

Summary Minutes
U.S. Environmental Protection Agency
Science Advisory Board
Perchlorate Advisory Panel

Panel Members: See Panel Roster¹

Date and Time: Tuesday July 18, 2012, 9:00 AM - 5:30 PM
Wednesday July 19, 2012 8:30 AM - 2:30 PM

Location: The Embassy Suites Hotel, 1250 22nd Street N.W., Washington, DC 20037

Purpose: To discuss responses to EPA's Charge questions related to the white paper:
Life Stage Considerations and Interpretation of Recent Epidemiological Evidence to Develop a Maximum Contaminant Level Goal for Perchlorate.

Attendees:

Panel Chair: Dr. Stephen M. Roberts

Panel Members:

Dr. Grant W. Anderson	Dr. Julie B. Herbstman
Dr. Hugh A. Barton	Dr. David G. Hoel
Dr. Nancy Carrasco	Dr. Judy LaKind
Dr. Claude Emond	Dr. Paul H. Lipkin
Dr. Jeffrey Fisher	Dr. Jennifer Peck
Dr. Mary A Fox	Dr. Joanne F. Rovet
Dr. Wendy J. Heiger-Bernays	Dr. Cheryl R. Stein

SAB Staff Office: Mr. Thomas Carpenter, Designated Federal Officer
Dr. Vanessa Vu, Director SAB Staff Office

Others Present: See Attachment A

Meeting Materials: All meeting materials are available on the SAB Web site at the Perchlorate Advisory Panel Meeting Page:

<http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/C99D0AF3224EA17F852579E2004F282D?OpenDocument>

Convene Meeting

The meeting was announced in the Federal Register² and proceeded according to the meeting agenda, as revised. Mr. Thomas Carpenter, Designated Federal Officer (DFO) for the Perchlorate Advisory Panel, convened the meeting at 9:00 a.m. on July 18, 2012. He stated that the EPA Science Advisory Board (SAB) was a chartered federal advisory committee and he reviewed Federal Advisory Committee Act (FACA) requirements. He stated the members of the panel are in compliance with Federal ethics requirements. He noted that the SAB Staff Office has determined that there are no issues with conflict of interest or appearance of a loss of impartiality for any of the panel members.

He stated that for this review, the SAB Staff Office had convened an ad-hoc panel of experts to review available data and information to support a Maximum Contaminant Level Goal (MCLG) for perchlorate. The panel will be asked to consider exposed individuals at different life stages, epidemiologic and biomonitoring data, and physiologically based pharmacokinetic (PBPK) analyses, as well as provide advice on approaches to develop an MCLG for perchlorate. The determinations necessary to form the panel are summarized on the SAB web page³. Mr. Carpenter stated that as DFO, he would be present during the panel's business and deliberations. He stated that summary minutes of the meeting would be prepared and certified as accurate by the Chair.

Welcoming Remarks

Dr. Vanessa Vu, Director of the EPA SAB Staff Office, welcomed the panel members and thanked them for providing advice through the SAB to EPA on approaches to develop an MCLG for perchlorate and information identified in the EPA white paper⁴.

Introduction of Members, Purpose of Meeting, and Review of the Agenda

Dr. Stephen Roberts, Chair of the SAB Perchlorate Advisory Panel, hereafter referred to as the panel, provided introductory remarks.

Dr. Roberts welcomed the Panel and members of the public participating in the meeting. He stated that the meeting was convened to respond to the charge provided to the SAB and to consider data and information that would support approaches to develop an MCLG for perchlorate. Dr. Roberts reviewed the meeting agenda⁵ and provided an overview of how the panel would conduct their deliberations to provide advice in response to the charge questions. He noted that after the panel discussions, they would develop an advisory report for distribution among panel members for further discussion with the goal of reaching consensus on the recommendations and advice.

Dr. Roberts noted that EPA would provide introductory remarks to the panel and would be available throughout the meeting for clarifying questions as they arose. He also acknowledged the four members of the public that requested to provide oral comments for the Panel's consideration, after which lead discussants and the Panel members would deliberate on responses to the Charge questions and discuss their comments. Dr. Roberts invited members of the public to register to provide public comments on the issues raised during the Panel's discussions for a public comment period at the end of the first day. Dr. Roberts asked panel members if they had any clarifying questions. Hearing none, he proceeded to the agenda and introduced the Agency staff for presentations.

Remarks from EPA's Office of Water

Ms. Pamela Barr, Acting Director for the Office of Ground Water and Drinking Water, provided the history and context for developing a National Primary Drinking Water Regulation (NPDWR) for perchlorate. She noted that the EPA has initiated the process to develop a MCLG and NPDWR for perchlorate and provided the statutory context for EPA's action and how the Charge to the SAB fits into that regulatory context under the Safe Drinking Water Act (SDWA). She noted that the MCLG is a non-enforceable goal defined under the SDWA as "the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety." For perchlorate, the NPDWR will likely specify an enforceable Maximum

Contaminant Level (MCL) and monitoring and reporting requirements for public water systems. The SDWA specifies that the enforceable MCL be set as close to the MCLG as feasible using the best available technology, treatment techniques, and other means (taking cost into consideration). She noted that SDWA further requires that when proposing any NPDWR that includes an MCL, the Administrator must analyze “[t]he effects of the contaminant on the general population and on groups within the general population such as infants, children, pregnant women, the elderly, individuals with a history of serious illness, or other subpopulations that are identified as likely to be at greater risk of adverse health effects due to exposure to contaminants in drinking water than the general population.”

Ms. Barr informed the panel that the EPA has a regulatory schedule established by SDWA that requires EPA to publish a proposed MCLG and NPDWR within 24 months of making a determination to regulate a contaminant and promulgate a final regulation within 18 months of the proposal. EPA also must develop and publish a Health Risk Reduction and Cost Analysis that includes an assessment of the quantifiable and non-quantifiable health risk reduction benefits likely to occur as a result of treatment to remove the perchlorate.

In February 2011, EPA published the Final Regulatory Determination to regulate perchlorate under SDWA. The Final Regulatory Determination stated that EPA was evaluating the potential alternative health reference levels (HRLs) and considered them to be levels of public health concern for the purposes of final determination.

Dr. Elizabeth Doyle, Chief of the Health Effects and Criteria Division, Office of Science and Technology in the Office of Water, provided an overview of the technical issues EPA has identified in developing an MCLG for perchlorate. She noted that the purpose of this white paper is to seek guidance from the SAB on how best to consider and interpret the life stage information, the epidemiologic and biomonitoring data since the NRC report, physiologically based pharmacokinetic (PBPK) analyses, and the totality of perchlorate health information to derive an MCLG for perchlorate.

Dr. Doyle noted that the agency is interested in the SAB’s advice to strengthen the scientific defensibility of information and analyses to consider sensitive subpopulations and potential adverse health effects for exposure to perchlorate. She noted that iodide deficiency and the subsequent reduction in thyroid hormones has strong associations to inhibited neuro-development; however, research has not been developed for direct linkages to perchlorate in humans. She noted the agency is considering data and analyses to further evaluate factors for sensitive subgroups within the general population in developing an MCLG.

Dr. Doyle noted that in addition to the science on sensitive subpopulations and thyroid interactions, the agency is using physiologically based pharmacokinetic (PBPK) modeling of radioactive iodide uptake (RAIU) from perchlorate exposure and recent epidemiological studies to understand perturbations from perchlorate exposure from drinking water. Dr. Doyle noted the PBPK modeling efforts have built on several iterations of the models and are presented in two analyses in the white paper. She noted that the panel was provided recent epidemiological and biomonitoring studies for review and their use in developing the MCLG. Lastly Dr. Doyle noted the agency’s interest in how best to use all the information in an integrated approach to develop the MCLG.

One member pointed out that the panel’s focus was on exposure through drinking water and not additional exposure pathways (i.e., ingestion of agricultural produce containing to perchlorate through processing rinse water or irrigation). Dr. Doyle confirmed that the focus was on drinking

water, acknowledged other pathways exist and described the use of relative source contributions in developing MCLGs.

Dr. Roberts noted that the Charge to the SAB focused on approaches to develop an MCLG for drinking water and not to changes in the Reference Dose (RfD). Dr. Doyle noted the Agency agrees with the mode of action framework used as the basis for the RfD.

Public comments

Four individuals registered to address the panel and 9 others provided written comments. The presentations given by the registered speakers are posted on the SAB website. Dr. Michael Lumpkin of Environ International Corporation⁶ spoke on behalf of the Chlorine Institute. Dr. Richard C. Pleus of InterTox Incorporated⁷ spoke on behalf of the Perchlorate Study Group. Dr. Kimberly Wise with American Chemistry Council⁸ and Dr. Kevin Morley with the American Water Works Association⁹ also presented at the meeting.

Additional written comments provided by nine individuals are posted on the SAB website for this meeting.¹⁰ The commenters were:

- Dr. Richard Pleus, Intertox Inc.
- Dr. William Mendez, Jr. ICF International Inc.
- Mr. Paul Yaroschak, Department of Defense
- Dr. David Kimbrough, Pasadena Water & Power
- Mr. Jonathan Bode, The Perchlorate Study Group
- Dr. Kimberly Wise, American Chemistry Council
- Mr. Michael Wallis, East Bay Municipal Utility District
- Ms. Teresa Cirone, The Chlorine Institute
- Mr. Tom Curtis, American Water Works Association

Members of the panel asked several clarifying questions after Dr. Lumpkin's presentation. One member asked about the statistical significance of the Tellez 2005 study he presented and noted that the Tellez study was in the group of studies provided to the panel for consideration. Another member noted that the Braverman (2005) study cited by Dr. Lumpkin had included occupational airborne exposure level considerations and another member noted that nitrate and thiocyanate were identified as confounders in that study. Other members sought clarification about whether there were gender considerations for the 2005 Braverman study.

Members of the panel asked several clarifying questions after Dr. Pleus' presentation. One member asked Dr. Pleus to elaborate on the severity of adverse effect in the thyroid risk assessment model on page 5 of his slides. Another member asked Dr. Pleus to elaborate on the events after iodide uptake inhibition, and specifically, is there post exposure reversibility of the sodium iodide symporter (NIS), and once damaged or slowed development occurs, is the NIS adaptable or regenerated? Another panel member asked if Dr. Pleus had a recommendation for the MCLG? Dr. Pleus replied that he believes the RfD is protective.

After Dr. Wise's presentation one panel member asked for clarification on her interpretation of the adverse effect discussed in the presentation.

After Dr. Morley's presentation panel members asked clarifying questions about the extra conservatism AWWA believes may be provided by the RfD based on a no observed effect level (NOEL) and no observable adverse effect level (NOAEL). They also asked if any additional analyses on the extra sensitivity he attributed to using a NOEL were available.

Discussion of EPA's Charge questions

Panel members discussed the charge questions and asked the EPA staff clarifying questions on the charge questions. Members noted that there are overlapping issues between the charge questions and the life stage issues that still need to be addressed in each of the charge questions. Members agreed that responses need to be consistent and should refer to the responses to sensitive life stage charge questions as appropriate.

Sensitive Life Stages

Members noted that the charge questions in the analysis of sensitive life stages refer to the RfD and the standard formulaic MCLG approach. One member noted that the second bullet of this question refers to hazard identification and dose response issues. Another member noted that margins of exposure (MOE) are incorporated into the RfD. EPA Staff confirmed that the margin of exposure in the standard MCLG approach is incorporated in the RfD and the SDWA does not define an MOE. Members also noted that the charge questions introduce qualitative aspects to the point of departure recommended by the National Research Council and that the NRC provided advice on qualitative aspects in addition to the recommendations for further research.

PBPK Modeling

Panel members noted that the charge questions seem to be asking about uncertainty in the current model. Members noted that models usually used the RfD level as a parameter. Members noted that the charge questions ask what can be added to the PBPK model to improve the current analysis.

Epidemiology and Biomonitoring

Members noted that these issues questions are very closely related the questions in the sensitive life stage section (i.e., biomonitoring and epidemiological studies of sensitive life stages). Other members noted that the review also needs to focus on the suitability of the identified studies and recent studies not identified by EPA to develop an MCLG.

Integration of Information

Members noted that the premise of this charge question is on moving forward with the current RfD and whether re-evaluating the RfD may be a better approach than introducing new concepts into the standard MCLG approach. Other members noted that the algebraic formula to develop an MCLG limits the options to address sensitive life stages. Members agreed to discuss options and approaches to develop an MCLG as they addressed the response to the previous three charge questions. Members noted that the panel should not limit their discussion to the papers identified by EPA in the charge to the SAB. The panel discussed the balance between providing scientific advice to develop an MCLG and solutions to develop an MCLG within the statutory schedule. The panel agreed that the response to charge questions should address the schedule as appropriate. However, the panel also agreed they should not provide any advice that is based on the schedule at the expense of scientific rigor of the advice.

Members discussed whether or not the PBPK modeling approach was appropriate to meet the agency's statutory schedule. The panel agreed to focus on a mode of action approach using the PBPK model to introduce quantitative information in developing the MCLG. One member noted that the PBPK approach allows explicit opportunity to document the selection of biologically based parameters into the development of an MCLG.

Discussion of Responses on Charge Questions

Sensitive Life Stages

There are currently no data available to directly link perchlorate to neurobehavioral effects in infants and children. How should EPA consider the following life stage factors in deriving an MCLG?

- *Life stage specific differences in body weight and food and drinking water intake;*
- *Differences in greater severity and permanence of potential adverse effects in neonates, infants and young children compared to adults;*
- *Shorter half-life and lower reserves for thyroid hormone in infants compared to adults; and*
- *Intrauterine exposure to perchlorate and impact on thyroid status in fetuses.*

Drs. Anderson, Carrasco, Lipkin and Rovet were the lead discussants for this area and provided a summary of their respective reviews for the panel.

The lead discussants addressed the need to consider sensitive life stages in developing a MCLG for perchlorate based on the importance of thyroid hormone and potential inhibition of iodine uptake by perchlorate and the subsequent reduction in thyroid hormones for human development in fetuses, neonates, infants, and young children. They noted that thyroid hormone is essential for the developing brain and is involved in a number of fundamental neurobiological processes such as neurogenesis, neuronal migration, process growth, synaptogenesis and myelination. Thyroid hormone's specific mode of action is to up- or down-regulate major brain genes that underlie these processes. Timing of need for thyroid hormone within the brain varies among the different processes with some (e.g., neurogenesis, neuronal migration) needing thyroid hormone earlier than others (e.g., myelination). Additionally different brain regions also vary in when they need thyroid hormone both *in utero* and after birth. Since most aspects of brain development are complete by the second year of life, normal thyroid hormone levels must be maintained from conception through to at least the age of two years. The discussants explained that thyroid hormone also plays a role in later brain functioning by regulating key neurotransmitters, and normal levels of thyroid hormone are also required throughout life. Furthermore, because iodine is a key component of thyroid hormone and it cannot be manufactured within the body, adequate dietary iodine is essential, particularly during pregnancy when the need for iodine and thyroid hormone increase by as much as 40-50%.

These members generally agreed that human studies have not assessed the thyroidal status of the fetus in context of maternal perchlorate ingestion, which is not unexpected due to the difficulty of conducting such a study. They also noted that data in humans or animals of the effects of perchlorate dosing on brain thyroid hormone levels are limited. This is not a trivial issue to address experimentally but is extremely important as the brain hormone levels do not necessarily

follow blood levels of hormone due to the requirement for thyroid hormone transport across the blood brain barrier. They also elaborated that the studies on thyroid hormone and effects are complex and evaluate different bodily fluids, limiting comparison among studies without a complete panel of thyroid function indicators and making it is difficult to draw solid conclusions.

Because the fetal thyroid system has a protracted development, lead discussants noted that the fetus, early in gestation, has to rely totally on the maternal supply of thyroid hormone transferred via the placenta. Further, since the fetal thyroid does not secrete its own centrally regulated thyroid hormone until the third trimester, an adequate maternal thyroid hormone supply is essential in the first half of pregnancy and also serves a supplementary role later until the fetal thyroid matures fully by term. Discussants identified research that found by term as much as 40% of fetal thyroid hormone still may be from the mother. After birth, small amounts of thyroid hormone continue to be transferred to the infant in breast milk. Conditions resulting in thyroid hormone insufficiencies during critical stages of early brain development include clinical or subclinical hypothyroidism in the mother, whereby effects are presumably worse in early gestation; iodine deficiency, which affects both maternal and fetal/infant supplies of thyroid hormone; congenital hypothyroidism, which typically begins at the end of gestation and continues postnatally for one to two months; and exposure to natural goitrogens or other chemicals that have thyroid-disrupting effects on both the mother's and the fetal/child thyroid gland. Conditions that disturb thyroid hormone production later in childhood when most thyroid hormone dependent brain development has occurred include juvenile acquired hypothyroidism as well as exposure to thyroid hormone-disrupting environmental toxicants.

Members acknowledged that no data currently exist linking perchlorate to neurobehavioral effects in infants and children and any inferences on neurobehavior must be drawn from studies of early thyroid insufficiencies and iodine deficiency, for which a considerable literature exists.

Members noted that the specific differences in body weight and intake are difficult to respond to in the standard MCLG approach. The panel agreed to respond to this question in terms of using the PBPK modeling approach.

Panel members noted that permanence of effects is not addressed in the EPA white paper. The panel agreed to address this in terms of thyroid hormone levels in adults and the developing human. Members noted that exposure at different lifestages leads to differences of treatability in adults and fetuses and children. That is, adults may return to a normal thyroid state while children may suffer a range of permanent outcomes across exposure scenarios. The panel agreed to include the rationale and information to demonstrate that treatment after exposure during early development may not ameliorate the adverse effects.

One member pointed out that shorter reserves and lower reserves may have an effect in infants compared to adults as well. The issue is that neonate reserves tend to be lower and the elevated demand for thyroid hormone remains constant.

Members agreed that the intrauterine exposure is an important period for thyroid hormone and neurodevelopment. They also noted that thyroid hormone source is maternal thyroid hormone during early trimester until the fetus begins to use maternally supplied iodide to produce thyroid hormone itself. They also pointed out that the hypothyroxinemic pregnant women are of concern in addition to the hypothyroid pregnant women. Within the thyroidal state, hypothyroxinemia is not as severe as hypothyroidism and would increase the population of concern. Members pointed to animal studies on low dose with subsequent effect.

Members asked the lead discussants if there are ways to address the lack of data between perchlorate exposure and neurodevelopmental effects. Lead discussants pointed out there are studies that support the neurological effects from iodide deficiency and they could provide a reasonable foundation base on the inhibition of iodide uptake from perchlorate exposure. They also suggested using the clinical data and information for iodide deficiency as an alternative for specific studies on perchlorate and adverse effects. They also identified several recent studies that may provide additional support.

Physiologically based Pharmacokinetic (PBPK) Modeling

How should EPA consider PBPK modeling to derive an MCLG for perchlorate?

What are the strengths and limitations of the two PBPK model results described in this effort?

Drs. Barton, Emond, and Fisher were the lead discussants for this section.

Lead discussants found that the PBPK model used the MOA framework described by the NRC report (2005) and could be used to develop a clear and transparent approach to derive an MCLG. They noted that analyses that EPA presented in the White Paper using PBPK modeling were appropriate and useful and such analyses should continue to be part of deriving an MCLG for perchlorate.

They noted that the questions on developing a health-protective MCLG (e.g., charge questions for integration of information) reflect a lack of information that directly link perchlorate in drinking water with adverse outcomes. Absent that direct link, an alternative approach would be to use a mode of action analysis, defining the steps involved in the process to the extent possible and asking about linkages among these steps. In this context, the PBPK model provides a relationship (for the average individual at each life stage) between drinking water intake and perchlorate pharmacokinetics. They noted that the current model also predicts the key first pharmacodynamic step, which is inhibition of the target, the sodium-iodide symporter, by perchlorate. The steps after that (i.e., alterations in thyroid hormones and neurodevelopmental impacts) are not included in the model but there is some literature cited that addresses these aspects. Lead discussants noted if EPA wants to begin to estimate the extent of effects and the size of the populations involved, focusing more on a mechanistic mode of action analysis might begin to provide useful estimates in a way that focusing on 0.7 ug/kg/day does not.

The discussants noted that the various epidemiological papers sometimes report water concentrations, but often report other measures, notably urinary perchlorate; it also would be beneficial to use the PBPK model to impute the water concentrations that would give rise to the measured urinary perchlorate so that there was a common metric for comparing all the studies.

Lead discussants presented the strengths and limitations of the two PBPK model results described in the White Paper. They recognized that using a PBPK model to calculate RAIU estimates for life stages is daunting because of the lack of data to verify the estimates in the fetus and young, or a pregnant mother but, the modeling provides a theoretical construct, with uncertainty, to evaluate life stages, going beyond the limits of data. Thus the computational evaluation has merit and value because the model is focused on the primary mode of action for perchlorate. By far, the most sensitive elements in the RAIU model are the model predicted radioiodide and perchlorate concentrations in serum because the K_m or K_i for the NIS protein is

so much greater than the model predicted serum levels (V_{\max} not sensitive). In this regard, assumptions about systemic clearance of perchlorate or radioiodide (see comment earlier) may affect model predictions for percent inhibition of RAIU for the young. An evaluation of this aspect of the model is worthwhile to ensure similar outcomes (or not).

These members noted that the second analysis (presented in Table A-4) is a more appropriate analysis asking what the predicted RAIU inhibition would be for different life stages assuming different drinking water concentrations. This analysis shows that, using the upper 90th percentile for drinking water intake, the inhibition at the different life stages is 2% or less for a “biologically average” individual for perchlorate drinking water concentrations of 15 ug/L.

Members discussed the challenge of deriving an MCLG and how to consider the RfD. One interpretation is that it is necessary to avoid exposure to more than 0.7 ug/kg/day (the RfD), the approach in Table 1 of the white paper. EPA can take this approach and then have no idea to what degree it is being protective and for what proportion of the population as is clearly evident in the materials they have provided. Members pointed out that the other interpretation is that one is trying to prevent neurological effects that would arise from inhibiting iodide uptake into the thyroid and thus thyroid hormone production, so the key value of the RfD was basing it on a perchlorate dose that resulted in a decrease in radioactive iodide uptake (RAIU) of approximately 2%. This level of inhibition in the Greer et al., 2002 study was felt to be within the individual intraday variability of iodide uptake as well as being approximately the detection limit of the assay.

Members noted that previous peer reviews of the PBPK model have supported its use, although there are limitations on how well one can know that the parameter values at the different life stages capture the average behavior at each stage. EPA made a number of modest changes and improvements to the model following its peer review supporting its continued use.

Another member noted that the current modeling work only reflects uptake (and binding) of radioactive iodide in the thyroid gland, and as such, represents only a precursor event in terms of the potential disturbances of the HPT axis. The relationships between iodide intake, perchlorate exposure, disturbances in the HPT axis (RAIU and thyroid hormone changes) and adverse outcomes are complex. He commented that a computational effort is ongoing to evaluate serum thyroid hormone changes (e.g., free serum T4) in the pregnant mom and fetus for a range of dietary iodide intakes (70 to 250 $\mu\text{g}/\text{day}$) and exposures to perchlorate (0.001 – 1000 $\mu\text{g}/\text{kg}/\text{day}$). A portion of this work was presented at Society of Toxicology conference in 2012 (Lumen et al., 2012).

Members presented and discussed several analyses that should be considered in PBPK modeling of perchlorate.

- For the maximum contaminant level goal (MCLG) calculation, we should consider the newborn to be in the sensitive life stage; therefore, the neonate should be protected if this prediction is relevant to the observation for this group age (most important if data exist).
- A better characterization of the life stage between Day 0 and Day 7 should be investigated using the model to understand why this stage is so sensitive.
- Considering that life stage, we may also characterize the feeding of newborns with bottles.

- With the physiologically based pharmacokinetic (PBPK) model, we have a way to describe the mode of action; however, we still have some gaps concerning kinetic or dynamic behavior. Despite these gaps, the PBPK model should be useful.
- According to the results presented in Table 3 of the white paper, the PBPK model used on a sensitive population seems to protect the general population. However, we could introduce a supplementary uncertainty factor of 3.16 (≈ 3) depending of the availability of the data.
- The most important question is whether we have enough data for this subpopulation to support this PBPK modeling prediction.

Epidemiological Evidence

How should EPA consider the post-NRC epidemiology data in deriving an MCLG?

Drs. Hoel, Herbstman, Peck, and Stein were the lead discussants for this focus area.

Lead discussants noted that while there are several new epidemiological and biomonitoring studies published since the 2005 NRC report, there are still no studies examining the association between prenatal and/or early life perchlorate exposure and child cognitive and behavioral development. They found that the epidemiological data on the association between perchlorate-exposure and thyroid function in humans remain inconclusive, most likely because of the divergent study populations and methodological differences among the studies. Some studies did observe changes in thyroid function among subpopulations of perchlorate exposed individuals, but there does not appear to be information on when thyroid perturbation in these groups becomes sufficient to result in neurological or other impairments, especially among fetuses or neonates. The largest studies of newborn thyroid function relied on ecological epidemiological assessments of perchlorate levels in drinking water. Drinking water represents only a portion of total perchlorate exposure, so fetal exposures based on average maternal drinking water concentrations would likely underestimate total perchlorate dose. Lead discussants noted that in the absence of more relevant epidemiological studies, the MCLG must rely on numerous uncertainty factors, especially since the reference dose is based on a study of just 37 healthy adults. A plan to monitor the state of the science with respect to adverse health effects of perchlorate exposure, and adjust the MCLG if needed, could be implemented.

Several studies examine maternal iodine deficiency and/or maternal thyroid impairment in relation to neonatal and early childhood behavior and development, and report adverse effects. Only one study, however, appears to have followed the offspring beyond age 2.5 years. This study (Vermiglio 2004) reports dramatic decreases in IQ, but the study was small and iodide sufficiency was determined ecologically. Existing birth cohorts with longitudinal follow-up may help identify limits for iodide sufficiency and thyroid function with respect to cognitive and behavioral development.

Lead discussants also found – and members concurred - that the current epidemiological evidence for a potential effect of perchlorate exposure on maternal and neonatal thyroid function is limited and insufficient to draw definitive conclusions regarding the drinking water exposure range of concern. The guidance offered from existing studies of thyroid function during pregnancy indicates that alterations in maternal thyroid hormone concentrations have not been

observed in populations with average urinary perchlorate concentrations as low as 2.1 µg/L (Pearce et al. 2010) or as high as 13.5 µg/L (Pearce et al. 2011).

Members noted that the two positive studies of associations with thyroid hormone alterations in women of reproductive age and neonates were also the largest studies (Blount et al. 2006; Steinmaus et al. 2010). General considerations for the interpretation of the existing epidemiologic evidence would include lack of individual exposure assessment, appropriate model specification, adequate evaluation of potential confounders and in some instances limited statistical power to evaluate vulnerable subgroups. Additionally, all studies are based on the assumption that the perchlorate exposure measurements represent stable, long-term environmental exposures.

Integration of Information

How can EPA best use the total body of information to derive a health protective MCLG, while considering the results of epidemiology and biomonitoring data in establishing bounds on potential values?

How can EPA use the available data to estimate reductions in adverse health effects (i.e., dose response) that are likely to result from reducing perchlorate levels in drinking water?

Drs. Fox, Heiger-Bernays, and LaKind were the lead discussants for this focus area.

Based on the discussion of the previous sections of the white paper and the responses to Charge questions the lead discussant identified several options for approaches to develop an MCLG for Perchlorate for discussion.

Discussants noted that members had identified many concepts that need to be evaluated in order to consider the sensitive life stages to develop an MCLG for perchlorate. One approach is to incorporate these elements in the current approach. However they also note that the current formulaic approach introduces difficulty in that uncertainty and consideration about lifestages is accounted for in several of the elements used to developing the MCLG (i.e., intraspecies uncertainty age extrapolations used to develop the RfD, specific body weights and ingestion rates for specific life stages factors in the MCL). This approach could lead to “double counting” of the elements and increase the uncertainty of the MCLG.

One lead discussant noted the NRC (2005) report recommended the RfD of 0.7 µg/kg-day which included an uncertainty factor meant to be protective of the most sensitive subpopulation – fetuses of pregnant women who have hypothyroidism or iodide deficiency. In its White Paper, EPA noted that it believes that “this RfD is the most scientifically defensible endpoint available at this time for assessing risk from perchlorate exposure.” However, it also noted that at the RfD, RAIU inhibition is 1.1-6.7 times greater than adults. This is less than the uncertainty factor of 10 used to derive the RfD. Given the current state of the literature a discussant raised the issue of revisiting the RfD rather than introducing the necessary life stage analysis in the standard MCLG approach.

Another possible approach would place the most weight on epidemiology studies of mothers and infants. The Agency could conduct a meta-analysis using weighting for quality of study. This approach would require evaluating the results from the cross-sectional epidemiology studies and

applying life-stage specific body weights, water consumption and RSC and the current RfD to consider if an MCLG is sufficiently protective of sensitive life stages.

Discussants also noted that during the discussion of PBPK modeling some members noted that using the PBPK model is an option to developing the MCLG for perchlorate. The model provides an opportunity to evaluate different life stages and the data and information that would be needed to consider the adverse effects from perchlorate exposure and is consistent with the MOA framework.

Members discussed the possible options and the approaches and how they could account for the thyroid mode of action, differences in life stage exposure, perchlorate kinetics, the NIS, and iodide inhibition. The discussion focused on the ability of the approaches to incorporate the needed elements of the life stage analysis and to transparently document the Agency's analysis.

The panel's discussion identified difficulty in conducting additional meta analysis using the epidemiological and biomonitoring studies. The difference in the study designs, inconsistent results and confounding factors used in the studies lead members to identify conducting this type of analysis as a least desirable option. Members thought that the analysis may provide an opportunity to validate the analysis conducted in the other options.

Members also identified difficulties in developing an option modifying the formulaic algebraic approach. They noted that simply running the MCLG analysis with different factors for life stages did not provide a simple comparison. Elements that considered lifestages consideration as uncertainty factors would again be included in simple comparisons.

Members acknowledged that the MOA framework used for the RfD accounts for many of these factors and that the point of departure from the Greer 2002 study is a precursor effect No Observed Effect Level. They noted that a 10-fold uncertainty factor for intraspecies extrapolation was used account for sensitive lifestages. Some members noted that this approach is consistent with previously developed RfDs. They noted that the uncertainty factor was developed considering the use of the NOEL, not a No Observed Adverse Effect Level.

Members discussed how the PBPK model could more clearly document the analysis of specific parameters used to predict iodide uptake inhibition from perchlorate exposure and the subsequent downstream adverse effects. Members noted that the PBPK models can account for the prenatal lifestages. The model also predicts multiple exposure pathways such breast feeding or formula feeding of neonates. For example, members discussed the ability of the model to use a range of data for a parameter rather than assume a mean or 95% interval for a parameter.

Some members expressed concern that the use of a complex model may be seen as a black box of parameters while the RfD approach is well understood. Other members found that the model is transparent and provides an opportunity for the Agency to better document the science and parameters used to develop the model results and therefore the MCLG.

Members discussed the current model and noted that it is based on iodide uptake inhibition – the same POD as the RfD. Some members identified recent efforts to improve the PBPK modeling and suggested that improvements to the model are forthcoming and could be relatively easy to include in developing the MCLG.

The panel discussed the level of effort to develop a model to predict serum level of thyroid hormones and possibly neurodevelopmental outcomes. The PBPK modelers on the panel noted that fully developing the model to include neurodevelopmental outcomes would require

additional resources and time that do not meet EPA regulatory schedule. Members discussed options to develop the model to predict serum thyroid hormone levels and use clinical literature to support extrapolation to neurodevelopmental effects.

Panel members also discussed available guidance that Agency should consider in developing a MCLG with the recommended approach. In devising a framework the EPA should consider the advice of NRC 2011 (Review of EPA's Draft IRIS Assessment of Formaldehyde) and devise a consistent framework or approach to analysis that clearly presents the scientific information. The Agency should critically evaluate the quality and content of each type of information in a transparent manner. The Agency should take advantage of available quality evaluation tools (STROBE¹¹, GRADE¹², others?) and synthesis methods (systematic review, meta-analysis) for epidemiological literature to document the strengths and limitations, variability, and uncertainty of the information underlying the analysis.

Public Comment on the Panel's Deliberations

Four individuals registered to address the panel and provide oral comment on the panel's discussion.

Dr. Kevin Morely, American Water Works Association, reiterated his presentation from the morning and urged the panel to reconsider AWWA's written comments and his presentation from the morning. He noted the use of the NOEL rather than a NOAEL and that is a conservative approach. He conveyed AWWA's position that regulating perchlorate doesn't present a meaningful opportunity to protect public health as is required by SDWA.

Dr. Kimberly Wise, American Chemistry Council, encouraged the panel to develop a weight of evidence approach in their recommendation particularly in the consideration of life stages. She noted that the PBPK approach seems to have benefits over the algebraic MCLG approach. She also noted the risk reduction and any available data should be identified by the panel.

Mr. Kevin Bromberg, Small Business Administration, Office of Advocacy, raised concerns over what a perchlorate regulation may mean to water utilities characterized as small entities (serving fewer than 10,000). He used the arsenic regulation as an example of a regulation using high cost technologies to remove contaminants from drinking water and noted perchlorate treatment costs are similarly high. He noted that the panel should focus on the scientific questions at hand. He further stated that the RfD is a life stage analysis and is appropriate. He stated that the NOEL, used in the RfD, is not based on an adverse effect and is therefore conservative. He also noted that iodide uptake is relative to the life stage considered and should be accounted for in the analysis. Dr. Roberts thanked Mr. Bromberg and noted his points were discussed by the panel. Dr. Barton pointed out that the discussion on the PBPK analysis and Table A-3 in the EPA white paper addressed Mr. Bromberg's points as well.

Dr. Richard Pleus, InterTox, Inc. reiterated two main points from his morning presentation and urged the panel to consider the complete literature on perchlorate toxicity and consider whether the Charge to this panel is overly narrow. Dr. Pleus offered to provide the panel with information from the database to assist their deliberations upon request.

RECESS FOR THE DAY

At 6:00 p.m., Mr. Carpenter, DFO, adjourned the panel in recess until 8:00 am Thursday July 19, 2012.

RECONVENE

Mr. Carpenter reconvened the Perchlorate Advisory Panel at 8:00 am. Mr. Carpenter called roll and asked that members of the public send an email to document their attendance to the teleconference line.

Members participated in writing sessions and conferred among the 4 issue areas to develop preliminary draft panel responses for discussion. These preliminary responses for discussion are available on the SAB website and the discussions are summarized below.

Discussion of draft Responses

Sensitive Life Stages

Lead discussants suggested providing a preamble to the response to sensitive life stage charge questions presenting the biology of thyroid hormones and underscoring the essential need for the developing brain and involvement in a number of fundamental neurobiological processes such as neurogenesis, neuronal migration, process growth, synaptogenesis and myelination. Panel members agreed that a preamble in this charge question would be appropriate and would provide an introductory understanding of thyroid hormone biology that would benefit the subsequent sections of the report.

Is there a need to have a sensitive life stage analysis?

Members of the panel agreed that there is significant need to consider sensitive life stages in developing a MCLG for perchlorate. They identified key factors to include in the consideration of fetuses, neonates and infants of hypothyroxinemic pregnant women rather than the hypothyroxinemic pregnant women considered by the NRC. The group identified several lines of evidence to support this recommendation that should be expanded upon in the report:

- The specific adverse effects of low thyroid hormone levels and inadequate iodide uptake on brain development vary at different life stages
- Infants are more susceptible to perchlorate exposure effects than adults, especially if exposure is acute. Although no data exist on the long-term adverse neurodevelopmental effects of perchlorate *per se*, the data on the adverse effects of thyroid hormone perturbations (a downstream target) on the developing brain justify the need for a life stage approach
- The evidence suggests that the most sensitive life stages for the permanent adverse effects of perchlorate for permanent effects on brain development are (i) the pregnant woman and her fetus, (ii) infancy and (iii) the lactating woman.
- At different life stages, there are multiple organs targets and depending on the life stage, those numbers may change. For example, in the third trimester, maternal thyroid, placenta, and fetal thyroid are all affected.

How should the EPA consider differences in severity and permanence of potential adverse effects in neonates, infants, and young children compared with adults?

Members agreed that there is a difference in the adverse effects when comparing perchlorate exposure of adults to exposure in neonates and infants. Members noted that exposure pathways for fetuses, neonates and infants differ from that of adults and must consider fetal exposure and breast milk exposure in addition to drinking water and formula preparations. Members also noted that adult exposures may be ameliorated over time while exposure to children may have permanent adverse effects from suppressed brain and neurological development in fetuses, neonates and children. Members also noted that modest reductions in thyroid hormone, even as early as the first trimester, can have deleterious and potentially permanent effects on the developing brain.

How should the EPA consider the effect of shorter half-life and lower reserves for thyroid hormone in infants compared to adults?

Members noted and agreed that the neonate and young infant have lower thyroid reserves. They also have a more rapid turn-over of iodide and thyroid hormone suggesting greater need for iodide than in the older person. Differences in half-life in thyroid hormones and lower reserves suggest greater vulnerability to acute and chronic exposures to perchlorate. In discussing approaches to develop an MCLG for perchlorate, the shorter half lives and reserves can be more readily addressed in a modeling approach rather than the algebraic approach based on the RfD. The modeling approach may better account for and document these factors.

How should the EPA consider the impact of intrauterine exposure to perchlorate on thyroid status in fetuses?

Members noted that thyroid status in the fetus cannot be readily or safely determined. Therefore, one needs to monitor maternal thyroid status as a biological indicator of perchlorate exposures. If the mother's thyroid status is impacted, then one can assume the fetal status is definitely affected. However, if the mother's thyroid status is not affected, one cannot assume that the fetal thyroid has not been affected. Members discussed clinical literature that could be cited to provide markers of fetal effects from iodide deficiency and could be used as surrogates to effects from perchlorate exposure. Members also noted that the neonatal screening value, albeit at parturition, is an indicator of thyroidal impact at the end of pregnancy.

Physiologically based Pharmacokinetic (PBPK) Modeling

How should EPA consider PBPK modeling to derive an MCLG for perchlorate?

Members agreed that EPA should utilize a mode of action (MOA) framework for developing the MCLG that links the different steps in the proposed mechanism leading from perchlorate exposure through NIS inhibition to thyroid hormone changes and finally neurodevelopmental impacts. Within this MOA framework, the PBPK model provides a tool for integrating aspects of exposure (e.g., different drinking water consumption rates) with the biological changes occurring at the different lifestages to obtain predictions of inhibition as would be observed if a radiolabeled iodide uptake inhibition study were done.

The EPA PBPK model describes inhibition of NIS (as observed in RAIU inhibition study), so it includes the first key pharmacodynamic step, target modulation. Extension of models to

incorporate dietary iodide intake and thyroid hormone synthesis is underway and would be desirable to improve the quantitative linkages in the MOA framework. This would strengthen both the analysis of the biological variability and the combined impact of exposure differences with the biological variability.

Future model developments that would be valuable include i) extending the model to describe iodide intake and thyroid hormone regulation, and ii) population variability beyond life stage differences. These would be longer term efforts for improved analyses to support the MCLG.

What are the strengths and limitations of the two PBPK model results described in this effort?

Members discussed the specific analyses that EPA presented in the white paper noting the model predictions strengths and applicability in supporting an MCLG for perchlorate. For example members noted that the first analysis (Table A3) evaluates the predicted RAIU inhibition for the same perchlorate dose (7 ug/kg/day) that arises from biological variations captured in the PBPK model for different lifestages. This analysis helps support the use of the UF in deriving the RfD.

The second analysis (Table A4) evaluates the combined impacts of the differences in exposure (e.g., drinking water consumption) with the biological variability by assessing the predicted RAIU inhibition at fixed drinking water concentrations. In comparing the two analyses members pointed to a limitation of the first analysis is the selection of the urinary excretion rate for perchlorate. Literature for iodide excretion indicates the rate is faster in neonate/infants than at later ages, which might then be expected to be the case for perchlorate. This needs to be carefully assessed and justified.

Members noted that life-stage variations in the model are based on average human values at each life stage. Extension of the model to a full population description would be useful, but it is recognized that this would be a major effort.

The second analysis is more valuable for asking what extent of NIS inhibition would be predicted for different potential MCLG concentrations. It provides perspective on the protection offered by different concentrations. Since it uses 90th percentile drinking water consumption rates, it also starts to address population issues, though the biological aspects of the model are for an average individual.

Epidemiological Studies

How should EPA consider the post-NRC epidemiology data in deriving an MCLG?

Lead discussants found that the epidemiology data and studies published since the NRC cited in the White Paper are insufficient to guide casual inference with regard to perchlorate exposure and thyroid dysfunction. Members also noted that none of these studies are useful as validation of a safe level of perchlorate in drinking water. However, these data do provide evidence that the iodine insufficiency rates in the U.S. (based on NHANES) are higher than previously appreciated.

Members also provided comments and summaries of several new studies not cited by the EPA. They agreed that detailed summaries of the studies should be included in the report to identify confounding analyses, uncertainty, and possible exposure misclassifications, co-exposures to

other goitrogens or neurological toxins (lead), and possible epidemiological modeling misspecifications.

They also noted that among the studies there are limitations and confounding factors. For example the inference from epidemiologic (association) studies are limited (large studies are powered but ecologic; small studies are underpowered)

Members presented recommendation for future studies to improve the understanding of perchlorate exposure assessment. Recommendations for future studies included: repeated measures of perchlorate, i.e., know half life in urine); improved understanding of variability over time (e.g., diurnal, etc.); methods to increase the validity of epidemiological studies using a single samples to represent exposure and using longitudinal epidemiological studies as they are completed.

Integrating Information

How can EPA best use the total body of information to derive a health protective MCLG, while considering the results of epidemiology and biomonitoring data in establishing bounds on potential values?

The panel recommended using the MOA of perchlorate to form the basis of MCLG as derived from the body of available literature. The members agreed that the PBPK model is a tool that can provide the appropriate rigor and transparency to developing the MCLG and is preferable to the standard formulaic approach to MCLG development. The panel noted that EPA needs to provide documentation and justification for using the PBPK. The Agency should include robust, accessible and transparent documentation for each module of the model; describe the role of the underlying data (including the Greer study) in development of the model; and clearly identify and address limitations and uncertainties.

The panel discussed developing the PBPK model to predict serum free T4 and thyroid stimulating hormones based on the clinical human and animal literature on iodine deficiency. To further develop the model and predict neurobiological outcomes – specifically defining an adverse event or effect, recognizing that these range from changes in gene expression, neurophysiology, and behavior and learning will need to come from the clinical literature.

The panel also discussed EPA's regulatory schedule and whether the recommendation should account for completion of the MCLG within the statutory construct. Members agreed to recognize the schedule and provided a recommendation that acknowledged the available resources EPA may have to meet the preferred recommendation. Panel members agreed to provide a preferred recommendation and note that there were milestones that could be used to develop an MCLG. They also noted that the recommendation should be clear that using the alternate approach would have uncertainties and assumptions the Agency should appropriately identify and discuss in its proposed MCLG.

At a minimum, the panel recommended to use the PBPK modeling approach to NIS inhibition as a surrogate for perchlorate exposure quantitatively. The panel noted that a preferred approach would be to use the PBPK-PD approach to model the entire MOA but acknowledged that the EPA would need to consider the resources need to accomplish the improvements needed for the currently available PBPK models.

The panel discussed using the a structured framework to capture the evaluation of each type of data and decision to document the framework. The panel noted there are several organizations, including the National Academy of Sciences, that provide guidance and these should be included into their documentation of the modeling and analyses.

How can EPA use the available data to estimate reductions in adverse health effects (i.e., dose response) that are likely to result from reducing perchlorate levels in drinking water?

As EPA evaluates the SAB recommendations, it must define the adverse effects it can document. These adverse effects range from changes in gene expression, neurophysiology, and behavior and learning. EPA must define the sensitive populations. The panel finds that the fetuses and infants of hypothyroxinemic pregnant women are the most sensitive subpopulation.. Shifts in exposure to sensitive populations can begin to address impact and benefit of reduced perchlorate in drinking water. Quantitative procedures described above may also be helpful in describing dose response.

Tools the Agency can use are available in the NAS report on Science and Decisions report. The panel noted that conceptual models for unified dose-response may be useful.

Key Points for the Letter to the Administrator and Executive Summary

The panel finds that it is important for the Agency to consider sensitive life stages explicitly in the development of a Maximum Contaminant Level Goal for perchlorate.

- The mode of action of perchlorate is well understood and involves the potential for disturbance of thyroid homeostasis. Interference with thyroid is known to produce adverse effects on neurodevelopment in humans, with the fetus and infants most vulnerable. Although adverse neurodevelopmental effects of perchlorate in infants and children have not been reported in the literature, their risk can be reasonably inferred from other lines of evidence.
- The panel recommends that the Agency derive perchlorate MCLGs that address sensitive life stages through PB/PK modeling based upon its mode of action. The panel believes that this approach is a more facile, transparent, and rigorous way to address differences in biology and exposure between adults and sensitive life stages than is possible with the traditional approach for deriving an MCLG.
- The panel notes that Agency already has a PB/PK model for perchlorate that could be used for this purpose.
- The model could be used in its present form, although expansion of the model to address important aspects of vulnerability to perchlorate is strongly recommended. In particular, expanding the model beyond prediction of inhibition of thyroid uptake to effects on thyroid hormone levels will be especially important to capture factors that could contribute to perchlorate sensitivity, such iodine intake, underlying thyroid disease, etc. As a long-term goal, additional research could be used to extent the model to prediction of adverse effects resulting from specific concentrations of perchlorate in drinking water.
- The panel has made specific recommendations on ways in which information from clinical and epidemiological studies can be used to inform the model.
- The panel notes that as perchlorate research continues, studies in animals may provide important insights into neurobehavioral consequences of perchlorate exposure. A PB/PK

framework is well suited to help place these findings in the context of human perchlorate exposure.

Although this approach is a departure from the usual method for MCLG calculation, it is consistent with the Agency's increasing use of PB/PK modeling in support of risk assessment.

The Agency will need to develop a technical document for the approach and have it peer reviewed.

Discussion of Remaining Issues and Next Steps

Dr. Roberts reviewed the points the panel members identified as key issues and asked the panel for any additional thoughts. Panel members agreed that the key issues were identified and did not identify any additional issues or comments. Dr. Roberts asked the DFO to summarize the next steps for panel members to develop the Advisory Report.

Mr. Carpenter stated that writing teams would work to develop draft sections of the Advisory Report and submit them to the DFO. The DFO and the Chair would develop the draft Advisory report with the Letter to the Administrator and Executive Summary based on key issues from the panel's discussion and draft submissions. The panel would then reconvene to review the draft Advisory Report by teleconference in approximately 6 weeks. Based on the discussion, a second draft Advisory report would be distributed for consensus review. After consensus, the draft Advisory report would be submitted to the chartered Science Advisory Board for Quality Review prior to finalization. Mr. Carpenter will develop a writing schedule and request available times for the teleconference from panel members.

Dr. Roberts asked the panel for any questions or clarifications. He then called upon the DFO to adjourn the meeting

The Designated Federal Officer adjourned the meeting at 2:30 p.m.

Respectfully Submitted:

Certified as Accurate:

/Signed/

/Signed/

Mr. Thomas Carpenter
SAB Designated Federal Officer

Dr. Stephen Roberts
Chair

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the meeting. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the panel members. The reader is cautioned not to rely on the minutes represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations

Materials Cited

All meeting materials for the Perchlorate Advisory are available on the SAB Web site. <http://www.epa.gov/sab>. The materials cited below for this meeting are available at the [July 18-19, 2012 Meeting](#) Page:

¹Roster SAB Perchlorate Advisory Panel

² Federal Register Notice Announcing the Meeting (77 *FR* 31847-31848)

³ Determination Memorandum and Biosketches of Candidates

⁴ *Life Stage Considerations and Interpretation of Recent Epidemiological Evidence to Develop A Maximum Contaminant Level Goal (MCLG) for Perchlorate*

⁵ Meeting Agenda

⁶ Presentation by Dr. Michael Lumpkin , Environ International

⁷ Presentation by Dr Richard C. Pleus InterTox International

⁸ Presentation by Dr. Kimberly Wise, American Chemistry Council

⁹ Comments submitted by Dr. Kevin Morley, American Water Works Association

¹⁰ Written Public Comments received by the DFO

¹¹ Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

<http://www.strobe-statement.org/index.php?id=available-checklists>

¹² Grading of Recommendations Assessment, Development and Evaluation (GRADE)

<http://www.gradeworkinggroup.org/index.htm>

Attachment A
Members of the Public Participating in the
Perchlorate Advisory Panel Meeting
July 18 -19, 2012

Members of the Public Present¹

Dr. Nancy Beck, American Chemistry Council
Mr. Scott Biernat, Association of Metropolitan Water Agencies
Ms. Miranda Brannon, U.S. Air Force
Ms. Sarah Bresolin, Small Business Administration
Mr. Kevin Bromberg, Small Business Administration
Mr. Eric Burneson, U.S. EPA
Mr. Bob Cantilli, U.S. EPA
Dr. Gail Charney, Health Risk Strategies
Dr. Kevin Crofton, U.S. EPA
Dr. Elizabeth Doyle, U.S. EPA
Ms. Ann Johnson, U.S. Environmental Protection Agency
Dr. William Eck, Department of Defense
Dr. Michael Firestone, U.S. EPA
Dr. Lynn Flowers, U.S. EPA
Mr. Malcolm Garo, U.S. Army
Dr. Ann Marie Gebhart, ToxServices, LLC
Dr. Mary Gilbert, U.S. EPA
Mr. Jonathan Gledhill, Policy Navigation Group
Ms. Maria Hegstad, Inside EPA
Mr. Chris Knight, Pesticide and Chemical Policy
Mr. Thomas Hale Kupiec, U.S. Food and Drug Administration
Ms. Katherine Lenz, Federal Aviation Administration
Dr. Mike Lumpkin, Environ, International Corporation
Mr. Jake Lynn, Lockheed Martin
Dr. William Mendez, ICF International
Ms. Mary Morningstar, Lockheed Martin
Dr. Kevin Morley, American Water Works Association
Mr. Jason Leuck, Lockheed Martin
Ms. Emily McGavisk, American Water Works Association
Lt. Cmdr. Eva McLanahan, U.S. EPA
Ms. Jacqueline Moya, U.S. EPA
Ms. Sara Mustafa, U.S. EPA
Mr. John O'Donnell, City of Phoenix
Mr. Dan Olson, U.S. EPA
Mr. Phil Oshida, U.S. EPA
Mr. Darrell Osterhoudt, Association of State Drinking Water Administrators
Dr. Mary Ostrozocki, American Chemistry Council
Mr. Larry Pearl, Pesticide & Chemical Policy
Mr. T.J. Pepping, Environmental Working Group
Mr. Russ Perkinson, U.S. EPA

¹ Members of the public who signed in at the meeting

Dr. Richard Pleus, Intertox
Dr. Resha Putzrath, Navy and Marine Corps Public Health Center
Mr. Drew Rak, Noblis
Dr. Santhini Ramasany, U.S. EPA
Mr. Alan Roberson, American Water Works Association
Ms. Meredith Russell U.S. EPA
Dr. Jennifer Sass, Natural Resources Defense Council
Dr. Paul Schlosser, U.S. EPA
Ms. Nicole Shao, U.S. EPA
Ms. Cheryl Siege Scott, U.S. EPA
Ms. Anne Speismen, Washington Aqueduct
Ms. Mina Suh, ToxStratgies
Ms. Patricia Ware, BNA Daily Environment Report
Dr. Paul White U.S. EPA
Ms. Julia Winfield, University of Michigan Public Health
Dr. Kimberly Wise, American Chemistry Council

Member of the Public Requesting Teleconference Access²

Gail Charnley, PhD, HealthRisk Strategies
Nancy B. Beck, Ph.D., American Chemistry Council
Michael P. Firestone, Ph.D., U.S. Environmental Protection Agency
Ann Marie Gebhart, PhD., ToxServices, LLC
Ms. Ann Johnson, U.S. EPA
Ms. Maria Hegstad, Inside Washington Publishers
Mr. Larry Pearl, Pesticide & Chemical Policy
Dr. Deborah Proctor, Tox Strategies
Mr. John O'Donnell, City of Phoenix AZ
Mr. Phil Oshida, U.S. EPA
Ms. Mina Suh, Tox Strategies
Ms. Pat Ware, BNA's Daily Environment Report

² Based on members of the public requesting the teleconference dial in information