioconcentration” defines the
34 bioaccumulation issue, but the rest of the section is a scattered set of observations that do
35 not help define what is unique to metals about bioaccumulation, what is of concern with
36 how the issue is used (the specific construct), or how it might be used in risk
37 assessments. The discussion should be revised to address these questions.
38
- 39 • Subsection 2.1.6, “Acclimation, Adaptation, and Tolerance”, is an important component
40 that should be linked to the discussion of essentiality in subsection 2.1.2. Also,
41 subsection 2.1.6 should include the potential costs (e.g., genetic erosion) of the
42 acclimation, adaptation, and tolerance phenomena when or where they occur (some
43 discussion should be brought forward from Section 4), as well as their influence on
44 toxicity testing.
45
- 46 • Section 2.1.7 discusses toxicity testing and implies that toxicity is the metal impact of

1 primary concern. However, the SAB notes that metal effects on the environment can be
2 much broader than effects measured in a toxicity test endpoint (e.g., long-term impacts
3 on ecosystem structure). The SAB therefore recommends that the factor be re-named
4 and discussed as “toxicity”. The terrestrial part of Section 3 (Sections 3.3.3.4 and
5 3.3.3.5) extends “toxicity testing” to include “extrapolation to effects” (in nature). The
6 SAB recommends that the problem definition of “Toxicity” in Section 2 be clarified in a
7 similar way. It is important to take into account limits and linkages between toxicity
8 testing and adverse effects. Both Section 4 and EPA’s Metals Issue Papers include
9 useful discussions of effects of metals on populations and communities of organisms.

- 10
- 11 • The mixtures discussion in the Framework document focuses on metal mixtures. The
12 SAB notes however, that the document should also contain a discussion of mixtures of
13 metals and organic contaminants. Mixtures of metals and certain organic compounds
14 can behave additively, synergistically and/or antagonistically with respect to cancer risk,
15 depending on the mixture and the context. There is ample evidence of this from
16 laboratory experiments with simple mixtures (e.g., arsenic and PAHs) showing a variety
17 of complex effects not well predicted by knowledge of either agent alone. In addition, it
18 would be useful to include a discussion indicating that metals can react with organics to
19 form organometallic compounds, thus transforming a metal to a state in which its fate
20 and risk will be governed by processes more relevant to organic compounds (e.g.,
21 biodegradation, partitioning to dissolved organic carbon [DOC]).
- 22

23 **6.2.2 Charge question 2.2. Please comment on how well the conceptual model presents** 24 **key metal processes and whether or not it is complete.**

25 *Completeness of Conceptual Model*

26

27

28 The SAB finds that the conceptual model as depicted in Figure 2-3 of the Framework is fairly
29 complete. It is closely related to a conventional multimedia exposure model. A key difference
30 between metals and most organic compounds with respect to fate and transport is the
31 biogeochemical cycling of metals. The role of biogeochemical cycling for metals may not be
32 adequately represented in Figure 2-3, though it may be considered under the “Environmental
33 Chemistry” (M1) part of the diagram. At a minimum, the text related to Figure 2-3 should
34 mention the role of biogeochemical cycling. As currently presented, the conceptual model lacks
35 the feedbacks involved in biogeochemical cycling.

36

37 *Linkage of Conceptual Model to Text in the Framework*

38

39 The SAB notes that Figure 2-3 of the Framework is a compact summary of the conceptual
40 model upon which the risk assessment framework is based. The text in the various parts of
41 Section 2 should therefore be related to Figure 2-3. This can be accomplished with some modest
42 revision of the existing text. More detail will be needed in some parts in order to explain the
43 relevance of some of the components of Figure 2-3 not currently addressed in the text (e.g.,
44 transport models). In revising the parts of Section 2 to explain linkage with the relevant
45 components of Figure 2-3, links to related parts of Sections 3 and 4 should be included where
46 appropriate.

1
2 The SAB believes that the linkage of Figure 2-3 to the text could be enhanced by modifying
3 the footnote box “Key Metal Issues” in Figure 2-3 to include references to specific subsections in
4 the text. The footnote box should be reconsidered to determine how well it clarifies the figure
5 and relates the figure’s components to the text. The SAB suggests that the footnotes to Figure 2-
6 3 might be improved by listing just the key factors that impact the conceptual model components
7 shown. The SAB offers the following specific comments on Figure 2-3.

- 8
- 9 • In the footnotes to Figure 2-3 it would be better if the words were not abbreviated in the
10 description of M1 through M9 in the figure legend.
 - 11 • The footnote referring to M1 of Figure 2-3 should include organic carbon cycling.
 - 12 • The meaning of “concentration dependency” in the footnote referring to M2 of Figure 2-3
13 is unclear.
 - 14 • In the blocks on Figure 2-3, the word “chemical” should be changed to “metal”.
- 15

16 The SAB finds that Figure 2-2 of the Framework is also an important organizing graphic, but it
17 focuses on detailed processes that are not discussed in detail in Section 2 of the document. As
18 Section 2 is an overview of basic factors to be considered in metals risk assessment, Figure 2-2 is
19 too detailed to be included in this section. Figure 2-3 provides the high level of aggregation
20 appropriate for Section 2. Figure 2-2 is well structured and informative, but should be moved to
21 Section 4 where it can be introduced and explained in detail, and linked to the topics discussed in
22 that part of the Framework document.

23
24 *Classes of Metals Considered in the Conceptual Model (Table 2-1)*

25
26 The conceptual model represented in Figure 2-3 was developed to describe the assessment of
27 classes of metals identified in Table 2-1 in Section 2 in the Framework. The SAB offers the
28 following specific comments on the lists of metals in Table 2-1:

- 29
- 30 • Mg is an essential metal and should be added to Table 2-1.
 - 31 • Cr (III) is a nutritional supplement, not an essential metal.
 - 32 • Silicon is in Table 2-4 but not in Table 1-2 of Section 1. For consistency, these tables
33 should have the same elements.
 - 34 • It is unclear why the particular metals in Tables 1-2 and 2-1 were selected to be included
35 in the tables, and why others were omitted. Some comment should be included
36 concerning risk assessment for other metals such as tungsten, uranium, or tellurium that
37 may be important in local, regional, or national settings. This is discussed in lines 9 to 13
38 of page 1-3 in the Framework, but the relevance to all metals should be repeated in
39 introducing Table 2-1.
- 40

41 Additional comments on the list of metals included in Table 2-1, and the classifications
42 presented there, are provided in the response to Charge Question 3.9.

43
44 *Key Concepts to be Emphasized in the Conceptual Model*

45
46 The conceptual model in the Framework is closely related to conventional organic multimedia

1 models, both in the component models chosen and in the linear sequence in which they are
2 applied. Much of the Framework is devoted to distinguishing concepts used in metals risk
3 assessment from organic risk assessment. The following key concepts that are not indicated in
4 the conceptual model diagram should be emphasized either by modifying the diagram or by
5 adding accompanying text where Figure 2-3 is introduced:
6

- 7 • Precipitation/dissolution of mineral phases that contain a metal can lead to a decoupling
8 of the usual linear relationship between the total mass of a metal in an environmental
9 compartment and the free ion or other dissolved metal concentrations.
- 10
- 11 • Cyclical metal transformation processes, such as oxidation/reduction and
12 methylation/demethylation, are not readily handled by organic fate and transport models
13 since metal reactions do not result in a permanent transformation to another compound.
14
- 15 • Natural loadings of metals differ from anthropogenic loadings in that they may come
16 from inside the system of interest at rates controlled by natural processes.
17
- 18 • The fate and transport of both organic compounds and metals are coupled to the major
19 biogeochemical cycles, such as carbon and nutrients. In general, metals interact with the
20 cycles of more elements (especially sulfur and other metals) than organic compounds.
21 For organic compounds, the coupling to natural biogeochemical cycles is essentially
22 unidirectional (i.e., the major biogeochemical cycles affect the fate and transport of
23 organics, but not vice versa). For metals, exceptions to this rule are more common since
24 metals can be limiting nutrients or toxicants to organisms that drive the major
25 biogeochemical cycles such as higher plants, phytoplankton, or bacteria. This aspect of
26 metal biogeochemistry cannot be simply accounted for in a linear framework. In the
27 absence of a comprehensive model, a means of allowing metals model outputs to feed
28 back into values selected for model input parameters that govern the major cycles may
29 need to be devised.
30
- 31 • The “metalloregions” approach (briefly discussed on page 2-12 of the Framework) of
32 defining “metal-related ecoregions” for regional- or national-scale assessments is an
33 evolving approach that may have merit. Because no details on the approach are
34 presented in the Framework, however, it is difficult for the reader to evaluate the strength
35 of its potential value. The panel recommends that an expanded description of the
36 approach be provided, and that it be presented as just one example of how regional-scale
37 risk assessment might be approached. The challenges that result from uncertainty and
38 variability inherent in the approach should be addressed.
39

40 **6.3.1 Charge question 3.1. Please comment on how well the recommendations under**
41 **Section 3 are supported by the detailed information in Section 4. Are there**
42 **recommendations that should be included? Are there any inorganic metals or**
43 **metal compounds for which any of the recommendations would not apply?**

44 The SAB has reviewed the recommendations in Section 3 of the Framework document and
45 provides the following general and specific comments. The SAB recommends that EPA provide

1 “guidelines” for formulating the recommendations. To be most helpful, the recommendations
2 should be tiered, with the most critical recommendations (those with the greatest impact)
3 presented first, followed by specific recommendations that would be of value to the assessor.
4 This would help focus the different sections of the Framework to ensure that the most important
5 issues are addressed. Guidelines for formulating recommendations would also provide a
6 platform for subsequent documents so the assessor can prioritize how a risk assessment site is
7 addressed. The SAB notes that recommendations pertaining to various topics in the Framework
8 are distributed throughout Section 3 of the document. For example, recommendations pertaining
9 to environmental chemistry are included in Sections 3.2.1 and 3.3.1 that present
10 recommendations on environmental fate and transport.

11
12 *General Comments on the Recommendations in the Framework*

13
14 The SAB provides the following general comments on the recommendations in the
15 Framework.

- 16
17 • To ensure that the document is not prescriptive, as stated in the document purpose in
18 Section 1, the SAB recommends that prescriptive recommendations throughout the
19 document be generalized. For example, instead of recommending a particular model or
20 approach (such as recommendation 3 on page 3-24), the models should be described as
21 alternatives amongst several approaches.
22
- 23 • Section 3 of the Framework should be reorganized to make it comparable to other
24 sections. For example, the headings for aquatic risk assessment should be more similar to
25 those for terrestrial risk assessment. There is a lack of parallelism between the aquatic
26 and terrestrial recommendations and balance needs to be achieved. The terrestrial
27 recommendations, in general, include a broader range of approaches and include specific
28 guidance to the risk assessor regarding the current state-of-the science (i.e., tools for
29 today) as well as the direction of future tools and approaches. A similar level of
30 recommendations and guidance needs to be reflected in the aquatic discussion.
31
- 32 • Recommendations should be highlighted by minimizing textual justification and cross
33 referencing the justification directly to those parts of Section 4 that support or discuss the
34 recommendations. Additionally, any references to the scientific literature contained in
35 the recommendations should be removed. References should be provided in the sections
36 of the Framework that support the recommendations.
37
- 38 • As opposed to the broad environmental chemistry recommendations given in Section
39 3.2.1 of the Framework, the recommendations provided at the end of Section 3.3.1 (pages
40 3-23 and 3-24) are very specific. The SAB notes that it is unclear whether this level of
41 specificity is appropriate for a “Framework” document. A greater degree of consistency
42 is needed with respect to the specificity of the recommendations as a whole.
43
- 44 • In general, the recommendations in Section 3 with respect to environmental chemistry are
45 supported by the discussion in Section 4. However, it is difficult to determine which
46 parts of Section 4 correspond to particular recommendations in Section 3. In order to

1 better assess the support for the recommendations in Section 3, it would be helpful to
2 provide a “section identifier” indicating the source of the supporting information.
3 Similarly, this might serve as a better way to organize Section 4.
4

- 5 • The recommendations concerning environmental chemistry lack consistency with respect
6 to scope. Some recommendations are broad statements that may be of little practical use
7 to a risk assessor, while others are more specific statements. Instead of providing a non-
8 hierarchical list of recommendations, it would be helpful to organize recommendations
9 with respect to importance or specificity.
10
- 11 • The focus of many of the environmental chemistry recommendations is on modeling.
12 Little information is provided, however, on activities related to model validation or other
13 data collection efforts that may be important for a given location. For example, the
14 complex environmental conditions at a specific site may not be amenable to application
15 of available models and may require substantial site-specific data.
16
- 17 • While it may be logical to separate the discussion of soil and sediment for the purposes of
18 assessing exposure or toxicity, from an environmental chemistry perspective it would
19 make better sense to combine the discussion of the two media in one section. In this
20 format, geochemical origins and resulting similarities among soils, aquatic sediments,
21 and subsurface sediments can first be highlighted. Risk assessment approaches that have
22 evolved to depend upon different factors such as controlling solid phases, solution
23 composition, and redox conditions, can then be discussed.
24
- 25 • The SAB recommends that EPA reduce the number of specific recommendations in the
26 Framework by omitting statements and condensing similar or redundant
27 recommendations.
28

29 *Comments on Recommendations in Specific Sections of the Framework*

30

31 The SAB provides specific comments addressing the question of whether the
32 recommendations set forth in Section 3 of the Framework are directly supported by the more
33 detailed discussion in Section 4. The SAB also provides additional comments addressing the
34 question of whether the specific recommendations in the Framework are justified or germane to
35 an understanding of the risks of metals. SAB comments are provided on recommendations in the
36 following specific sections of the Framework.
37

38 Framework Section 3.1.1 - Fate and Transport.

39

- 40 • The fate and transport section (Section 3.1.1) of the human health risk assessment
41 recommendations provided in the Framework currently refers to the ecological and
42 environmental chemistry sections for recommendations in this area. The SAB finds that
43 this is appropriate.
44

45 Framework Section 3.1.2.1 - Background.

46

- 1 • Recommendation 1 (page 3-3, line 9) in Section 3.1.2.1 regarding background exposures
2 should be modified such that the word “ambient” replaces the word “background.” In
3 support of this word change, the following definition for the word “ambient” should be
4 added to the glossary section:

5
6 Ambient Levels: The amount of metals occurring in soil, water, sediment, or air that
7 represent the combined contributions from natural and various anthropogenic sources.
8 This ambient level may be highly region-specific but can be used as a baseline against
9 which elevated levels from other natural or anthropogenic sources can be compared.

- 10
11 • Recommendation 2 (page 3-3, line 15) in Section 3.1.2.1 should be expanded by the
12 addition of the following phrase: “It is also important to consider speciation of the metals
13 wherever and whenever possible.”
14
15 • An additional recommendation should be included in this section to state: “Ranges rather
16 than averages should be used in risk assessments, especially for site specific evaluations.”
17

18 Framework Section 3.1.2.2 - Air Pathways and Inhalation Exposure.

- 19
20 • Recommendation 1 in Section 3.1.2.2 (page 3-3, line 32) should be revised. Particulate
21 matter that is less than 2.5 micrometers in size (PM_{2.5}) and nanoparticles are now of
22 critical concern for the exposure and delivery of metals to humans and should be added
23 as separate entities at the end of this recommendation. Support for the recommendation
24 in Section 3.1.2.2 to focus inhalation exposure only on the small particles (PM₁₀) is given
25 in Atmospheric Behavior and Chemistry Section (4.1.7) where the long atmospheric
26 lifetime of small compared to large particles in the atmosphere is discussed. In general,
27 the section on atmospheric chemistry of metals is rather short and not comprehensive but
28 it does support the recommendation. EPA may want to consider addressing in this
29 recommendation other larger size classes that can be important for long range transport
30 and subsequent adverse effects. However, these considerations were not addressed in
31 Section 4. In order to do so, the discussion will have to be expanded.
32
33 • The SAB notes that a new recommendation should be added regarding the need to
34 consider other particle characteristics in addition to size, such as surface properties,
35 solubility, and particle chemistry. The characteristics of inhaled particles are critical
36 determinants how they react with biological membranes and can affect the efficacy of the
37 uptake of metals across those membranes.
38
39 • The SAB also notes that another recommendation should be added to include the need to
40 consider the biological effects associated with inhaled mixtures such as metals in
41 combination with other airborne pollutants including gases such as ozone (which can
42 alter the permeability of the cell membrane so as to increase metal uptake by the cells).
43 In addition, particulate matter (PM) itself is a unique mixture of metals, other inorganic
44 compounds such as sulfates, and organic compounds (e.g., PAHs) adsorbed onto solid
45 carbon cores, and should be addressed as such.
46

- 1 • The SAB finds that recommendation 2 (page 3-4, line 1) in Section 3.1.2.2 is appropriate
2 as written.
3

4 Framework Section 3.1.2.3 - Soil, Dust and Dietary Exposure Pathway.
5

- 6 • The SAB recommends deletion of the first recommendation in this section.
7
8 • Recommendation 2 (page 3-4, line 16) in Section 3.1.2.3 should be revised starting at line
9 20 (page 3-4) to read “consider dermal sensitization, contact dermatitis and other direct
10 skin effects. For example, nickel and chromium are both common allergens in sensitized
11 people (approximately 2-5% of the population for each metal), and arsenic can cause both
12 local irritation as well as increased risk of cancer at sites of repeated high dose
13 application. Although dermal exposure in general is of less concern for metals, the
14 potential skin effects of some metals should be considered by the risk assessor in the
15 overall health evaluation.”
16
17 • Recommendation 3 (page 3-4, line 23) in Section 3.1.2.3 is acceptable to the SAB.
18
19 • Recommendation 4 (page 3-4, line 27) in Section 3.1.2.3 should be modified by deleting
20 text starting on line 28 (page 3-4) at the semicolon to end of paragraph (line 31). The
21 SAB recommends this modification because, depending on the exposure situation,
22 specific metals/metal forms, and skin conditions, dermal effects can be an issue.
23 Assessors should be aware of potential uptake of metals in specific forms (e.g.,
24 nanoparticles), potential uptake of metals via unique exposure conditions (e.g., bathing,
25 showering, swimming), and the uptake of metals through damaged skin (e.g., irritated
26 skin, sunburn). Co-exposures of metals with other toxicants can also affect dermal
27 uptake. Dermal metal exposures can produce allergic dermatitis (e.g., chromium, nickel,
28 gold), irritation (e.g., arsenic, chromic acid), and skin cancer (e.g., arsenic) under certain
29 exposure conditions.
30

31 Framework Section 3.1.2.4 - Water Pathway and Oral Exposure.
32

- 33 • The SAB finds that recommendation 1 (page 3-5, line 12) in Section 3.1.2.4 is acceptable
34 in its current form.
35
36 • Recommendation 2 (page 3-5, line 17) in Section 3.1.2.4 should be amended to read:
37 “It is recommended that site-specific assessments use measured metal concentrations
38 within water distribution systems and at the tap.”
39
40 • Recommendation 3 (page 3-4, line 20) in Section 3.1.2.4 should be amended by changing
41 the word “negligible” to “less important”. The term “surface” should be deleted.
42

43 Framework Section 3.1.2.5 - Integrated Exposure Approaches.
44

- 45 • Recommendation 1 (page 3-5, line 35) in Section 3.1.2.5 should be amended to indicate
46 that the Integrated Exposure Uptake Biokinetic (IEUBK) Model should be “considered”

1 rather than “recommended” and should make use of all available site-specific data, in
2 particular factors that may influence oral uptake such as nutritional status of the affected
3 population.
4

- 5 • With regard to recommendation 1 in Section 3.1.2.5, the SAB finds that the IEUBK
6 Model is not applicable for all metals and, thus, similar models should be developed for
7 other toxic metals/metalloids of concern.
8

9 Framework Section 3.1.2.6 - Bioavailability.

- 10 • The SAB finds that recommendations 1 , 2, and 3 (page 3-6, lines 19, 23, and 28) in
11 Section 3.1.2.6 are acceptable in their current forms.
12
- 13 • The SAB finds recommendation 4 (page 3-6, line 32) in Section 3.1.2.6 to be acceptable
14 in its current form for lead, arsenic and potentially other metals.
15
- 16 • The SAB recommends deletion of recommendation 5 (page 3-6, line 35) in Section
17 3.1.2.6. The SAB notes that this is actually a research need and not a recommendation.
18
19

20 Framework Section 3.1.3.1 - Physiologically Based Pharmacokinetic (PBPK) and
21 Pharamcodynamic (PBPD) Modeling.
22

- 23 • Recommendation 1 (page 3-7, line 16) should be amended by replacing “bone” with
24 “storage compartments such as bone.” This change de-emphasizes bone and makes a
25 more general recommendation that encompasses other metals.
26
- 27 • Recommendation 2 (page 3-7, line 21) should be amended by deleting “and” on line 21
28 and adding “(4) bioavailability, and (5) routes of exposure.” at the end of the sentence
29 (line 22, page 3-7). This change is necessary because these other important factors also
30 need to be included. The SAB also recommends expansion of the discussion of PBPK
31 and PBPD modeling in Section 4.2.6 to include these parameters. References cited in
32 Section 4.2.6 are appropriate, but the specific information from these citations should be
33 summarized and included in the section; for example, from the O’Flaherty 1998 review
34 article on metals PBPK modeling (cited on page 4-68 of the Framework)
35
- 36 • Recommendations 3 (page 3-7, line 24) and 4 (page 3-7, line 30) in Section 3.1.3.1
37 should both be deleted and the following new Recommendation 3 should be added:
38 “Although there is a useful PBPK model for lead, similar models for other metals are
39 lacking and need to be developed and validated.”
40

41 Framework Section 3.1.3.2 – Essentiality.
42

43 The SAB accepts the recommendation in this Section, but feels that additional material is
44 needed in the introductory paragraph of the section. It should be stated in this Section
45 that, “for some metals, there may be an apparent discrepancy between the Recommended
46 Daily Allowance (RDA) and the calculated Reference Concentration (RfC) or Reference

1 Dose (RfD). The EPA should consider the RDA for essential metals when considering
2 the RfC/RfD. However, it should be noted that the RDA is typically satisfied by normal
3 dietary intake of food and water, and therefore the RfC/RfD value may still represent a
4 potential additional body burden of that metal from other dietary or extrinsic sources.”
5 Phrased another way, RfD/RfC values are presented as increments to RDAs. The SAB
6 also notes that there is a need for a definition of essentiality and in this definition there is
7 a need to demonstrate the role of the metal in an essential physiological or biochemical
8 process.

9
10 Framework Section 3.1.3.3 - Toxicity Testing.

11 The SAB recommends the following changes to this section (page 3-8):

- 12 • The first sentence in this section (lines 9-12) should be changed to “At least five metals
13 are accepted as human carcinogens – arsenic, beryllium, cadmium, chromium (VI) and
14 nickel.”
- 15 • Recommendation 1 in this section (line 22) should be amended by adding “with
16 particular attention to route of exposure, speciation and life stage.” to the end of the
17 sentence.
- 18 • Recommendation 2 (line 26) in this section should be amended by adding, “with
19 particular attention to route of exposure, speciation and life stage.” to the end of the
20 sentence.
- 21 • A new recommendation should be added to this section stating that, “Animal models for
22 metal toxicity need to be selected carefully with respect to species, diet, age, and sex.
23 Rats, for example, sequester metals in their red blood cells; laboratory diets frequently
24 fail to reflect human diets; early development and senescence are periods of enhanced
25 sensitivity to toxic challenges; and, sex differences in response to both deficiencies and
26 excesses are universally acknowledged.”
- 27 • The last paragraph (lines 28-31) of the section should be deleted. Neither statement in
28 this paragraph is true, nor does it add any value to the section.
29
30
31
32

33
34 Framework Section 3.1.3.4 - Metals Mixtures.

- 35 • The SAB recommends that the opening paragraph of this section mention the importance
36 of metals-organic mixtures. Also, the sentence in this section about selenium being
37 protective against mercury should be deleted. This is not a good example. In addition,
38 the SAB recommends the following changes to the recommendations in this section
39 (pages 3-8 to 3-9)
- 40 • Recommendation 1 (page 3-9, lines 9-11) in this section should be revised to include the
41 National Academy of Sciences/National Research Council (NAS/NRC) 1988 report on
42 the toxicity of mixtures as a reference (National Research Council, 1988). Replace
43
44
45
46

1 recommendation 1 with the following rephrasing:
2

3 “Metal mixtures interactions and toxicity need to be clearly demonstrated by the use of:
4 a) proper experimental design (National Research Council, 1988), b) appropriate plotting
5 of diagrams, and c) rigorous statistical evaluation to demonstrate synergism, additivity,
6 sub-additivity, potentiation and antagonism”
7

- 8 • The SAB finds Recommendation 2 (page 3-9, line 13) in this section to be acceptable.
9
- 10 • Recommendation 3 (page 3-9, line 13) in this section should be revised to include the
11 need for identifying synergy, additivity, potentiation or antagonism using appropriate
12 statistical analysis.
13
- 14 • Recommendation 4 (page 3-4, line 22) in this section should be revised to read as
15 follows: “There are established interactions that are based on molecular mimicry as a
16 mechanism of action for metals. Future research goals should determine how
17 considerations of metal mimicry may affect risk assessments and metal toxicity.”
18

19 Framework Section 3.1.3.5 - Sensitive Subpopulations and Life Stages.
20

- 21 • The SAB finds that the recommendation in this section should be revised to read as
22 follows: “Assessors should consider subpopulations with differing sensitivities that may
23 arise as a result of differential exposure (e.g., children ingest dirt) or susceptibility (e.g.,
24 elderly, immune compromised individuals, malnourishment, gender, ethnicity, genetic
25 polymorphisms, etc).”
26

27 Framework Section 3.2.1 - Fate and Transport
28

- 29 • The SAB notes that Recommendation 1 (page 3-11, line 7) in this section is a statement
30 and not a recommendation. Recommendation 1 as currently written should therefore be
31 inserted as part of the supporting text.
32
- 33 • Recommendation 2 (page 3-11, line 14) in this section is discussed in Section 4 of the
34 Framework (Section 4.1.6.3.1 and Section 4.4.1.1.1). However, the treatment of this
35 Recommendation in Section 4 does not provide enough detail to support the
36 recommendation. The SAB finds, however, that Recommendation 2 in Section 3.2.1 is
37 appropriate.
38
- 39 • Recommendation 3 (page 3-11, line 19). The details of Recommendation 3 (page 3-11,
40 line 19) in this section are discussed in Sections 4.4.1.2 and 4.4.1.1.1 of the Framework.
41 Recommendation 3 may be an important recommendation, but it is not clearly articulated
42 from the accompanying support material. In addition, the recommendation is very long
43 (almost longer than the supporting text). Recommendation 3 should be shortened and
44 supporting comments should be put back into the main text. The SAB also notes that a
45 linkage in these models with carbon cycling is potentially important in understanding the
46 cycling and ultimate effects of metals.

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- Recommendation 4 (page 3-11, line 34) in this section addresses the use of chemical equilibrium models such as MINTEQ. The utility of computer based chemical speciation models like MINTEQ for characterizing forms of metals is given in section (4.1.4.1.2 and 4.1.6.4.1). The SAB finds that adequate support is provided for this recommendation.
 - Recommendation 5 (page 3-11, line 38) in this section is discussed in Section 4 of the Framework, starting on page 4-99, and is consistent with EPA policy. The SAB notes, however, that Recommendation 5 is not written as a recommendation, but rather as a statement. Recommendation 5 should be shortened and re-stated in the form of a recommendation.
 - Support for Recommendation 6 (page 3-12, line 6) in Section 3.2.1 of the Framework is provided in the environmental chemistry section of the document, specifically in the discussion of the limitations of solution speciation computer based models (Section 4.1.6.4.2). This issue is also given some support in the discussion on the limitation of the equilibrium partition approach in the discussion of limitations (Section 4.4.1.1.2) of the aquatic transport models. This limitation is certainly one of the most important for modeling.
 - Recommendation 7 (page 3-12, line 12) of this section is supported, but not in the section of the Framework that is referenced. Rather, the limitation of the equilibrium partition coefficient and equilibrium approach is given in the discussion of limitations of the aquatic transport models. This discussion is provided in Section 4.4.1.1.2 but not in Section 4.1.4. However, the equilibrium assumption for modeling metal partitioning to and from aged soils is a limitation that is not mentioned in Recommendation 7. The SAB notes that metals are not likely to be in readily reversible associations with solid phases in aged soils. This point on aging is made in Section 4.1.6.3. Recommendation 7 should not stand alone as a recommendation, but rather be included in the supporting text. The SAB notes that Recommendation 6 in Section 3.2.1 can encompass the issue of partition coefficients. The SAB also notes that there should be less emphasis given to static “partition coefficients” and more emphasis on dynamic partitioning processes.
 - Support for Recommendation 8 (page 3-12, line 22) of this section is provided throughout the document in the discussion of the importance of oxidation state changes for certain metalloids, and in the environmental chemistry section (Section 4.1). For example, the environmental chemistry section on the importance of pH and redox conditions (Section 4.1.3.2), and the atmospheric behavior/chemistry section (Section 4.1.7) address Recommendation 8. However, the SAB feels that it may be inappropriate to change input parameters to overcome the shortcomings of the process modeled. As such, the SAB suggests removing this recommendation and the text on page 4-101 (lines 25-33) from which it was taken.

45 Framework Section 3.2.2 – Water Column Exposure, Bioavailability and Effects

46

- 1 • The SAB feels that the recommendations contained in this section were generally well-
2 stated and well-supported in Section 4.
3

4
5 Framework Section 3.2.3 - Background.
6

- 7 • The SAB finds that the recommendations in Section 3.2.3 (background) are generally
8 supported by the text in Sections 4.5.4.1-4.5.4.2 of the Framework, but statements in
9 Section 3.2.3 are not really "justified" by data (i.e., graphs showing variability). This
10 type of "support" is probably not absolutely necessary, but in a strict sense, the
11 Framework fails to justify the conclusion in Section 3.2.3 with data.
12
- 13 • The recommendation addressing the importance of considering background
14 concentrations in metals risk assessment is discussed in various places throughout the
15 document. It is identified as a key metal issue in the problem formulation and metals
16 principles section (Section 2) and given specific emphasis in the human exposure
17 pathway analysis section (Section 4.2.2.1). Background concentration effects are also
18 discussed in the section on characterization of ecological effects (Section 4.5.4). The
19 SAB notes that it would be useful in all the recommendation statements provided in the
20 Framework to indicate where the information is discussed in Section 4.
21
- 22 • Background metal concentrations issues are not discussed in the environmental chemistry
23 section (Section 4.1) of the Framework. The SAB notes that it would be useful to include
24 a section on the natural occurrence of metals in the environmental chemistry part of the
25 document. It would be useful for the environmental chemistry section to highlight those
26 metals and regions for which background concentrations would be important. The issue
27 of aging as discussed in Section 4.1.6.3 is suggestive of the relative importance of
28 background versus recent metal inputs into soils and sediments and its implied
29 significance to bioavailability and mobility. Similarly, a discussion of the effect of early
30 diagenetic reactions on the fate and effects of metals would be helpful.
31
- 32 • The SAB finds that the relationship between the recommendations in Section 3.2.4 on
33 bioaccumulation and the support in Section 4.5.8 is muddled by the lack of a clear
34 presentation and consistent use of definition of "bioaccumulation factor" and
35 "bioconcentration factor" (BAF/BCF). Once BAF/BCF are clearly defined and used
36 consistently, it will be possible to assess these sections critically.
37

38 Framework Section 3.2.4 – Bioaccumulation
39

40 The SAB finds that the recommendations in this section are unclear, contradictory,
41 inconsistent, and ill supported. As discussed in the responses to charge questions 3.11,
42 3.12, and 3.13 below, Section 4 of the Framework does not adequately reflect the
43 recommendations made. In general, the SAB feels the EPA needs to revise the
44 recommendations in this section to increase clarity and conciseness. For example, the
45 SAB recommends that EPA consider: 1) combining and reconciling Recommendations 1
46 and 3 (page 3-17, lines 16 and 27) in this section; 2) Combining and clarifying
47 Recommendations 4, 5, (page 3-17 lines 31 and) and 8 (page 3-18, line 12) in this

1 section; and 3) Combining Recommendations 6 and 7 (page 3-18, lines 1 and 5) in this
2 section. The issue of diet must be reflected as a route of exposure in the revision. The
3 SAB finds that Recommendation 9 (page 3-18, line 16) in this section can stand as
4 drafted.

5
6 Framework Section 3.2.5 – Trophic Transfer, Biomagnification, and Dietary Toxicity
7

- 8 • The SAB finds that Recommendation 1 (page 3-19, line 9) in this section of the
9 Framework needs to reflect the importance of trophic transfer. It is suggested that the
10 statement be revised by adding the phrase: “...classifying hazards or risks of inorganic
11 metal compounds, [whereas, trophic transfer should be considered.]”. Recommendation
12 2 (page 3-19, line 17) in this section needs to be revised to be more directed and concise.
13 As written, the recommendation is contained in the 1st sentence. The remainder of the
14 text is clarifying information and should be moved into the supporting text description.
15

16 Framework Section 3.2.6 – Sediment Exposure and Effects
17

- 18 • The SAB finds that all of the recommendations in this section of the Framework need to
19 be reconsidered in light of the discussion contained in the response to charge question
20 3.14 below.
21

22 Framework Section 3.2.7 – Metals Mixtures
23

- 24 • The SAB feels that the discussion in Chapter 4 needs to be further developed as it relates
25 to the recommendations in Section 3.2.7 of the Framework. EPA should consider the
26 addition of a recommendation to address the inclusion of empirical studies of metals
27 mixtures in the field. Field assessment should be included here – the field part is left out
28 and there should be a recommendation to assess toxicity in the empirical studies of metal
29 mixtures as they occur in the field. Finally, the SAB feels that the concept of
30 Quantitative Ion Activity Relationships (QICAR) is not well developed in Sections 3 or
31 4. EPA needs to justify that this is sufficiently well developed and validated to be
32 included in such a specific recommendation.
33

34 Framework Section 3.3.1.1 - Atmospheric Chemistry and Behavior.
35

- 36 • The SAB finds that Recommendation 1 (page 3-22, line 18) in this section is not a
37 recommendation. It should therefore be removed and included as commentary in the
38 paragraph description. The SAB also notes that the Community Multi-Scale Air Quality
39 (CMAC) Model is not mentioned by name in Section 4.1.7 as implied by the referencing
40 to Section 4.1.7.
41

42 Framework Section 3.3.1.2 – Soil Mobility.
43

- 44 • Recommendation 1 (page 3-23, line 6) in this section is simply a list of measurement
45 techniques and not necessarily a recommendation. Little supporting information is given
46 on the utility of each technique and how the information may be useful in a risk analysis

1 context. Some chemical techniques and speciation tools are covered in the referenced
2 environmental chemistry section (Section 4.1.8). However, if the point to be made in this
3 section of the Framework is that these tools should be used to help with site specific
4 assessment of metals, and for providing guidance on relative mobility, then this should be
5 stated in Recommendation 1. The SAB also notes that little information is provided in
6 the Framework about analytical chemical methods that are currently commonly used for
7 metal ion speciation.
8

- 9 • Recommendation 2 (page 3-23, line 15) in this section is not a recommendation but a
10 statement. Supporting information on the need to use computer models for predicting
11 speciation changes in soil solutions is provided in the environmental chemistry section
12 (Section 4.1.6.4.1.1.). The SAB suggests that an appropriate statement to be included in
13 Recommendation 2 would be that computer speciation models should be considered
14 when a more definitive analysis of the impact of metal ion speciation in metal risk
15 assessment is required for site specific level risk characterization, the model assumptions
16 are appropriate for the application, and sufficient site characterization data is available.
17
- 18 • The SAB finds that Recommendation 3 (page 3-23, line 20) in this section is well
19 supported in the Framework. However the recommendation is not stated in the form of a
20 recommendation. The SAB suggests that Recommendation 3 might be restated to
21 emphasize that K_d values can only be used when they are either calibrated for a specific
22 site, or have sufficient functionality built in to account for the variability of K_d with
23 important changes in solution conditions such as pH and soil composition effects.
24 Discussion of K_d is provided in the environmental chemistry section of the Framework
25 (Section 4.1.4.1.3) and the section of the Framework addressing the limitations of using
26 K_d (Section 4.1.4.1.4).
27
- 28 • The SAB finds that Recommendation 4 (page 3-23, line 26) in this section is not a
29 recommendation. Supporting information about the MINTEQ model is provided in the
30 environmental chemistry section on metal sorption modeling (Section 4.1.4.1.2). In
31 Sections 4.1.4.1.2 and 4.1.4.1.5 of the Framework it is indicated that the Diffuse Layer
32 Surface Complexation Model (DL Model) can be used to generate generic partition
33 coefficients, and that one can use the DL sorption model for screening level assessment
34 of metal ion mobility and in the site specific definitive assessment of sorption and
35 mobility. However, the SAB notes that as the recommendations are not meant to be
36 prescriptive, the Framework should mention other applicable models with the same
37 capabilities as MINTEQ, such as MINEQL+ and PHREEQC.
38
- 39 • Recommendation 5 (page 3-23, line 30) of this section is not a recommendation but
40 rather a statement. Support for this statement with respect to metal cations is provided in
41 the environmental chemistry section (Section 4.1.4.1.3.), but support for the statement is
42 not provided with respect to oxyanions. The applicability of a varying pH K_d value for
43 anion sorption should be added to the chemistry section, although the motivation for an
44 inverse dependency of anion sorption with increasing pH is given in Section 4.1.6.2.2.
45

- 1 • Recommendation 6 (page 3-23, line 38) in this section concerning estimation of metal
2 adsorption is not a recommendation but a statement. Support for this statement is
3 provided in the environmental chemistry section (Section 4.1.4.1.3.) but this support is
4 not backed up with reference to literature reporting on where this approach has been
5 previously used successfully. Recommendation 6 is a condensed version of two
6 statements that are given without supporting information in the environmental chemistry
7 section. For example, the Framework does not indicate in the section of the document
8 discussing models that it would be difficult in practice to estimate the amounts and
9 surface areas for composite soil and sediment materials. The SAB also notes that a
10 statement should be included in the Framework to indicate that, in addition to obtaining
11 relevant sorption parameters, quantifying the amount for the major sorbing fractions is
12 one of the major challenges for applying surface complexation sorption models. In
13 practice, this would probably be a fitting parameter in the way models might be applied
14 for screening or site specific assessments. It is not clear whether or not this should stand
15 alone as a recommendation, or be a part of the discussion in the supporting text.
16
- 17 • Recommendation 7 (page 3-24, line 2) in this section is not a recommendation but a
18 statement. Discussion of this statement is provided in the environmental chemistry
19 section (Section 4.1.4.1.5). In view of the discussion of the potential shortcomings of
20 using single or averaged literature K_d values or generic forms that depend on soil
21 properties, Recommendation 7 is amply supported by the information provided in the
22 environmental chemistry section. As stated previously, one must also account for
23 changing environmental conditions.
24
- 25 • Recommendation 7 (page 3-24, line 5) in this section is not a recommendation.
26 Discussion of the Generalized Two-Layer Model (GTLM) is provided in Section
27 4.1.4.1.2 of the Framework. However, support for the requirement of isotropic fluid flow
28 and fast, reversible, and linear sorption is not given in the environmental chemistry
29 section of the Framework. The inherent assumption of isotropic fluid flow, however, is
30 common to transport models. While the need for fast and reversible sorption is true,
31 linear sorption is not required per se. One of the attributes of the GTLM is that it can
32 account for the nonlinearities in sorption as a function of pH and changing amounts of
33 solid to liquid. Not much discussion was provided in the Framework on the conditions
34 under which the use of models is appropriate. Perhaps a more elaborate discussion of the
35 limitations (data or field conditions) should be added to the metal sorption section to
36 describe the types of scenarios where such models are appropriate. In general, the SAB
37 feels that the discussion in the Framework of sub-surface transport is limited.
38
- 39 • Recommendation 7 (page 3-24, line 10) in this section of the Framework addresses the
40 PHREEQC model. It is not clear why a separate recommendation is needed concerning
41 PHREEQC unless the point to be made is that three dimensional models are also now
42 available that couple metal ion surface complexation models with transport. The SAB
43 finds that Recommendation 7 is largely a repeat of the same sentence from Section
44 4.1.4.1.2 of the Framework that is given there without further discussion.
45

1 Framework Section 3.3.2.2 – Soil Invertebrates and Plants

- 2
- 3 • The SAB finds that the recommendations in this section of the Framework should be
- 4 revisited and revised in light of comments in the response to charge question 3.11 below.
- 5

6 Framework Section 3.3.2.1 – Soil Invertebrates

- 7
- 8 • The SAB finds that the recommendations in this section of the Framework are well-stated
- 9 and well-supported.
- 10

11 Framework Section 3.3.2.2.2 – Plants

- 12
- 13 • The SAB finds that the recommendations in this section of the Framework (as drafted)
- 14 need to be reduced in scope such that the actual recommendations are clearly stated and
- 15 the explanatory statements are moved to the supporting text. The text in
- 16 Recommendation 1 (page 3-28, line 33) in this section, reflecting the soil plant barrier
- 17 concept, needs to be shortened but expanded in supporting paragraphs. Recommendation
- 18 3 (page 3-29, line 12) in this section, discussing the issue of aerial deposition, needs to be
- 19 reconsidered and dropped or revised to reflect supporting information. The SAB finds
- 20 that this recommendation is not adequately supported by text. Recommendation 4 (page
- 21 3-29, line 16) in this section is a statement not a recommendation and should be moved to
- 22 the supporting text.
- 23

24 Framework Section 3.3.2.3 – Wildlife

- 25
- 26 • The SAB finds that the recommendations in this section of the Framework are well
- 27 defined and adequately supported. It is suggested that Recommendation 5 in this section
- 28 be revised as follows: “Although bioaccumulation and trophic transfer of metals does
- 29 occur [and should be considered], biomagnification (i.e., increases in concentration
- 30 through the food web) is a less important consideration and may be assumed to be
- 31 unimportant.” Recommendations 3, 4, and 5 in this section should be combined into a
- 32 single recommendation. Recommendation 5 in this section contains a reference to the
- 33 general scientific literature, the SAB feels that this should be relocated to another part of
- 34 the document.
- 35

36 Framework Section 3.3.2.4 – Food Chain Modeling

- 37
- 38 • The SAB finds that the recommendations in this section need to be revised to make them
- 39 more concise. Recommendation 2 (page 3-31, line 9) in this section of the Framework is
- 40 not a recommendation and should be moved to the supporting text. Recommendations 3,
- 41 4, and 5 (page 3-31, lines 11, 25, and 29) of this section should be consolidated into a
- 42 single recommendation.
- 43

44 Framework Section 3.3.2.5 – Bioaccumulation

- 45
- 46 • The SAB recommends that EPA reconsider and re-evaluate the recommendations in this

1 section in the light of previous comments, and make sure that parallels between soils and
2 sediments are developed.

3
4 Framework Section 3.3.3.1 – Adaptation and Acclimation

- 5
6 • The SAB finds that there is confusion about what is intended in the Framework by the
7 term “acclimation.” It is unclear whether EPA is the question of “true” metals
8 acclimation and the resulting increase in tolerance and/or resistance, or suggesting that
9 care should be taken in culturing organisms for testing to ensure that they are not “overly
10 sensitive” owing to the fact that they were raised in metals-deficient conditions.

11
12 Framework Section 3.3.3.2 – Essentiality

- 13
14 • The SAB finds that Recommendations 1 (page 3-35, line 23) and 5 (page 3-36, line 2) in
15 this section need to be removed and incorporated into the supporting text of the
16 document; they are not recommendations, rather, they are informational statements.

17
18 Framework Section 3.3.3.3 – Metals Mixtures

- 19
20 • In general, the SAB finds that the metals mixtures recommendations in this section of the
21 Framework are adequate. However, the SAB notes that there is a need to be mindful of
22 the importance of evaluations conducted in the “real world.”

23
24 Framework Section 3.3.3.4 – Toxicity Testing

- 25
26 • The SAB finds that the recommendations for toxicity testing and extrapolation of effects,
27 as developed for terrestrial ecosystems, need to be developed and included in the aquatic
28 section of the Framework. Toxicity testing has strengths and limits that are unique to
29 metals. For example, limits derive from: the use of surrogate species versus the diversity
30 of responses to metals, among metals and among species; and the lack of dietary
31 exposures in the toxicity testing data bases usually used by risk assessors. There are
32 unique effects of metals that are well known in some aquatic environments (e.g., stream
33 insect communities; selenium and mercury effects on upper trophic levels) and poorly
34 known in others. In light of these considerations, the finds that the recommendations in
35 this section are not well articulated with regard to evaluation of national and site specific
36 risk from metals. The recommendations contained in this section need to be concise and
37 explanatory text needs to be moved into the supporting body of text. The SAB finds that
38 the recommendations in the section were generally supported by the text in Section 4 of
39 the Framework.

40
41 Framework Section 3.3.3.5 – Extrapolation of Effects

- 42
43 • The SAB finds that actual recommendations need to be made and “statements” moved
44 into the text. For example, Recommendation in this section is a statement. The SAB
45 finds that the recommendations in this section are not well-supported by information in
46 Section 4 of the Framework.

1
2 *Specific Comments on Section 3 of the Framework*

3
4 The SAB provides the following specific comments on Section 3 of the Framework document.
5 The pertinent pages and line numbers in Section 3 of the Framework are referenced below.
6

- 7
- 8 • Many of the recommendations in Section 3 of the Framework are not sufficiently specific
9 to be useful. On page 3-11, for example, the following recommendation is made about
10 use of chemical equilibrium models: "Most of the available transport models do not
11 currently include chemical speciation subroutines. In such cases, chemical equilibrium
12 models such as MINTEQ serve as useful alternatives for characterizing the forms of
13 metal that are present." This statement is not incorrect, but it is not clear how chemical
14 equilibrium models can be used to consider speciation in transport assessments.
 - 15 • Page 3-10, lines 31-32: In light of discussions in Section 4 of the Framework and in the
16 issue paper on the environmental chemistry of metals, it would be more appropriate to
17 state that partitioning (and not partition coefficients) are important. This statement
18 should be followed by a discussion of how chemical speciation calculations are preferred
19 in determining metal partitioning, but in situations where sufficient data and modeling
20 tools are not available, partition coefficients should be assigned with great care to account
21 for the effects of pH, inorganic and organic ligand concentrations, competitive
22 interactions, and redox chemistry. Although the comments on partitioning and partition
23 coefficients may seem minor, it is important that the Agency begin to move away from
24 the paradigm of partition coefficients for metals and place greater emphasis on the more
25 appropriate concept of metal speciation.
26
 - 27 • Page 3-11, line 24: In complex models, organic carbon cycling should specifically be
28 included to account for temporal and spatial changes in particulate organic carbon (POC),
29 dissolved organic carbon (DOC), redox conditions, and for Hg assessments, sulfate
30 reduction rates. It is therefore recommended that EPA add organic carbon modeling to
31 line 24 (e.g., as "hydrodynamic, sediment transport, organic carbon cycling, and chemical
32 transport algorithms").
33
 - 34 • Page 3-12, line 12-20: The focus should be on metal partitioning (and not partition
35 coefficients). In addition to the recommendation for further consideration of equilibrium
36 assumption, it may be even more important to recommend an appropriate approach for
37 calculating metal partitioning from chemical speciation calculations, and when sufficient
38 data and modeling expertise is not available, to state what factors need to be considered
39 in assigning a partition coefficient.
40
 - 41 • Page 3-14, lines 36-37: Quantitative Ion Character Activity Relationships (QICARs)
42 appear to be an important tool for extrapolation metal availability and toxicity data.
43 However, the detailed discussion of QICARs on pages 4-153 and 4-154 is very brief.
44
 - 45 • Page 3-18, lines 1-3: Discussions in Section 4 of the Framework on biotic ligand models
46 focus on bioavailability and toxicity from metal binding at the gill. The SAB notes that

1 there are no discussions on how biotic ligand models have been used in estimating
2 bioaccumulation.

- 3
- 4 • Page 3-19, lines 9-15: In discussing the rarity of metal bioaccumulation, a qualifying
5 statement should be added for the methylmercury and organoselenium exceptions.
6
- 7 • Page 3-21, lines 22-23: It is not clear from discussions in Section 4 of the Framework that
8 the BLM has been applied to metal mixtures.
9
- 10 • The recommendations in Section 3 of the Framework are often given without the
11 precautionary statements that were part of discussions in Section 4 of the document. For
12 example, Section 4 indicates the limitations of several approaches when applied to clay-
13 rich sediments and soils.
14
- 15 • In general, all of the "recommendations" under soil mobility (Section 3.3.1.2) need to be
16 reworded and stated in the form of recommendations or it should be stated at the
17 beginning of Section 3 of the Framework that the lists are guidance statements or
18 recommendations rather than just recommendations.
19
- 20 • Although organo-metal transformation processes are discussed in the environmental
21 chemistry section of the Framework (Section 4.1.9), the recommendations at the end of
22 Section 3.3.1.3 (transformation in soils, page 3-25) are not taken directly from the
23 information provided. Any recommendation listed in Section 3, should follow naturally
24 from the information and context provided in Section 4. The summary paragraph in
25 Section 3 and the recommendations listed in Section 3.3.1.3 do not seem to be taken from
26 the Section 4 summary on organo-metal transformations.
27
- 28 • Page 3-10, lines 23-25: Regarding model complexity, the statement that more complex
29 models are not necessarily better gives no basis for decision. Calibration is arguably the
30 key issue in making this choice. Discussion of this point would be helpful.
31
- 32 • Page 3-11: The discussion of partitioning seems out of place given critique of partitioning
33 that is provided later in the Framework.
34
- 35 • Page 3-14: Hardness (competing cationic metals) is an independent factor from
36 speciation. The suggestion to only use it when speciation data are not available does not
37 make sense.
38
- 39 • Section 3.2.3: Default use of state averages for backgrounds would be erroneous if non-
40 point sources are significant in comparison to geological sources. The SAB notes that
41 this could be ascertained on a metal-by-metal basis prior to adopting state average as a
42 background.
43
- 44 • Section 3.2.4: The discussion in the Framework concerning the appropriate use of
45 BCF/BAF is confusing. Paragraphs at the bottom of page 3-16 and top of page 3-17
46 seem to offer conflicting statements concerning the use of BCF/BAF.

- Page 3-17, lines 8-9: The statement concerning whole body concentration and potential for toxicological impact is likely to be true, but the question of correlation between whole body concentrations and concentrations in specific organs/sites should be considered.
- Section 3.2.6: Recommendation of the use of the SEM-AVS approach without considering other approaches is neither balanced nor justified.
- Section 3.2.7: Concerning metals mixtures, a pre-defined set of interactions should be checked. EPA should start by looking at ratios of toxic to interacting essential metals.

6.3.2 Charge Question 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.

Human Exposure and Health Effects

The SAB finds that the information concerning human health effects in Section 4 of the Framework is not complete and has numerous errors. Much of the human health information in Section 4 was derived from the issue paper on human health effects of metals (EPA, 2004), which was not comprehensive and needs to be expanded to improve this key resource for the Framework document. The following are examples of key items that need to be addressed.

- The SAB notes the importance of considering nanoparticles and their associated metal content in assessing human exposure to metals. Dermal exposure is also of considerable importance with regard to nanoparticles.
- The SAB notes that PM₁₀ and PM_{2.5} need greater attention as mixtures with regard to human exposure and health effects.
- The SAB notes that the discussion of Hg speciation was not given sufficient attention especially with regard to the source of exposure. Additionally, Hg speciation *in vivo* is very complex and measurements of blood Hg levels do not distinguish between, for example, dental exposure to metallic Hg vapor and Methyl Hg from eating fish.
- There is reference in Section 4 of the Framework to the principle of metal accumulation in organisms that can be eaten by humans. The SAB notes that and this general principle applies to many metals, in particular Cd. However, with regard to Cr (VI), this general principal does not apply; and in fact, plants, fish, and game that consume and take up hexavalent Cr convert it to the less toxic trivalent form. Thus, humans can safely consume most plants and animals exposed to hexavalent Cr.
- The SAB notes the omission of any discussion in Section 4 of toxic effects of metals at low doses. This is a crucial issue because a number of metals exhibit a biphasic dose response curve with distinct adverse effects at low doses and a different type of toxic

1 response at higher concentrations. The SAB recommends the inclusion of a section in the
2 Framework that describes low dose toxic responses to metals and their compounds. For
3 example, it is now apparent that the slope describing Pb toxicity versus blood Pb
4 concentrations is greater at low exposure levels.

- 5
- 6 • The SAB suggests that Section 4 should include an analysis of the extent to which the use
7 of Benchmark Dose Modeling decreases uncertainty and improves the derivation of RfDs
8 for metals compared to the use of no observed adverse effects levels (NOAELs), and the
9 importance of updating current RfDs using the Benchmark dose modeling approach.
- 10
- 11 • The SAB notes the importance of including more summary tables in the Framework to
12 enhance the understanding of the complex information presented in section 4.
- 13 • The SAB notes an insufficient discussion of the interactions between metals and organic
14 chemicals as it applies to the problem of mixtures. There needs to be more discussion in
15 the Framework of how metals interact with organics and how this interaction can lead to
16 potentiation or antagonism. The SAB also notes the importance of applying proper
17 objective criteria to assessing these interactions, including correct statistical tests.

18 19 *Environmental Chemistry*

20
21 The SAB finds that, with respect to environmental chemistry, the coverage of available tools
22 for risk assessment and methods for metals analyses is fairly comprehensive, with an emphasis
23 on tools and methods unique to metals. Detailed descriptions of tools and methods are not given
24 in the Framework, but adequate references are cited. In many instances however, critical
25 evaluations of the tools and methods are not provided and the justification for many
26 recommendations is not clear. Two examples are given below:

- 27
- 28 • In recommending analytical techniques to characterize metal speciation (page 3-23, lines
29 6-13), no evaluations were presented in Section 4 to help distinguish between methods
30 commonly available through contract laboratories and those that presently are only
31 available through research universities and laboratories.
- 32
- 33 • In recommending computer modeling to predict metal speciation in soil solutions (page
34 3-23, lines 15-18), the computer programs Windermere Humus Aqueous Model
35 (WHAM) and Non-Ideal Competitive Absorption Model (NICA) are cited without any
36 discussion in Section 4 of the strengths, weaknesses, and limitations in the modeling
37 approaches.

38
39 The SAB therefore recommends that more emphasis be placed on developing comparative
40 assessments of available tools and methods, and on providing additional information to aid risk
41 assessors in deciding when particular tools and methods are and are not appropriate.

42
43 The SAB also recommends that the balance of coverage in Section 4 be reviewed. The
44 following issues are cited:

- 1 • Modeling tools, and to a lesser extent, analytical methods are included in the Framework.
2 Limited information however is provided on what should be considered in data collection
3 efforts (e.g., such as the type of data to be collected, appropriate temporal and spatial
4 time scales to be considered, and data quality requirements that are unique to metals
5 evaluations).
6
- 7 • EPA should provide a more balanced discussion of approaches for measuring solution
8 speciation versus techniques for assessing solid phase speciation. In Section 4, no
9 mention is made of current methods to assess free metal ion concentrations in the solution
10 phase for some metals directly (e.g., through specific ion electrodes, voltametry, or
11 standard EPA methods) or for measuring solution speciation for some metalloids.
12
- 13 • Although it could be argued that several of the modeling tools presented apply equally
14 well to marine and freshwater systems, specific issues for the marine environment (e.g.,
15 background concentrations and ion strength corrections) are barely addressed in
16 comparison to the specific issues for freshwater environments.
17

18 The SAB also recommends that Section 4 of the Framework contain additional consideration
19 of data requirements and model uncertainty. Issues that should be addressed include: criteria for
20 designing a sampling plan, data requirements for model calibration, suitable techniques for
21 estimating parameter values (and associated uncertainties) for simple and complex models, and
22 evaluation of model uncertainty in model simulation results that are specific to metals.
23

24 In addition, the SAB recommends that biogeochemical cycles be discussed in Section 4 of the
25 Framework. This includes the effects of organic carbon (and possibly iron, manganese, etc.) on
26 the fate of metals in the environment, and the effects of metals on organic carbon and other
27 ecological cycles through nutritional limitations or through toxic response.
28

29 The SAB notes that the following statements in Section 4 should be checked for accuracy and,
30 as warranted, corrected:
31

- 32 • Page 4.3, line 1: The order of the metal sulfides appears to be incorrect. Iron should be
33 moved between zinc and manganese. The solubility constants cited should be checked
34 against established compilations of thermodynamic data.
35
- 36 • Page 4-40: The equation showing dimethyl mercury photolysis should be checked.
37 Dimethyl mercury does not absorb sunlight directly and direct photolysis is unlikely.
38 Formation of two methyl radicals is also unlikely. Atmospheric oxidants, however,
39 would be expected to oxidize dimethyl mercury (as discussed in the last paragraph on the
40 page). Also, demethylation is unlikely to occur via sorption to particulate matter, as
41 suggested in line 31 of the same page.
42
- 43 • Page 4-42, lines 15-16: The statement that 15-30 percent of arsenic is volatilized is
44 almost certainly due to arsine (AsH₃), rather than methylation. Thus, the statement is out
45 of place in a methylation paragraph.
46

- 1 • Page 4-40: The atmospheric transformation section appears to be written in a manner
2 that is inconsistent with other sections in regard to paragraph length and formatting. The
3 sections are very short, relative to the previous or following sections.
4
- 5 • Page 4-39, line 7: The following text should be reworded “. . . formation of less
6 bioavailably charged metal-sulfur complexes”. The SAB questions whether the metal
7 sulfur complexes are actually charged?
8
- 9 • Page 4-39, line 11: Use of the word “unbioavailable” is a bit awkward.
10

11 *Ecological Exposure and Effects*

12

13 With respect to ecological exposure and effects, the SAB finds that Section 4 of the
14 Framework offers a great deal of supporting information for the recommendations that are
15 articulated in Section 3. However, the manner of treatment for the various parts of Section 4
16 relative to ecological metals risk assessment should be more parallel in format across the
17 pathways of exposure. This is particularly evident in the uneven treatment of topics such as
18 aquatic sediment and bulk sediment chemistry when in comparison to the treatment of soils. A
19 critical shortcoming of the treatment of ecological metals risk assessment is the lack of a
20 discussion of levels of uncertainty, both in the knowledge base as well as in metals risk
21 assessment implementation. A discussion of uncertainty should be more explicit and more
22 uniformly distributed throughout the presentation of the current state of knowledge. The
23 following specific shortcomings are noted.

24 The Biotic Ligand Model (BLM) approach is highlighted in Section 4 of the Framework but
25 the reader is never provided with a clear definition of the concept. The concept is treated as
26 though the reader is already familiar with this approach. The SAB feels that the BLM concept
27 should be clearly defined. Trophic transfer is discussed extensively in Section 4 of the
28 Framework but not with respect to the BLM.

29 There is very little attention given in Section 4 of the Framework to the importance of
30 parameter, model, and laboratory validation in the field. There is a great deal of emphasis in this
31 section on models as tools for metals risk assessment as appropriate, but the section lacks a
32 discussion of field validation needs and the consequences of this deficiency in the current state of
33 knowledge. There is little discussion of ecosystem assessment or habitat assessment, the
34 discussion focuses on biotic indicators only.

35 Section 4 of the Framework contains a good discussion of dietary exposure and trophic
36 transfer but the tools to deal with these processes are not comparably developed. For example,
37 tools such as dynamic modeling (i.e., biodynamic or biokinetic modeling) should be included in
38 the discussion.

39 The concept of soils and the terminology associated with soil substrates needs to be clearly
40 defined and improved to accommodate modern nomenclature in soil science for organic and
41 mineral soil horizons and soil types. Concepts used should accommodate soil substrates in

1 urban, wetland, forested, agronomic and disturbed ecosystem contexts consistent with U.S.
2 Department of Agriculture (USDA) Natural Resource Conservation Service (NRCS)
3 terminology. Several soil properties (e.g., pH, cation exchange capacity [CEC]) are often
4 discussed in this chapter because of their appropriate importance in metal risk assessment
5 activities. These properties can be highly operationally defined based on the methods chosen but
6 there is only a passing mention of the importance of methods. This subject should be explicitly
7 developed.

8 Section 4 of the Framework should also include a discussion of acclimation and adaptation.
9 This is discussed in more detail in the response to charge question 3.11. Species sensitivity
10 distributions (SSDs) are mentioned in Section 4 but not discussed and should be more fully
11 described in this section. There is limited discussion of vascular plant risk assessment for metals
12 and this could be developed further and parallel to other sections of the chapter.

13 **6.3.3 Charge Question 3.3. Please comment on the state of the science (i.e., data, tools
14 and methods) to address inorganic metals speciation in all environmental
15 compartments for any given inorganic metal from the point of environmental
16 release to the point of toxic activity as discussed in the document. Please comment
17 on whether the framework identifies appropriate research needs to overcome any
18 limitations in the state of the science. Please address these questions separately for
19 each of the three types of assessments presented (i.e., site-specific, national level, and
20 ranking and categorization.)**
21

22 The SAB notes that the major limitation in addressing inorganic metal speciation in risk
23 assessment is the lack of analytical tools for the direct measurement of metal species/fractions.
24 Although tools to directly measure metal species exist and are improving with time, they are
25 relatively rare in the metals risk assessment arena. The need to develop these tools, and the data
26 to support modeling of speciation, should be discussed in the Framework. The SAB feels that
27 the Framework should not recommend specific analytical tools, but it should discuss the
28 importance of determining speciation in environmental media and human biomonitoring
29 samples. The paucity of data to support modeling of speciation limits the risk assessor's ability
30 to adequately include speciation in metal risk assessment tasks at the site to national scales. The
31 SAB notes, however, that metal speciation determination is more applicable for site-specific
32 investigations than the setting of national standards.

33 The lack of analytical tools for direct measurement of metal species/fractions affects models
34 related to environmental transport and fate as well as exposure. Section 5 of the Framework lists
35 needs that would address this limitation but these needs are only listed in a bulleted form. In
36 comparison, the discussion of the Unit World Model which may address other risk assessment
37 needs is more extensive. All research needs, however, should be addressed at a similar level of
38 detail if this section is to have relevance. As it stands now, this section is just a collection of
39 limitations with no systematic or comprehensive development of them. It would be preferable to
40 include these limitations within the discussions of Section 4 and omit Section 5 of the
41 Framework. The SAB provides the following specific comments in response to charge question
42 3.3.

- 43 • The SAB notes that it would be useful to collect the discussions of metal speciation in

1 one location in the document.
2

- 3 • The Framework should contain a discussion of how to bound uncertainty in site and
4 national efforts employing speciation.
5
- 6 • The SAB notes that a section needs to be added to the Framework on the importance of
7 speciation of metals in human toxicity, not only from the point of view of exposure, but
8 also the diversity of species that can be formed within the body, (i.e. Cr (VI) and Cr (III),
9 As methylation, elemental Hg and inorganic Hg, Cd metallothionein and other Cd
10 ligands, etc.). It is important to identify the chemically and toxicologically active species
11 of the metal as well.
12
- 13 • The SAB notes the importance of developing techniques to measure, in biological tissues,
14 different species of metals to which humans can become exposed as well as to understand
15 the species formed within the human body (e.g., methylated forms of As and Cr and
16 oxidation states).
17
- 18 • The SAB notes the importance of considering metal speciation for each individual metal
19 since this concept makes sense only when considering each individual metal.
20
- 21 • The SAB notes that numerous tools in the form of models and operationally defined
22 analytical methods to address inorganic metal speciation are listed and discussed in the
23 Framework. There are several well developed models for establishing the theoretical
24 distribution of metals among species for given conditions in solution, although only
25 specific ones are considered in much detail in the Framework. Similar models for
26 understanding speciation in other media such as soils and sediments are not as well
27 developed. However, as noted above, analytical tools to measure inorganic metal species
28 are not very advanced. Analytical tools that are discussed in the Framework (e.g.
29 simultaneously extracted metals [SEM], sequential extractions) are, in reality, methods
30 designed to fractionate an environmental matrix. With regard to application of these
31 tools to the three types of assessments discussed in the Framework, models using the
32 Hard and Soft Acids and Bases (HSAB) concept are probably most suitable for national
33 assessments. The other tools appear to be applicable across the assessment types.
34
- 35 • The SAB notes that all discussions in the document related to speciation should adhere to
36 the definition in the glossary. The use of consistent terminology when discussing forms
37 of metals in various environmental matrices is recommended. This is discussed more
38 fully in Appendix A of this report where a terminology proposed by an international
39 expert body is provided.
40
- 41 • The SAB finds that the discussion of inorganic metals speciation is well developed and
42 successful in describing the importance of inorganic metals speciation in determining
43 biological or ecological risk. However, the focus of the discussion is largely on the metal
44 cations of greatest commercial interest, which represent only about one third of the
45 metals of interest noted in the Framework scope (Section 1.2). This section should
46 discuss all of the metals of interest, particularly the anionic metals Se, Sb, As, and V

1 where speciation is critically important in mobility and toxicity. The discussion should
2 bring forward its treatment of metals that do not behave like the metal cations.

- 3 • The discussion of speciation should also include a biogeochemical context which
4 provides a more complete understanding of processes influencing metal exposure and
5 metal transformations. The discussion should point out where methods are available to
6 directly measure metal species of interest and where modeling is the most suitable
7 approach.
- 8 • The framework is selective in its treatment of speciation and transformations in the water
9 column and in sediment, and would benefit from a more parallel organization of the
10 discussion.

11 **6.3.4 Charge Question 3.4. In an earlier draft of the framework, EPA had included three**
12 **Summary Recommendation Tables in Section 3 on human health, aquatic, and**
13 **terrestrial risk assessment, covering the three general assessment categories (i.e.,**
14 **site-specific, national level, and ranking and categorization). An example of this**
15 **table is included as Appendix A in the draft provided to the SAB. To minimize**
16 **confusion for users of the framework, the initial idea behind the recommendations**
17 **and adjoining table was to have concise recommendations on the science, followed**
18 **by a separate accounting of how these recommendations could then be applied to**
19 **the different assessment categories. Reviews have been mixed on the utility of these**
20 **tables as a sufficient communication tool. Please comment on whether tables of this**
21 **type are useful for the final version of the framework. Does the panel have**
22 **alternative suggestions for effectively communicating how the recommendations can**
23 **be considered for each of the three assessment levels?**

24
25 The SAB believes that tables such as the example presented in Table A-1 of the Framework
26 are a good way to summarize important points and capture the structural character of the
27 document. Tables have an advantage as a way of presenting a summary, arranging complicated
28 material to allow it to be viewed from different perspectives, and facilitating organizing and
29 cross referencing of materials. However creation of a summary table for a complex document
30 such as the Framework is not straightforward. Issues that arise include: the difficulty of
31 representing complex concepts in short statements in the table; the temptation to accept the
32 abbreviated representation of the material in the table and ignore the full complexity of the
33 matter; and the fact that as the length and completeness of the table increases, it expands across
34 multiple pages and loses the advantage of a compact representation of the material.

35
36 The SAB recommends that the tables in the Framework be formatted differently and moved
37 up to a lead position near the beginning of Section 3. The tables should be structured to capture
38 the recommendations presented in Section 3 in an organized manner that relates them to their
39 utility for the categories of risk assessment discussed in this document (i.e. national ranking and
40 categorization, national level assessments, and site specific assessments), with recognition that
41 within these three categories there are both screening and definitive risk assessments. In this
42 regard the tables should include key but limited information on currently available tools as well
43 as future directions not yet readily available for operational risk assessment activities. The tables
44 should provide, at a glance, an outline of the framework, key elements of the framework

1 recommendations, and available approaches (now and in the near future) to accomplish these
2 metals risk assessment goals. Use of the term “tools” as presented in the Table A-1 needs to be
3 reassessed, because “fate and transport” and “bioaccumulation” are not specific tools, but are
4 aspects of risk assessment that require application of specific tools (e.g., extraction techniques
5 for estimating bioavailability).
6

7 The SAB recommends that the tables not include references to the scientific literature but
8 rather references to the specific parts of Section 4 of the Framework to explain the information
9 and recommendations in the table. Table footnotes could be added to reference the relevant
10 sections of the text and provide justification for each recommendation listed and summarized in
11 the table. In this way, the tables become an operational, rapid index to the document. Such
12 tables, if created for each of three broad subject areas covered in the Framework (i.e., ecological
13 exposure and effects; human exposure and health effects, and environmental chemistry), would
14 help ensure consistency between the three areas. These tables could be placed at the end of
15 each relevant part of Section 3. The SAB notes that an alternative to using summary tables as a
16 way of complementing the text would be to include a series of examples.
17

18 Section 4 of the Framework should be a thorough discussion of the background science that
19 supports the rationale for the framework structure and recommendations, a practical overview of
20 current practice and the technical and political context of those activities, and opportunities for
21 improved approaches in metals risk assessment now and in the future. Section 4 should embody
22 a state of science analysis that leads to sound assessment practices, and thereby highlights some
23 of the logical research needs in the metals risk assessment arena. Section 3 of the Framework
24 should ideally include much less text, focusing on providing the broader intent and context for
25 the table.
26

27 Table 1 below illustrates a possible approach to capturing the elements of the Framework into
28 a table, and providing a gateway to the information contained in Section 4 of the document. The
29 SAB notes that there are other approaches. It is suggested that the challenges in developing
30 tables will be identifying brief descriptors of key elements of the Framework recommendations,
31 providing appropriate references to the sections of the document that fully discuss these
32 sometimes complex issues, and ranking otherwise complex and subjective aspects of information
33 related to each recommendation such as uncertainty. The SAB suggests that the overriding
34 benefit of developing tables will be providing a visual summary of the essence of the Framework
35 that offers information of value to metal risk assessors and directions to relevant information in
36 the document. Table 1 below is a skeletal representation of a possible table structure, with an
37 ecological exposure and effects example filled in for the purpose of illustration.
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Table 1.

DRAFT RECOMMENDATIONS TABLE - FRAMEWORK FOR METALS ASSESSMENT										
No.	Recommendation	National Screening	National Ranking	National Complex	Site Scale Screening	Site Scale Complex	Tools Current	Tools Future	Uncertainty	Data
HUMAN										
1										
Ref										
2										
Ref										
AQUATIC										
3	BLM for use in assessing bioavailability.	0	0	0	1	1	1		1	1
Ref	4.3.2		4.4.1.1	4.8.1	x.x.x.x	x.x.x	x.x.x.x.x	x.x.x.x	x.x	x.l.x.x
4										
Ref										
5										
Ref										
TERRESTRIAL										
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Notes on Table 1:

- Each recommendation in the table would occupy a block, but not all cells would be filled in. In most cases Current and Future tools available would not be filled in, particularly when the recommendations deal specifically with a tool. Where specific tasks are recommended, it is possible current and future tools would exist.
- Most cells would be filled by a numeric system where 0 = not good or not applicable, 1 = somewhat available/applicable or other qualifier, and 2 = excellent option or application. No verbiage is included in the BLM example although it is possible that a few words might accompany the numbers in the boxes.
- With each recommendation there is a row (blue in Table 1) that includes references to the parts of Section 4 of the Framework. Only single sections are listed although multiple pointers could be included in any box, and should represent the roadmap to the relevant discussions.
- Uncertainty is an important column even though it is highly subjective. Including this column elevates the need to consider the uncertainty in the approach or tools being used by the risk assessor, and offers a judgment of how much uncertainty is associated with that approach or factor or tool in risk assessment could be due to natural factors, characteristics of the methodology, or other factors.

- 1
2 - Data represents a range of possible issues associated with data in risk assessment, most often related to
3 either the availability of the necessary data of the target metal for different types of national or regional risk
4 assessments, or the availability of ancillary data at any scale that is necessary to appropriately determine
5 risk.
6

7 **6.3.5 Charge Question 3.5. Please comment on the objectivity of the Hard Soft Acid Base**
8 **concept to applications of stability of metal complexes in toxicity assessments. See**
9 **Section 4.1.2. (Emphasis added by SAB.)**
10

11 Although charge question 3.5 specifically seeks comments on the objectivity of the Hard Soft
12 Acid Base (HSAB) concept to applications of stability of metal complexes in toxicity
13 assessments, the SAB finds that the question could also apply more generally to risk assessment.
14 The SAB has commented on the objectivity of HSAB regarding both toxicity assessments and
15 the broader issue of risk assessment.
16

17 The SAB concludes that the application of the Hard Soft Acid Base (HSAB) concept to the
18 stability of metal complexes in the general context of *risk assessment* is generally presented in an
19 unbiased manner, with perhaps one possible exception. General statements that hard acids are
20 more toxic than soft acids should be worded more carefully to ensure that the statements are not
21 interpreted in a broader context than warranted by the available data.
22

23 The application of the HSAB concept specifically to *toxicity assessment* is a more complex
24 issue. Whereas the HSAB concept is generally useful for assessing the strength of binding of a
25 metal to a receptor (if the chemical structure of the receptor is known), the extent of the toxic
26 response once the metal is bound is not really addressed by the HSAB concept. Clarification of
27 this distinction would improve the objectivity of this section of the Framework.
28

29 The clarity and completeness of the presentation could be improved by expanding the
30 introduction with the following context for the application of the HSAB concept. The HSAB
31 concept is a valuable way to summarize a considerable amount of qualitative chemical
32 information and to allow the user to develop an intuitive feel for which complexes are likely to
33 be more and less stable. The concept is well established in mainstream chemistry. However, the
34 user should be aware that, while HSAB is useful for qualitative assessments of complex stability,
35 quantitative calculations still depend on thermodynamic data such as stability constants and
36 solubility products. These thermodynamic data are the basis of the models of metal speciation.
37 The SAB also notes that additional citations to applications of the HSAB concept in
38 environmental science would be useful (e.g., Sposito, 1989). In addition, the SAB recommends
39 that, to ensure the accuracy of the presentation, the solubility constants in the Framework should
40 be checked against established compilations of data.
41

42 The following specific revisions are also recommended but the SAB to improve the clarity of
43 Section 4.2.1.
44

- 45 • Page 4-2, lines 8-10: The introductory paragraph contains broad generalities that are not
46 all strictly accurate; it should be completely rewritten. EPA should define “acids” and
47 “bases” and then state which metal species are usually acids and which ligand atoms are

1 usually bases.
2

- 3 • Page 4-2, lines 12-13 and 15: Revise the document to qualify and/or provide references
4 for the statement about “toxic reaction” being directly related to the nature of the metal at
5 the surface of the organism, and the statement about toxicity. This is addressed in the
6 comment above on toxicity.
7
- 8 • Page 4-2, line 16: Change “introduced” to “described” because the concept was
9 introduced earlier by Pearson (1963) and others (Arhland et al., 1958; Schwarzenbach,
10 1956) in the 1950’s.
11
- 12 • Page 4-2, line 17: Delete “in this concept” because the statement is true in general.
13
- 14 • Page 4-2, line 21: Delete “mobile and easily moved” to avoid confusion with oxidation-
15 reduction reactions; deformable and polarizable are the appropriate terms.
16
- 17 • Page 4-2: If a box is necessary to define “ligand,” a box should also be used to define
18 “complex.”
19
- 20 • Page 4-3, line 1: Delete the clause “which are less toxic;” such statements about relative
21 toxicity are made better in the text, where appropriate justification and qualification can
22 be given, than in the title, where it appears without justification and qualification.
23
- 24 • Page 4-3, line 2: The U.S. spelling of sulfur should be used.
25
- 26 • Page 4-3, lines 2-3: The appropriate term to be used is “extent of binding,” not “strength
27 of binding” because the strength is intrinsic to the metal and ligand, and the pH effect is
28 more accurately described as a competition effect.
29
- 30 • Page 4-3, line 5: Change “many of the hard metals” to “some of the hard acids;” to
31 avoid confusion, use the terminology “hard and soft acid” consistently, don’t switch to
32 “hard and soft metals.”
33

34 **6.3.6 Charge Question 3.6. Please comment on the objectivity of the atmospheric metal**
35 **chemistry discussion and its application to exposure assessments. See Sections**
36 **3.3.1.1 and 4.1.7. (Emphasis added by SAB.)**
37

38 In responding to this charge question, the SAB notes that none of the Metals Risk
39 Assessment Framework Review Panel members has an active research program in atmospheric
40 chemistry. The SAB therefore recommends that an atmospheric chemist review these sections of
41 the Framework to ensure that there are no gaps in coverage, beyond those cited below.
42

43 The SAB cannot recognize much evidence of critical thought in the recommendation
44 provided in Section 3.3.1.1 of the Framework. There is no recommendation in Section 3.3.1.1
45 specifically addressing *exposure assessment*. The one bulleted recommendation in Section
46 3.3.1.1 addresses models for metal speciation in the atmosphere, and there is no text in Section

1 4.1.7 of the Framework to support that one recommendation. The rest of the text in Section
2 3.3.1.1 is a summary of some of the key points of Section 4.1.7, but it is not cast in the form of a
3 recommendation.

4
5 Section 4.1.7 of the Framework describes metals adsorbed to particles as the principle route
6 of *direct* exposure to metals in the atmosphere and cites the importance of particle size in
7 transport and exposure. The SAB concurs, within the limits of our knowledge of the subject, that
8 this assessment of *direct* exposure is generally accurate for most metals. However, the
9 discussion of atmospheric chemistry and its application to exposure assessment would be more
10 complete if the following issues were addressed.

- 11
12 • A statement should be included about the potential for longer-scale transport of metals
13 from a source through the atmosphere to soil, water, or air, from which exposure
14 ultimately occurs. Even if the process for metals follows principles already established
15 and described for organic compounds and EPA does not want to repeat that description in
16 the Framework, a statement about the similarities and differences between inorganic and
17 organic compounds would improve the completeness of the Framework. For example,
18 while many metals are transported in the atmosphere primarily only on the surfaces of
19 particles, many organic compounds are transported in the atmosphere primarily as a
20 component of the vapor phase.
- 21
22 • A statement about the potential importance of volatile inorganic species of metalloids
23 (e.g., $\text{H}_2\text{S}(\text{g})$, $\text{AsH}_3(\text{g})$) should be included in the discussion.
- 24
25 • A statement about the potential importance of atmospheric transport to “background”
26 concentrations of metals in the environment should be included either in the section of
27 the Framework discussing atmospheric chemistry or in the “background” section.

28
29 **6.3.7 Charge Question 3.7. Please comment on the objectivity of the metal chemistry and**
30 **environmental parameters incorporated in the various metal surface complexation**
31 **and partition coefficient models and their applications to exposure assessments. See**
32 **Sections 3.3.1.2 and 4.1.4.1.**

33
34 The SAB finds the Framework discussion of surface complexation models to be generally
35 accurate and unbiased, but notes the following areas where the presentation seems to lack
36 completeness.

- 37
38 • The limitations of the models, particularly the data needs for the surface complexation
39 models and the potential difficulty of obtaining the data, should be made more clearly
40 obvious. The SAB questions, for example, how realistic it is to propose routine
41 application of surface complexation models in risk assessment.
- 42
43 • A statement should be made in the Framework about balancing detail and uncertainty
44 over the entire assessment. The SAB questions, for example, whether it is appropriate to
45 combine a detailed, molecular-level model of one process with an empirical, “black-box”
46 model of another process, within the same risk assessment.

- 1
- 2 • A statement should be made about the applicability of the surface complexation and
- 3 partition coefficient models as a function of ionic strength, particularly with regard to
- 4 estuarine and marine environments.
- 5
- 6 • The sediment chemistry and soil chemistry sections should be coordinated to ensure that
- 7 similar recommendations are given for similar circumstances. Combination of the
- 8 environmental chemistry of soils and sediments into a single section should be seriously
- 9 considered (whereby it is recognized that ecotoxicity in the two environments should still
- 10 be treated separately.)
- 11
- 12 • A statement should be made to the effect that, if a K_d partitioning model is ultimately
- 13 used, one should still be aware of factors considered in more detailed models. It is
- 14 important to ensure that all relevant factors on which K_d depends (e.g., pH, etc.) have
- 15 been appropriately considered; information should be given on how to test applicability
- 16 of a K_d model. The usefulness of surface complexation modeling in evaluating the
- 17 potential variability of K_d for a specific situation should be noted.
- 18
- 19 • Emerging alternatives to the surface complexation models and K_d models should be
- 20 mentioned. Alternatives include distributed ligand models, which are similar to WHAM.

21

22 **6.3.8 Charge Question 3.8. Please comment on the objectivity of the discussion and**

23 **recommendations on natural background of metals. See Sections 3.1.2.1 and**

24 **4.2.2.1.1).**

25 The SAB strongly recommends that the EPA use the term “ambient” or “ambient levels” in the

26 Framework rather than “background,” both in the glossary and throughout the text and

27 recommendations. The following changes should be made in the glossary.

28 *Glossary recommendation:*

- 29 1. Delete the term – “Background”
- 30 2. Add – “Ambient Levels”: The amount of metals occurring in soil, water, sediment, or air
- 31 that represent the combined contributions from natural and various anthropogenic
- 32 sources. This ambient level may be highly region-specific but can be used as a baseline
- 33 against which elevated levels from other natural or anthropogenic sources can be
- 34 compared.

35

36 The SAB suggests that information discussed below be included in Section 4 of the

37 Framework. The term background is often incorrectly assumed to connote “natural” and

38 therefore “safe” or of no significant human or ecological health concern. However, ambient

39 levels can vary, or can be inherently high enough to represent a potential health concern in and of

40 themselves. They can also represent a total level from a combination of natural and

41 anthropogenic sources, some of which may be historical or unknown. For metals in particular,

42 the concept of background levels is complicated by several factors, as described in the

43 Framework document, which include the sometimes highly variable natural levels of metals in

44 soils, sediments, air and water, various historical anthropogenic sources or activities, and air

1 deposition from distal anthropogenic sources.
2

3 For example, natural levels of arsenic in soils can vary over a wide range from region to
4 region depending on the sediment types from which the soils are derived, by as much as a factor
5 of 10- to 20-fold. In addition, arsenical pesticides have been used over the past hundred years in
6 agricultural and other settings; smelting and other air emissions can also contribute to local
7 arsenic soil levels. Also, certain conditions, such as the chemistry of landfills, can lead to
8 mobilization and release of natural sources of arsenic from rocks and soil, leading to greatly
9 elevated arsenic levels in groundwater, but from entirely natural sources of arsenic. However,
10 this can be distinguished from normal ambient levels with appropriate sampling and/or
11 modeling. Use of the term “ambient” does not connote an ability to identify the various
12 contributions from natural and anthropogenic sources, but does distinguish between setting a
13 benchmark level for a site or region against which other anthropogenic or anthropogenically-
14 influenced inputs of concern can be measured. Anthropogenic metals can be those that are
15 released into the environment from a specific human activity (i.e. a point source emission) or
16 “natural” metals that may move from one environmental compartment to another (i.e. soil to
17 groundwater) due to a change in environmental chemistry related to a human activity.
18

19 Since the concept of “background” is even more difficult to characterize in a human context,
20 the SAB recommends defining and using the term “body burden” in this instance, since it is also
21 a neutral term that attempts to quantify an individual’s steady-state level using biomonitoring of
22 one or more sample matrices (for example, blood, urine, hair, toenails, bone scan, etc.). The
23 Centers for Disease Control’s (CDC) National Health and Nutrition Examination Surveys
24 (NHANES) study is currently attempting to quantify and characterize body burdens in
25 individuals so as to develop a national database that can serve as the equivalent of a baseline
26 measure against which the levels in an individual can be compared. Section 4 of the Framework
27 currently does not discuss this important issue. The SAB, therefore, recommends that the
28 following definitions be added to the glossary, and also be discussed in new sections in the
29 human health effects parts of Section 4.
30

31 *Glossary recommendation:*

- 32 1. Add – Body Burden: An estimate of the concentration(s) of a metal or metal species in
33 specific tissues or the entire body, determined by the use of biological monitoring data in
34 the appropriate matrix.
- 35 2. Add – Human Biological Monitoring: Use of measurements in specific tissues or matrices
36 (blood, urine, hair, toenails, bone, etc.) of specific metals or metal species in order to
37 assess exposure or estimate body burden.
38

39 The SAB also feels that Section 4 of the Framework does not adequately describe
40 biomonitoring. This is an important emerging area of risk assessment that should be addressed.
41 As with other aspects of metals analysis, speciation, method of analysis and choice of the
42 appropriate matrix are critical aspects of effective biomonitoring in humans. For example,
43 analysis of chromium in blood, serum or urine does not provide a way to distinguish between
44 nutritional forms of chromium from food or supplements versus environmental or occupational
45 exposures to hexavalent chromium that may be of concern. Likewise, analysis of total arsenic in
46 blood or urine does not reflect body burdens or recent exposures to inorganic arsenic since food

1 contains high but variable levels of organic arsenic forms. However, arsenic in toenails provides
2 both specificity for inorganic arsenic and an integration of arsenic exposures and steady-state
3 levels over several weeks or months of exposure. Thus, metal-specific issues need to be
4 considered for any biomonitoring program. However, effective biomonitoring can provide
5 excellent data on individual body burdens that may reflect both exposures of concern and
6 potential health risks. The lack of discussion on this topic is a serious deficiency of both
7 Sections 3 and 4 of the Framework. The SAB strongly recommends amending these sections to
8 include this discussion, and further recommends that the EPA consider partnering with CDC
9 through its ongoing NHANES and State pilot biomonitoring programs in this important area.

10
11 **6.3.9 Charge Question 3.9. Please comment on the objectivity of the discussion of**
12 **essentiality versus toxicity, including the relationship between Recommended Daily**
13 **Intakes (RDAs) and thresholds such as Reference Doses (RfDs) and Reference**
14 **Concentrations (RfCs). See Sections 3.1, 4.3.2, and 4.3.3**

15
16 The SAB provides the following comments and recommendations in response to charge
17 question 3.9.

- 18
- 19 • The SAB notes that for some metals, there might be an apparent discrepancy between the
20 RDA and the calculated RfC or RfD. The EPA should consider the RDA for essential
21 metals when considering the RfC/RfD. However, it should be noted that the RDA is
22 usually satisfied by normal dietary intake of food, so that the RfC/RfD may be defined as
23 a potential increment to the body burden of that metal from other dietary or extrinsic
24 sources.
 - 25
 - 26 • The SAB notes a need to define essentiality and, in this definition, to include the role of
27 the metal in an essential physiological or biochemical process.
 - 28
 - 29 • The SAB notes that in Section 4.3.2 of the Framework it is important to restrict the
30 discussion of essentiality to humans and to revise tables 2-1 and 4-12, which are
31 identical. Table 2-1 could include a list of essential and non-essential metals in all
32 organisms, with footnotes to denote those known to be essential in just plants, animals or
33 humans, while Table 4-12 should be restricted to a list applicable solely to humans.
 - 34
 - 35 • The SAB notes that the current versions of tables 2-1 and 4-12 need major revisions. The
36 following recommendations apply specifically to the human table. It is recommended
37 that Mg be added to the list of nutritionally essential metals. In addition, the middle
38 column of the table should be eliminated and the metals in that column moved to the third
39 column that lists metals with no known beneficial effects. The metals in the second
40 column to be moved to the third column include: As, B, Ni, Si and V. Barium, B and Sr.
41 These particular metals should be noted by asterisks in the third column to denote that
42 there are limited human data for these metals.
 - 43
 - 44 • The SAB notes that a summary table should be added that includes RDA, RfDs, and
45 RfCs available for the essential metals. The table should also include the adverse effects
46 that occur at concentrations near or below the RDA for a given metal. This section

1 should also specifically reference recent U.S. Department of Agriculture (USDA) and
2 National Research Council (NRC) reviews on essentiality of elements in humans.

3
4 **6.3.10 Charge Question 3.10. Please comment on the objectivity of the discussion and**
5 **recommendations presented for assessing toxicity of mixtures, including how to**
6 **assess additivity versus departure from additivity (See sections 3.1.3.4 and 4.3.6).**
7

8 The SAB provides the following specific comments and recommendations in response to
9 charge question 3.10.

- 10
- 11 • The SAB believes the Framework discussion of the mixtures topic (Section 4.3.6) is
12 limited and needs clarification and expansion. This section needs to be expanded to
13 address co-exposures with organic pollutants (e.g., TCE, solvents, hydrocarbons) and air
14 pollutants (e.g., gases such as ozone and particulates). The section needs more and
15 improved examples of interactions for each of the conditions, and would benefit from a
16 table that lists typical interactions and the ensuing effects on toxicity.
17
 - 18 • The SAB recommends that the example of the selenium and mercury interactions on the
19 bottom of page 4-78 be deleted. It is not an appropriate example since it leaves the
20 impression that Se supplementation should be used to prevent Hg toxicity.
21
 - 22 • The SAB recommends that the mixtures topics part of the Framework (currently Section
23 4.3.6) contain the following sections:
24 a.) Exogenous non-essential metal(s) effect on nutritionally essential metals.
25 i) effects via molecular/ionic mimicry
26 b.) Interactions between non-essential metals
27 i) effects via interactions at a common site
28 ii.) effects via one metal affecting one site and another metal affecting another site
29 c.) Interactions of metals with non-metals
30 i.) interactions with organics
31 1) effects on toxicity of the metals
32 2) effects on toxicity of the organics
33 ii.) interactions with gasses and/or particulates
34 1) affecting metal uptake
35 2) affecting metal toxicity
36
 - 37 • The SAB suggests the inclusion of a new Framework recommendation that states:
38 Metal mixture interactions and toxicity need to be clearly demonstrated by the use of:
39 a.) proper experimental design (National Research Council, 1988)
40 b.) appropriate plotting of diagrams
41 c.) rigorous statistical evaluation to demonstrate synergy, additivity, potentiation, sub-
42 additivity and/or antagonism.
43
 - 44 • The recommendations in Section 3.1.3.4 of the Framework need to address the National
45 Academy of Sciences/National Research Council (NAS/NRC) *Complex Mixtures* report
46 (National Research Council, 1988). Recommendation 1 (page 3-9, line 9) in Section

1 3.1.3.4 should address the NRC report. Recommendation 4 (page 3-9, line 22) in Section
2 3.1.3.4 should be rephrased to say: "There are established interactions that are based on
3 metal mimicry. Future research goals should determine how considerations of metal
4 mimicry affect risk assessments and metal toxicity."

- 5
- 6 • A definition of metal mimicry is needed in the glossary of the Framework. The SAB
7 suggests the following definition, "Metals that exhibit structural similarity which results
8 in competition for essential receptors thus disrupting normal functions, such as chromate
9 or arsenate substituting for sulfate or phosphate, lead replacing Ca or Zn and Cd
10 substituting for Zn or Ca." It might also be helpful to include in Section 4 of the
11 Framework a table that presents examples of well-established metal mimicry. It is also
12 important to note that metals can profoundly influence each other's biology through
13 mechanisms other than mimicry.
- 14

15 **6.3.11 Charge Question 3.11. Please comment on the objectivity of the discussion and**
16 **recommendations concerning natural background, bioavailability, bioaccumulation,**
17 **biomagnification, and trophic transfer in both aquatic and terrestrial environments.**
18 **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.**

19

20 The SAB finds that many aspects of the discussion in Sections 3 and 4 of the Framework are
21 objective and of reasonable utility for risk assessors. The level of detail seems appropriate for a
22 document of this type (i.e., screening level guidance document). There are sections that could be
23 improved and there are issues of balance among the sections that should be addressed. For
24 example, the discussions of bioaccumulation, biomagnification and trophic transfer are confusing
25 at times. Some of the recommendations in Section 3 are inconsistent with the discussion in
26 Section 4 and the issue papers. The Framework brings up some very important issues reasonably
27 well. But it also seems to advocate some methods without reflecting important uncertainties,
28 unknowns, or lack of informed consensus in their base of scientific support. After revisions, the
29 greatest utility of the Framework will be its value as a statement of considerations unique to
30 metals. The major issues lie in: the need for balance in integrating sections, the imbalance
31 among recommendations, the need to integrate discussions of uncertainties, and some omissions.

32

33 *Routes of Exposure*

34

35 The SAB notes that the fairly nice discussion of dietary exposure and trophic transfer in
36 Section 4 of the Framework was lost in Section 3. Section 4.4.2.3.2 discusses limitations to the
37 SEM-AVS that are not mentioned in Section 3 (see details below). Both sections are more
38 conciliatory than analytical. The statement that "the most widely used approach of assessing
39 metal exposure in sediments is based upon EqP theory" is not true. Many more agencies and
40 scientists use the methods detailed in documents referenced by National Oceanic and
41 Atmospheric Administration (NOAA) and/or Canadian guidelines (Long & Morgan, 1990;
42 1991; McDonald et al, 1996; McDonald et al., 2000). These methods and concepts are discussed
43 in the Chemistry section, but not mentioned in Section 4.4.2.3.

44

45 *Natural Background*

46

1 In the Framework, “background” is defined as both natural and anthropogenic levels of metal.
2 This lack of clear definition confuses the issue. As discussed in the response to charge question
3 3.8 above, natural background should be a consideration, but the Framework document treats it
4 as a non-issue. In the Framework discussion of background, no medium (e.g., soil, sediment,
5 water) is specified and the issue of background is different in different media. This issue is
6 acknowledged to be complex when evaluating sediments if particle size is ignored and no
7 sediment cores are available. The Framework states that background concentrations can vary by
8 as much as five orders of magnitude. The SAB finds that five orders of magnitude variation in
9 metal concentration is most likely an exaggeration when described in reports and literature. In
10 part, large variances may be the result of using earlier sediment and water chemistry data, when
11 adequate” clean chemistry” methods were not used. Mention of the EPA Storage and Retrieval
12 (STORET) database, with some casual caveat about quality assurance, does little to help the risk
13 assessor. STORET is full of data that could be incorrect by five orders of magnitude because it
14 represents earlier, non-clean chemical analyses. The Framework needs to emphasize the
15 importance of ultra-clean chemistry in determining all metal concentrations, but especially those
16 values that might be background.

17
18 The Framework Document should distinguish between “natural” and higher-level
19 anthropogenically-induced backgrounds. In the response to charge question 3.8 above, the SAB
20 recommends that the EPA use the term “ambient” or “ambient levels” rather than “background.”
21 In discussing ambient or background levels, the Framework needs to specify the need for
22 determining what background is and, consequently, what to consider. Using the term “natural”
23 likely complicates the task of defining a base concentration for comparison in metal risk
24 assessment. The Framework should provide guidance to establish a “background” concentration
25 that would be operationally defined for the assessment taking into consideration realistic
26 concentrations that often will reflect both natural and anthropogenic influences. Acknowledging
27 “background” concentrations becomes assessment specific. For example, San Francisco Bay
28 sediments have high nickel concentrations stemming from historical times. Arsenic at regional
29 scales presents a similar situation. Background concentrations ultimately dictate the kinds of
30 organisms, the nature of ecology, and types of chemistry at that site or region.

31 *Bioavailability*

32
33
34 Bioavailability is a useful concept and should be brought up into the Framework
35 recommendations. The Framework statement on the “bioavailable fraction” is very important,
36 both in terms of the science and moving the Framework forward. The Framework document
37 does handle the concept of bioavailability more extensively than other aspects. It is clear that in
38 the view of the document “bioavailability” concerns speciation and other water chemistry
39 effects. “Trophic transfer”, “dietary exposure” and “biomagnification” are mentioned in a few
40 places, but there is little effort in Section 3 to help the risk assessor understand and employ these
41 concepts. The discussion of dietary toxicity leaves out important examples and understates the
42 importance of this route of exposure, as well as the increasing knowledge of it. Dietary exposure
43 is an important consideration, or at least uncertainty, in any assessment of the ecological risks of
44 metals. The Framework does not adequately integrate this uncertainty into the overall view it
45 presents to risk assessors. There is no integrated view of how an organism might respond to all
46 sources in different circumstances; the routes of exposure are treated as if they are not related.

1
2 The problem with the hazard assessment of metals in water is that very small deviations from
3 background concentrations result in very large amplification through the environment because of
4 high Kds and relatively high BCF/BAFs for many metals. No guidance concerning this issue is
5 provided in the Framework document nor is the essence of the issue discussed to any length.
6 Bioavailability as shown in the conceptual model in the Framework should include both
7 exposure and dietary uptake. The Framework text provides an uneven approach and should be
8 expanded to address the influence of dietary uptake. The conceptual model in Figure 2-2 of the
9 Framework includes dietary uptake, as it should, and provides a rationale for including food type
10 and food choice. There is also an ecological need to incorporate dietary uptake into the
11 Framework discussion. There should be an emphasis in the Framework on the need to
12 understand species presence and the nature of the food web. Trophic transfer, for example, has
13 been shown to be an important route of uptake of metals from sediments into fish via planktonic
14 invertebrates and into epibenthic invertebrates feeding on periphyton.

15 16 *Bioaccessibility*

17
18 The SAB finds that “bioaccessibility” is properly considered in the document and represents
19 the labile portion of the metal.

20 21 *Bioaccumulation*

22
23 Bioaccumulation is a concept that is different from biomagnification. This presents some
24 level of confusion in the discussion of the different levels of risk assessments in the Framework..
25 The important point that should be made is that metals bioaccumulate, and trophic transfer is
26 important. It is less important that biomagnification through the food web is likely to occur only
27 in some circumstances (although examples exist for selenium and methylmercury).

28
29 Bioaccumulation should be reviewed in the Framework as a concept for use in risk
30 assessments, particularly in the site-specific risk assessments. The issues of what construct to
31 use to express bioaccumulation (BCF, BAF, models) is separate from consideration of the
32 bioaccumulation processes. Sections 3 and 4 of the Framework place great emphasis on the
33 limits of a ratio approach and little emphasis on bioaccumulation processes that are relevant to
34 exposure analysis in a risk assessment. A concern of the SAB is that coefficients in the ratios are
35 not independent of exposure concentrations. The coefficients are calculated and used but are
36 highly variable. The concept of using BAF or BCF ratios can be appropriate, but it should never
37 be assumed they are constant(s) as is the typical assumption in uses like hazard assessment. This
38 is discussed in the response to charge question 3.12. below. The SAB recommends that a box
39 text be included in the Framework document that identifies the concept of BCF versus the use of
40 this as a tool in site specific or national assessments. The SAB also feels there is a strong need
41 for presentation of a conceptual model of bioaccumulation in the Framework. Such a
42 conceptual model should tie bioaccumulation to toxicity. If bioaccumulation and
43 bioconcentration factors are treated more comprehensively, the Framework will be a more
44 cohesive document. The SAB’s discomfort with the treatment of BCF and BAF has to do with
45 difficulties in measuring bioaccumulation, which involves estimates of uptake, depuration, etc.
46 Any method that can be related to a dynamic intake, and that relates site of target toxicity with

1 effects, would be of value. Such models need to be better incorporated into the bioaccumulation
2 discussion in the Framework. Until this is incorporated, toxicity tests will be utilized or
3 concentrations in tissues will be used, without any understanding.

4
5 *Essentiality*

6
7 The SAB finds that the discussion of essentiality in the Framework also needs to be
8 expanded, particularly with regard to how essentiality influences accumulation factors. Tissue
9 concentrations can vary by a large amount and there is a need to discuss the factors influencing
10 the site specific characteristics that lead to a given BCF. In this regard the Framework
11 document should discuss the state of the science (versus what might simply be included in a
12 Framework).

13
14 *Concentrations in “Metallo-regions”*

15
16 The SAB recommends using a geometric progression (log-normal distribution) for metal
17 concentrations in either “metallo-regions” or catchment basins and describing the low-end of the
18 distribution (e.g., 95th or 90th percentile exceedence zones) as potential problem areas. In a
19 national or ranking risk assessment, a conservative approach would need to be taken by using
20 medians and the 90th (or so) percentile. For national-level risk assessments, one would
21 necessarily want to err on the side of conservatism.

22
23 *Soil Measurements and Soil Concepts*

24
25 The SAB notes that, EPA has used the term, “duff”, in the terrestrial section of the
26 Framework (3-27) when discussing factors influencing metal availability and accumulation.
27 This term is many decades out of date. The SAB therefore recommends that EPA delete the term
28 and instead use the “O horizon or litter layer.” Use of the correct terminology is important in
29 order to address concerns about soil measurements and soil concepts. In a forest region, the
30 forest floor horizon is the O horizon. Standardizing soil to the top 10 – 12 cm is not appropriate
31 across a range of ecosystem conditions to include urban, wetland, undisturbed forest, agronomic,
32 and disturbed systems. A more appropriate nomenclature for soil horizons and types consistent
33 with USDA NRCS terminology should be defined and used.

34
35 *Critical Body Residues*

36
37 The SAB finds that the concept of critical body residues (CBR) is handled unevenly in the
38 Framework and is overly emphasized. The fact that CBR can be measured does not necessarily
39 mean it is the concentration at the site of toxic action. Further, there are few data on this and it
40 has been measured in only a few species. The concept may be an idea that can be used in the
41 future.

42
43 *Acclimation*

44
45 The SAB notes that there is much discussion in the Framework of acclimation and adaptation.
46 The costs of adaptation are discussed well in Section 4, but that does not carry over to section 3.

1 It is well known that organisms have developed a variety of physiological and/or biochemical
2 strategies for dealing with metals exposure due to the ubiquitous presence of metals in the
3 natural environment. In many cases these strategies have permitted organisms to survive and
4 thrive in areas where they would not normally be able to exist. The importance of considering
5 these strategies has long been debated among the regulatory and regulated communities. It is
6 also true that many metals are essential for the health and development of organisms and in some
7 cases it has been observed that organisms used in toxicity tests that have been cultured in
8 “metals-deficient” media have been shown to be more sensitive to subsequent metals exposure
9 than are wild organisms raised in natural environmental conditions. The general
10 recommendation that has come from the scientific community is that researchers should ensure
11 that organisms used in conducting toxicity tests are cultured (or at least acclimated for a period
12 of time) to test media that contain metals concentrations that are “similar” to natural background
13 concentrations, not concentrations similar to the site in question, but to “natural background
14 levels.” It is assumed that this approach will reduce the potential of overestimating toxicity from
15 “metals-deficient” stressed organisms, while ensuring that underestimations of toxicity are not
16 reached from tests conducted with “metals-acclimated” organisms. To this end, it is equally
17 important that risk assessors are mindful of this potential concern and consider it in conducting
18 their evaluation of effects data. The SAB feels that the discussion and recommendations
19 contained in Sections 3 and 4 relative to this issue do not adequately describe and delineate the
20 difference between true metals acclimation and test organism stress due to metals deficiency.
21

22 **6.3.12 Charge Question 3.12. Please comment on the objectivity of the framework**
23 **statement that the latest scientific data on bioaccumulation do not currently support**
24 **the use of bioconcentration factor (BCF) and bioaccumulation factor (BAF) values**
25 **as generic threshold criteria for hazard classification of inorganic metals (see**
26 **recommendation on page 3-17, lines 27-29 of the document). By this, the**
27 **framework means that various assumptions underlying the BCF/BAF approach,**
28 **including the independence of BCF/BAF with exposure concentration and the**
29 **proportionality of hazard with increasing BCF/BAF do not hold true for the vast**
30 **majority of inorganic metals assessed. Please comment on the framework's**
31 **acknowledgement that the appropriate use of BCFs/BAFs to evaluate metal**
32 **bioaccumulation, including the degree to which BCFs/BAFs are dependent on**
33 **exposure concentrations, needs to consider information on bioaccessibility,**
34 **bioavailability, essentiality, acclimation/adaptation, regulation of metals (uptake**
35 **and internal distribution), detoxification and storage, dependence on exposure**
36 **concentration, and background accumulation. While the ability to quantitatively**
37 **address all these factors may be limited at the present time, the framework states**
38 **that their potential impacts should at least be qualitatively addressed. See Sections**
39 **3.2.4, 3.3.2.5, and 4.5.8.**
40

41 The SAB agrees with the statement that BCF/BAFs do not apply for metals. The language of
42 the Framework is useful in describing the context of use for BCF/BAF. As stated, it is
43 appropriate largely for use in a site assessment. The Framework acknowledges that these
44 methods may not be the best approach for use in a national assessment, and especially for hazard
45 rankings. However, guidance is offered in the Framework on how to derive BCFs/BAFs (e.g.,
46 pages 3-17, and 3-33). The SAB finds that the Framework document needs a clearer discussion

1 of when to use these tools and their deficiencies, and when they should not be used. The
2 justification of why or why not to use them needs to be more explicit and coherent.

3 4 *BCF/BAF*

5
6 The SAB notes that the Framework does not mention that BCF/BAFs vary 50 fold or more
7 for every metal, partly because of inherent biological diversity in response to metals. A careful
8 analysis of the literature would show alternatives to the BCF/BAF approach that are much more
9 flexible and less variable (biodynamic models).

10
11 The Framework correctly assesses the state of the science. Section 4.5.8 of the Framework
12 clearly expresses the issues and identifies shortcomings of the BCF/BAF approach. There is a
13 difference in the utility of the BCF/BAF approach for assessing the risks associated with
14 organics and inorganics and the Framework appropriately addresses these differences. The SAB
15 supports the call for more data on bioavailability, acclimation, storage, metal regulation, and
16 accumulation as modifiers of BCF or BAF. There is no doubt that the better the data for metal
17 storage, disposition in the body, and consequent potential toxicity, the better the predictions of
18 risk will be. However, in some cases where data are limited, a precautionary stance of using
19 potential BAFs might be called for and not simply ignored. For example, it would be much
20 clearer if the Framework were to state that the BCF/BAF does not work for national assessments
21 but it has value for site-specific assessments.

22
23 The Framework should specifically address the hazard assessment issue and consider trophic
24 transfer. The Framework needs to consider options beyond dissolved metals toxicity tests. In
25 this regard, the SAB suggests considering options that address: 1) the potential for trophic
26 transfer, and 2) the potential for transformation into bioavailable organometal compounds.

27
28 **6.3.13 Charge Question 3.13. Given the variety of organism responses to inorganic metals**
29 **exposure, based on factors such as bioaccessibility, bioavailability, essentiality,**
30 **uptake/excretion mechanisms, and internal storage/regulation, as described in**
31 **Section 3.2.4, the framework states that BAFs/BCFs should be derived using**
32 **mathematical relationships that represent the concentration in the organism or**
33 **tissue as a function of the bioavailable concentration in the exposure medium/media**
34 **for each set of exposure conditions. Please comment on whether this is the best**
35 **approach based on the current state of the science or if there are alternative**
36 **approaches that are more appropriate that can be routinely applied. See Sections**
37 **3.2.4, 3.3.2.5, and 4.5.8.**

38
39 The SAB finds that the mathematical relationships representing the metals concentration in
40 the organism or tissue as a function of the bioavailable concentration in the exposure
41 medium/media for each set of exposure conditions seem appropriate. However, it is worthy to
42 note that Section 4.5.8 of the Framework indicates that steady-state conditions are often the
43 primary concern in metals risk assessments, yet there certainly can be instances of non-steady
44 state conditions being of primary concern (e.g. episodic hydrologic events and related metal
45 mobilization). Further, if the recommendations to not apply BCFs and BAFs are supported, the
46 SAB questions why recommendations to derive them are included in the Framework.

1
2 The SAB finds that Sections 2 and 4.5.8.1 of the Framework clearly articulate issues
3 surrounding the derivation and utility of BCF/BAFs for metals. For all of the reasons discussed
4 in these sections, it appears that the concept of the BCF/BAF for metals holds little utility in
5 assessing the environmental toxicity of metals in hazards rankings. One optimal approach (least
6 uncertain) for deriving these values would be to use the tissue concentration at the site of action
7 and to relate this to the best estimate of the biologically available metal. However, few data exist
8 to allow derivation of such a value.

9
10 The SAB notes that one aspect not mentioned in Section 3.3.2.5 of the Framework is the use
11 of multi-species model ecosystems to verify BAF or BCF predictions. Often the results of such
12 real-world situations are to modify the growth (hence uptake and effects of metals). The
13 effective rate of uptake is very important, as the Framework states. Hence, BAFs are not
14 necessarily of value, as equilibrium situations are rarely found. The ideal is to have
15 concentration measures at site of action and in the surrounding environment, but adequate tools
16 are not immediately and widely available. Thus, the utility of the current construct is limited. If
17 the Framework were to include bioaccumulation dynamics, the variability would be narrowed.
18 On a site-specific basis, the ratios are better used than in national assessments because variability
19 may be less. For organics there are some well known and accepted assumptions. For metals
20 there is a large variability around the BCF/BAF estimates. However, there is little guidance as to
21 “where to draw the line.”

22
23 The SAB strongly concurs that one cannot use a BAF or BCF ratio for national assessments
24 or hazard ranking procedures. The SAB feels that a bioenergetics approach offers valuable
25 potential for understanding metal accumulation from air, sediments, soils or water (Wang et al.,
26 1996; Schlegel et al., 2002). In the interim, the Framework should address metals
27 bioaccumulation empirically for site assessments. In the future, there should be a concerted
28 attempt to generate data at the site of action (Escher et al., 2004).

29
30 **6.3.14 charge Question 3.14. Please comment on the objectivity of the information and**
31 **recommendations pertaining to the use of the acid-volatile sulfide-simultaneously**
32 **extracted metals (AVS-SEM) approach and the biotic ligand (BLM) model. Are**
33 **additional recommendations warranted? If yes, what are they? See Sections 3.2.6,**
34 **4.4.2.3, and 4.5.10.**

35
36 The SAB feels that the concepts of AVS-SEM and BLM are clearly on the agenda for
37 adaptation into risk assessment. The Framework comprehensively describes the theory and
38 evidence behind both methods. However, it is unbalanced throughout in comprehensively
39 evaluating the practical and theoretical challenges and inherent limitations that have been
40 encountered in implementing the use of AVS-SEM (Cantell, Burgess & Kester, 2002). The
41 primary literature contains a number of questions that are relevant with regard to implementation
42 of SEM-AVS in either risk assessment or regulation. The theory itself is attractive and a strong
43 literature supports its effectiveness in the environment of the typical sediment bioassay. There is
44 no question that sulfides are important in metal associations in anoxic sediments, or that sulfides
45 control pore water metal concentrations in bulk sediments. The questions about implementation
46 of the methodology lie in how the complex vertical gradients of sediments will be sampled, how

1 stable SEM-AVS characterizations will be for a site, and/or whether an SEM-AVS
2 characterization will hold for sediments that are moved during normal resuspension, flood or
3 bed-load transport events. Many such questions were raised in a very important review of
4 sulfide dynamics and its relationship to the stability of AVS in the cover article of Environmental
5 Science and Technology (Morse & Rickard, 2004).
6

7 A second issue is that, although AVS controls bulk pore water concentrations, it does not
8 control metal concentrations in what an animal eats. The literature that considers dietary
9 bioaccumulation from sediments raises important issues with regard to the design of most
10 sediment bioassay experiments: the living nature of sediments and how that affects
11 bioavailability, and the biases that can occur in sediment bioassays of the type typically used for
12 the AVS concept. These issues are not necessarily resolved one way or the other, but they are
13 substantial and well enough documented that risk assessors must be made aware of the debate
14 and be prepared to consider the pros and cons of the SEM-AVS method in a balanced way (Lee
15 et. al., 1988; Lee & Luoma, 1998).
16

17 The BLM is in the relatively early stages of development and also has inherent limits. For
18 example, the BLM: 1) has no dietary component; 2) no chronic component; and 3) no cross-
19 species comparisons among differing mechanisms for binding and effects-level metal
20 concentrations. The published literature on animals other than trout and fathead minnow show
21 simple, and not unexpected, correlations between toxicity test outcomes and metal speciation, in
22 the guise of a biological model. The BLM definitely does account for speciation better than any
23 methods to date; but the BLM does have limits, at the present state of knowledge
24

25 The information presented in the Framework regarding the use of the BLM and AVS-SEM
26 approaches is appropriate and reflects the current state-of-the-science. It is, however, interesting
27 that the use of techniques relating to bulk sediment concentrations are conspicuously absent, at
28 least in terms of their applicability to large scale assessments. Methods such as sediment quality
29 criteria (SQC), threshold effect level (TEL), probable effect level (PEL), etc. have a good role in
30 conducting metals risk assessment, especially when data are not available to address metals
31 sediment toxicity through methods such as AVS/SEM. Further, the implied lack of
32 bioavailability of metals associated with sulfides has come into question (Lee et al., 2000). For
33 risk assessments of a broader nature, e.g., at the national level, clearly the only viable approach
34 to be implemented may be through the assessment of bulk sediment numbers.
35

36 The future of toxicity testing is moving toward mechanistic approaches and the BLM
37 approach is a step in the right direction. An important feature of the BLM is that it addresses the
38 site of action. For chronic effects, BLM may not apply since site of effect may change with
39 exposure time frame. The risk assessor has to be aware that there is not an available
40 comprehensive tool and that there are limits to each approach. However, anything that moves
41 risk assessment toward consideration of bioavailable fraction, mode of action, and a mechanistic
42 approach is in the right direction.

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Appendix A. Speciation

Among risk assessors and scientists working on the environmental chemistry and ecotoxicology of metals, the concept of “chemical speciation” is fundamental. Despite this fact, or perhaps because of it, a variety of context-specific uses of the term, along with the related term “chemical species,” have developed. This practice can confuse newcomers to the field, perhaps even hindering their apprehension of concepts that are not in themselves difficult. To remedy this situation, the SAB recommends that the environmental chemistry section begin with a set of definitions adapted from recent IUPAC recommendations (Templeton et al., 2000). Quotations from this source are in italics.

Species: *Chemical compounds that differ in isotopic composition, conformation, oxidation or electronic state, or in the nature of their complexed or covalently bound substituents, can be regarded as distinct **chemical species**.*

In environmental chemistry, the phase the species occurs in - gas, liquid, aqueous solution, mineral, or adsorbed on an interface between phases - generally is also specified in a complete definition.

Note that this definition applies equally to the environmental chemistry of organic compounds and of metal ions, although there are important differences in how the term is used in practice. In the context of the environmental chemistry of metals, chemists speak of a metal species as a “*specific form of an element defined as to isotopic composition, electronic or oxidation state, ... complex or molecular structure*” and phase. In the context of environmental organic chemistry, chemists do not usually refer to an organic compound as specific form of carbon, although every organic compound is one. Rather, as long as its core structure remains intact, each different protonation state, complex of a metal ion, and occurrence in different phases of an organic compound may be referred to as a different *species of the compound*.

Speciation: According to the above definition of species, it is apparent that the reactants and products of any properly written chemical reaction are distinct chemical species. Indeed, the concepts of species and reactions are intimately related since any process that brings about a chemical change by definition results in the formation of a new species. As a result of this logical relationship, and possibly also its parallel to the concept of evolutionary “speciation” in biology, some geochemists and environmental chemists have “*applied the word speciation to describe the transformations taking place during cycling of the elements.*” However, the IUPAC has recommended against this use of “speciation,” instead suggesting the term **species transformation**. Given its consistency with the usage of “transformation” in the field of environmental organic chemistry, this recommendation should be easily accepted and put into practice.

The IUPAC also recommends against using the term *speciation* to indicate the analytical activity of identifying chemical species and measuring their distribution. Sometimes, it is used to indicate that a method gives more information on the form in which the element is present than other

1 *more commonly applied techniques (e.g., measuring distinct organomercury compounds as*
2 *opposed to a total mercury determination). In order to avoid confusion, [IUPAC] recommends*
3 *using the term **speciation analysis** when referring to the analytical activity of identifying and*
4 *measuring species.*

5
6 Instead, the IUPAC-recommended use of **speciation** *is the distribution of an element amongst*
7 *defined chemical species in a system.* Normally, a quantitative description of the speciation of an
8 element is implied. Such a distribution could be the result of: i) one or more chemical analyses
9 of a sample, ii) chemical modeling of a laboratory solution of known composition, or iii)
10 chemical modeling of an environmental system. When not clear from the context, the terms
11 *analytical speciation and modeled speciation* may be helpful in distinguishing these methods
12 used to obtain the speciation.

13
14 As a practical matter, the degree of resolution adopted in any description of the speciation of a
15 system will depend on:

- 16
17 i) *the relevance of the species differences for our understanding of the system under study,*
18 ii) *our ability to distinguish between the various species analytically,*
19 iii) *our ability to model the speciation in some operationally-defined or experimentally-*
20 *controlled fraction of an analyzed substance.*

21
22 While some analytical methods directly determine the concentration of a single species in an
23 environmental sample or matrix, most common environmental analyses measure several related
24 species, or **fractions**. IUPAC recommends that the *process of classification of an analyte or a*
25 *group of analytes from a certain sample according to physical (e.g., size, solubility) or chemical*
26 *(e.g., bonding, reactivity) properties* undertaken by a chemical analyst be referred to as
27 **fractionation**.

28
29